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Advances in Scoliosis, Spinal Deformity and Other Spinal Disorders

Edited by
Zach Pennington, Daniel M. Sciubba and Benjamin D. Elder

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About the Editors

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Zach Pennington is a graduate of the Johns Hopkins University School of Medicine and is a current resident in neurologic surgery at the Mayo Clinic in Rochester, Minnesota. His areas of clinical interest include spinal oncology and complex spinal deformity, and he has published over 200 peer-reviewed manuscripts on these topics. He is a member of the American Association of Neurological Surgeons, the Congress of Neurological Surgeons, the Lumbar Spine Research Society, the North American Spine Society, and AOSpine.

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Benjamin Elder, M.D., Ph.D., is a neurosurgeon, who is fellowship-trained in complex spinal surgery and spinal oncology, practicing at the Mayo Clinic. He completed a four-year BS/MS degree at Yale University, prior to completing an MD/PhD at the combined Rice University/Baylor College of Medicine program. He then matriculated to a neurosurgical residency at the world-renowned Johns Hopkins Hospital. Following his residency, he completed an Orthopedic Surgery Fellowship in spinal deformity surgery with Khaled Kebaish. He specializes in the treatment of adult spinal deformity, scoliosis surgery, and revision spine surgery of the cervical, thoracic, and lumbar spine. He also has extensive experience in the surgical management of a variety of spinal conditions, including spinal tumors, spinal stenosis, neck and back pain, herniated discs, and pinched nerves, and holds particular expertise in the treatment of normal-pressure hydrocephalus. His research focuses on developing novel approaches for tissue engineering and the regeneration of bone and cartilage for the treatment of spinal pathologies, aiming to develop new motion-sparing techniques for spine regeneration and optimize patient outcomes after fusion surgery. Additionally, he studies idiopathic normal-pressure hydrocephalus (iNPH), seeking to improve imaging and functional diagnostic tests for the diagnosis and characterization of iNPH, as well as to develop new tools to assess and optimize gait apraxia.

Preface

In the present Special Issue, we have collated articles focusing on the contemporary management of spinal deformity, including contributions discussing both adult and pediatric spinal deformity. Our aim in compiling this Special Issue was to highlight current points of investigation in spinal deformity research with contributions covering topics such as instrumentation level selection, durotomy prediction during pedicle subtraction osteotomy, the application of robotics to minimally invasive spinal deformity surgery, and the use of bracing in adolescent idiopathic scoliosis. This Special Issue is directed at current practicing spine surgeons and practitioners involved in the management of patients with spinal deformities. We appreciate the contributions of all the authors in this Special Issue, who include leaders from around the world. We hope that readers enjoy the present Special Issue and use it as a talking point to pursue additional investigations into improving the care of patients with spinal deformity.

Zach Pennington, Daniel M. Sciubba, and Benjamin D. Elder
Guest Editors

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Article

The Predictors of Incidental Durotomy in Patients Undergoing Pedicle Subtraction Osteotomy for the Correction of Adult Spinal Deformity

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Abstract: Background: Pedicle subtraction osteotomy (PSO) is a powerful tool for sagittal plane correction in patients with rigid adult spinal deformity (ASD); however, it is associated with high intraoperative blood loss and the increased risk of durotomy. The objective of the present study was to identify intraoperative techniques and baseline patient factors capable of predicting intraoperative durotomy. **Methods**: A tri-institutional database was retrospectively queried for all patients who underwent PSO for ASD. Data on baseline comorbidities, surgical history, surgeon characteristics and intraoperative maneuvers were gathered. PSO aggressiveness was defined as conventional (Schwab 3 PSO) or an extended PSO (Schwab type 4). The primary outcome of the study was the occurrence of durotomy intraoperatively. Univariable analyses were performed with Mann–Whitney U tests, Chi-squared analyses, and Fisher's exact tests. Statistical significance was defined by $p < 0.05$. **Results**: One hundred and sixteen patients were identified (mean age 61.9 ± 12.6 yr; 44.8% male), of whom 51 (44.0%) experienced intraoperative durotomy. There were no significant differences in baseline comorbidities between those who did and did not experience durotomy, with the exception that baseline weight and body mass index were higher in patients who did not suffer durotomy. Prior surgery (OR 2.73; 95% CI [1.13, 6.58]; $p = 0.03$) and, more specifically, prior decompression at the PSO level (OR 4.23; 95% CI [1.92, 9.34]; $p < 0.001$) was predictive of durotomy. A comparison of surgeon training showed no statistically significant difference in durotomy rate between fellowship and non-fellowship trained surgeons, or between orthopedic surgeons and neurosurgeons. The PSO level, PSO aggressiveness, the presence of stenosis at the PSO level, nor the surgical instrument used predicted the odds of durotomy occurrence. Those experiencing durotomy had similar hospitalization durations, rates of reoperation and rates of nonroutine discharge. **Conclusions**: In this large multisite series, a history of prior decompression at the PSO level was associated with a four-fold increase in intraoperative durotomy risk. Notably the use of extended (versus) standard PSO, surgical technique, nor baseline patient characteristics predicted durotomy. Durotomies occurred in 44% of patients and may prolong operative times. Additional prospective investigations are merited.

Keywords: pedicle subtraction osteotomy; complication; adult spinal deformity; revision surgery

1. Introduction

Adult spinal deformity (ASD) is represented by sagittal and/or coronal plane imbalance, and is common in patients with degenerative spinal pathology [1]. It has been reported to affect 6% of adults older than 50 years of age [1], though some reports, notably

that of Schwab et al. [2] have reported radiographic scoliosis to affect upwards of two-thirds of patients over 60 years of age. ASD has a significant negative impact on the mental and physical well-being of affected patients, with prior quality-of-life (QoL) studies suggesting sagittal imbalance is correlated with the overall degree of disability [3]. To this end, Pellisé et al. [4] noted that the negative impact of ASD on reported QoL exceeds that of other chronic conditions, including diabetes, congestive heart failure and chronic lung disease, and is greatest in those requiring surgical intervention. Among these surgical patients, intervention often involves multilevel posterior instrumented fusion with interbody placement and osteotomies to reduce the deformity [5].

A nontrivial proportion of patients experience mechanical complications, including proximal junctional kyphosis (PJK) [6], that require surgical revision. Additionally, some patients initially undergo a less invasive focal treatment, designed to treat radicular pain due to foraminal stenosis within the kyphoscoliotic deformity, but subsequently require definitive management. Such revision operations have an increased risk for durotomy [7], and may require aggressive bony work, including a three-column (3CO) or pedicle subtraction osteotomy (PSO) to achieve sagittal and/or coronal plane correction, particularly in a previously fused spine [8]. Such aggressive correction has a high associated morbidity, with work from the Scoliosis Research Society [9] noting complications in nearly a third of patients. One complication—durotomy—occurred in 6% of cases, and can lead to meningitis due to the free communication between the wound and the intrathecal space and complicated drain management and wound healing, and can potentially inhibit wound healing by inhibiting local angiogenesis [10]. Incidental durotomy, therefore, has a significant potentially negative impact on ASD surgeries involving pedicle subtraction osteotomy. The objective of the present study is to identify those risk factors for incidental durotomy in patients undergoing surgical correction of ASD with PSO.

2. Materials and Methods

After obtaining IRB approval, a single institution database comprising three tertiary care centers was queried for all patients who underwent 3CO as part of an instrumented spine procedure between February 2008 and February 2023. All patients treated at these centers were prospectively enrolled in the registry as a part of an ongoing quality improvement effort. The registry can be searched based upon patient demographics, procedural codes and diagnostic codes, among other details pulled directly from the electronic medical record. In the present study, the database was queried by diagnosis with the search terms "adult spinal deformity" or "scoliosis", and the procedural terms "pedicle subtraction osteotomy" and "spinal fusion" or "lumbar fusion" or "thoracolumbar fusion". After identifying potential patients from the registry, patient records were individually queried to ensure that surgery was performed for ASD, as defined by the Schwab criteria: coronal Cobb angle $\geq 20^{\circ}$, sagittal vertical axis (SVA) ≥ 5 cm, thoracic kyphosis $\geq 60^{\circ}$, or pelvic tilt $\geq 25^{\circ}$ [11]. Patients were included if: (1) they met radiographic criteria for adult spinal deformity, (2) underwent long-segment thoracolumbar instrumented fusion including one or more pedicle subtraction osteotomies and (3) had complete medical records including prior spine surgery history, operative notes and postoperative follow-up detailing the need for surgical revision. Patients were excluded if they: (1) were pediatric patients (<18 years of age), (2) underwent surgery for an indication other than adult spinal deformity (including infection, pathologic fracture, trauma, or malignancy) or (3) underwent sagittal plane correction with only a combination of Schwab 1 and Schwab 2 osteotomies (i.e., did not undergo a PSO or extended PSO).

For patients that met these criteria, details were collected on demographics (e.g., age, sex), medical comorbidities (including modified Frailty Index-5 item (mFI5) and Charlson comorbidity Index (CCI)), chronic ($\geq$6-week) corticosteroid use, surgical history (index versus revision surgery), surgeon details (specialty, fellowship training, experience/years post-residency), operative details (construct length, type of osteotomy, osteotomy level), and durotomy details (where durotomy occurred). For this study, durotomy was defined as

the intraoperative detection of a complete dural tear with cerebrospinal egress; partial thickness dural tears were not considered, given the argument by prior authors that repairing with sealant alone is sufficient for these defects [12]. Additionally, preoperative radiology reports were queried to identify whether the patient had documented radiographic stenosis at the level of the PSO (defined as radiologist report of moderate or severe stenosis).

2.1. Procedure Description

The details of pedicle subtraction osteotomy have been described in details by others, including this recent description by Gupta and colleagues [9]. In short, patients in this study all underwent open thoracolumbar instrumented fusion with a PSO or extended PSO. Midline incisions were made, and the target vertebral levels were exposed in subperiosteal fashion. Pedicle screws were placed using established landmarks (leaving out the planned PSO level). Laminectomy of the PSO level was performed, or, where prior decompression had been performed, the scar was debulked to prevent buckling of the dura with closure of the PSO. Complete bilateral facetectomies were then performed and the pedicles were taken down bilaterally. Temporary rods were placed across the planned PSO site to stabilize the spinal column during resection of the middle and anterior columns. If an extended PSO was performed, the diskectomy was completed prior to placement of the temporary rods. Using a nerve root retractor to protect the thecal sac, the osteotomy wedges were completed bilaterally using a combination of osteotomes, rongeurs, a high-speed drill, and an ultrasonic bone cutting device, as determined by surgeon preference. Once the PSO was completed, the rods were compressed across the PSO site and, one at a time, final rods were placed. The wound was then closed in standard fashion.

2.2. Statistical Analysis

Data were collected using Microsoft Excel Version 2207 (Build 15427.20308 Click-to-Run) (Redmond, WA, USA) and checked by three independent reviewers (AH, ZP, MAP). Data were summarized as mean ± standard deviation for continuous data and counts with percentages for discrete data. Statistical Analysis was performed using SPSS 28.0.0 (IBM, Armonk, NY, USA). Univariable comparisons between patients who did and did not experience durotomy were compared using Mann–Whitney U tests for continuous variables, Fisher's exact tests for dichotomous variables and χ^2 analyses for ordinal and categorical data. Those variables identified as significant at the $p < 0.05$ level on univariable analysis were entered into multivariable analysis to identify independent statistically significant predictors of durotomy. Results of the logistic regression were expressed as odds ratio (OR) with associated 95% confidence intervals (95% CI).

3. Results

A total of 116 patients were identified (mean age 61.9 ± 12.6 yr; 44.8% male), of whom 51 (44.0%) experienced intraoperative durotomy, though none resulted in new neurological deficits (Table 1). All patients underwent only a single PSO or extended PSO; none underwent more than one three-column osteotomy. A comparison of baseline characteristics between the "durotomy" and "no durotomy" groups showed no statistically significant differences with respect to age ($p = 0.55$), sex ($p = 0.35$), smoking history ($p = 0.85$), mFI5 ($p = 0.21$), CCI ($p = 0.76$) or chronic steroid use ($p = 0.24$). The sole exceptions were that patients not experiencing durotomy had a higher weight BMI (30.9 ± 5.5 vs. 28.5 ± 5.6 kg/m^2; $p = 0.04$) than those experiencing durotomy.

Table 1. Demographics of included patients and univariable comparisons for risk factors for intraoperative durotomy.

Variable		All Patients	Durotomy	No Durotomy	*p*
Demographics	N	116	51	65	
Age (yr)	116	61.9 ± 12.6	63.2 ± 11.1	60.9 ± 13.7	0.55
Sex (% male)	116	52 (44.8)	20 (39.2)	32 (49.2)	0.35
Race	116				0.49
White		112 (96.6)	49 (96.1)	63 (96.9)	
Black		3 (2.6)	1 (2.0)	2 (3.1)	
Other		1 (0.9)	1 (2.0)	0 (0)	
BMI (kg/m^2)	116	29.8 ± 5.6	28.5 ± 5.6	30.9 ± 5.5	**0.04**
Smoking History	116				0.80
Current		14 (12.1)	5 (9.8)	9 (13.8)	
Former		38 (32.8)	17 (33.3)	21 (32.3)	
Never		64 (55.2)	29 (56.9)	35 (53.8)	
Any		52 (44.8)	22 (43.1)	30 (46.2)	0.85
Medical Comorbidities					
ASA	116	2.7 ± 0.6	2.7 ± 0.5	2.6 ± 0.6	0.27
mFI5	116	0.9 ± 0.9	0.8 ± 0.8	1.0 ± 0.9	0.21
Diabetes Mellitus	116	22 (19.0)	7 (13.7)	15 (23.1)	0.24
HTN Requiring Medication	116	64 (55.2)	23 (45.1)	41 (63.1)	0.06
Functional Dependence	116	12 (10.3)	8 (15.7)	4 (6.2)	0.13
COPD or Pneumonia	116	9 (7.8)	3 (5.9)	6 (9.2)	0.73
CHF Exacerbation in Past 30 d	116	1 (0.9)	0 (0)	1 (1.5)	0.99
CCI	116	1.0 ± 1.4	1.1 ± 1.4	1.0 ± 1.3	0.76
MI	116	3 (2.6)	1 (2.0)	2 (3.1)	0.99
CHF	116	7 (6.0)	4 (7.8)	3 (4.6)	0.70
PVD	116	8 (6.9)	2 (3.9)	6 (9.2)	0.46
CVA	116	3 (2.6)	1 (2.0)	2 (3.1)	0.99
Dementia	116	2 (1.7)	1 (2.0)	1 (1.5)	0.99
COPD	116	10 (8.6)	6 (11.8)	6 (9.2)	0.76
CTD	116	10 (8.6)	6 (11.8)	4 (6.2)	0.33
PUD	116	0 (0)	0 (0)	0 (0)	0.99
Liver disease	116				
Mild		5 (4.3)	0 (0)	5 (7.7)	0.07
Moderate/Severe		0 (0)	0 (0)	0 (0)	0.99
DM	116				
Without EOD		19 (16.4)	6 (11.8)	13 (20.0)	0.31
With EOD		3 (2.6)	1 (2.0)	2 (3.1)	0.99
Hemiplegia	116	2 (1.7)	2 (3.9)	0 (0)	0.19
Moderate/Severe CKD	116	12 (10.3)	5 (9.8)	7 (10.8)	0.99
Malignancy	116				
Without metastases		8 (6.9)	6 (11.8)	2 (3.1)	0.14
With metastases		0 (0)	0 (0)	0 (0)	0.99
Leukemia	116	1 (0.9)	0 (0)	1 (1.5)	0.99
Lymphoma	116	0 (0)	0 (0)	0 (0)	0.99

Table 1. *Cont.*

Variable		All Patients	Durotomy	No Durotomy	*p*
AIDS	116	0 (0)	0 (0)	0 (0)	0.99
≥6-week Steroid Use	116	7 (6.0)	5 (9.8)	2 (3.1)	0.24

AIDS—acquired immunodeficiency syndrome; ASA—American Society of Anesthesiologists; BMI—body mass index; CCI—Charlson Comorbidity Index; CHF—congestive heart failure; CKD—chronic kidney disease; COPD—chronic obstructive pulmonary disease; CTD—connective tissue disease; CVA—cerebrovascular accident; d—day; HTN—hypertension; kg—kilogram; m—meter; mFI—modified frailty index; MI—myocardial infarction; PUD—peptic ulcer disease; PVD—peripheral vascular disease; yr—year.

An evaluation of surgeon characteristics (n = 18 unique surgeons) showed no statistically significant difference in the odds of intraoperative durotomy between patients treated by a neurosurgeon versus an orthopedic spine surgeon ($p = 0.40$) or a surgeon with fellowship training versus one without fellowship training ($p = 0.99$). A review of surgical details (Table 2) showed that the only significant predictors of intraoperative durotomy were having undergone prior thoracolumbar surgery, (82.4 vs. 63.1%; $p = 0.02$) and more specifically, having previously undergone a decompression procedure at the level of the PSO (72.5 vs. 38.5%; $p = 0.001$). There was no significant inter-group difference regarding the surgical tool(s) employed to perform the osteotomy, including use of the ultrasonic bone cutter ($p = 0.17$). Though, of note, the use of the ultrasonic bone cutter for osteotomy formation was less common in the durotomy group. The placement of an interbody device at the PSO level ($p = 0.99$), aggressiveness of the PSO—Schwab 3 vs. Schwab 4 PSO ($p = 0.25$), PSO level ($p = 0.74$), nor the presence of canal stenosis at the PSO level ($p = 0.24$) predicted durotomy risk.

Table 2. Operative details for the included patients and univariable comparisons for risk factors for intraoperative durotomy.

Variable		All Patients	Durotomy	No Durotomy	*p*
Surgical Details					
Revision [vs Index]	116	83 (71.6)	42 (82.4)	41 (63.1)	**0.02**
Prior lami at PSO level	116	62 (53.4)	37 (72.5)	25 (38.5)	**<0.01**
Osteotomy Tool Used	116				
Curette		39 (33.6)	22 (43.1)	17 (26.2)	0.08
Drill		51 (44.0)	22 (43.1)	29 (44.6)	0.99
Rongeur		63 (54.3)	29 (56.9)	34 (52.3)	0.71
Ultrasonic Bone Cutter		15 (12.9)	4 (7.8)	11 (16.9)	0.17
Osteotome		95 (81.9)	42 (82.4)	53 (81.5)	0.99
Cage Placed at PSO Level	116	57 (49.1)	25 (49.0)	32 (49.2)	0.99
PSO Type	116				0.25
Schwab 3		69 (59.5)	27 (52.9)	42 (64.6)	
Extended PSO (Schwab 4–5)		47 (40.5)	24 (47.1)	23 (35.4)	
PSO Level	116				0.74
L1		6 (5.2)	3 (5.9)	3 (4.6)	
L2		16 (13.8)	6 (11.8)	10 (15.4)	
L3		35 (30.2)	14 (27.5)	21 (32.3)	
L4		49 (42.2)	25 (49.0)	24 (36.9)	
L5		9 (7.8)	3 (5.9)	6 (9.2)	
S1		1 (0.9)	0 (0)	1 (1.5)	

Table 2. *Cont.*

Variable		All Patients	Durotomy	No Durotomy	*p*
Stenosis at PSO Level	116				0.24
None		64 (55.2)	29 (56.9)	35 (53.8)	
Mild		28 (24.1)	15 (29.4)	13 (20.0)	
Moderate		13 (11.2)	5 (9.8)	8 (12.3)	
Severe		11 (9.5)	2 (3.9)	9 (13.8)	
Surgeon Specialty	116				0.40
Neurosurgery		86 (74.1)	40 (78.4)	46 (70.8)	
Orthopedic Surgery		30 (25.9	11 (21.6)	19 (29.2)	
Fellowship-Trained	116	105 (90.5)	46 (90.2)	59 (90.8)	0.99
Outcomes					
Length of Stay (d)	116	8.6 ± 5.8	9.5 ± 7.5	7.9 ± 3.9	0.67
Non-home Discharge	116	53 (45.7)	22 (43.1)	31 (47.7)	0.71

PSO—pedicle subtraction osteotomy.

The bivariate logistic regression of durotomy odds as a function of surgical history showed that patients with a history of prior lumbar procedures had nearly three-fold higher odds of intraoperative durotomy (OR 2.73; 95% CI [1.14, 6.58]; $p = 0.025$). A history of prior decompression at the PSO level was even more closely associated with durotomy odds, portending a more than four-fold increase (OR 4.23; 95% CI [1.92, 9.34]; $p < 0.001$). On multivariable analysis, only having undergone a prior laminectomy at the planned PSO site was predictive of intraoperative durotomy (OR 4.12; 95% CI [1.41, 12.03]; $p = 0.009$); BMI (OR 0.93; 95% CI [0.87, 1.00]; $p = 0.061$) nor undergoing revision [vs index] thoracolumbar surgery alone (OR 0.93; 95% CI [0.28, 3.10]; $p = 0.93$) were predictive of durotomy.

Primary durotomy closure was achieved in 48 of 51 patients. The sutures' materials included nylon (Nurolon™, Ethicon, Raritan, NJ, USA), polypropylene monofilament (Prolene™, Ethicon, Raritan, NJ, USA) and polytetrafluoroethylene (Gortex, Gore Medical, Flagstaff, AZ, USA)™. In 35 cases, a dural sealant was employed (32 employed sealant to reinforce the primary closure). Closures were bolstered with a muscle pledget in 22 patients, an acellular collagen graft (DuraGen®, Integra LifeSciences, Princeton, NJ, USA) in 11 cases, and gelatin foam in 4 cases. None of the patients underwent the placement of a lumbar or external ventricular drain. Six patients required reoperation for wound complications. Of the fifty-one cases of durotomy, two patients were symptomatic, both presenting with headaches. One patient was successfully treated with an epidural blood patch. The second patient was initially managed with an epidural blood patch, which was unsuccessful and required a return to the operating room for an ongoing CSF leak. The durotomy was originally repaired with a muscle pledget, polypropylene suture, and fibrin glue. The wound was reopened and repaired with a running 5-0 Prolene™ (Ethicon, Raritan, NJ, USA), a gelatin sponge onlay, and fibrin glue.

4. Discussion

Three-column osteotomies, including pedicle subtraction osteotomies (Schwab type 3 osteotomy) and extended pedicle subtraction osteotomies (Schwab type 4 osteotomy) [13], are associated with complications in approximately one-third of patients [14], even in the hands of experienced surgeons. One complication, durotomy, can result in impaired wound healing, requiring surgical revision and potentially persistent cerebrospinal fluid (CSF) leaks and meningitis in the setting of wound infections. In the present multicenter study, we examined 116 patients undergoing open corrections of ASD using one or more PSOs. Interestingly, we found that the only significant predictors of durotomy were prior lumbar surgery, and, more specifically, prior decompression procedure at the PSO level, which was associated with an over four-fold risk in the odds of durotomy. While BMI was also

statistically higher in the "no durotomy" group, we feel this is most suggestive of sampling bias, given a recent meta-analysis by Alshameeri et al. [15] failed to find any significant association between obesity and the risk of intraoperative dural tear. Interestingly, neither surgeon training nor the need for extended PSO predicted the occurrence of durotomy. Of note, the intraoperative durotomy rate (44%) was high relative to rates quoted by studies examining general spine practices (7–10%) [7,16–18], though similar rates have been reported in other single-institution series exclusively examining adult spinal deformity surgery, including that of Chan et al. [19].

4.1. Prior Studies of Risk Factors for Durotomy in ASD Surgery

4.1.1. Revision Surgery and Scarring

As in the present study, multiple other studies have suggested prior surgery portends an increased risk of intraoperative durotomy. Ehresman and colleagues [7] presented a retrospective cohort of 1279 patients who underwent thoracolumbar surgery, of whom 8.4% experienced durotomy. They noted that the independent risk factors for durotomy were a delayed surgical start, undergoing revision surgery, advanced patient age and increasing surgical time. In their series of 1430 lumbar surgeries (10% with durotomy), Baker and colleagues [13] similarly noted advanced patient age, revision surgery and increased surgical invasiveness as risk factors for durotomy, with revision surgery being the strongest individual risk factor. Herren and colleagues [14] subsequently reported revision surgery to be associated with 78% increased odds of dural tears in their multicenter series of 3254 lumbar surgeries, of which 328 (10.1%) were complicated by durotomy. Subsequently, Iyer et al. [17] described durotomy risk based upon 564 patients from the multicenter ISSG dataset. Durotomy occurred in 10.8% of cases. As in the present study, the authors reported a history of prior decompression to be the only significant risk factor for intraoperative durotomy. Of note, this earlier cohort had a lower prevalence of revision surgery (47.2%) compared to the present study (71.5% of patients), which may in part account for the observed difference in durotomy rates.

Increased durotomy risk in the context of revision surgery is likely related to epidural scarring, which has been noted by multiple prior groups [18]. In the context of ASD surgery requiring osteotomy for correction, Arlet [19] recommended performing the osteotomy away from the level of scarring. The present results support this as a potential protective maneuver, as the biggest predictor of durotomy in the present study was having previously undergone a decompression procedure at the PSO level. However, avoiding PSO execution at the prior laminectomy site may be infeasible, depending upon the level and location of the fixed deformity in revision cases. It may also place the lordosis in a non-physiological location, and thereby be an unfavorable strategy from the perspective of achieving alignment goals. In such cases, decompression should start from regions of normal anatomy and then move towards taking down the scar and exposing the landmarks for the osteotomy. The dural tube should be freed of all adhesions to the pedicles and vertebral body of the PSO level prior to initiating the osteotomy. Though clinical experience suggests it is during this step that the surgeon is at highest risk of durotomy, such maneuvers are necessary to create a working channel for the osteotomy tools and to prevent the excessive buckling of the dura during the closure of the PSO.

The above strategies have been described as potential methods for decreasing durotomy risk while performing a PSO, though there are no surefire techniques for preventing this outcome. In general, our strategy is the first to consider performing the PSO at a level other than the level of the prior decompression. This allows the surgeon to work with a preserved/normal anatomy and to avoid regions of epidural scarring, which the current literature suggests is likely a driver of durotomy risk. However, if the PSO must be performed at a level of prior decompression in order to achieve the necessary sagittal correction, then the dissection should start from a region of normal or relatively preserved anatomy. The scar should then be taken down piecemeal from the region of normal anatomy to that which is most abnormal. All scar material need not be removed if the combined scar/dura is

pliant enough to tolerate compression across the PSO site without the buckling of the dura. During the decompression, the adhesions to the pedicles and vertebral body of the PSO level should be lysed, so that an incidental durotomy is not encountered during execution of the PSO. Such a tear will likely be very eccentric/lateral and likely not amenable to primary repair, increasing the potential risk of persistent CSF leaks.

4.1.2. Surgeon Experience

There have been limited investigations into the influence of surgeon experience on durotomy risk. Recently, Winter and colleagues [20] examined a retrospective cohort of 650 patients who underwent lumbar surgery. They found that laminectomy versus sublaminar decompression increased the risk of durotomy, but neither surgeon experience nor revision (versus index) surgery predicted durotomy occurrence. By contrast, Enders et al. [21] published an earlier series of 541 patients who underwent lumbar interbody fusion over a 10-year period, finding that inexperienced surgeons (defined as having performed <40 prior interbody fusions) were more than twice as likely to experience a durotomy than experienced surgeons (a minimum of 150 prior interbody fusions performed). Prior surgery (OR 2.63; $p < 0.001$) and multi-segment (versus single segment) surgery (OR 1.43; $p = 0.03$) were also risk factors for durotomy. Sin et al. [22] reported similar findings in their series of 76 patients, of whom 12 suffered durotomies. The authors reported that 75% of the durotomies were caused by residents in training, suggesting again that increased experience may reduce the risk of intraoperative durotomy. McMahon et al. [23] similarly noted residents to be responsible for the largest portion of durotomies, with fellows and attending surgeons accounting for far smaller proportions. Lastly, Raad and colleagues [24] reported on a single surgeon series of 197 PSOs. Though durotomy was not specifically examined, neurological injury—an often-related outcome—was examined and was noted to decrease with increased experience (estimated at 8% per 100 cases). This echoed earlier findings by Lau et al. in a 12-year cohort, where they found that increased years of surgeon operative experience was associated with a decreased risk of neurologic injury amongst patients undergoing 3CO for ASD. They noted a relative plateau after 3–5 years of independent operative experience.

4.1.3. Schwab Grade of Osteotomy

To our knowledge, there has been no previous investigation of the association between osteotomy size and odds of durotomy. Previously, it has been reported that the risk of durotomy is increased in patients undergoing osteotomy for sagittal or coronal alignment correction. Using the ISSG database, Iyer et al. [17] reported that the performance of a PSO was associated with a 2.8-fold increased risk of durotomy, though this association was only significant in univariable analyses. There has been no such examination comparing risk following PSO, extended PSO, or vertebral column resection. Additionally, the data of Iyer et al. [17] showed a greater PI–LL mismatch and a more severe sagittal deformity (as measured by SVA) preoperatively, with no significant difference postoperatively, suggesting that sagittal plane correction may have been more aggressive in the durotomy group, though this was not formally examined.

4.1.4. Ultrasonic Bone Curette and the Influence of Osteotomy Tools

The influence of the decompression instrument on durotomy risk has been only superficially examined, with most studies reporting Kerrison rongeur use to be associated with the occurrence of durotomy, though without formalized statistical examination [22,23]. Here, we sought to examine the influence of osteotomy tools (high-speed drill/burr, ultrasonic cutting instrument, osteotome, etc.) on the occurrence of durotomy. The ultrasonic cutting tool has been reported to have a decreased associated risk of durotomy in small series, including that of Bydon et al. [25] and Steinle et al. [26], though this association has been inconsistent [27]. Some authors [19] advocate against the use of this tool in the context of epidural scars, as they believe it actually increases the risk of durotomy. In the present

series, we found that the performance of osteotomy cuts with an ultrasonic bone cutter was not associated with an increased risk of durotomy. In fact, though a non-significant finding due to the small sample size, the use of an ultrasonic cutting device was potentially protective of durotomy, as it was used nearly two-fold more commonly in the group that did not suffer durotomy (16.9 vs. 7.8%; $p = 0.17$).

4.2. Limitations

The present study has several limitations, including its reliance on retrospective data. This precludes us from reaching any conclusion about the potential causal linkage between the identified risk factors and durotomy occurrence. Additionally, the present study makes use of data from a single institution. Nevertheless, the data were gathered from three tertiary care sites staffed by surgeons trained at multiple distinct centers from both orthopedic and neurosurgical disciplines, so they help to improve the generalizability of the present results. An additional limitation is the potential for incompleteness in the operative notes. While many surgeons employ several tools during the execution of a PSO, all may not be named in their operative report, leading to potential under-reporting. It is therefore possible that there is an association between intraoperative durotomy and one of the osteotomy techniques, which was not captured due to incompleteness of the operative notes. Furthermore, while the use of a PSO versus an extended PSO was investigated as a risk factor for intraoperative durotomy, the classification was based upon surgeon reports of the procedure. An alternative radiographic method for assessing the osteotomy (i.e., the bony wedge angle) may be an aspect to explore in future investigation and may reveal a threshold for osteotomy "aggressiveness", above which there is an elevated risk of durotomy. A final limitation is the relatively small sample size. While a multiyear, multicenter dataset was employed, the power of the results can be improved in further iterations through the inclusion of additional centers or study groups. Finally, prospective data collection could facilitate the determination of causal factors for durotomy, which may better identify potential points for therapeutic intervention.

5. Conclusions

In the present multicenter retrospective cohort study, a history of prior lumbar surgery was the only significant predictor of intraoperative durotomy during adult spinal deformity surgery incorporating one or more pedicle subtraction osteotomies. Specifically, a history of a prior decompressive procedure at the planned PSO site was the greatest risk factor, portending a more than four-fold increase in the odds of durotomy. Pedicle subtraction osteotomy size (Schwab 3 vs. 4) nor surgeon training successfully identified patients' risk of durotomy. Additional investigations using prospectively gathered data are merited to validate these results.

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Informed Consent Statement: Patient consent waived for the present study as it was retrospective, non-interventional and posed minimal risk to the patients included.

Data Availability Statement: The data presented in this study are available on request from the corresponding author (accurately indicate status).

Conflicts of Interest: The authors declare no conflict of interest.

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Systematic Review

Assessing the Accuracy of Spinal Instrumentation Using Augmented Reality (AR): A Systematic Review of the Literature and Meta-Analysis

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Abstract: Technological advancements, particularly in the realm of augmented reality (AR), may facilitate more accurate and precise pedicle screw placement. AR integrates virtual data into the operator's real-world view, allowing for the visualization of patient-specific anatomy and navigated trajectories. We aimed to conduct a meta-analysis of the accuracy of pedicle screw placement using AR-based systems. A systematic review of the literature and meta-analysis was performed using the PubMed/MEDLINE database, including studies reporting the accuracy of pedicle screw placement using AR. In total, 8 studies with 163 patients and 1259 screws were included in the analysis. XVision (XVS) was the most commonly used AR system (595 screws) followed by the Allura AR surgical navigation system (ARSN) (462 screws). The overall accuracy was calculated as 97.2% (95% CI 96.2–98.1% $p < 0.001$). Subgroup analysis revealed that there was no statistically significant difference in the accuracy rates achieved by XVS and Allura ARSN ($p = 0.092$). AR enables reliable, accurate placement of spinal instrumentation. Future research efforts should focus on comparative studies, cost effectiveness, operative time, and radiation exposure.

Keywords: augmented reality; mixed reality; XVision; pedicle screw

1. Introduction

Pedicle screw placement is a fundamental spine surgery technique classically performed via an anatomy-based freehand technique or with fluoroscopic guidance [1]. However, screw misplacement is not uncommon and can have significant consequences [1]. Therefore, novel techniques and technologies have been developed to improve the accuracy and precision of pedicle screw placement. Augmented reality (AR) is an emerging technology that allows for virtual data to be integrated into the operator's field of view in real time [2,3]. AR can provide the surgeon with real-time access to their patient's three-dimensional (3D) anatomy without disrupting the surgical workflow [4]. AR was first used within spine surgery for pedicle screw placement but is now facilitating pelvic fixation, osteotomy planning, interbody placement, and tumor resection [5]. Recent studies have shown that AR-based systems can significantly enhance the accuracy of pedicle screw placement [6]. In this study, we aimed to perform a systematic review of the literature to assess the accuracy of AR-based systems for spinal pedicle screw placement. We also discuss the requirements, limitations, and barriers associated with such systems, providing insights that could assist in identifying gaps in the adoption of AR technology.

2. Methods

2.1. Literature Search

A systematic search of the literature was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The MEDLINE database was screened from inception until 31 May 2023, using the search syntax *(spine OR spinal) AND ("augmented reality" OR "mixed reality" OR "AR" OR Xvision OR HMD OR "head mounted" OR "head-mounted") AND (screw OR pedicle OR fixation OR hardware)*.

2.2. Study Selection

Studies were reviewed after establishing the inclusion and exclusion criteria. We included the studies if they met the following criteria: involved $\geq$1 patient undergoing pedicle screw fixation using an AR-based system; provided accuracy data on screw placement; reported in English. Studies were excluded if they were conducted on cadavers or phantom models or if they were conference abstracts, reviews, technical notes, commentaries, or case reports. Articles were independently reviewed by the first two authors, using title/abstract screening followed by full-text evaluation. Any disagreements were resolved by the senior author. The reference lists of included studies were also manually screened to capture any additional studies not included by the initial search strategy.

2.3. Data Extraction

The required data were extracted by one author (B.P.) and then independently verified by an additional author (T.D.A.). The data included the patients' demographics, comorbid medical conditions, number of screws, spinal level of screw placement, type of AR system, accuracy of screw placement, accuracy assessment scale, grade-wise accuracy, complications, and follow-up.

2.4. Evidence Assessment

The 2011 Oxford Center for Evidence-Based Medicine guidelines were utilized to assess the level of evidence of each study.

2.5. Statistical Analysis

The meta-analysis was conducted using MAJOR (Jamovi software, Version 2.4.11). A fixed-effects model was created to study the effect size of the screw accuracy achieved using AR. The fixed-effects model was chosen over the random-effect model because of the moderate heterogeneity detected using the I^2 test (I^2 = 31.87%). This could be attributed to the utilization of two different AR systems, the type of study design, and the involvement of a variety of spinal levels. A subgroup analysis was conducted to compare the accuracy of the Allura augmented-reality surgical navigation (ARSN) system with that of the XVision system (XVS) using the Student's *t*-test; all statistics were two-tailed with a $p < 0.05$. To assess for publication bias, the Egger's test was performed.

3. Results

3.1. Study Selection

The initial search strategy returned a total of 388 potential studies for the meta-analysis (Figure 1). Following title/abstract screening, 349 studies were excluded, and the full texts of 39 studies were reviewed. After full-text review, 31 additional studies were excluded, resulting in 8 studies for quantitative meta-analysis (Table 1).

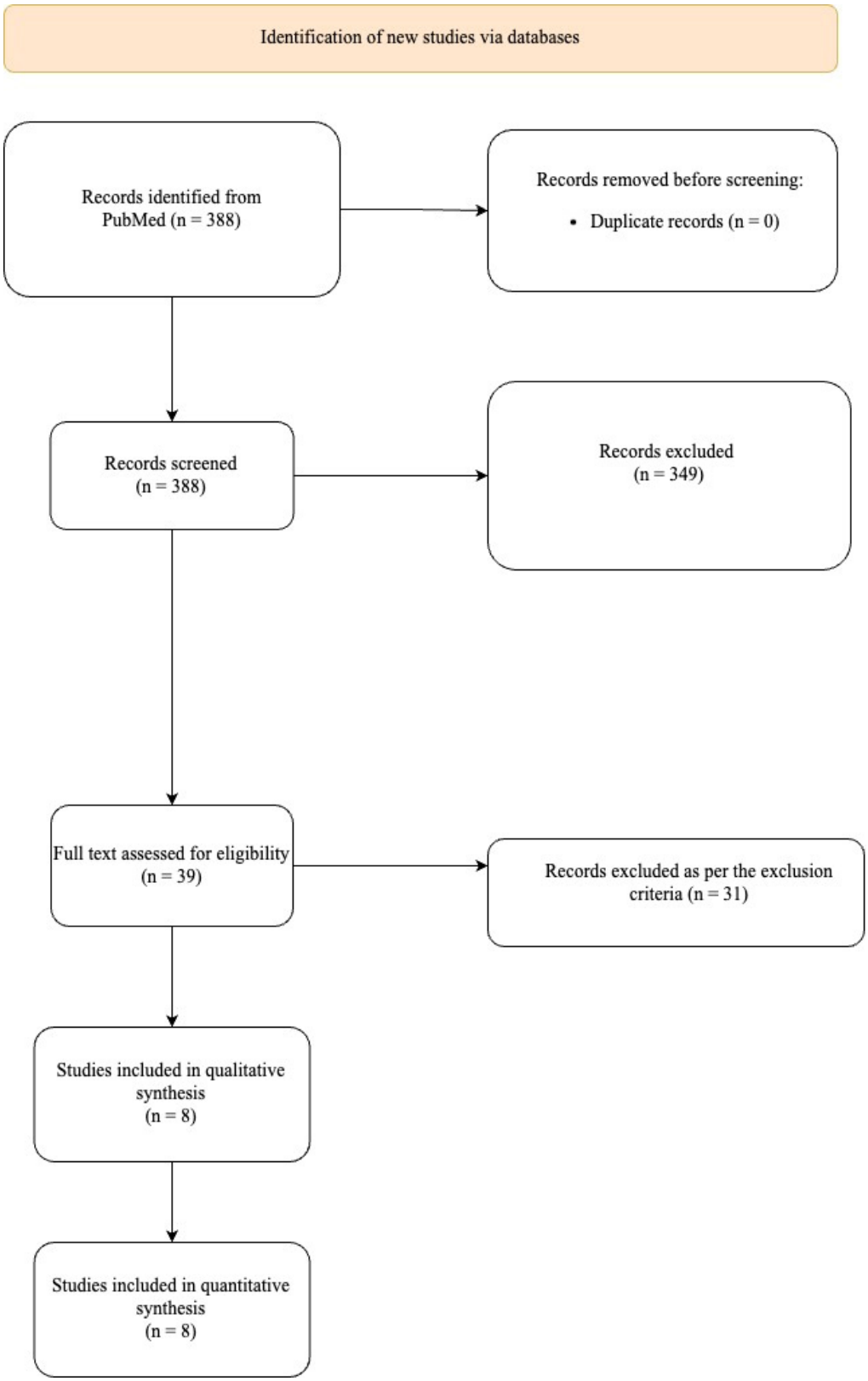

Figure 1. Detailed process of selection of studies according to PRISMA guidelines.

Table 1. Summary findings of studies included in meta-analysis.

Author, Year	Study	Technology	No. of Screws	No. of Patients	Gender	Mean Age (yrs)	Spinal Level	Pathology	Accuracy Assessment Tool	Accuracy (%)	Breach Grade
Gu et al., 2020 [7]	RCT	MR	142	25	11 M 14 F	44.32	142 L	Lumbar spondylolisthesis (n = 7)	NR	95.77	NR
Emi-Terander et al., 2020 [8]	Prospective	Allura ARSN	262	20	9 M 11 F	30	166 T, 96LS	Scoliosis (n = 13), kyphosis (n = 2), other (n = 5)	G	93.9	63.4% Grade 0 30.5% Grade 1 6.1% Grade 2
Liu et al., 2021 [9]	Retrospective	XVS	205	28	11 M 17 F	62.5 *	67 T, 112 L, 26 S1	12 degenerative disease; 12 deformity correction; 3 tumor; and 1 trauma	GR scale	98	94% Grade A 4% Grade B 1.5% Grade C 0.5% Grade D
Yahanda et al., 2021 [6]	Retrospective	XVS	63	9	5 M 4 F	71.9	32 T, 31 L	4 tumors, 3 degenerative disease, 1 spinal deformity, and 1 infection	GR scale	100	96.8% Grade A, 3.2% Grade B
Burström et al., 2021 [10]	Retrospective	Allura ARSN	260	20	9 M 11 F	30.5	166 T, 94 LS	13 scoliosis, 2 kyphosis, 3 lumbar spondylolisthesis, 1 lumbar spinal stenosis, 1 lumbar degenerative disk disease	GR scale	97	NR
R Bhatt et al., 2022 [11]	Prospective	XVS	218	32	13 M 19 F	50.9	TLSP	6 deformity, 5 instability, 9 postlaminectomy syndrome, 2 pseudoarthrosis, 10 stenosis	GR scale	97.1	91.8% Grade A, 5.3% Grade B
Harel et al., 2022 [12]	Prospective	XVS	86	17	7 M 10 F	60.23	40 L, 46 LS	17 spondylosis	GR scale	97.7	84.9% Grade A, 12.8% Grade B, 2.3% Grade C
Judy et al., 2023 [13]	Retrospective	XVS	23	12	4 M 8 F	63 *	S2 alar-iliac	3 degenerative disease, 8 deformity, 1 tumor	G	95.6	91.3% Grade 0, 4.3% Grade 1, 4.3% Grade 3

* Median age. Abbreviations: MR, mixed reality; XVS, XVision system; ARSN, augmented-reality navigation system; G, Gertzbein classification; GR, Gertzbein and Robbins grading; T, thoracic; L, lumbar; S, sacral; LS, lumbosacral; NR, not reported; P, pelvic.

3.2. Patient Characteristics

A total of 1259 screws were placed in 163 patients (female, N = 94 (57.7%)) (Table 2).

Spinal deformity was the most common indication (N = 74, 45.4%) followed by degenerative spine disease (N = 35, 21.5%). The thoracic spine was the most frequent site of pedicle screw placement using AR (N = 431, 34.2%) followed by the lumbosacral spine (N = 221, 17.6%). One study did not mention the spinal level. The most commonly used AR system was the XVS (595 screws) followed by Allura ARSN (426 screws) and mixed reality (MR) (146 screws).

Table 2. Patient characteristics.

Parameter	Frequency
Number of Screws	1259
Thoracic	431 (34.2%)
Lumbar	194 (15.4%)
Lumbosacral	221 (17.6%)
S1	26 (2.1%)
S2 alar-iliac	23 (1.8%)
No. of Patients	163
Males	69 (42.3%)
Females	94 (57.7%)
Conditions	
Deformity	74 (45.4%)
Tumor	8 (5%)
Degenerative disease	35 (21.5%)
Spondylolisthesis	10 (6.1%)
Trauma	1 (0.6%)
Infection	1 (0.6%)
Pseudoarthrosis	2 (1.2%)
Postlaminectomy syndrome	9 (5.5%)
Others	5 (3.1%)
AR System	
XVision, head mounted	595 screws
Allura ARSN	462 screws
Mixed reality	142 screws

3.3. Accuracy

Most studies (N = 6, 75%) utilized the Gertzbein and Robbins (GR) classification to assess screw accuracy while two studies utilized the original Gertzbein classification. GR grading is a modification of the Gertzbein classification [14] as depicted in Table 3.

Table 3. Relation between Gertzbein classification and Gertzbein and Robbins grading of accuracy for pedicle screw placement.

Gertzbein Classification	Gertzbein and Robbins Grading	Interpretation
Grade 0	Grade A	No cortical breach or screw within pedicle
Grade 1	Grade B	0–2 mm breach
Grade 2	Grade C	2–4 mm breach
Grade 3	Grade D	4–6 mm breach
	Grade E	>6 mm breach

Six studies deconstructed their data to provide grade-specific accuracy (Table 1). Placement was termed "accurate" if the grading was below and inclusive of grade 1/B. Screw accuracy within individual studies ranged from 94% to 100%. The overall weighted accuracy was 97.2% (95% CI, 96.2–98.1% $p < 0.001$) (Figure 2a), meaning that, of 1259 screws, 1224 were accurately placed using AR (grade1/B or better) while 25 screws could not be accurately placed and were, therefore, placed freehand, guided either by fluoroscopy or other techniques, which were not explicitly reported by the studies. The effect size for accuracy achieved by the XVS was 98% (95% CI 97–99.2% $p < 0.001$) (Figure 2b). There was no statistically significant difference in the mean accuracy achieved by the XVS and the Allura ARSN (97.7 $\pm$ 1.6% vs. 95.5 $\pm$ 2.2%, $p = 0.092$).

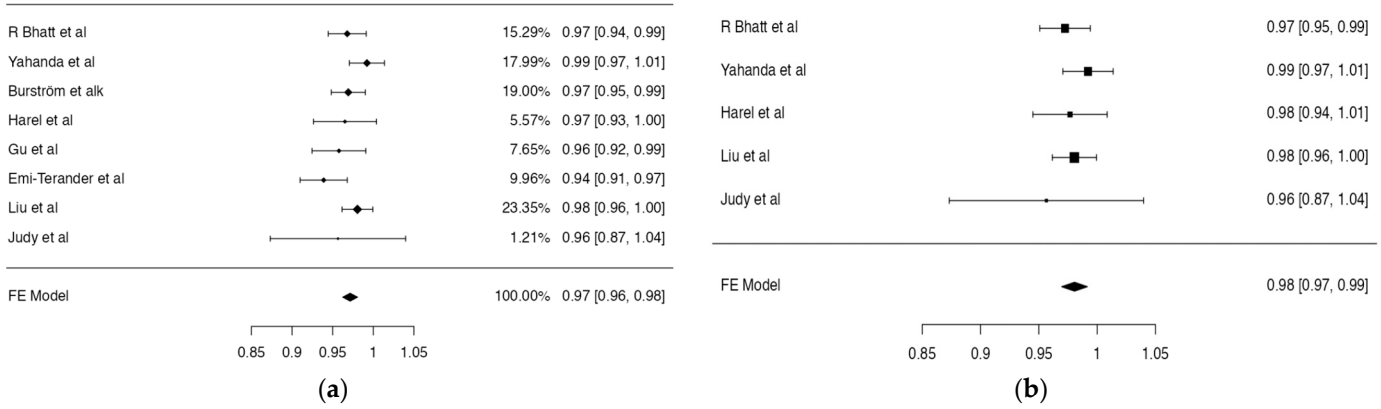

Figure 2. (**a**) Meta-analysis of the accuracies of spinal screw placement using augmented reality. (**b**) Meta-analysis of studies reporting the accuracy of the XVision system. Estimates for the main effect are provided by a shape and error bars, with estimates for summary effect provided by a diamond [6,8–13].

3.4. Publication Bias Assessment

The *p* value of the Egger's test was 0.131 (>0.05), suggesting low-to-minimal publication bias (Figure 3).

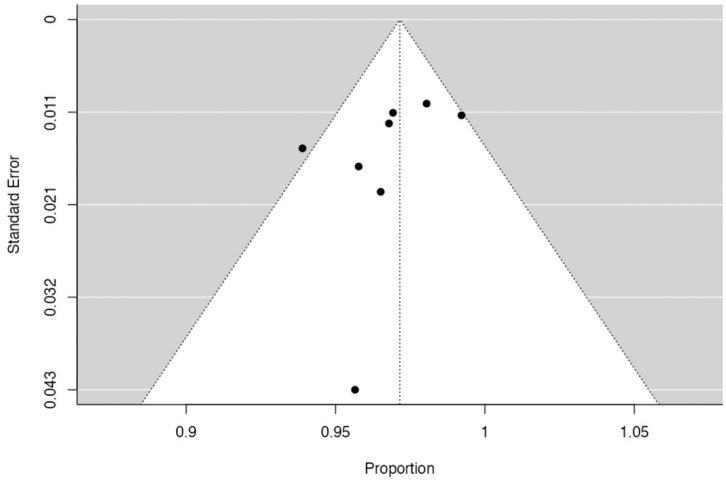

Figure 3. Funnel plot for the studies included in the analysis. Each dot represents and included study.

4. Discussion

Pedicle screw placement can be divided into two major schools of thought, namely freehand and imaging guided. Image guidance, classically, involves fluoroscopic guidance. Technological advancement has seen the emergence of new techniques for intraoperative navigation, i.e., robot assistance and AR [1]. Regardless of the technique utilized, an in-depth understanding and accurate identification of the anatomical landmarks remains critical for safe and precise screw insertion [6]. A systematic review reported an accuracy of 95.5% achieved by 3D fluoroscopy, demonstrating consistent success across all spinal levels. However, this technique often results in greater levels of radiation exposure [15]. Verma et al. found that the accuracy of computer-assisted screw placement (CASP) was significantly higher than that achieved freehand (93.3% vs. 84.7% $p < 0.001$) [16]. Additionally, the complication rate was 0% in patients undergoing CASP as compared to 2.3% for patients who underwent freehand screw placement [15]. However, the accuracy of CASP may depend on the angle between the camera and the surgical tool, the quality of the camera, the hand movement of the surgeon, the duration of surgery, and the environmental conditions. In an attempt to mitigate these challenges, robot-assisted screw placement (RASP) was

introduced [9]. In our meta-analysis, an average weighted accuracy of 97.2% was achieved for patients undergoing pedicle screw placement using AR, comparable to rates cited in the most accurate freehand, CASP, and RASP studies [9,17]. These findings support the use of AR as a valuable tool for ensuring accurate and safe spinal instrumentation. The accuracy of individual studies varied from 94% (Emi-Terander et al. [6]) to 100% (Yahanda et al. [8]). Emi-Terander et al. intentionally chose larger screw diameters to maximize screw bony purchase and biomechanical stability. While this decision may have led to their higher incidence of cortical breaches, the authors posit that, without AR, it may not have been possible to place a screw at these levels due to miniscule pedicle diameters. The strength of AR lies in its potential to mitigate human limitations, such as mild hand tremors or trajectory variations. However, AR on its own might not entirely eliminate these challenges. Ultimately, the decision on surgical adjunct lies with the surgeon and the technology they are most comfortable with. AR and robot assistance both have pros and cons. While these adjuncts may have different ideal applications, currently, the decision on which adjunct to use should be made based on surgeon comfort. The recent literature, including the study by Vörös et al., has explored a mixed-model approach, combining the strengths of both AR and robotic systems [18].

Two AR systems have been utilized in spinal screw instrumentation, namely XVision AR-HMD and Allura ARSN. XVS is the only AR-HMD system approved by the Food and Drug Association (FDA), while Allura is currently only used as an off-label prototype [8]. XVS has a head-mounted display system that projects holographic images directly into the surgeon's field of view, eliminating the need to look at a computer screen and facilitating an uninterrupted operative visual field. In contrast, the ARSN system features a C-arm panel with integrated video cameras and a monitor displaying AR-enhanced images. The most significant advantage of the ARSN system is its capacity to intraoperatively image misplaced screws via a built-in cone beam computed tomography device. In the context of thoracolumbar instrumentation, Burstrom et al. found comparable sensitivity and specificity in the identification of pedicle screw breaches using intraoperative CT compared to traditional postoperative CT imaging [10]. Intraoperative CT may minimize the need for returns to the operative room and postoperative follow-up imaging [10]. Two studies have described their human-trial results using ARSN in thoracolumbar spinal pedicle screws with a mean accuracy of 95.5% (94% Elmi-Terander et al. [8] and 97% Burstrom et al. [10]).

Comparatively, Gu and colleagues conducted a randomized prospective study to compare outcomes in patients undergoing lumbar pedicle screw insertion using mixed-reality (MR) versus freehand techniques. MR, a hybrid of augmented- and virtual-reality technologies, allows surgeons to superimpose virtual 3D holographic images onto the operative field. Gu and colleagues demonstrated a screw accuracy rate of 96% [7] when using MR, consistent with the accuracies observed in AR systems (Table 1) [19,20]. However, Gu et al. failed to mention the scale followed to calculate this accuracy rate, which needs to be mentioned to avoid confounded findings.

Navigated techniques appear to outperform freehand techniques in terms of operative time for actual screw placement. Butler et al. reported that the time taken to place each screw was 3 min 54 s using AR [21], which was less than that reported for fluoroscopy-guided (6.3 ± 3.0 min/screw) and robot-assisted screw placement (4.0 ± 1.1 min/screw) [22]. Khan et al. reported similar findings of 6.8 ± 0.9 min/screw for fluoroscopy-guided placement and 3.7 ± 1.8 min/screw for robotic placement [23]. However, these findings did not account for the setup time required for the robot or the AR system. The average total operative time required by the ARSN system was greater than that needed for fluoroscopy-guided placement, though statistically insignificant (403 min vs. 361 min, p =0.31) [8]. A similar effect was observed for deformity patients using this system [24]. It is likely that the entire operative team's familiarity with the system and a standard imaging and registration process are necessary to achieve durable reductions in operative time when using AR.

Gu et al. reported a reduction in operative blood loss when using the MR system, when compared to the freehand group (MR, 382 cc; FH, 450 cc, p = 0.01) [7]. Similarly,

intraoperative blood loss utilizing the ARSN system was nearly half of that lost during fluoroscopy-guided placement (628 ± 386 cc vs. 1165 ± 1103 cc, respectively $p = 0.06$) [8]. The ability of AR technology to potentially reduce operative time and blood loss suggests that AR may have the capacity to enhance intraoperative decision making and workflow.

Importantly, Boyaci et al. [25] sought to explore the use of AR technology for surgical education. The authors tested the ability of AR guidance on medical students and physicians (without formal surgical training) safely and accurately placing C2-3 transpedicular screws on cadaver models. Unsurprisingly, individuals in the AR group achieved a statistically higher Grade 0 safety ratio as compared to the freehand-alone group [25]. Thus, as AR technology becomes more accessible, surgical education will benefit from earlier hands-on experience as well as more standardized training.

While the potential benefits of AR technology in spinal instrumentation are significant, the associated capital costs are likely less than that of robotic systems [26,27]. These start-up costs most significantly impact on the technology's expansion into lower-middle-income countries (LMICs) where AR systems could potentially provide the greatest long-term cost savings. Furthermore, considering that AR is a relatively new technology, it can be argued that outstanding accuracy outcomes may be predominately achieved in the hands of the highly experienced surgeons, as exemplified by the 100% accuracy rate by Yahanda et al. [6] The correlation between accuracy and the surgeon's experience is directly proportional, as revealed by Rivkin et al., who noted an accuracy increase from 86.8% for 30 cases to 98.9% for 270 cases [28].

Limitations

Factors such as obesity, age, and osteoporosis are pivotal in such studies since they can affect screw breach [29,30]. However, our meta-analysis aimed to consolidate the findings of individual studies, and as such, we relied on the data provided in those studies. Many of the original articles with relatively small cohorts did not provide detailed patient demographics or did not statistically analyze these potential risk factors. Incorporating a new statistical analysis based on these factors would require access to raw, patient-level data, which is unfortunately beyond the scope of our current meta-analysis. Additionally, limited follow-up was reported for the included studies. Only one study reported a short-term follow-up at two weeks postoperation. Future studies would benefit from extended follow-up periods to provide a more comprehensive understanding of AR applications. Furthermore, only two studies reported the operative duration as a variable. While AR navigation requires additional steps for setup including intraoperative imaging and navigation array registration, it may expedite intraoperative decision making and enable faster instrumentation placement. Future studies should evaluate the overall effect of AR navigation on total operative time, as well as time specifically for hardware placement. Another limitation was the inability to further stratify results based on the anatomical risk associated with pedicle screw placement. Specifically, screws placed in high-risk areas could present different challenges. Future studies with a more detailed dataset would be beneficial in shedding light on this crucial aspect.

5. Conclusions

Augmented reality (AR) is an emerging technology with promising results in spinal surgery. The early data indicate that AR navigation for pedicle screw placement is safe and accurate. Future investigations into long-term patient outcomes the cost effectiveness of AR navigation will be important to help determine the best role for this technology in the future of spinal surgery.

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Nighttime versus Fulltime Brace Treatment for Adolescent Idiopathic Scoliosis: Which Brace to Choose? A Retrospective Study on 358 Patients

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Abstract: The purpose of this study is to retrospectively compare the effectiveness of fulltime Boston Brace (BB) and Providence Nighttime Brace (PNB) treatments in moderate scoliotic curves (20–40°) at a single institution and to carry out analyses for different subgroups. Inclusion criteria: idiopathic scoliosis, age $\geq$ 10 years, curve 20–40°, Risser $\leq$ 3 or Sanders stage $\leq$ 6 and curve apex below T6 vertebra. Exclusion criteria: incomplete radiological or clinical follow-up and previous treatment. The primary outcome was failure according to the SRS outcome assessment: increase in main curve > 5° and/or increase in main curve beyond 45° and/or surgery. The subgroup analyses were secondary outcomes. In total, 249 patients in the PNB and 109 in the BB groups were included. The BB showed a higher success rate compared to the PNB (59% and 46%, respectively) in both crude and adjusted comparisons (p = 0.029 and p = 0.007, respectively). The subgroup analyses showed higher success rates in pre-menarchal females, thoracic curves and curves > 30° in the BB group compared to the PNB group. Based on the findings, fulltime braces should be the treatment of choice for more immature patients and patients with larger and thoracic curves while nighttime braces might be sufficient for post-menarchal females and patients with lumbar and smaller curves.

Keywords: brace treatment; nighttime brace treatment; adolescent idiopathic scoliosis; scoliosis; Providence brace; Boston brace

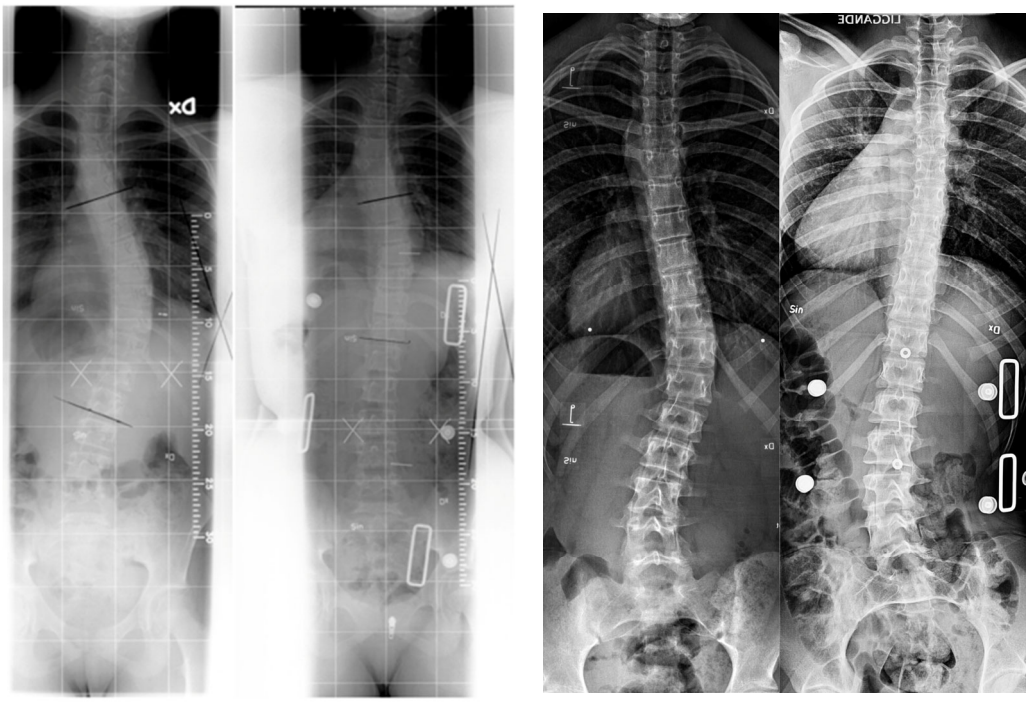
1. Introduction

Adolescent idiopathic scoliosis (AIS) mostly affects healthy adolescent females [1]. The yearly incidence is 3–5%; however, only 0.3–0.5% require treatment. In AIS, the growing spine starts to rotate shortly before the growth spurt and creates a typical lateral scoliotic curve. The deterioration usually continues until full maturity is reached and can lead to a severe spine deformity if it is left untreated. Meanwhile, severe scoliotic deformities (radiologic Cobb angle > 45°) are treated surgically, and milder forms of progressive deformities (20–40°) can respond to brace treatment [2,3]. Although there are many different brace types and designs, their common goal is to align the spine during the growth spurt by external forces and limit the progression of the scoliotic curve (Figure 1).

A traditional fulltime brace (e.g., Boston brace) is sought to be worn for 18–23 h per day, even though some treatment effect is still noticeable after 12 h of daily wear [2,4]. The treatment is demanding for the patient as well as their family, and adherence to the treatment varies substantially (33–93%) [5,6]. Nighttime braces (e.g., Providence, Charleston) are supposed to limit the negative psycho-social effects of brace treatment and increase adherence to the treatment while maintaining equal treatment effect. Even though early studies showed promising results on nighttime bracing, later works showed inconclusive results, with treatment success ranging from 15% to 93% [7–17]. This discrepancy might be due to different inclusion criteria, outcome measures for success, compliance assessment

and/or maturity staging. Therefore, new guidelines for brace studies in AIS patients were created by the Scoliosis Research Society (SRS) Committee [18]. However, only a few studies on nighttime bracing have attempted to follow these guidelines [9,10,13,14].

Here, we present what is to our knowledge the largest study comparing treatment effectiveness in 358 consecutive AIS patients treated either with a fulltime Boston brace (BB) or a Providence nighttime brace (PNB) at a single institution. Both the SRS assessment criteria of effectiveness for brace studies and the increase in the Cobb angle until final follow-up were primary outcome measures for treatment effectiveness. In addition, compliance as well as treatment effectiveness in different subgroups were compared as secondary outcome measures.



(**a**) (**b**)

Figure 1. Pre-brace and in-brace radiographs for Boston and Providence brace treatments: (**a**) left: pre-brace (40° curve); right: in Boston brace (17°); (**b**) left: pre-brace (31° curve); right: overcorrection in Providence brace (−4°).

2. Materials and Methods

2.1. Study Design

A retrospective observational case–control study approved by the Swedish Ethical Review Authority (DN: 2020-04364) was conducted at a single institution specialized in the treatment of spinal deformity. The patients were identified within the records of the institution's Orthotics Department, where all orthotic/brace treatments performed at the clinic were registered. Patients treated between 2003 and 2019 were included. Although the BB was gradually replaced by the PNB in the 2010s, the indication criteria for brace treatment have remained the same over time. The inclusion criteria were idiopathic scoliotic curves 20–40° Cobb angle, age over 10 years, Risser stage ≤ 3 and/or Sanders stage ≤ 6 and apex of the main curve below T6 vertebra. Exclusion criteria were incomplete clinical and radiological follow-up or previous treatment for scoliosis. In total, 590 consecutive AIS patients from the Orthotics Department's records were cross-referenced with the medical records and reviewed. Of these, 102 patients were excluded due to advanced radiological skeletal maturity, 85 patients due to missing radiological or clinical data, 44 patients due to having curves >40° or <20° and 1 patient due to having apex at the T4 vertebra. Thus, 358 patients were included in the study (Figure 2).

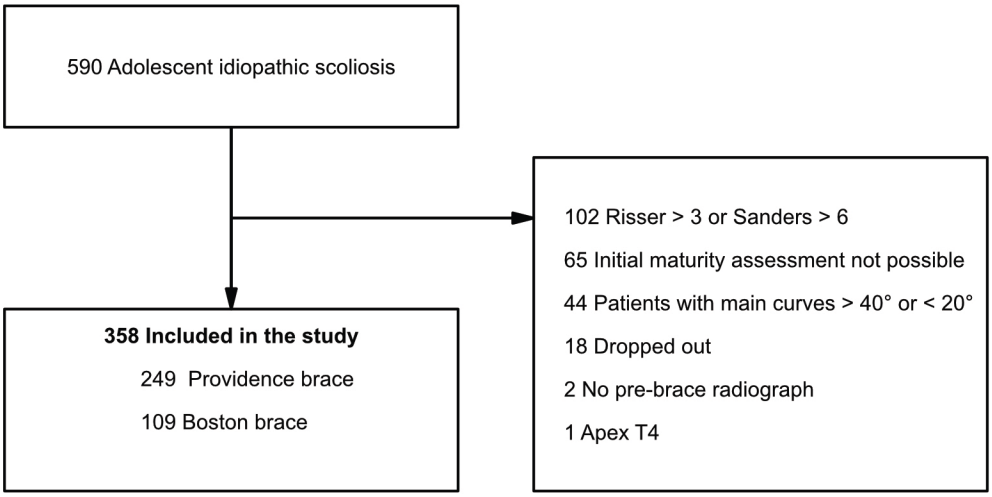


Figure 2. Study flowchart.

2.2. Treatment Procedure

Both studied braces, the Boston brace (BB; Allard UK Ltd., Dunalk, Ireland) and the Providence nighttime brace (PNB; Spinal Technology, LLC, West Yarmouth, MA, USA), are semi-custom-made devices; their treatment principles, measurement and manufacture are described elsewhere [7,19]. The BB is a fulltime brace intended for 23 h of daily wear, whereas the PNB is prescribed for night-wear only. After the brace was fitted, the radiographs were taken to ensure an acceptable (50%) in-brace correction (i.e., supine or standing radiographs in PNB or BB patients, respectively). Brace adjustments were usually necessary during the first 4–6 weeks to reach an optimal fit. Clinical and/or radiological follow-ups were taken every 6–12 months depending on the risk of curve progression. The brace was checked for a good fit at each visit by a dedicated team consisting of a spine surgeon, physiotherapist and orthotic engineer. Any treatment changes and compliance issues were documented. The treatment was discontinued when skeletal maturity was reached (Risser $\geq$ 4 and/or Sanders $\geq$ 7 and/or 2 years after menarche). At least one post-treatment follow-up visit was performed about 1 year after discontinuation of the treatment.

2.3. Outcome Measures and Variables

The primary outcome measure was determined based on the recommendation of the SRS Committee on Bracing and Nonoperative Management [18]. Thus, treatment failure was defined as: (1) increase in the scoliotic curve by $\geq 6^\circ$ before the 1-year follow-up visit and/or (2) increase in the curve beyond 45° and/or (3) surgery being recommended or performed within 2 years after discontinuation of the treatment. The brace groups were also compared with respect to increase in the main curve during the treatment period. A simplified Lenke classification was used for five major curve patterns: Major Thoracic, Double Thoracic, Double Major, Triple Major and Thoracolumbar/Lumbar (Lenke 5 and 6). In the case of double curves, the larger curve was labeled as the primary curve.

Since inclusion in the study stretched over a prolonged period of time, the Risser skeletal maturity assessment was gradually replaced by the Sanders staging system. In order to enable comparison between different maturity assessments, a modified Sanders stage (MSS) variable was introduced. This variable was constructed in agreement with the previous work by Sanders et al. [20] and consists of either a true Sanders stage, where available, or a Risser stage changed to a Sanders stage, i.e., MSS 3 $\approx$ Risser 0 and pelvic triradiate cartilage (TC) open, MSS 4 $\approx$ Risser 0 and TC closing, MSS 5 $\approx$ Risser 0 and TC closed, MSS 6 $\approx$ Risser 1–3, MSS 7 $\approx$ Risser 4, MSS 8 $\approx$ Risser 5. The radiographs of 76 patients included in a previously published randomized study were assessed independently by two observers [21]. The remaining radiographs were assessed by one individual.

Additionally, a per-protocol analysis was performed excluding patients whose initial brace treatment was changed to a different one. Finally, an analysis of certain subgroups was performed, and the compliance was compared between the groups.

2.4. Compliance

A physiotherapist specialized in brace treatment took records of patients' well-being, compliance and brace-fit at each follow-up visit. Based on these records, the patients were retrospectively divided into four groups: excellent, good, fair and poor. The patients with excellent compliance throughout the whole treatment or those with minor compliance issues during less than 25% of the prescribed time were assigned to the "excellent" group. The patients with minor compliance issues in less than half of the prescribed time were assigned to the "good" group, e.g., a PNB patient who involuntarily "opened up" the brace on fewer than half of the nights or a BB patient who was not able to wear the brace at school. The patients who had major compliance issues were assigned to the "fair" group, e.g., a PNB patient who was not able to wear the brace more than 3 nights/week, a BB patient who was able to use the brace during nights only or any patient who discontinued the treatment after less than half of the predicted treatment period. All patients who discontinued bracing after less than 25% of the prescribed time or used the brace less than 25% of the daily recommendation were assigned to the "poor" group.

2.5. Statistical Analyses

The main results were presented as proportions of treatment failures/successes in each brace group and/or a mean difference in outcome between the groups. The 95% confidence intervals (95% CI) were bootstrapped or robust where normal distribution or homoscedasticity were violated, respectively. Both crude and adjusted differences in outcome between the brace groups were calculated. A multivariable logistic regression analysis was performed for dichotomous outcome measures adjusted for propensity score. Similarly, analysis of covariance (ANCOVA) was used for comparison of adjusted continuous data. Significantly different variables at baseline with effect size > 0.2 were selected as covariates/factors for adjusted calculations. The within-groups point estimates of continuous variables were presented as means (SD) and medians (IQR—interquartile range). Student's t-test was used for continuous and Fischer's exact test for dichotomous variables between groups. The Mann–Whitney U test and Chi square test were used for ordered and non-ordered categorical data, respectively. The significance tests were two-sided at the 5% significance level. The statistical analysis was performed using SPSS v 28.0 (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Study Population

Age at bracing, gender, delay to bracing, proportion of pre-menarchal females and curve characteristics were similar in both groups (Table 1). Patients in the BB group had significantly larger initial main curves, longer follow-up and inferior in-brace correction (IBC). A majority of patients presented with thoracic curves followed by the group with TL/L curves. The MSS was significantly different between the groups ($p = 0.042$), i.e., the MSS 6 was overrepresented in the PNB group. Of 358 patients included in the study, 88% were females, and more than half of these were pre-menarche. The patients were treated for a mean of 1.9 years and followed up for a mean of 1.5 years after treatment cessation.

Table 1. Baseline characteristics for patients in Providence and Boston brace treatments groups.

	Total (n = 358)	Providence (n = 249)	Boston (n = 109)	p	Effect Size
Age at bracing	13.41 (1.28) 13.42 (12.53; 14.35)	13.42 (1.32) 13.43 (12.50;14.38)	13.41 (1.21) 13.38 (12.57; 14.28)	0.49	0.003
Gender					
Female	314 (87.7%)	215 (86.3%)	99 (90.8%)		
Male	44 (12.3%)	34 (13.7%)	10 (9.2%)	0.30	0.06
Initial Cobb angle main curve	31.1 (4.7) 31 (27; 35)	30.7 (4.5) 30 (27; 34)	32.1 (4.9) 32.5 (28; 36)	**0.006**	−0.29
Delay to bracing (years)	0.20 (0.08) 0.19 (0.15; 0.24)	0.20 (0.06) 0.19 (0.15; 0.24)	0.19 (0.11) 0.17 (0.13; 0.23)	0.56	0.08
Time spent in brace (years) *	1.91(0.94) 1.81 (1.28; 2.42) n = 295	1.87 (0.90) 1.69 (1.28; 2.31) n = 195	2.00 (1.01) 1.98 (1.34; 2.53) n = 100	0.12	−0.15
Follow up after finishing bracing (years) *	1.45 (0.73) 1.19 (1.02; 1.64) n = 295	1.39 (0.66) 1.15 (1.00; 1.53) n = 195	1.56 (0.86) 1.25 (1.04; 1.94) n = 100	**0.045**	−0.23
Initial modified Sanders stage					
2	7 (2.0%)	3 (1.2%)	4 (3.7%)		
3	48 (13.4%)	31 (12.4%)	17 (15.6%)		
4	109 (30.4%)	74 (29.7%)	35 (32.1%)		
5	58 (16.2%)	37 (14.9%)	21 (19.3%)		
6	135 (37.7%)	104 (41.8%)	31 (28.4%)		
7	1 (0.3%)	0 (0.0%)	1 (0.9%)	**0.042**	
Risser 0	164 (45.8%)	109 (43.8%)	55 (50.5%)		
Risser > 0	194 (54.2%)	140 (56.2%)	54 (49.5%)	0.25	0.062
Main curve size					
Cobb 20–29°	142 (39.7%)	106 (42.6%)	36 (33.0%)		
Cobb 30–40°	216 (60.3%)	143 (57.4%)	73 (67%)	0.10	0.089
Type of curve					
MT (Lenke 1)	169 (47.5%)	125 (50.2%)	44 (40.4%)		
DT (Lenke 2)	29 (8.1%)	18 (7.5%)	11 (10.1%)		
DM (Lenke 3)	37 (10.3%)	22 (8.8%)	15 (13.8%)		
TM (Lenke 4)	1 (0.3%)	1 (0.4%)	0 (0.0%)		
TL/L (Lenke 5 and 6)	122 (34.1%)	83 (33.3%)	39 (35.8%)	0.32	0.11
Menarche at bracing					
Pre-menarche	173 (55.6%)	119 (55.9%)	54 (55.1%)		
Post-menarche	138 (44.4%) n = 311	94 (44.1%) n = 213	44 (44.9%) n = 98	0.90	0.007
In-brace main curve correction (%)	54.7 (23.8) 55.8 (38.5; 71.4)	63.3 (20.2) 64.0 (50.0; 76.7)	34.9 (19.2) 33.3 (19.2; 46.9)	**<0.0001**	−1.4

For categorical variables, n (%) is presented. For continuous variables, Mean (SD)/Median (IQR) is presented. Mann–Whitney U test was used for ordered categorical variables, X^2 test for non-ordered categorical variables, Fischer's exact test for dichotomous variables and t-test for continuous variables. MT—major thoracic, DT—double thoracic, DM—double major, TM—triple major, TL/L—thoracolumbar/lumbar. Effect sizes are presented as Cohen's d and Cohen's w for continuous and categorical variables, respectively. * Only those who did not interrupt the treatment or underwent early surgery are included.

3.2. Main Outcome

The overall success rates according to the SRS criteria were 46% and 59% in PNB and BB groups, respectively, and they differed significantly in favor of the Boston brace (p = 0.029; Table 2). In order to take into account other variables that might influence the outcome, a logistic regression was performed with failure according to the SRS assessment criteria as the dependent variable adjusted for the propensity score. The initial curve magnitude and MSS were selected as factors in the propensity score based on the baseline differences for these variables. The other baseline characteristics, e.g., menarche, age and type of the curve, lacked both the statistical significance and effect size and, therefore, were not included in the model. In the adjusted analysis, the risk for failure after being treated by the PNB was 1.91 times higher (OR: 1.91 [1.19, 3.05]) than if treated by the

BB (p = 0.007; Table 2). Surgery was either performed or recommended within 2 years after brace treatment cessation in 28.9% and 22.9% of patients in the PNB and BB groups, respectively (p = 0.30). When adjusted for propensity score, the patients in the PNB group had 1.93 times significantly higher odds for surgery than patients in the BB group (95% CI [1.08, 3.42]; p = 0.025; Table 2).

Table 2. Primary analysis: comparison of treatment failure/success according to the SRS criteria for the Providence group and the Boston group.

	Providence	Boston			Adjusted Analysis		
			Mean D (95% CI)	p Value	OR (95% CI)	p Value *	Effect Size **
Total, n	249	109					
Failure, n	135 (54.2%)	45 (41.3%)	12.9% (1.8, 24.0)	**0.029**	1.91 (1.19, 3.05)	**0.007**	0.12
Success, n	114 (45.8%)	64 (58.7%)	−12.9% (−24.0, −1.8)				
Surgery							
Yes	72 (28.9%)	25 (22.9%)	6% (−3.7,15.7)	0.30	1.93 (1.08, 3.42)	**0.025**	0.06
No	177 (71.1%)	84 (77.1%)	−6% (−15.7,3.7)				

SRS criteria for failure were as follows: increase in the main curve by > 5° at follow-up or main curve reaching 45° or surgery. Fischer's exact test was used for crude comparisons. OR [95% CI] is the odds ratio for failure in the Providence treatment (1) compared to the Boston treatment (0) adjusted for propensity score. Propensity score is the predicted probability of being treated by the Providence brace adjusted for the initial curve magnitude and Modified Sanders stage 1–3. D = difference * Adjusted p value. ** Effect size of crude comparison is Cohen's W.

The main curve in the PNB group increased more during the treatment until the 1-year follow-up compared to in the BB group (Table 3). The average increase in Cobb angle during the treatment period was 7.3° and 4.5° in the PNB and BB groups, respectively (p = 0.009). Subsequently, the Analysis of Covariance (ANCOVA) model was built with the same covariates as in the former analysis, i.e., the initial Cobb angle and MSS 1–3 vs. MSS 4–7. Comparing the groups, the difference in the curve progression after adjustment was 3.1° with 95% CI [1.1°, 5.1°], showing a significantly worse outcome in the PNB group (p = 0.002; Table 3).

Table 3. Comparison of crude and adjusted means of main curve progression from the start of treatment to the 1-year follow-up.

	Providence		Boston					
	Crude Mean (SD) Median (IQR)	Adjusted Means * (95% CI)	Crude Mean (SD) Median (IQR)	Adjusted Means * (95% CI)	p	Adjusted p *	Difference between Groups Adjusted Means (95% CI)	Effect Size **
Cobb angle change (°) of main curve	7.3 (9.3) 6.0 (0.5; 12.5) n = 249	7.4 (6.2, 8.5) n = 249	4.5 (9.1) 3.0 (−2; 10) n = 109	4.3 (2.6, 6.0) n = 109	**0.009**	**0.002**	3.1 (1.1, 5.1)	0.30

* For adjusted means, Analysis of Covariance (ANCOVA) was used with Initial Cobb angle of main curve and Modified Sanders stage 1–3 as baseline covariates. The confidence interval for adjusted mean difference is robust because heteroscedasticity was assumed. ** Effect size is Cohen's d of crude means. For crude comparison between groups, t-test was used. p value is two-sided, significance level 0.05.

3.3. Per Protocol Analysis

In total, 12 (3.4%) patients crossed over to another brace group, i.e., 9 BB patients moved to the PNB group, 1 PNB patient moved to the BB group and 2 patients started treatment with another type of brace. Thus, the per protocol analysis was performed on the remaining 346 patients. The ANCOVA for adjusted means comparison and the multivariable logistic regression were performed with the same covariates as in the main analysis. The crossovers did not have any impact on the main results. The adjusted mean difference of the main curve progression until follow-up was 3.0° [0.9°, 5.1°], showing less progression in the BB group. The multivariable logistic regression with adjustment for

propensity score showed 1.8 times higher odds for failure in the PNB group compared to the BB group (95% CI [1.1, 2.9]; $p = 0.013$), thus showing similar results as in the main analysis.

3.4. Secondary Outcomes

The subgroup analysis was performed for certain subgroups selected by gender, menarchal status, type of main curve and curve magnitude (Table 4). Both outcomes, i.e., failure according to the SRS and increase in the main curve until follow-up, were calculated. The BB performed better in females compared to males, in pre-menarchal females, in patients with thoracic curves and in those with 30–40° curves. On the other hand, the two braces performed similarly in males, post-menarchal females and patients with lumbar curves. In the patient subgroup with minor curves (20–29°), the PNB showed a larger increase in the curve angle, although there was no significant difference in odds for failure between the groups. The patients in the PNB group, further, showed significantly better compliance with the treatment (Table 5), whereas 74% of the PNB patients had excellent compliance while only 55% in the BB group did.

Table 4. Subgroup analyses—comparison of the main results from the start of treatment to 1-year follow-up in selected subgroups.

		Failure SRS Rates				Adjusted Increase in Cobb Angle		
Selected Subgroup	**Brace Group**	**Proportion of Failures**	**Mean Difference between Groups [95% CI]**	**OR [95% CI] ***	***p* ***	**Within Groups Mean (°) [95% CI] ****	**Difference between Groups Adjusted Means [95% CI] ****	***p* ****
Females	Providence *n* = 215	117 (54.4%)	15.0% [3.3, 24.7]	2.0 [1.2, 3.3]	**0.005**	7.1 (5.9, 8.3)	3.2 (1.1, 5.2)	**0.002**
	Boston *n* = 99	39 (39.4%)				3.9 (2.2, 5.7)		
Males	Providence *n* = 34	18 (52.9%)	−7.1% [−41.8, 27.6]	1.1 [0.2, 5.3]	0.88	9.0 (5.2, 12.7)	1.3 (−8.3, 10.9)	0.79
	Boston *n* = 10	6 (60.0%)				7.7 (0.3, 15.0)		
Pre-menarche	Providence *n* = 119	78 (65.5%)	17.4% [1.6, 33.2]	2.2 [1.1, 4.3]	**0.02**	9.8 (8.1, 11.5)	4.8 (1.8, 7.8)	**0.002**
	Boston *n* = 54	26 (48.1%)				5.0 (2.4, 7.6)		
Post-menarche	Providence *n* = 94	38 (40.4%)	13.1% [−3.4, 29.6]	2.0 [0.9, 4.4]	0.095	3.7 (2.3, 5.1)	1.3 (−1.5, 4.1)	0.34
	Boston *n* = 44	12 (27.3%)				2.4 (0.3, 4.5)		
Thoracic curve	Providence *n* = 155	96 (61.9%)	18.0% [3.8, 32.2]	2.4 [1.3, 4.3]	**0.005**	8.8 (7.3, 10.4)	3.6 (0.9, 6.2)	**0.008**
	Boston *n* = 66	29 (43.9%)				5.3 (3.0, 7.6)		
Lumbar curve	Providence *n* = 94	39 (41.5%)	4.3% [−13.2, 21.8]	1.3 [0.6, 2.8]	0.47	4.9 (3.3, 6.5)	2.2 (−0.8, 5.1)	0.15
	Boston *n* = 43	16 (37.2%)				2.8 (0.4, 5.2)		
Curves 20–29°	Providence *n* = 106	55 (51.9%)	13.0% (−5.6, 31.6)	2.3 (1.0, 5.4)	0.05	8.1 (6.3, 9.9)	3.8 (0.3, 7.3)	**0.034**
	Boston *n* = 36	14 (38.9%)				4.3 (1.1, 7.4)		
Curves 30–40°	Providence *n* = 143	80 (55.9%)	13.4% (−0.6, 27.4)	1.9 (1.04, 3.3)	**0.036**	6.9 (5.4, 8.3)	2.7 (0.2, 5.2)	**0.035**
	Boston *n* = 73	31 (42.5%)				4.2 (2.2, 6.2)		

* OR = odds ratio for SRS failure of Providence brace treatment (1) compared to Boston (0) brace treatment in multivariable logistic regression with propensity score adjustment. ** Analysis of Covariance (ANCOVA) was used with adjustment for Modified Sanders stage 1–3 and Initial Cobb angle. The confidence intervals for ANCOVA were robust where homoscedasticity was not assumed. *p* value is two-sided, significance level 0.05.

Table 5. Comparison of compliance between the groups.

	Providence (n = 243)	Boston (n = 109)	p
Compliance			
Excellent	180 (74.1%)	60 (55.0%)	
Good	32 (13.2%)	15 (13.8%)	
Fair	15 (6.2%)	18 (16.5%)	
Poor	16 (6.6%)	16 (14.7%)	**<0.001**

For categorical variables, n (%) is presented. For comparison between groups, Mann–Whitney U test was used for ordered categorical variables.

4. Discussion

4.1. Main Results

This, to our knowledge, is the largest study comparing fulltime and nighttime bracing for AIS at a single institution. Further, it is the first brace study attempting to compare two different treatments using the two most common outcome measures, i.e., the failure rates based on the SRS recommendation and the increase in the main curve at follow-up. Interestingly, both outcome measures converged toward similar results. The BB showed overall superior performance compared to the PNB. Within different subgroups, the BB showed a better outcome in pre-menarchal females and patients with larger curves and thoracic curves. Moreover, in an attempt to control for potential confounders, the results were adjusted for important differences in baseline characteristics between the groups.

Previously published studies comparing nighttime and fulltime bracing showed different success rates ranging between 15% and 78% in the fulltime group and 31% and 73% in the nighttime group [9,10,13,15,21]. In contrast to the present study, however, no significant differences in treatment success between the groups were found. The possible explanation might be a limited ability to detect a difference in treatments, lack of data on skeletal maturity and/or failure to account for other predictors influencing the outcome in these studies. In the present study, the mature patients were rigorously excluded, and the covariates were methodically selected based on baseline differences between the groups.

The treatment success rates of 45% and 59% for the PNB and BB, respectively, are poorer than expected. The rigorous inclusion criteria, high proportion of pre-menarchal females in both groups and application of SRS outcome assessment criteria might explain these results. Indeed, in the study by Janicki et al., where the SRS outcome criteria were first applied, the results were even more disappointing, with treatment success rates of 15% and 31% in fulltime (TLSO) and nighttime (PNB) groups, respectively [13]. On the other hand, those studies using a certain cutoff value for failure, e.g., the curve exceeding 45° magnitude or the need for surgery, usually present higher success rates for brace treatment [2,15].

4.2. Secondary Outcomes

The main result of the comparisons within the subgroups was that the fulltime brace might better protect against failure in more immature patients, thoracic curves and larger curves compared to the nighttime brace, whereas patients with lumbar curves and more mature patients, e.g., post-menarchal females, might be treated by either of the braces. This finding is supported by the meta-analysis by Buyuk et al., who carefully concluded that nighttime bracing might be an alternative to fulltime bracing in Risser 1 or 2 patients with lumbar curves [22]. Indeed, a pioneer study by D'Amato showed excellent results in PNB treatment especially for lumbar curve patterns (94% success) [7]. Also, the BB performed better in the treatment of patients with curves > 30° regarding both outcomes, while the results for curves < 30° were not conclusive. This finding is in agreement with those of previous studies showing that patients with larger initial curves are at a higher risk of failing brace treatment [23,24]. Therefore, more intensive (i.e., fulltime) brace treatment might be warranted.

Compliance with the treatment is a crucial prerequisite for treatment success [2,25,26]. In the present study, the PNB patients demonstrated significantly better compliance with the treatment than the BB patients. This finding is supported by other studies where nighttime braces were generally better accepted than fulltime braces, even though the range of good compliance between the studies is wide (49–93% nighttime, 33–73% fulltime) [5,27–33]. Surprisingly, the BB in the current study performed better despite poorer compliance. This might be due to an absolute amount of time spent in the brace. The results of our study suggest that nighttime bracing might be an insufficient treatment in certain highly progressive curves even with good compliance.

4.3. Limitations

This is a retrospective study, and, thus, 67 (16%) patients were excluded due to an incomplete radiological assessment. Moreover, 18 (4%) patients dropped out from the follow-up. Also, despite the mean follow-up in the PNB and BB groups of 1.4 and 1.6 years, respectively, not all of the patients reached a minimum of 1-year follow-up. Nevertheless, the average growth velocity after brace discontinuation was 0.5 cm per year, and the mean age at follow-up was 16.4 years and 17.4 year for females and males, respectively. Also, one of the three criteria for failed treatment was that the surgery had to be performed or recommended within two years after the treatment discontinuation. Since an average follow-up was less than two years, some patients could have been lost to follow-up and/or operated at another hospital. However, all the patients that showed progress of scoliosis in mature age or those whose scoliotic curves had progressed close to the cut-off for surgery (45° Cobb angle) were further followed. Moreover, our institution is the only scoliosis center in the region. Due to the rules for the reimbursement system between the regions, it is unlikely that a significant number of patients would undergo the surgery outside the region.

Next, we could not adhere to the SRS recommendations on objective compliance measurement due to the prolonged time period spanned by this study. Instead, we attempted to categorize the patients according to the subjective reports obtained at each visit. Thus, the compliance is not an exact objective measure, although we believe that the brace groups were comparable, which was the purpose of the categorization. Lastly, due to the change of skeletal maturity assessments along the course of the data collection, we attempted to match the Risser sign to the Sanders staging system, which might have added some bias.

4.4. Clinical Implications

The findings of the current study provide additional guidance for decision-making in AIS brace treatment. At our institution, the PNB has been the brace of choice for all AIS patients since the 2010s, irrespective the skeletal maturity stage, curve type, curve magnitude or menarche. However, based on the current results, we must reconsider our treatment standards. We now think that the fulltime brace should be the treatment of choice for more immature patients and larger curves, especially in combination with stiffer thoracic curves. On the other hand, other factors, such as compliance and patients' psychological and emotional status and preferences, should be taken into account when counselling the family. Although it is not possible to generalize our results, we encourage caution regarding nighttime bracing in general as the PNB's performance was inferior even with good compliance and excellent IBC. It seems that highly progressive curves close to the peak height velocity need to be addressed more aggressively with fulltime regimes irrespective of chronological age. The PNB can probably still be offered to more mature patients and to non-compliant patients as an alternative for treatment of lumbar and smaller curves.

5. Conclusions

The Boston fulltime brace is more effective than the Providence nighttime brace in the treatment of adolescent idiopathic scoliosis in pre-menarchal female patients, patients with thoracic curves and patients with curves > 30° Cobb angle.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/jcm12247684/s1, File S1. Original dataset.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Swedish Ethical Review Authority (DN: 2020-04364, date: 1 December 2020).

Informed Consent Statement: Patients consent was waived due to retrospective nature of the study. All the results are presented on a group level without any information that could identify the study subjects.

Data Availability Statement: The original dataset is available within the Supplementary Materials.

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A Change in Global Sagittal Alignment after Transforaminal Epidural Steroid Injections in Lumbar Spinal Stenosis

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Abstract: Patients' functional adaptation to pain can affect global sagittal alignment. This study evaluated the short-term spinal sagittal alignment change after transforaminal epidural steroid injection (TFESI) in lumbar spinal stenosis patients. Patients with lumbar spinal stenosis who underwent TFESI were retrospectively examined. Clinical outcomes were assessed using the Visual Analog Scale (VAS) and Oswestry Disability Index (ODI). Before and two weeks after the intervention, whole-spine lateral standing view radiographs were taken. Radiographic parameters including the Sagittal Vertical Axis (SVA), C2C7 Cobb, Thoracic Kyphosis (TK), Lumbar Lordosis (LL), Pelvic Incidence (PI), Pelvic Tilt (PT), Sacral Slope (SS), and Lumbopelvic Mismatch (PI-LL) were measured. Ninety-nine patients (mean age 64.3 ± 9.2 years) were included in this study. Both VAS and ODI outcomes were statistically improved after two weeks of intervention. Radiographic parameters showed that SVA, PT, and PI-LL mismatch were significantly decreased, while C2C7 Cobb, TK, SS, and LL were significantly increased after the intervention. SVA was improved by 29.81% (52.76 ± 52.22 mm to 37.03 ± 41.07 mm, $p < 0.001$). PT also decreased significantly from 28.71° ± 10.22° to 23.84° ± 9.96° ($p < 0.001$). Transforaminal epidural steroid injection (TFESI) significantly improves VAS, ODI, and global sagittal parameters in lumbar spinal stenosis patients.

Keywords: global sagittal balance; transforaminal epidural steroid injections; lumbar spinal stenosis

1. Introduction

Global sagittal balance is important for patient well-being. Previous studies have reported that spinal imbalance causes more muscle energy expenditure [1] to maintain body balance and movement, resulting in pain, fatigue, and disability [2,3]. For this reason, accurate planning for global sagittal alignment correction is essential for spinal surgeons to achieve the best outcomes and improve patients' quality of life [4].

Other than structural spinal deformity, which causes global spinal imbalance, a patient's functional adaptation can also affect global sagittal alignment [5]. Lumbar canal stenosis may compensate for the pain they feel by leaning forward or adopting a flexion posture. This has been proven to alleviate pain due to an increase in the spinal canal diameter [6,7]. From previous studies, spinal surgical procedures for treating spinal canal stenosis, such as decompression alone [8], discectomy [9,10], or short-segment fusion [11], result in an improvement in sagittal spinal imbalance. However, to our knowledge, no study is yet to report the effect of transforaminal epidural steroid injection (TFESI) in sagittal spinal alignment.

TFESI is recognized as a conservative treatment in lumbar spinal stenosis to alleviate symptoms [12,13], and as a diagnostic procedure [14] to identify pathologic levels in complex cases. TFESI is commonly used as an initial procedure before considering surgical management, and this study aims to evaluate the short-term spinal sagittal alignment change after TFESI.

2. Materials and Methods

All patients provided written informed consent. We retrospectively reviewed cases from electronic medical records and radiographs of lumbar spinal stenosis patients aged between 18 and 85 years old at Thammasat University Hospital, who underwent transforaminal epidural steroids injections from January 2017 to January 2020. The inclusion criteria were patients who have a history of clinical radiculopathy from spinal stenosis and lumbar disc herniation with complete pre-intervention and post-intervention data records. The exclusion criteria were spinal infection, clinical progressive neurologic deficit, symptoms of cauda equina or conus medullaris syndrome, a history of spinal surgery, ankylosing spondylitis, active hip disease, and a history of other conditions that can mimic spine pathology (such as urologic, gynecologic, or great vessel disease).

Demographic data were collected from the electronic medical records, including age, sex, and the vertebra level injected. Clinical outcomes were recorded pre-intervention and two weeks after intervention. The Visual Analog Scale (VAS) and Oswestry Disability Index (ODI) (Thai version) [15] were collected.

2.1. Radiological Measurement

Whole-spine anteroposterior (AP) and lateral standing radiographs were taken before intervention (pre-intervention) and two weeks after intervention (post-intervention) by using 36-inch full-length films. To standardize the imaging process, all patients were instructed to stand in a comfortable position with full hip and knee extension, and with the elbow flexed at 45° [16].

Two spine surgeons independently performed digital radiograph interpretations. The patients' data and identifications were blinded to the evaluators. The sagittal parameters were measured by PACS (SYNAPSE, Fujifilm's) measurement tools on the 27-inch monitor. The Sagittal Vertical Axis (SVA), Thoracic Kyphosis (TK), Lumbar Lordosis (LL), Pelvic Incidence (PI), Pelvic Tilt (PT), Sacral Slope (SS), and PI-LL (PI minus LL) were measured according to the Scoliosis Research Society-Schwab classification [1]. C2C7 Cobb was measured from the angle between C2 and the C7 lower endplate [17] (Figure 1).

2.2. Intervention

TFESI was performed with triamcinolone acetonide 40 mg/1 cc (40 mg for one-level injection and 80 mg for two- to four-level injection) and normal saline mixed up to 2 cc for each injection point. In addition, 0.5–1 cc of Iohexol (Omipaque 300 Contrast) was administered as a contrast media to confirm the position prior to steroid injection under biplanar (AP and lateral) fluoroscopic guidance (C-arm Fluoroscope, Philips BV Pulsera, Amsterdam, The Netherlands). Quincke spinal needles, size 23, gauge 9 cm, were used, and they were angled towards the safe triangle [18,19] in the AP view and towards the middle of the neural foramen in the lateral view (Figure 2).

2.3. Statistical Analysis

Percentages were used for categorical data. The mean and standard deviation were used for continuous data after the normality assumption was validated, and a paired *t*-test was used in the analysis. Characteristics of the data between groups were analyzed by analysis of variance (ANOVA). The correlation of the data was measured using Pearson correlation coefficients. An r value of more than 0.3 or less than -0.3 confirmed a statistical correlation [20], and a p value of less than 0.05 indicated statistical significance. Interobserver reliability testing was performed using the Intraclass Correlation Coefficient (ICC). All statistical calculations were performed on IBM SPSS Statistic version 25.0 (IBM Corporation, Armonk, NY, USA).

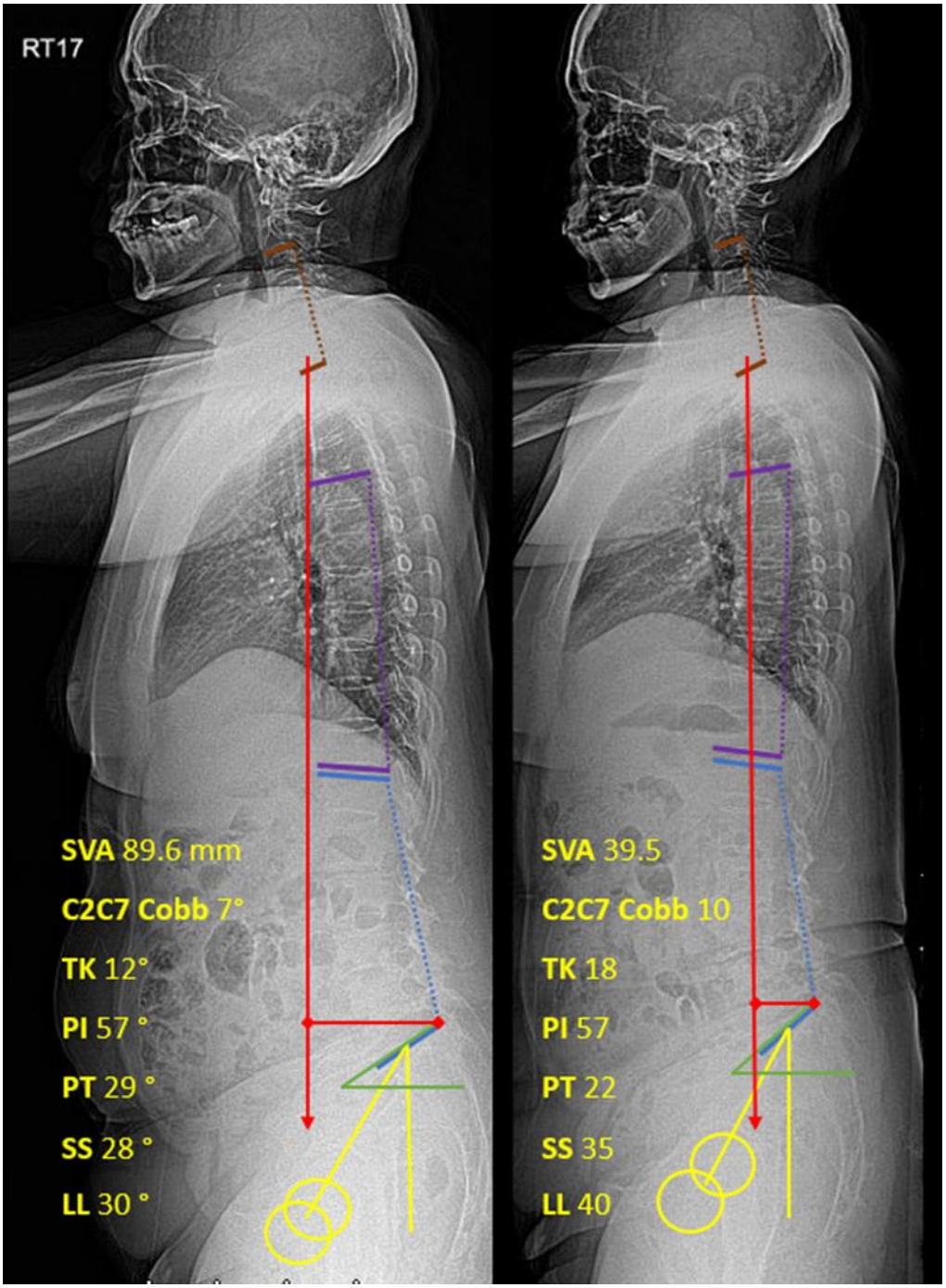

Figure 1. Whole-spine lateral standing films with measured sagittal parameters ((**left**): pre-intervention; (**right**): post-intervention). Red: Sagittal vertical axis, Purple: Thoracic kyphosis, Blue: Lumbar lordosis, Yellow: Pelvic tilt, Green: Sacral slope.

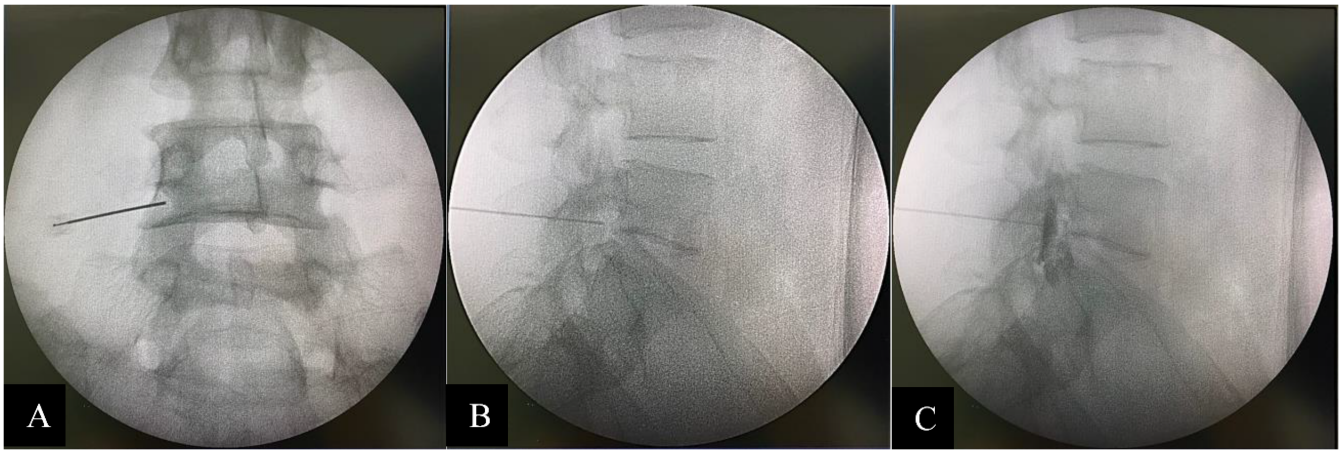

Figure 2. (**A**) AP fluoroscopic view. The end of the needle is located in a safe triangle. (**B**) Lateral fluoroscopic view. The end of the needle is located in the middle of the neural foramen. (**C**) Lateral fluoroscopic view. After the L4 nerve root, contrast injection was outlined.

3. Results

We retrospectively reviewed 120 individual cases with 99 patients. A total of 21 males (21.2%) and 78 females (78.8%) underwent TFESI and were included in the study. The average age was 64.3 ± 9.2 years. The average vertebrae levels injected were 1.8 ± 0.8 levels.

3.1. Pre-Intervention and Post-Intervention Outcomes

Both VAS and ODI outcomes were statistically improved after the intervention: VAS decreased from 8.31 ± 1.11 to 3.38 ± 1.47 and ODI decreased from 31.06 ± 3.48 to 18.03 ± 4.17. All sagittal parameters were statistically significantly improved. SVA, PT, and lumbopelvic mismatch were significantly decreased, while C2C7 Cobb, TK, SS, and LL were significantly increased after the intervention. Post-intervention SVA showed an improvement of 30.12% (53.26 ± 51.67 mm to 37.22 ± 40.71 mm). Pelvic Incidence (PI) was not statistically affected by TFESI. All data are shown in Table 1.

Table 1. Pre-Intervention and Post-Intervention Outcomes and Sagittal Parameters.

Parameter	Pre-Intervention	Post-Intervention	*p*-Value [α]
VAS	8.31 ± 1.11	3.38 ± 1.47	<0.001
ODI	31.06 ± 3.48	18.03 ± 4.17	<0.001
SVA, mm	53.26 ± 51.67	37.22 ± 40.71	<0.001
C2C7 Cobb	12.15 ± 10.86	13.63 ± 10.26	0.004
TK °	19.22 ± 10.80	20.9 ± 10.46	0.001
PI °	56.25 ± 10.18	56.31 ± 10.13	0.296
PT °	28.65 ± 10.17	23.66 ± 9.96	<0.001
SS °	27.61 ± 9.00	32.65 ± 8.36	<0.001
LL °	33.35 ± 14.80	39.56 ± 13.34	<0.001
PI—LL °	22.89 ± 16.35	16.75 ± 14.82	<0.001

[α] Calculated with paired *t*-test.

3.2. Difference between the Number of Injection Levels and Sagittal Parameters

The collected data were divided according to the total number of vertebrae levels injected: 1 level, 2 levels, 3 levels, and 4 levels. The differences in outcomes and sagittal parameters in each group were assessed. The variations of VAS score and ODI among the different numbers of injection levels were not statistically significant, both before and after the intervention. The C2C7 Cobb and TK were found to not be statistically significant between injection levels. The sagittal parameters, including SVA, PT, and PI-LL mismatch, were statistically significantly higher in multiple-level injection groups compared to single-level injection groups, both before and after the intervention. In contrast, SS and LL were

statistically significantly lower in multiple-level injection groups compared to single-level injection groups, both before and after the intervention. All data are shown in Table 2.

Table 2. Outcomes and Sagittal Parameters between Number of Injection Levels.

	Parameter	Number of TFESI Injection Levels				
		1 (n = 40)	2 (n = 42)	3 (n = 14)	4 (n = 3)	p Value $^{\alpha}$
Pre-intervention	VAS	8.30 ± 1.04	8.17 ± 1.15	8.71 ± 1.14	8.67 ± 1.53	0.42
	ODI	30.93 ± 2.76	30.74 ± 3.78	32.29 ± 3.79	31.67 ± 7.23	0.53
	SVA	25.59 ± 33.29	64.08 ± 45.29	72.44 ± 57.25	164.76 ± 98.35	<0.001
	C2C7 cobb	12.05 ± 8.45	11.12 ± 10.93	13.57 ± 6.76	19.00 ± 39.15	0.619
	TK	19.40 ± 8.90	16.60 ± 11.45	18.21 ± 12.25	10.00 ± 8.71	0.487
	PI	56.55 ± 8.59	53.81 ± 9.31	60.57 ± 12.15	67.33 ± 13.61	0.027
	PT	2.45 ± 9.65	28.19 ± 8.78	36.14 ± 9.21	44.61 ± 13.78	<0.001
	SS	31.13 ± 8.26	25.69 ± 9.18	24.43 ± 7.98	22.67 ± 0.57	0.011
	LL	39.5 ± 13.57	30.90 ± 12.76	27.0 ± 15.80	12.33 ± 1.52	<0.001
	PI-LL	17.05 ± 15.38	22.90 ± 12.46	33.57 ± 16.79	55.0 ± 14.93	<0.001
Post-intervention	VAS	3.17 ± 1.50	3.37 ± 1.48	3.69 ± 1.10	5.00 ± 1.73	0.17
	ODI	17.47 ± 3.70	17.69 ± 4.42	19.84 ± 3.93	22.33 ± 4.93	0.08
	SVA	19.34 ± 28.96	44.8 ± 39.30	53.22 ± 47.44	97.76 ± 64.28	0.0002
	C2C7 cobb	13.70 ± 8.30	13.27 ± 10.67	13.5 ± 8.46	17.83 ± 31.05	0.907
	TK	21.83 ± 8.60	21.83 ± 10.93	18.19 ± 13	6.83 ± 4.25	0.071
	PI	56.7 ± 8.78	54.13 ± 9.98	59.84 ± 12.5	67.16 ± 11.62	0.067
	PT	20.8 ± 8.73	23.40 ± 9.24	29.00 ± 10.57	41.00 ± 10.44	0.0007
	SS	35.88 ± 6.75	30.60 ± 8.84	30.84 ± 9.22	26.16 ± 1.60	0.011
	LL	43.78 ± 11.85	38.61 ± 12.8	33.61 ± 15.67	22.5 ± 3.5	0.006
	PI-LL	12.9 ± 13.21	15.52 ± 12.01	26.23 ± 18.3	44.67 ± 14.9	0.0001

$^{\alpha}$ Calculated with ANOVA test.

3.3. Correlation between Sagittal Parameters

There was a strong negative correlation between the pre-intervention SVA and post-intervention SVA decrement (r = −0.646), shown in Figure 3. The pre-intervention LL showed a negative correlation with the post-intervention LL increment, shown in Figure 4 (r = −0.4). The pre-intervention PI-LL mismatch exhibited a negative correlation with the post-intervention PI-LL decrement (r = −0.394), shown in Figure 5. The significant correlation between pre-intervention parameters and post-intervention changes is shown in Table 3.

Table 3. Significant Correlation between Pre-Intervention Parameter and Post-Intervention Change $^{\alpha}$.

Pre-Intervention \ Post-Intervention Change	VAS	ODI	SVA	PT	LL	PI-LL
VAS	−0.444 *	−0.104	−0.04	−0.151	0.034	−0.038
ODI	−0.18	−0.43 *	−0.255	0.048	0.104	−0.104
SVA	0.268	0.133	−0.646 *	0.097	0.34 *	−0.298
PI	0.151	−0.004	−0.231	0.037	0.060	−0.041
PT	0.238	0.197	−0.253	−0.317 *	0.226	−0.226
LL	−0.236	−0.264	0.260	0.162	−0.4 *	0.411 *
PI-LL	0.304 *	0.235	−0.374 *	−0.123	0.369 *	−0.394 *

* r value more than 0.3 or less than −0.3; $^{\alpha}$ Calculated with Pearson correlation coefficient.

3.4. Interobserver Reliability

Interobserver reliability was calculated using the Intraclass Correlation Coefficient. The results were greater than 0.9 in all sagittal parameters. Thus, it was considered that the measurements were valid and achieved excellent reliability.

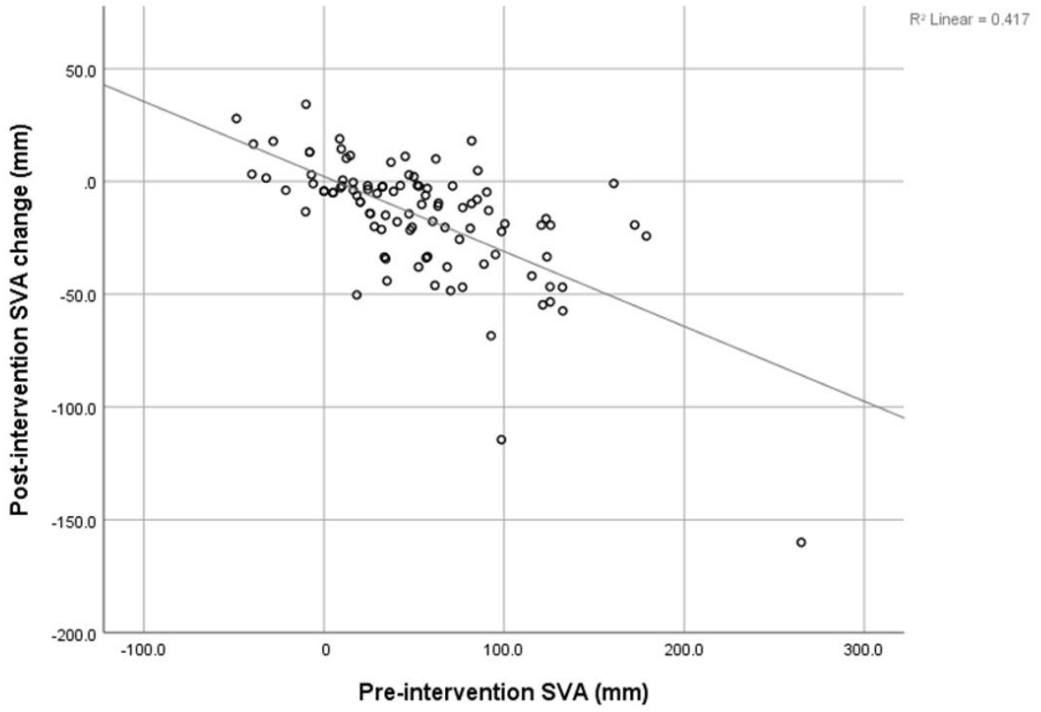

Figure 3. Correlation between pre-intervention SVA and post-intervention SVA change.

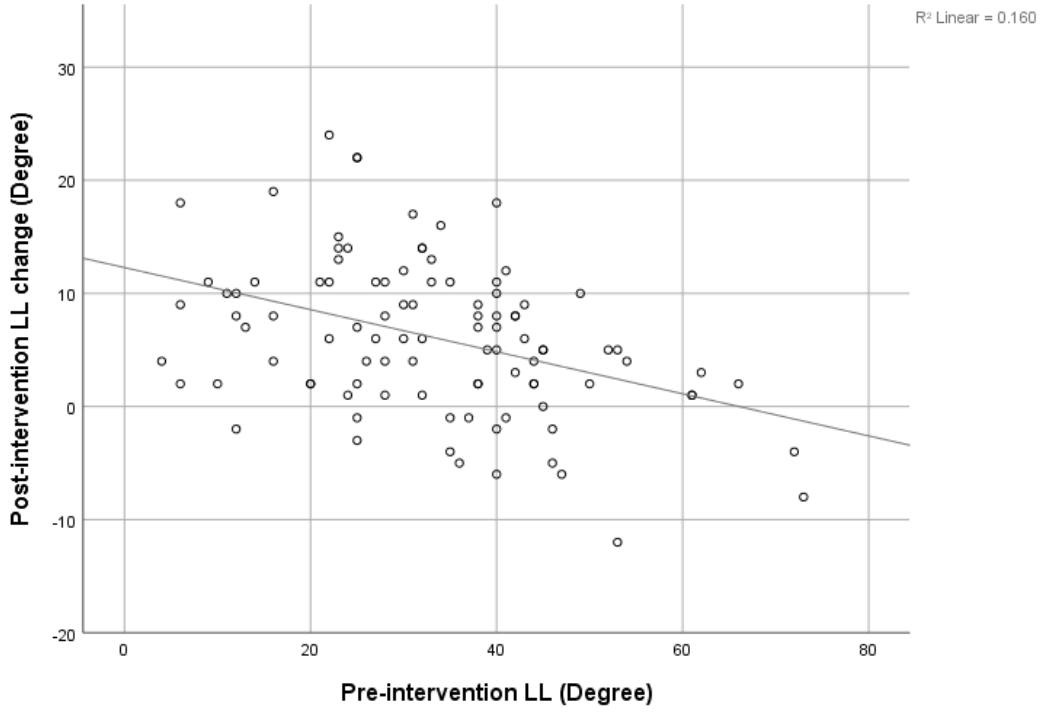

Figure 4. Correlation between pre-intervention LL and post-intervention LL change.

3.5. Case Example

A 63-year-old Thai man with low back pain and positive balance had pre-intervention parameters: SVA 124.5 mm, TK 21°, PI 53°, PT 26°, SS 27°, and LL 19°; and post-intervention parameters: SVA 70.6 mm, TK 32°, PI 53°, PT 31°, SS 25°, and LL 46°. After post-intervention parameters were evaluated, the operative planning was changed from long-segment fusion for correct SVA and multiple osteotomies for correct LL to short-segment fusion and single-level osteotomies instead (Figure 6).

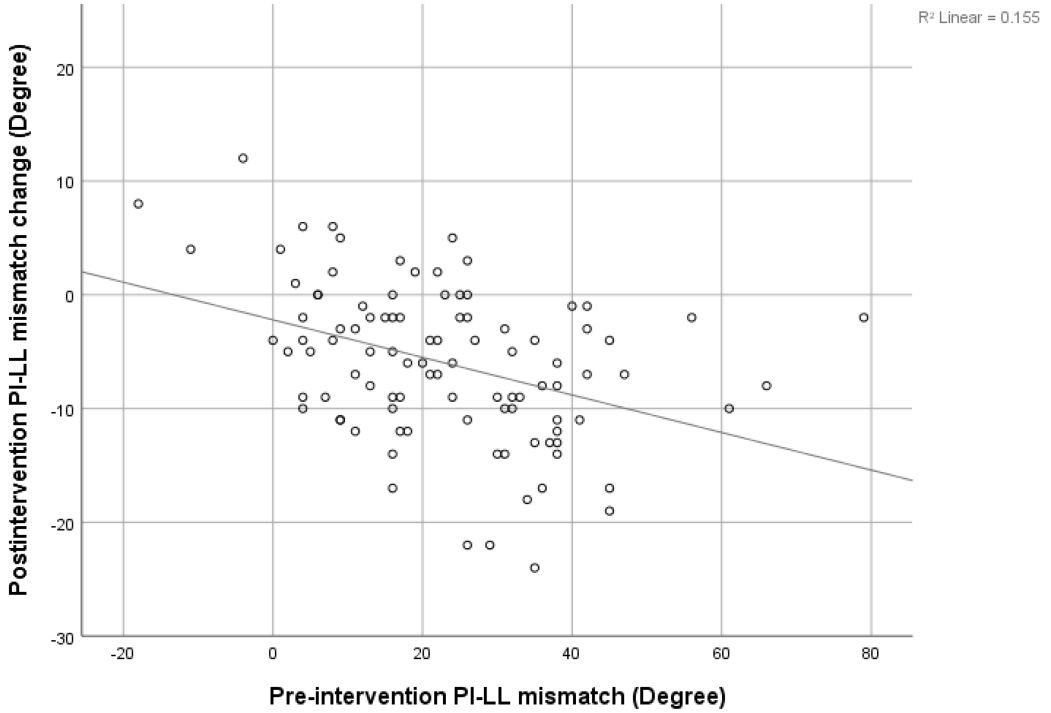

Figure 5. Correlation between pre-intervention PI-LL mismatch and post-intervention PI-LL mismatch change.

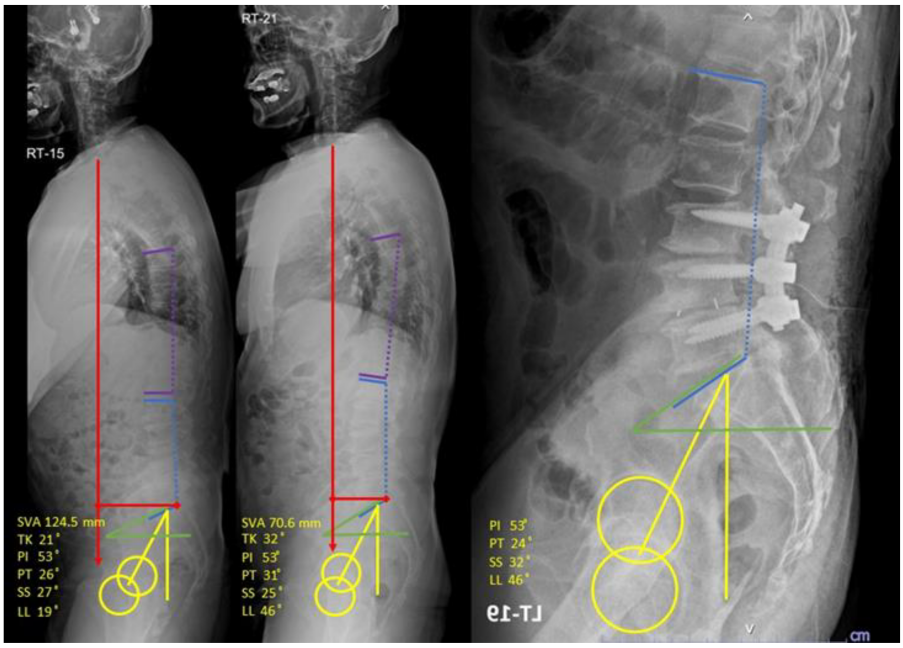

Figure 6. Whole-spine lateral standing films and post-operative films with measured sagittal parameters ((**left**): pre-intervention; (**middle**): post-intervention; (**right**): post-operative). Red: Sagittal vertical axis, Purple: Thoracic kyphosis, Blue: Lumbar lordosis, Yellow: Pelvic tilt, Green: Sacral slope.

4. Discussion

In our study, we collected data from patients with lumbar spinal stenosis who received TFESI. The results showed that both the VAS and the ODI improved significantly after the intervention. Ghahreman A. [21], Kabatas S. [22], and McCormick Z. [23] studied the short-term effects of TFESI, which significantly improved VAS and ODI in a similar study. The study of Karppinen et al. [24] showed that at 2 weeks of follow-up, a significant

improvement from baseline was observed in every outcome parameter (leg pain, back pain, ODI, degree of straight-leg-raising test). This could support the treatment of pain using TFESI for short-term efficacy in lumbar spinal stenosis.

Liang C. [10] conducted a study on lumbar disc herniation and found significant immediate improvement in all sagittal imbalance parameters on day one post-operation, and this improvement continued for three months before the parameters became close to their normal ranges. SVA improved from 11.6 ± 6.6 cm to 2.9 ± 6.1 cm, and three months post-operation, LL improved from 25.3° ± 14.0° to 42.4° ± 10.2°. Moreover, Fujii K. [8] retrospectively reviewed lumbar decompression without fusion in lumbar spinal stenosis and concluded that the SVA, TK, PT, LL, and PI-LL mismatch improved post-operatively. SVA was decreased from 49.1° ± 38.6° to 28.6° ± 30.7°, and LL was changed from 38° ± 13° to 44° ± 11°. A strong correlation was found between pre-op SVA/PI-LL and post-op SVA/PI-LL decrement post-operatively. Likewise, Salimi H et al. [25] also reported that minimally invasive lumbar decompression surgery could convert sagittal malalignment to normal alignment in 2 years and 5 years follow-up. The previous studies mentioned above indicated that spinal decompressive procedures without instrumentation have the ability to improve sagittal spinal parameters. Therefore, we believe that spinal interventions that reduce radicular pain, such as TFESI, can partially improve sagittal spinal parameters because when radicular pain was improved, compensating forward bending subsided.

This study may be the first study to collect data on the non-operative management of lumbar spinal stenosis. The present procedure did not interfere with the anatomical structure, but decreased the inflammation process to the neural structure and improved radicular pain. We found a significant change in SVA, C2C7 Cobb, TK, PT, SS, and LL after patients underwent TFESI. The SVA was improved by about 30% (from 52.76 ± 52.22 mm to 37.03 ± 41.07 mm), and PT and LL were improved by about 17% and 18%, respectively. This is compared to 42%, 15%, and 16% improvements reported by Fujii K. [8]. Patients with multiple levels of stenosis tend to have significantly more severe positive SVA, higher PT, and lower LL and SS. Furthermore, we found a strong negative correlation between pre-intervention SVA and post-intervention SVA decrement. This indicates that the more positive imbalanced patients were, the greater the resulting improvement in the SVA. This correlation has also been found in recent studies [8,10,26]. Similarly, a strong negative correlation between pre-intervention PI-LL and post-intervention PI-LL was found. The greater the PI-LL mismatch, the larger the PI-LL improvement could be predicted to be. In contrast, the pre-intervention LL was negatively correlated with the post-intervention LL increment, and this means that in a small cohort of pre-intervention LL patients, there may be more improvement in the post-intervention LL.

From a review of previous literature, it can be observed that many spinal pathologies are caused by sagittal imbalance, reduced muscle strength [10,27,28], adjacent disc degeneration [29], disc herniation [9], and spinal stenosis. Several authors have proposed that spinal stenosis patients have limited lumbar lordosis (LL) [5] due to the decreased pressure of the epidural venous plexus when bending forward. Furthermore, compensatory lumbar flexion posture lowers epidural pressure, thus reducing pain and neurogenic claudication [9,27,30,31]. The anatomical study showed that flexion for the lumbar spine increased spinal canal diameters [6,7]. We hypothesized that in global sagittal imbalance patients, there might be two factors that are involved in the imbalance. The first one is a structural imbalance, and the second one is the "functional compensation" of patients to radicular pain. We believe that after undergoing TFESI and the pain becoming less severe, compensation of lumbar flexion may be diminished. In this study, after TSESI, we found that SVA, PT, and LL were significantly improved. Recently, there has been little focus on the functional compensation of sagittal alignment before spinal surgical correction. We believe that it is better to evaluate the spinal surgical balance when the clinical pain of patients is subsiding, rather than when the pain remains severe.

Our most recent concern with this main issue was that we were uncertain whether we had to correct the deformity if a global sagittal imbalance existed in the surgical treatment of degenerative lumbar spinal stenosis. This study found that a considerable number of patients' global sagittal alignment significantly improved following TFESI. For this reason, in patients with degenerative lumbar spinal stenosis and global sagittal imbalance, reassessing global sagittal alignment after TFESI might show more accurate structural global sagittal imbalance. We advise obtaining whole-spine AP and lateral standing radiographs again after patients begin improving in terms of pain following TFESI.

This study has some limitations. First, this is a retrospective review of the database, so recall bias and selection bias may be present. Second, this radiographic study focuses on sagittal alignment, but the dynamic compensation of lower limbs, such as hip and knee flexion, is not investigated. It should be noted that we instructed all patients who received the whole-spine film to extend their hip and knee before imaging [32]. Third, due to the short-term effect of TFESI, the outcome and sagittal parameter data were collected only at a short-term follow-up. We suggest a long-term follow-up in future studies.

5. Conclusions

Transforaminal epidural steroid injection (TFESI) can improve SVA, C2C7 Cobb, TK, PT, SS, and LL parameters, as well as VAS and ODI, in a short-term follow-up study and also has benefits in that it is effective in correcting functional compensation to evaluate sagittal alignment correction before surgery to avoid postoperative overcorrection alignment. However, this could be the choice of treatment to improve quality of life factors in terms of pain and disability in sagittal malalignment patients who have contraindications or deny surgery.

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Evaluating Computer Vision, Large Language, and Genome-Wide Association Models in a Limited Sized Patient Cohort for Pre-Operative Risk Stratification in Adult Spinal Deformity Surgery

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Abstract: Background: Adult spinal deformities (ASD) are varied spinal abnormalities, often necessitating surgical intervention when associated with pain, worsening deformity, or worsening function. Predicting post-operative complications and revision surgery is critical for surgical planning and patient counseling. Due to the relatively small number of cases of ASD surgery, machine learning applications have been limited to traditional models (e.g., logistic regression or standard neural networks) and coarse clinical variables. We present the novel application of advanced models (CNN, LLM, GWAS) using complex data types (radiographs, clinical notes, genomics) for ASD outcome prediction. **Methods:** We developed a CNN trained on 209 ASD patients (1549 radiographs) from the Stanford Research Repository, a CNN pre-trained on VinDr-SpineXR (10,468 spine radiographs), and an LLM using free-text clinical notes from the same 209 patients, trained via Gatortron. Additionally, we conducted a GWAS using the UK Biobank, contrasting 540 surgical ASD patients with 7355 non-surgical ASD patients. **Results:** The LLM notably outperformed the CNN in predicting pulmonary complications (F1: 0.545 vs. 0.2881), neurological complications (F1: 0.250 vs. 0.224), and sepsis (F1: 0.382 vs. 0.132). The pre-trained CNN showed improved sepsis prediction (AUC: 0.638 vs. 0.534) but reduced performance for neurological complication prediction (AUC: 0.545 vs. 0.619). The LLM demonstrated high specificity (0.946) and positive predictive value (0.467) for neurological complications. The GWAS identified 21 significant ($p < 10^{-5}$) SNPs associated with ASD surgery risk (OR: mean: 3.17, SD: 1.92, median: 2.78), with the highest odds ratio (8.06) for the LDB2 gene, which is implicated in ectoderm differentiation. **Conclusions:** This study exemplifies the innovative application of cutting-edge models to forecast outcomes in ASD, underscoring the utility of complex data in outcome prediction for neurosurgical conditions. It demonstrates the promise of genetic models when identifying surgical risks and supports the integration of complex machine learning tools for informed surgical decision-making in ASD.

Keywords: adult spinal deformity; computer vision; large language model; genome wide associated study; sepsis; neurological complication; spine surgery

1. Introduction

Adult spinal deformity (ASD) is a condition characterized by abnormality in the three dimensional structure of the spine, most commonly the thoroco–lumbar segments [1]. Such deformities include scoliosis, kyphosis, and lordosis, where lumbar lordotic reduction is a significant driver of ASD [1]. Some specific deformities are more pathologic than others, and result in a reduction in quality of life (QOL) and increased disability [2]. ASD prevalence increases with age, with a general prevalence of 2–32% and a prevalence of 30–68% in the elderly population [3,4]. Surgery may correct the deformity; however, these surgeries are complex, with neurologic complications reported at 1–10% and non-neurologic complications reported at as much as 50% [3]. Elderly patients have an increased complication rate, likely due to diminished physiological reserve and greater frailty, but may gain greater QOL improvement from surgical correction, highlighting the complicated decision for ASD surgical intervention [4,5].

Surgical decision making for ASD correction is multifactorial, considering frailty, comorbidities, symptomatology, and degree of deformity [6]. These multi-factorial considerations underscore the need for accurate pre-operative risk stratification, which is challenging in ASD patients. To determine which patients would benefit from corrective surgery for ASD, traditional machine learning approaches (i.e., decision trees, nomograms, logistic regression, neural network) have been applied to predict outcomes such as complication, reoperation, readmission, and QOL metrics. Traditional approaches in ASD surgical risk stratification and existing predictive models are limited by the following three elements: (i) small patient cohorts due to the condition's relatively small incidence and prevalence (e.g., a prior prediction of QOL outcomes used only 191 patients) [7], (ii) limited data types included as predictive variables (i.e., demographic, clinical, radiographic, or operative variables), and (iii) utilization of traditional machine learning models rather than state-of-the-art advanced models. While some of these models have predicted outcomes including major complication (AUC of 0.89) [8] and health-related QOL (c-statistic of 0.739) [7], the validation of web-based predictive models for major complication, reoperation, and readmission in ASD using a cohort of adult symptomatic lumbar scoliosis patients found an AUC of only 0.6 for all outcomes, demonstrating that current feature-based models fail to accurately risk-stratify patients [9]. The poor performance of these traditional models in ASD outcome prediction motivates the need to survey the performance of state-of-the-art models.

Currently, there are advanced models, including computer vision and natural language processing (NLP) models (including large language models (LLMs)), that have been pre-trained on thousands to millions of patients and which can subsequently be fine-tuned for specific outcomes with smaller patient sets. We hypothesized that such pre-trained advanced models may be leveraged to address all three limitations in ASD surgical risk stratification, therefore improving surgical decision making. Therefore, in this work we investigate the application of advanced models, including computer vision, natural language processing, and genome wide association study (GWAS), for ASD risk stratification.

2. Methods

2.1. Inclusion and Exclusion Criteria

Adult patients, from 1 January 2016 to 26 June 2023, who underwent spine surgery to address ASD were included in the study. A procedure was determined as a spine surgery intervention for ASD if it involved any one of the following current procedural terminology (CPT) codes: 22800, 22802, or 22804. Patients younger than 18 were excluded.

2.2. Data Source

The Stanford Research Repository was used to identify patients who met the inclusion criteria. The patient population included patients with surgeries performed by any spine surgeon at Stanford University Hospital. ASD patients who experienced post-operative

complications had a higher mean age (entire cohort: 38.3, pulmonary complication: 41.1, delirium: 68.7, neurological complication: 54.8, sepsis: 43.1).

2.3. Variables and Outcomes

All X-ray imaging data, demographics, laboratory results, diagnostic and procedural codes, and clinical and procedural narrative reports were collected for each patient. There was variation in the word count of pre-operative clinical notes (mean: 808.3, SD: 564.6, min: 16, max: 2976). The surgical age of each patient was determined, and the most recent clinical notes and XR images were gathered and then manually screened for appropriate ASD-related notes and images. Clinical notes were deemed appropriate for the criteria if they were written by an attending surgeon and prior to the date of surgery. Therefore, despite prior demonstration of LLMs using operative notes [10], we did not include operative notes for the following two reasons: (1) they may include complication information, thereby biasing the model, and (2) the purpose of our model would be for improved patient counseling and selection, meaning that use of an operative note as input would not be appropriate. Primary outcomes for the study were selected based on the clinical consideration of frequency, predictive value, and data availability. These primary outcomes were the prediction of a pulmonary complication, neurological complication, sepsis, and delirium within 90 days of the index ASD surgery. These were selected based on the availability of sufficient positive instances for reliable model training. Other outcomes extracted were three-month revision, two-year revision, five-year revision, 90-days post-operative; altered mental status, confusion, mortality, and patient-reported outcome measures (PROMs); and PHQ2, PHQ9, ODI, and SRS. Due to the very low frequency of positive examples for these additional outcomes, models were only trained for the prediction of the primary outcomes.

2.4. Data Preprocessing

2.4.1. CNN

A CNN was trained and tested for the prediction of specific post-operative complications (pulmonary complication, neurological complication, sepsis, and delirium) in ASD surgery using pre-operative spine radiographs as input. A total of 1549 radiographs from 209 patients surgically treated for ASD were sourced from the Stanford Research Repository. For training and testing, we employed a 70–30 split via random allocation. Stratification was undertaken at the patient level to ensure that all radiographs from a single patient were allocated to either the training or testing set, preserving patient-level integrity in the data. Radiographs were extracted and processed in PNG format. All training images were scaled to 224 $\times$ 224 pixels and normalized by the mean and standard deviation of images. Only pre-operative radiographs were used for outcome prediction.

2.4.2. NLP

An LLM was developed and tested for the prediction of specific post-operative complications (pulmonary complication, neurological complication, sepsis, and delirium) in ASD surgery using pre-operative clinical notes as input. We extracted and utilized free-text clinical notes from the 209 patients, applying a 70–30 split for training and testing analogous to the CNN data preprocessing. We employed a large language model (LLM) (Gatortron) that has been extensively pre-trained on clinical notes by the University of Florida covering more than two million patients [11]. Patient-level stratification was similarly enforced to maintain consistency across all notes from an individual patient. Reports were truncated to 512 words as standard input for Gatortron.

2.5. Model Training and Evaluation

2.5.1. CNN

To evaluate the effect of pre-training the CNN, two separate models were developed, one of which was without any pre-training and used only our ASD patient radiographs. We trained two distinct CNNs, the first was trained from scratch using our dataset of ASD

radiographs and the second using a pre-trained, publicly available CNN from the VinDr-SpineXR database [12] and which was subsequently fine-tuning the model on our ASD dataset. The first 50 layers of the pre-trained model were frozen prior to fine-tuning. For each of the four clinical outcomes, a 70–30 training and validation split was used. Training used the stochastic gradient descent (SGD) optimizer, with an initial learning rate of 0.01 and batch size of 32. The validation set was used to determine epoch hyperparameter. The CNN trained from scratch was trained to the following epochs (pulmonary complication: 979, neurological complication: 619, sepsis: 199, delirium: 159), while the pre-trained CNN was fine-tuned to the following additional epochs (pulmonary complication: 519, neurological complication: 39, sepsis: 279, delirium: 19).

2.5.2. NLP

Due to the large data requirement associated with training a large language model, only one LLM was developed, which used the pre-trained Gatortron LLM model. A 70–30 training and validation split was similarly used. Training utilized the AdamW optimizer, with a learning rate of 1e-6, a batch size of 16, and L2 regularization set at 0.01. The LLM was fine-tuned to the following epochs (pulmonary complication: 4, neurological complication: 20, sepsis: 5, delirium: 3). Fine-tuning began to overfit after 10 epochs across all outcomes (Supplemental Figure S1).

2.5.3. Performance Metrics

To assess both the CNN and LLM, we calculated the AUC, F1 score, sensitivity, specificity, and positive predictive value (PPV).

2.6. Genome-Wide Association Study (GWAS)

2.6.1. Data Source

A GWAS was performed to identify genomic markers for ASD patients who required spine surgical intervention. Using the UK Biobank (N = 502,364), a cohort of patients who had undergone spine surgical intervention for ASD was defined (N = 540), as was a cohort of patients who had not undergone any spine surgical intervention but did have an ASD diagnosis (N = 7355). This outcome phenotype was selected due to the large (>500 patients) cohort available in the UK Biobank. Currently there is not a large cohort of ASD patients who have a specific post-operative complication available in the UK Biobank.

2.6.2. Inclusion and Exclusion Criteria

Both cohorts were restricted to subjects 18 years or older, with exclusion criteria of any diagnosis of a malignant neoplasm of the spinal cord, cauda equina, or a benign neoplasm of the spinal cord. The surgical cohort was defined so as to include any participants that had ever had an instrumented correction of deformity of their spine or other operative procedural correction of deformity of their spine, and to exclude any participants that had ever had an extirpation of a lesion of the spine, decompression of a fracture of the spine, other reduction of a fracture of the spine, or a fixation of a fracture of their spine. These exclusion criteria were employed so as to restrict cohorts to elective procedures and remove trauma as a third variable that may influence the need for operative correction of the ASD.

2.6.3. Phenotype Preprocessing

Quality control was run for subject phenotypes (i.e., ASD surgery, ASD no surgery). The standard UK Biobank filtering method was used and was restricted to the following: sex and genetic sex are the same, white British ancestry, no sex chromosome aneuploidy, no kinship found. Due to the UK Biobank's limited heterogeneity of racial identities, the standard filtering includes a restriction to those of white British ancestry in order to eliminate potential third variables associated with the inclusion of a small set of other races while attempting to identify phenotype-specific genomic factors that should later be validated across all racial groups. After phenotype quality control, the ASD surgery

group had 268 subjects, whereas the ASD no surgery group had 3803 subjects. There were 469,835 samples, where 254,616 were female and 215,156 were male.

2.6.4. Genotype Preprocessing

PLINK was used to perform quality control and filter the whole exome sequencing (WES) data, standard parameters were selected (minor allele frequencies (MAF): 0.0005, minor allele counts (MAC) = 20, missing call rates per variant (geno) = 0.1, missing call rates per sample (mind) = 0.1, minor allele maximum frequency (max-maf) = 0.9995). For each chromosome, a list of single nucleotide polymorphisms (SNPs) and WES ids that passed the filter were collected.

2.6.5. WES Association Study

Samples, variants, and phenotypes that passed the above quality control were used for the associated study. A logistic regression was run using PLINK2 on WES data for each chromosome. Sex and age were marked as covariates. SNPs were mapped to their genes, functional consequence, and clinical significance (if known) using the dbSNP database of the National Library of Medicine (NLM) National Center for Biotechnology Information (NCBI).

2.7. Ethical Considerations

This study was performed under IRB #69667 at Stanford University.

3. Results

3.1. Computer Vision Prediction of Surgical Outcomes Using Radiographs

A CNN was trained on pre-operative spine radiographs to predict the following four post-operative complications: pulmonary complications, neurological complications, sepsis, and delirium. To establish a baseline level of performance without transfer learning, we trained the CNN from scratch using our ASD dataset (Table 1). While the average AUC across outcomes (0.596) is low, an average specificity of 0.815 was achieved. The prediction of pulmonary complication was particularly successful (specificity: 0.822, PPV: 0.235, F1: 0.288).

Table 1. Performance metrics for the CNN trained from scratch (top) and the fine-tuned CNN from VinDr-SpineXR pre-training (bottom). A separate CNN was trained for each outcome. Area under the curve (AUC), F1 score, precision, sensitivity, and specificity metrics are included.

CNN	AUC	F1	Precision	Sensitivity	Specificity
Pulmonary Complication	0.579	0.288	0.235	0.326	0.822
Neurological Complication	0.619	0.224	0.137	0.447	0.766
Sepsis	0.534	0.132	0.066	0.198	0.917
Delirium	0.654	0.168	0.092	0.478	0.756
Pre-Trained CNN	**AUC**	**F1**	**Precision**	**Sensitivity**	**Specificity**
Pulmonary Complication	0.552	0.259	0.212	0.290	0.819
Neurological Complication	0.545	0.169	0.092	0.620	0.491
Sepsis	0.638	0.135	0.069	0.713	0.504
Delirium	0.414	0.000	0.000	1.000	0.000

The effects of using the pre-trained VinDr-SpineXR CNN with fine-tuning on the ASD patient cohort were surprising in this rare condition setting. The predictive power of the model was approximately similar for some outcomes (i.e., pulmonary complication), markedly lower for other complications (i.e., neurological complications and delirium), and markedly higher for sepsis prediction. In the case of sepsis prediction, large improvements in sensitivity (0.713 vs. 0.198) and AUC (0.638 vs. 0.534) of the model were achieved compared with the CNN without pre-training (Table 1). ROC curves for each model contrast the CNN trained from scratch with the CNN first pre-trained on VinDr-SpineXR (Figure 1).

3.2. Large Language Model (LLM) Prediction of Surgical Outcomes Using Clinical Pre-Operative Notes

A pre-trained LLM, Gatortron, was fine-tuned on the ASD cohort (Table 2). While the LLM achieved a low mean AUC across predicted outcomes (0.547), for the outcome with the greatest positive class frequency, pulmonary complication, it achieved successful performance across metrics (PPV: 0.410, F1: 0.545). Compared with the F1 achieved by the CNN for sepsis prediction (F1: 0.135), the LLM achieved evident improvement (F1: 0.383). Training and validation loss curves are given in Supplemental Figure S1.

Table 2. Performance metrics for the NLP models that were separately trained for each outcome. The NLP model is a fine-tuned Gatortron LLM. Area under the curve (AUC), F1 score, precision, sensitivity, and specificity metrics are included.

LLM	AUC	F1	Precision	Sensitivity	Specificity
Pulmonary Complication	0.565	0.545	0.410	0.814	0.317
Neurological Complication	0.559	0.250	0.467	0.171	0.946
Sepsis	0.557	0.383	0.440	0.338	0.776
Delirium	0.508	0.156	0.085	1.000	0.017

3.3. GWAS for Identification of Loci Associated with Surgical Intervention for ASD Patients

The patient cohort used for GWAS is derived from UK Biobank and distinct from the cohort used for CNN and LLM model development. A total of 21 SNPs were identified as significant using a 10-05 threshold in their association across a cohort of ASD patients who had undergone a surgical correction of their deformity and a cohort of ASD patients who had never undergone surgical correction (Figure 2, Table 3). The odds ratios (OR) for these SNPs ranged from 1.58 to 8.06, with a mean OR of approximately 3.17 and a median of 2.78, indicating variable but generally increased odds of the post-surgical state with these variants.

Analysis of the genomic distribution of these SNPs revealed involvement across 11 unique genes, with CELSR1 containing the highest number of significant SNPs (n = 8), followed by SLC6A9 (n = 4). The remaining genes each had one SNP associated with them. The functional consequences of these SNPs were predominantly intronic (n = 9), but also included missense variants and variants affecting gene expression regulation such as upstream and downstream transcript variants. Some SNPs were associated with more than one functional consequence, reflecting the complex and often unknown architecture of these genomic regions.

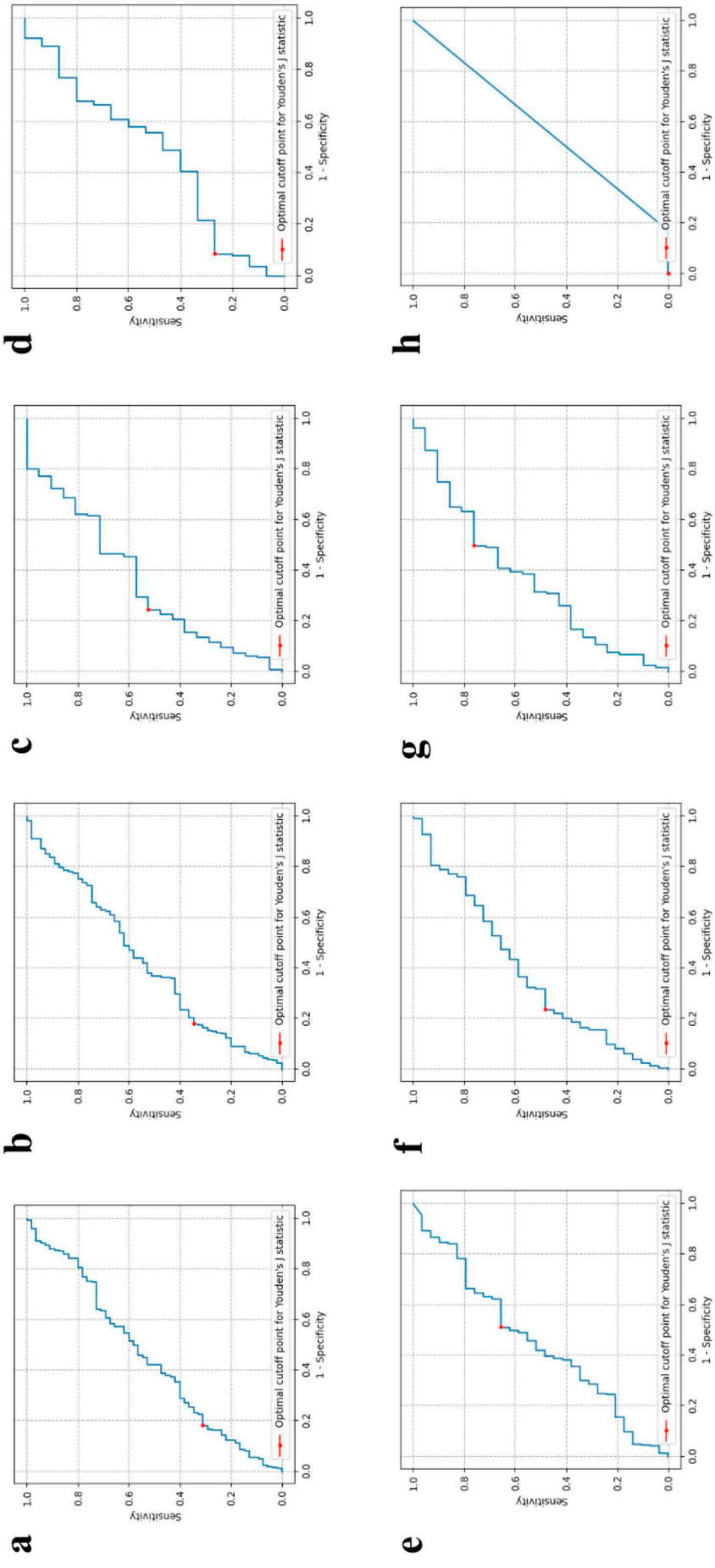

Figure 1. Receiver operating characteristic (ROC) curves for (**a**–**d**) CNN trained from scratch, and (**e**–**h**) fine tuning VinDr-SpineXR CNN on each outcome. The optimal cutoff threshold point (Youden's J statistic) is represented by a red point on each curve. Each model was trained independently for (**a**,**e**) pulmonary complications, (**b**,**f**) neurological complications, (**c**,**g**) sepsis, and (**d**,**h**) delirium.

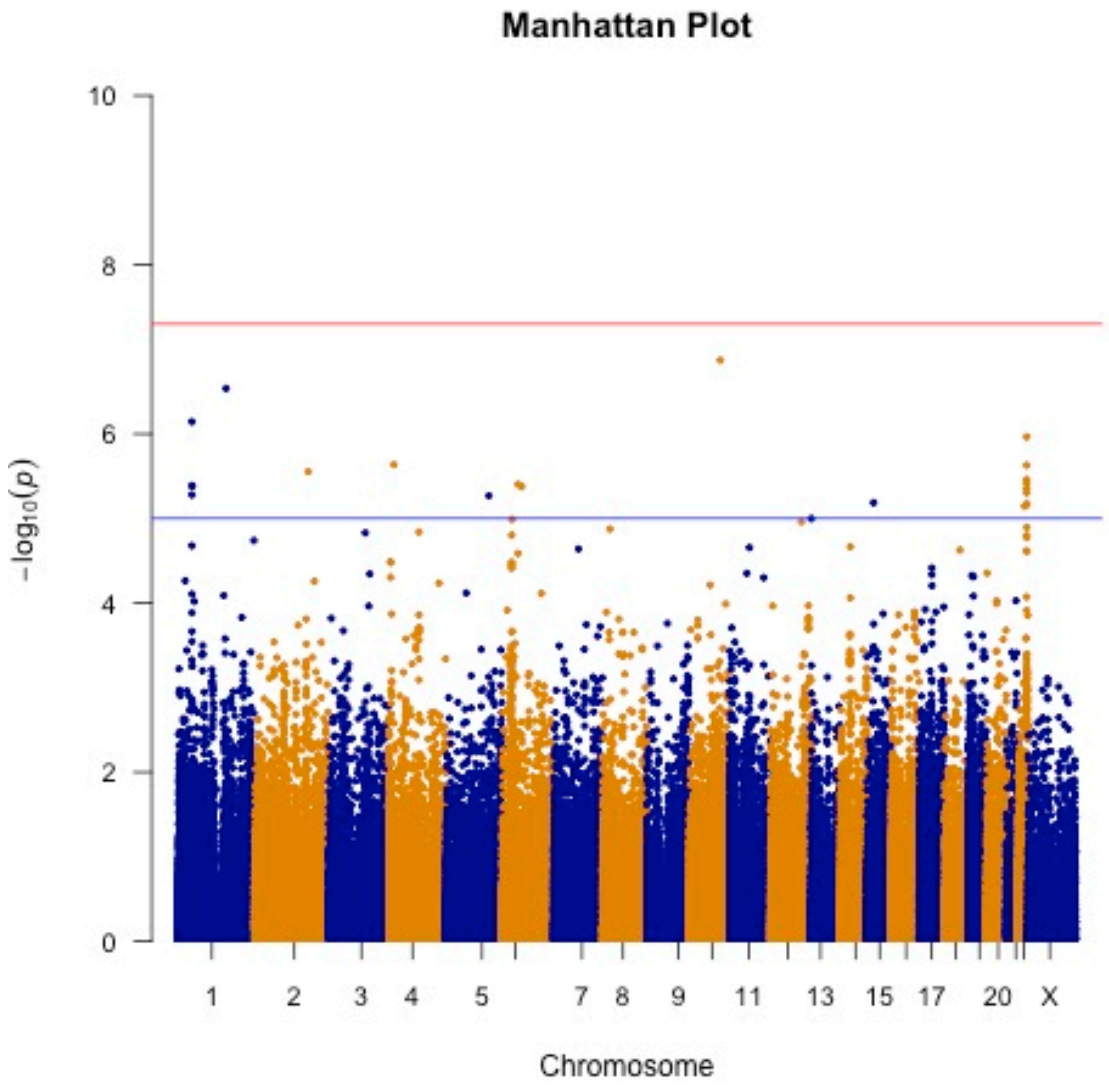

Figure 2. Manhattan Plot demonstrating 22 SNPs above a 1×10^{-5} threshold. Significant SNPs are spread across most chromosomes, with a high frequency of SNPs occurring on chromosomes 1 and 22. The blue line corresponds to a *p*-value above a 1×10^{-5} threshold. The red line corresponds to a *p*-value above a 5×10^{-8} threshold.

Table 3. GWAS results. Significant single nucleotide polymorphisms (SNPs) below a 10×10^{-5} threshold are included. SNPs are detailed according to their location, reference allele, alternate allele, standard rsID, and mapped to their respective gene by rsID.

Chromosome	SNP	rsID	Reference Allele	All Alternate Alleles	OR	*p*	Gene	Coding Variant	Clinical Significance
1	1:44000938:G:A	rs76038188	G	A	2.77567	5.3×10^{-6}	SLC6A9	No	Benign
1	1:44001675:C:T	rs188509294	C	T	4.31614	7.2×10^{-7}	SLC6A9	No	
1	1:44002768:C:T	rs41270407	C	T	2.80768	4.2×10^{-6}	SLC6A9	No	Benign
1	1:44010680:G:T	rs62621784	G	T	2.81042	4.1×10^{-6}	SLC6A9	No	Benign
1	1:155612177:T:C	rs470548	T	C	7.41008	2.9×10^{-7}	MSTO1	No	Benign
2	2:175964654:C:A	rs144765990	C	A	3.94093	2.8×10^{-6}	LNPK	No	
4	4:16674160:C:A	rs191683804	C	A	8.05679	2.3×10^{-6}	LDB2	No	
5	5:138150951:A:T	rs79552163	A	T	2.36997	5.4×10^{-6}	BRD8	Yes	
6	6:53097675:G:A	rs9474385	G	A	3.52686	3.9×10^{-6}	FBXO9	No	

Table 3. *Cont.*

Chromosome	SNP	rsID	Reference Allele	All Alternate Alleles	OR	p	Gene	Coding Variant	Clinical Significance
6	6:64626250:G:A	rs9445051	G	A	1.57604	4.2×10^{-6}	EYS	No	Benign
10	10:103406519:A:G	rs17735658	A	G	3.87312	1.3×10^{-7}	PDCD11	No	
15	15:42737116:C:T	rs190314153	C	T	5.62477	6.5×10^{-6}	CDAN1	No	Uncertain significance, Benign
22	22:39647872:C:A	rs57732048	C	A	4.384	7.2×10^{-6}	CACNA1I	Yes	
22	22:46365600:C:G	rs12165943	C	G	1.58045	4.4×10^{-6}	CELSR1	Yes	
22	22:46373108:T:C	rs6008779	T	C	1.64463	6.9×10^{-6}	CELSR1	No	
22	22:46378549:C:G	rs56344079	C	G	1.68868	2.3×10^{-6}	CELSR1	No	
22	22:46384624:T:C	rs6007897	T	C	1.69137	1.1×10^{-6}	CELSR1	Yes	
22	22:46391537:C:T	rs6008793	C	T	1.65223	3.8×10^{-6}	CELSR1	No	
22	22:46391797:A:G	rs6008794	A	G	1.64112	5.0×10^{-6}	CELSR1	Yes	
22	22:46391800:A:G	rs6008795	A	G	1.63249	6.7×10^{-6}	CELSR1	Yes	
22	22:46394132:G:T	rs11703679	G	T	1.6524	3.5×10^{-6}	CELSR1	No	

4. Discussion

This study demonstrates the effectiveness of cutting-edge ML models in forecasting post-surgical outcomes in ASD, highlighting the utility of complex data (patient imaging, clinical notes) for outcome prediction in neurosurgery. The recent external validation of ASD surgical outcome prediction models, which found poor performance (AUCs ~ 0.60) across complication, readmission, and reoperation outcomes, demonstrates that the current strategy for developing these models is insufficient to achieve clinically impactful machine learning decision-making support [9]. This strategy relies on standard predictive factors (demographic, surgical, radiographic) and traditional machine learning model types to leverage the small amounts of available data to predict outcomes. However, beyond the demonstrated poor predictive performance of this approach, there are clinical limitations. Firstly, models require manual input and become cumbersome and uninterpretable to the physician when including a large set of features [13,14], while, secondly, the models rely on predefined features which likely do not capture all relevant information [15]. To address these limitations, computer vision and natural language processing (NLP) offer the opportunity to use patient imaging and clinical notes, respectively, as inputs for a next-generation schema of spine surgery outcome prediction.

Computer vision and NLP have been identified as potentially powerful tools for surgical outcome prediction in the spine domain [16,17]. However, as of 2022, there were no computer vision tools [18] or NLP tools [19] widely used for diagnostics in spine surgery. The utilization of outdated models with low complexity has been identified as a limitation prohibiting clinical use [19]. The large amount of data needed to train these advanced models have restricted their development. However, advances in NLP [11] and computer vision [12] model pre-training on foundational clinical information allow for their application to data-limited domains such as ASD outcome prediction. In this paper, we demonstrate the success of computer vision, large language model (LLM), and genome-wide association studies (GWAS) in a limited ASD patient cohort for outcome prediction.

Both our CNN and NLP models achieve performance metrics comparable to the performance of the state-of-the-art models used for ASD outcome prediction [9] (Tables 1 and 2). The highest performance was achieved by the fine-tuned LLM on pulmonary complication and sepsis outcomes, with sensitivity, specificity, and F1 scores showing the potential for downstream clinical utilization. The LLM outperformed the CNN for prediction of pulmonary, neurological, and sepsis outcomes. This observed performance difference may be attributed to the fact that the LLM was pre-trained on a much greater extent of data as part of Gatortron development. However, the performance difference may show

the medical reasoning capacity of the LLM and how it is a more powerful model for outcome prediction. The use of advanced AI models offers several advantages in clinical practice. CNNs excel in image data analysis, such as MRI and CT scans, which are crucial in spine surgery. They can automate and enhance the accuracy of medical image interpretation, offering precise detection of spinal conditions [20,21] and of features that are too subtle for the human eye [22]. NLPs can extract insights from unstructured textual data, lowering the workload necessary to manually extract features, and can aid in rapid predictive modeling [19]. Analysis of free text reports have been used to detect outcomes such as incidental durotomies [23], intraoperative vascular injury in anterior lumbar spine surgery [24], postoperative wound infection after lumbar discectomy [25], and readmission after a posterior lumbar fusion [26]. Furthermore, CNN and NLP applications in spine surgery can streamline administrative tasks and optimize the allocation of resources, which can greatly enhance healthcare delivery. Finally, imaging data and clinical notes can be combined into a hybrid model to aid in preoperative planning and postoperative care, allowing neurosurgeons to tailor surgical approaches to individual patient needs [13].

Despite using a limited number of ASD patients who had undergone surgical intervention (N < 300), a GWAS identified 21 novel SNPs that differentiate ASD patients into a cohort which require surgical intervention, representing not only a novel research direction but also what we believe to be the first GWAS on a spine surgery utilization outcome. While the potential of GWAS for neurological disorders is known, the challenges of large required sample sets and resource requirements have limited its use in spine surgery research [27]. Our results show that GWAS designs can uncover SNPs for clinical risk stratification, patient counseling, and pathology forecasting (which may allow for earlier surgical decision making), even in rare spinal pathologies with limited numbers of patients. There are many factors which lead to the development and progression of spinal deformity and understanding specific genetic markers can differentiate which patients should receive intervention. CELSR1 (Table 3) was identified by the GWAS as a significant risk factor and a coding sequence variant in ASD patients who underwent surgical intervention. CELSR1, which has been previously implicated in neural tube defects [28], has been demonstrated to play a neuroprotective effect through neurogenesis promotion in cerebral ischemic injury through the Wnt signaling pathway [29]. These results suggest a potential role of CELSR1 to mediate neural functioning in spinal deformity, where its deficit leads to pathology. The identified risk genes (PDCD11, CDAN1, SLC6A9, MSTO1, CACNA1I, CELSR1, LNPK, LDB2, BRD8, FBXO9, EYS) should be further developed for the clinical stratification of ASD patients to allow for the earlier identification of appropriate surgical candidates before further (and often non-recoverable) deficits develop. The identified risk genes are for the prediction of spine surgery intervention in ASD, and not directly predictive of a complication following such intervention. However, the clinical application of these risk genes can allow for earlier intervention, which may improve outcomes and reduce complications in ASD surgery before the pathology and symptoms advance. This work focused on the intervention as an outcome due to the currently limited number of complications following ASD surgery in the UK Biobank. However, as this data availability grows, future work, motivated by our successful demonstration of GWAS in an ASD cohort, can develop GWAS to identify risk genes for specific complications and outcomes of ASD surgery.

This work introduces models that use imaging, clinical notes, and patient genomics to predict outcomes, including post-operative complications and the need for spine surgery intervention. Moreso, we show the potential of computer vision, large language models, and genome-wide associated models to interface with patient imaging, clinical notes, and genomics to predict relevant outcomes. Here we consider a potential workflow following the external validation and robust development of the models presented in this work to detail the clinical actionability of such models. When a patient presents with ASD, one of the first questions that a surgeon must consider is whether this patient is a surgical candidate. The patient may present with pathology that may not be intervened on, but that the surgeon worries will develop to cause non-reversible deficits. Such deficits may

include structural worsening that would change the surgery type to a procedure with greater risk or might result in the compression of the spinal cord or the exiting of spinal nerves that may result in non-recoverable function or pain. If such factors appear clinically relevant, the surgeon may genotype the identified set of SNPs that have been found to be markers for an ASD patient who will eventually need to undergo a spine surgery intervention. Therefore, if the patient is positive for these markers, their pathology may be likely to worsen, supporting the decision for earlier surgery. However, the decision for surgery is further determined by considering the potential for a patient to undergo a major post-operative complication. Using already available pre-operative imaging and pre-operative clinical notes, the CNN and NLP would be utilized for the prediction of such complications. The surgeon would then use these three models to support their decision making regarding the appropriateness of a surgical intervention, enriched with an understanding of personalized surgical risks and risk genes informing whether the patient's deformity is likely to develop to necessitate surgical intervention. To optimize the application of the models, future research should focus on broadening the spectrum of clinical inputs, enhancing the model's ability to forecast a wider array of actionable clinical outcomes. This expansion would refine the decision-making process. Additionally, future work should aim to integrate these models, leveraging the collective strength of genomic, imaging, and clinical data. Such integration promises a streamlined surgical workflow and a more robust decision support system that considers all facets of patient information.

There are several limitations to the study. First, due to the limited size of the cohorts, certain outcomes had too few positive examples for training. Second, these models were fine-tuned on patient data from a single institution and therefore require external validation. Such external validation, as for all clinical model development, should include diverse patient data across regions, race, and comorbidities. This is a limitation frequently faced by predictive models in spine surgery; however, our fine-tuning approach mollifies this limitation by using models that were pre-trained on large patient sets from other institutions. Therefore, it is likely that these fine-tuned models may perform better on external patient data than traditional models trained on single institution data. Furthermore, while this work sought to evaluate the efficacy of NLP and CNN models for outcome prediction, the final robust models for clinical use may benefit from the inclusion of other predictive variables (e.g., surgeon experience). Finally, the GWAS used the UK Biobank, whose population is homogenous. The identified SNPs must be validated on more diverse patient populations before being translated towards clinical utility. Future work should consider the development of multi-modal models with an expanded and diverse patient cohort from multiple sites. These models should consider other clinically relevant outcomes that may be well predicted by patient imaging and notes in ASD. Future models that seek to predict actionable clinical outcomes should define outcomes considering important parameters which impact the clinical outcome (i.e., fusion rate, screw malposition, screw breakage, and amount of correction) [30].

5. Conclusions

This study demonstrates that, while predictive efforts in neurosurgery are often limited by available patient samples, complex models (CNN, LLM, GWAS) offer predictive potential for surgical outcome prediction. These models, which incorporate more powerful machine learning technologies, can improve the clinical workflow by the elimination of manual input of patient features and the inclusion of patient images and clinical notes for prediction. The models can be developed in future work to robustly predict complications following surgical intervention for adult spinal deformity, improving patient selection and counseling.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/jcm13030656/s1, Figure S1: Loss curves for training (blue) and validation (red) cohorts for NLP model training on (a) pulmonary complications, (b) neurological

complications, (c) sepsis, (d) delirium. The NLP models begin to overfit to the training set after 10 epochs of fine tuning across the four outcomes.

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Data Availability Statement: Publicly available datasets were analyzed in this study. This data can be found here: https://vindr.ai/datasets/spinexr (accessed on 18 December 2023). Restrictions apply to the availability of some data analyzed in this study. Data was obtained from Stanford Research Repository and are under IRB and Stanford University restrictions.

Conflicts of Interest: A.V.: Consultant—Medtronic, Stryker, Nuvasive, Surgical Theater, Osteocentric, Higgs Boson; Stock Holder—ATEC. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Combined Anterior–Posterior vs. Posterior-Only Approach in Adult Spinal Deformity Surgery: Which Strategy Is Superior?

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Abstract: Introduction: Whether a combined anterior–posterior (AP) approach offers additional benefits over the posterior-only (P) approach in adult spinal deformity (ASD) surgery remains unknown. In a cohort of patients undergoing ASD surgery, we compared the combined AP vs. the P-only approach in: (1) preoperative/perioperative variables, (2) radiographic measurements, and (3) postoperative outcomes. **Methods:** A single-institution, retrospective cohort study was performed for patients undergoing ASD surgery from 2009 to 2021. Inclusion criteria were ≥5-level fusion, sagittal/coronal deformity, and 2-year follow-up. The primary exposure was the operative approach: a combined AP approach or P alone. Postoperative outcomes included mechanical complications, reoperation, and minimal clinically important difference (MCID), defined as 30% of patient-reported outcome measures (PROMs). Multivariable linear regression was controlled for age, BMI, and previous fusion. **Results:** Among 238 patients undergoing ASD surgery, 34 (14.3%) patients underwent the AP approach and 204 (85.7%) underwent the P-only approach. The AP group consisted mostly of anterior lumbar interbody fusion (ALIF) at L5/S1 (73.5%) and/or L4/L5 (38.0%). Preoperatively, the AP group had more previous fusions (64.7% vs. 28.9%, $p < 0.001$), higher pelvic tilt (PT) (29.6 ± 11.6° vs. 24.6 ± 11.4°, $p = 0.037$), higher T1 pelvic angle (T1PA) (31.8 ± 12.7° vs. 24.0 ± 13.9°, $p = 0.003$), less L1-S1 lordosis (−14.7 ± 28.4° vs. −24.3 ± 33.4°, $p < 0.039$), less L4-S1 lordosis (−25.4 ± 14.7° vs. 31.6 ± 15.5°, $p = 0.042$), and higher sagittal vertical axis (SVA) (102.6 ± 51.9 vs. 66.4 ± 71.2 mm, $p = 0.005$). Perioperatively, the AP approach had longer operative time (553.9 ± 177.4 vs. 397.4 ± 129.0 min, $p < 0.001$), more interbodies placed (100% vs. 17.6%, $p < 0.001$), and longer length of stay (8.4 ± 10.7 vs. 7.0 ± 9.6 days, $p = 0.026$). Radiographically, the AP group had more improvement in T1PA (13.4 ± 8.7° vs. 9.5 ± 8.6°, $p = 0.005$), L1-S1 lordosis (−14.3 ± 25.6° vs. −3.2 ± 20.2°, $p < 0.001$), L4-S1 lordosis (−4.7 ± 16.4° vs. 3.2 ± 13.7°, $p = 0.008$), and SVA (65.3 ± 44.8 vs. 44.8 ± 47.7 mm, $p = 0.007$). These outcomes remained statistically significant in the multivariable analysis controlling for age, BMI, and previous fusion. Postoperatively, no significant differences were found in mechanical complications, reoperations, or MCID of PROMs. **Conclusions:** Preoperatively, patients undergoing the combined anterior–posterior approach had higher PT, T1PA, and SVA and lower L1-S1 and L4-S1 lordosis than the posterior-only approach. Despite increased operative time and length of stay, the anterior–posterior approach provided greater sagittal correction without any difference in mechanical complications or PROMs.

Keywords: adult spinal deformity; anterior–posterior; posterior only; approach; sagittal malalignment; outcomes

1. Introduction

Adult spinal deformity (ASD) surgery requires complex operations to improve spinal alignment, which can lead to major improvements in quality of life; however, perioperative morbidity remains high [1,2]. Despite durable improvement in quality of life after ASD surgery, major variation exists in surgical technique. Various approaches to ASD surgery include the anterior, trans-psoas, pre-psoas, or traditional posterior approaches [3–5]. Minimally invasive techniques (MIS), mainly tubular work and percutaneous screw placement, have also become popular [6]. The two most popular approaches are the staged combined anterior–posterior (AP) approach and the traditional posterior-only (P) approach. The AP and P approaches have been compared in a small number of studies, with most data extrapolated from comparing transforaminal or posterolateral interbody fusion (TLIF/PLIF) to anterior lumbar interbody fusion (ALIF) [7–11].

The anterior approach in ASD surgery has been reported to have several mechanical advantages, mainly allowing a large, lordotic implant to be placed at low lumbar levels [4]. Moreover, the anterior approach allows for direct removal of anterior osteophytes that can help realign the lumbosacral fractional curve and indirectly decompress the low lumbar nerve roots. Furthermore, the anterior approach allows for the insertion of larger and more lordotic interbody grafts, allowing for increased surface area for fusion and the placement of bone grafts under compressive forces to boost fusion potential, which has been reported to decrease the rate of posterior implant loosening and failure [10].

There has been a steady rise in the number of reported combined AP approaches for ASD surgery [7–11]. Several factors, such as high complication rates with aggressive posterior column corrections and the availability of novel anterior implants, have contributed to this trend [3]. However, there is still a paucity of long-term data on the clinical, mechanical, and radiographic outcomes of the AP approach compared with the P-only approach. Therefore, we sought to compare the AP approach with the P-only approach for (1) preoperative/perioperative variables, (2) radiographic measurements, and (3) and postoperative outcomes.

2. Materials and Methods

2.1. Study Design

A retrospective, single-institution study of patients undergoing ASD surgery with at least 2-year follow-up was conducted from 2009 to 2021. A total of 5 fellowship-trained neurosurgery and orthopedic spine surgeons contributed to this registry. Postoperative patient-reported outcome measures (PROMs) were collected by five full-time research personnel. Institutional Review Board (IRB) approval was obtained (IRB#220894).

2.2. Patient Selection

All patients included in the study were $\geq$18 years old and underwent elective surgery for ASD. Inclusion criteria were: 5-level fusions or more, Cobb angle $\geq 30^{\circ}$, sagittal vertical axis (SVA) $\geq$ 5 cm, coronal vertical axis (CVA) $\geq$ 3 cm, pelvic tilt (PT) $\geq 25^{\circ}$, or thoracic kyphosis (TK) $\geq 60^{\circ}$. Patients were required to have a minimum of 2-year follow-up. Patients received either a combined AP approach within the same anesthetic setting or staged within 1–2 days or a P-only approach, most often performed within the same anesthetic setting. The decision for a combined AP or P-only approach was typically based on the surgeon's discretion, taking into consideration specific patient factors and the desired surgical goals. Generally, when a more extensive correction of sagittal alignment was needed, surgeons may have opted for the AP approach to achieve better correction.

2.3. Outcome Variables

Patient demographic and clinical data, including age, sex, body mass index (BMI), smoking status, and comorbidities (none, one, ≥two), were collected. Intraoperative measures, such as total instrumented levels, location of upper instrumented vertebra (UIV), number of interbody fusions, primary surgeon, blood loss as measured by estimated blood loss (EBL), calculated blood loss, and perioperative hemoglobin, were also collected.

Postoperative location of discharge and length of stay were documented. Complications, such as proximal/distal junctional kyphosis (PJK/DJK), rod fracture, and pseudoarthrosis, were recorded. The study examined patients who developed PJK. PJK was defined as an angle between the UIV inferior endplate and UIV + 2 superior endplate $\geq 10^{\circ}$ and a concomitant $\geq 10^{\circ}$ change compared to preoperative imaging [12]. PJF was defined as further progression on the PJK spectrum to include vertebral fracture of UIV or UIV + 1, subluxation between UIV and UIV + 1, failure of fixation, and/or neurological deficit [13,14].

Two-year PROMs, including Oswestry Disability Index (ODI), EuroQoL Group (EQ-5D), and numeric rating scale (NRS) for back and leg pain (NRS-BP and NRS-LP, respectively) were collected [15,16]. The minimally clinically important difference (MCID) was calculated for ODI, EQ-5D, and NRS [17,18].

Preoperative and postoperative radiographic measures were obtained, including coronal measurement of C7-PL and major Cobb, sagittal measures of L1-L4, lumbar lordosis (LL), pelvic incidence (PI), sacral slope (SS), sagittal vertical axis (SVA), pelvic tilt (PT), T1 pelvic angle (TPA), and L1-S1 angle. Variations in sagittal alignment were classified according to the Roussouly classification [19]. Clinically meaningful pelvic retroversion was defined as a PT > 50% of the PI.

2.4. Surgical Technique

Anterior surgery in the combined AP cohort primarily involved ALIF at L5/S1 or L4/5 or both. After exposure of the anterior part of the disc, the anterior longitudinal ligament was transversely incised, and the disc was completely removed. Next, the vertebral endplates were cleared of cartilage using sharp curettes, taking care that damage to the subchondral bone of the endplates was avoided. Maximum distraction of disc space was achieved by manual lordotic force. After a satisfactory trial implantation, the ALIF cage was filled with a morselized cancellous allograft and implanted. Bone morphogenic protein-2 (BMP-2) was used in almost all ALIFs but was left to the surgeon's discretion.

Posterior surgery in the combined AP group and the P-only group involved instrumentation via an open posterior approach. Subperiosteal exposure of the dorsal spine using a standard midline approach, adequate decompression, pedicle screw instrumentation, and with or without a TLIF was performed. The TLIF was performed in the standard technique as has been described, and use of a bullet or banana cage was left to the surgeon's discretion [20].

2.5. Statistical Analysis

Descriptive statistics were used to compare ASD patients who received combined AP vs. P-only approach for surgical correction. Continuous variables were reported as means and standard deviations, while categorical variables were reported as frequencies. To evaluate normal distribution and variance for continuous variables, the Shapiro–Wilk test and F-test were employed, respectively. Histograms were a qualitative assessment of normality. Normally distributed data with equal variance were analyzed using a two-tailed *t*-test, while nonparametric data were compared with the Wilcoxon signed-rank or Mann–Whitney test. For nominal data, χ^2 or Fisher's exact test was utilized in smaller samples. Univariate and multivariable analyses were conducted, controlling for patient age, BMI, and previous fusion. A significance level of p-value < 0.05 was considered statistically significant. All analyses were performed using R version 4.2.1 (The R Foundation, Vienna, Austria).

3. Results

3.1. Patient Demographics and Preoperative Data

Among the 238 patients undergoing ASD surgery, 34 (14.3%) patients underwent the combined AP approach, and the remaining 204 (85.7%) patients underwent the P-only approach (Table 1). The progression of the AP approach throughout the years is depicted in Figures 1 and 2.

Table 1. Demographic, preoperative, and radiographic variables.

Variables	Total Cohort = 238	Combined N = 34	Posterior Only N = 204	*p*-Value
Preoperative				
Age, mean ± SD	63.4 ± 17.4	62.8 ± 9.8	63.5 ± 18.4	0.048
Female, *n* (%)	181 (76.1%)	26 (76.5%)	155 (76.0%)	0.951
BMI, mean ± SD	28.9 ± 7.0	28.3 ± 7.6	29.4 ± 6.3	0.088
Race, white, *n* (%)	88 (37.0%)	15 (44.1%)	73 (35.8%)	0.13
Comorbidities, *n* (%)				0.269
0	51 (21.4%)	4 (11.8%)	47 (23.0%)	
1	90 (37.8%)	16 (47.1%)	74 (36.3%)	
2+	97 (40.8%)	14 (41.2%)	83 (40.7%)	
Diabetes, *n* (%)	44 (18.5%)	4 (11.8%)	40 (19.6%)	0.275
COPD, *n* (%)	64 (26.9%)	10 (29.4%)	54 (26.5%)	0.72
Heart failure, *n* (%)	34 (14.3%)	6 (17.6%)	28 (13.7%)	0.596
Hypertension, *n* (%)	154 (64.7%)	22 (64.7%)	132 (64.7%)	>0.999
Osteoporosis, *n* (%)	45 (23.9%)	11 (40.7%)	34 (21.1%)	0.027
Prior fusion, *n* (%)	81 (34.0%)	22 (64.7%)	59 (28.9%)	<0.001
Type of malalignment, *n* (%)				0.004
Predominantly sagittal	83 (32.7%)	14 (41.2%)	69 (33.8%)	
Predominantly coronal	11 (4.3%)	0	11 (5.4%)	
Predominantly combined	47 (18.5%)	13 (38.2%)	34 (16.7%)	
Others	97 (38.2%)	7 (20.6%)	90 (44.1%)	
Preoperative Radiographic Measurement				
PT, mean ± SD°	25.3 ± 11.5	29.6 ± 11.6	24.6 ± 11.4	0.037
T1PA, mean ± SD°	25.2 ± 14.0	31.8 ± 12.7	24.0 ± 13.9	0.003
L1-S1 lordosis, mean ± SD°	−22.9 ± 32.9	−14.7 ± 28.4	−24.3 ± 33.4	0.039
L1-L4 lordosis, mean ± SD°	−30.6 ± 15.5	−25.4 ± 14.7	−31.6 ± 15.5	0.055
L4-S1 lordosis, mean ± SD°	−30.6 ± 15.5	−25.4 ± 14.7	−31.6 ± 15.5	0.042
CVA, mean ± SD (mm)	26.5 ± 27.1	32.8 ± 27.6	25.3 ± 26.9	0.166
PI, mean ± SD°	52.7 ± 15.8	54.2 ± 15.6	52.4 ± 15.9	0.470
SS, mean ± SD°	27.5 ± 13.4	24.7 ± 10.7	28.0 ± 13.7	0.116
cSVA, mean ± SD (mm)	30.5 ± 16.5	26.9 ± 16.9	31.1 ± 16.4	0.256
SVA, mean ± SD (mm)	71.7 ± 69.8	102.6 ± 51.9	66.4 ± 71.2	0.005

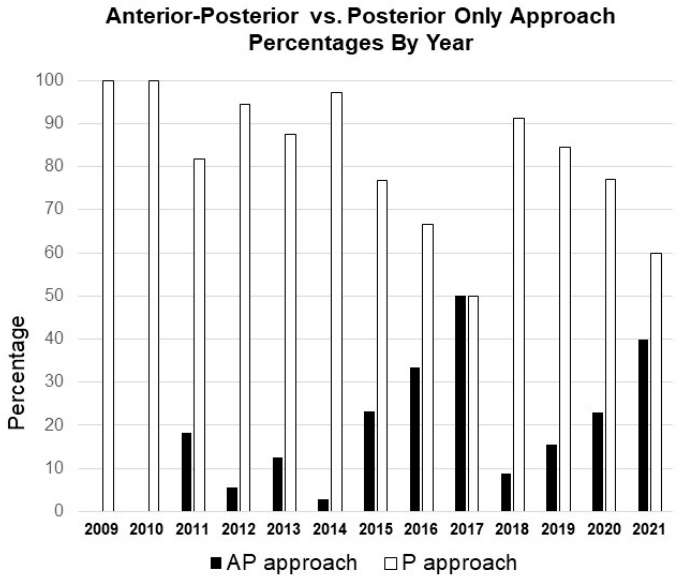

Figure 1. Bar graph comparing the rate of the combined AP vs. P-only approaches by year.

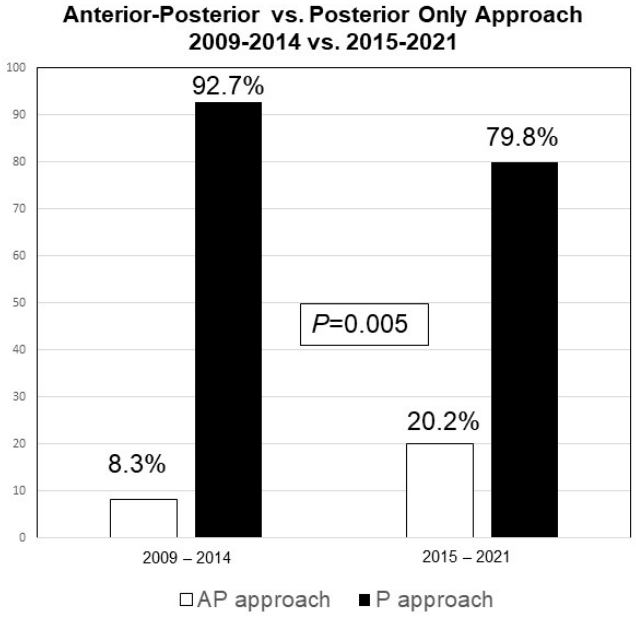

Figure 2. Bar graph comparing the rate of the combined AP vs. P-only approaches between 2009–2014 and 2014–2021.

Patients who underwent the AP approach were slightly younger (62.8 ± 9.8 vs. 63.5 ± 18.4years, p = 0.048) and had higher BMI (31.2 ± 7.6 vs. 28.5 ± 6.8, p = 0.026) compared to patients in the P-only approach. Aside from age and BMI, the two cohorts shared similar demographics with regards to sex (p = 0.951), race (p = 0.130), and comorbidities (p = 0.269).

Patients in the AP group were significantly more likely to have received prior fusions (64.7% vs. 28.9%, $p < 0.001$), which mainly consisted of < 5-level fusion, and the indications were predominantly associated with degenerative conditions. Radiographically, the AP group had higher preoperative PT (29.6 ± 11.6° vs. 24.6 ± 11.4°, p = 0.037), higher T1PA (31.8 ± 12.7° vs. 24.0 ± 13.9°, p = 0.003), less L1-S1 lordosis (−14.7 ± 28.4° vs. −24.3 ± 33.4°, $p < 0.039$), less L4-S1 lordosis (−25.4 ± 14.7° vs. 31.6 ± 15.5°, p = 0.042), and higher SVA (102.6 ± 51.9 vs. 66.4 ± 71.2 mm, p = 0.005). In both cohorts, the most common lordotic apex was at L5 (32.4% vs. 34.8%, p = 0.357), and the most common Roussouly classification was Type 2 (47.1% vs. 40.3%, p = 0.531). There was, however, a significantly higher number

of patients within the combined AP cohort with clinically meaningful pelvic retroversion with a PT > 50% of PI (64.7% vs. 41.6%, $p = 0.012$).

3.2. The Combined Anterior–Posterior Group

For patients in the AP group, the anterior approach consisted mostly of ALIF at L5/S1 (73.5%), L4/L5 (38.0%), L3/L4 (17.6%), L2/L3 (17.6%), and L1/L2 (2.9%). At L5/S1, the mean height of the implant was 10.9 ± 3.0 mm, and mean lordosis was −23.2 ± 32.5°. At L4/5, the mean height of the implant was 10.2 ± 3.0 mm, and mean lordosis was −10.7 ± 16.2°. Half of the AP cases were staged 18 (52.9%), separated by a mean of 2.1 (range 1–5) days. A three-column osteotomy was performed in 10 (29.4%) cases. A thoracolumbar UIV to sacrum/pelvis fusion was performed in 16 (47.0%) cases, and an upper/middle thoracic to sacrum/pelvis fusion was performed in 15 (44.1%) cases. A representative combined AP case is presented in Figure 3A–D.

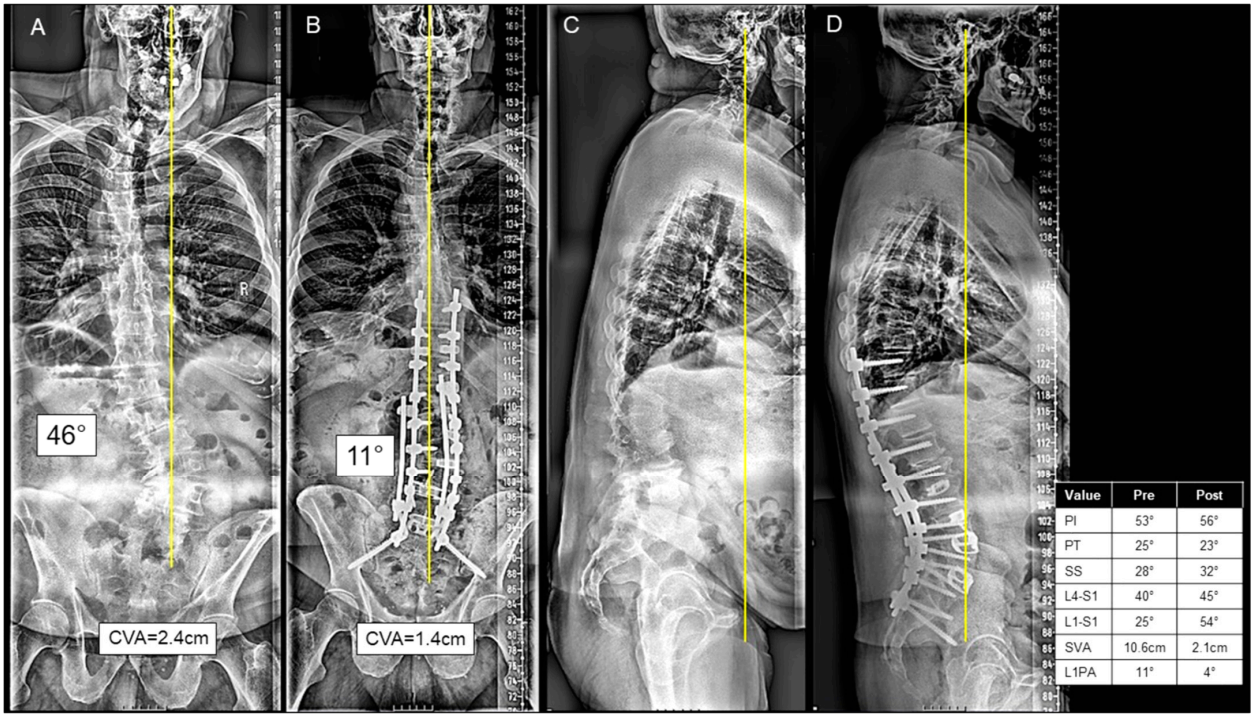

Figure 3. (**A**–**D**) A case presentation of a 67-year-old male presenting with L3-L4 left-sided radiculopathy and sagittal malalignment due to lumbar kyphosis causing severe mechanical back pain on the postero-anterior (PA) (**A**) and lateral X-rays (**C**). The patient underwent a stage 1 anterior lumbar interbody fusion at L4-5 and L5-S1. Two days later, the patient underwent a posterior approach consisting of T10-ilium instrumentation, posterior column osteotomies from T12-L5, inferior facetectomies from T10-S1, and L2/L3 and L3/L4 transforaminal lumbar interbody fusion, as seen on the postoperative PA (**B**) and lateral X-rays (**D**). The patient was discharged to IPR at postoperative day 9.

3.3. The Posterior Only Group

For the P-only group, the posterior approach included lumbar interbodies in 36 (17.6%) patients. These were most commonly L4-L5 (36.1%), L5-S1 (58.3%), L3-L4 (25.0%), and L2-L3 (11.1%). The majority of P-only cases were performed in one anesthetic setting. A three-column osteotomy was performed in 34 (16.7%) cases. A thoracolumbar UIV to sacrum/pelvis fusion was performed in 58 (28.4%) cases, and an upper/middle thoracic to sacrum/pelvis fusion was performed in 103 (50.4%) cases. A representative P-only case is presented in Figure 4A–D.

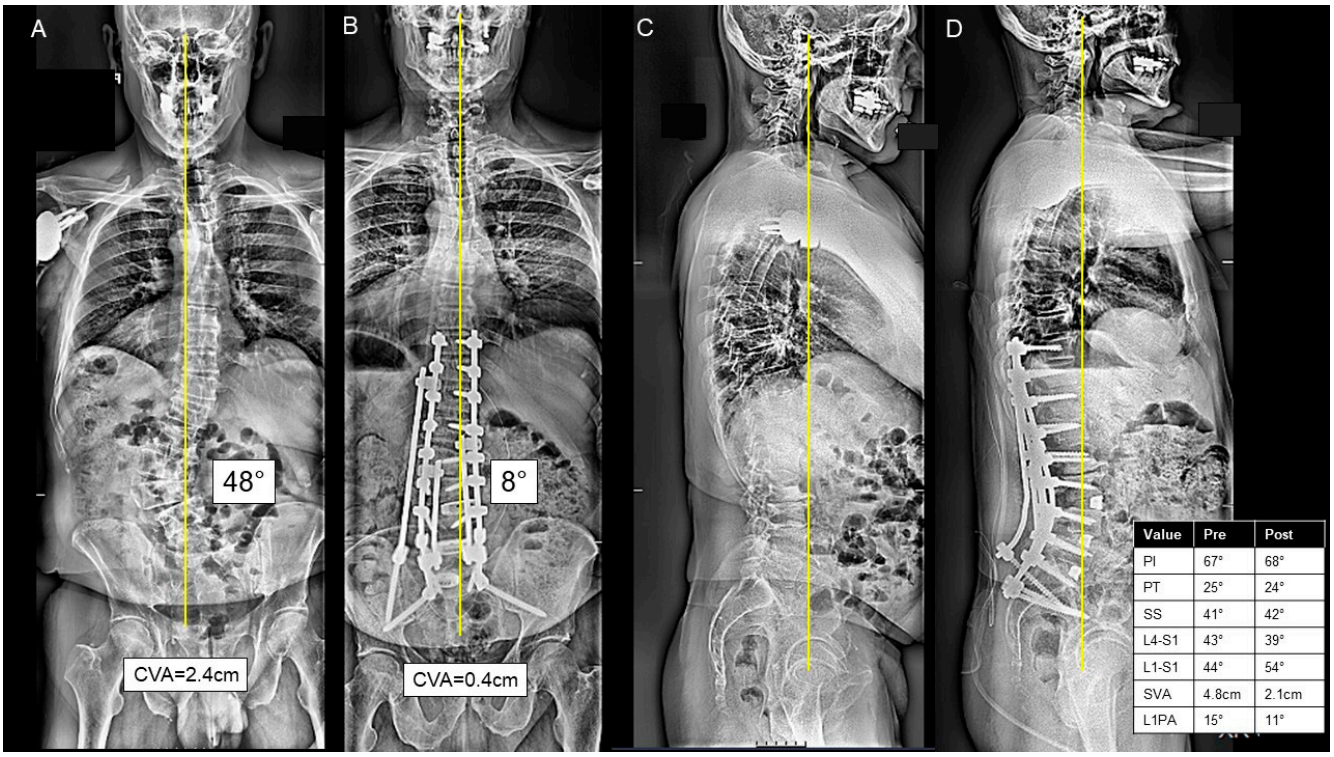

Figure 4. (**A**–**D**) A case presentation of a 67-year-old male with severe L2 and L3 right-sided radiculopathy, left-sided L4 radiculopathy, severe mechanical back pain, and inability to walk for more than 5–10 min, who was found to have a significant degenerative scoliosis in the thoracolumbar and lumbar spine on the postero-anterior (PA) (**A**) and lateral X-rays (**C**). The patient underwent a posterior-only approach consisting of T10-ilium posterior spinal instrumentation; T10-S1 inferior facetectomies; L1-S1 posterior column osteotomies; a total of 3 transforaminal lumbar interbody fusions at L3/L4, L4/L5, L5/S1; decompressive foraminotomies at L5/S1, L4/L5, L3/L4 and L2/L3; and a cobalt kickstand rod from T11/12-S1 with compression and distraction forces to correct the scoliosis, as seen on the postoperative PA (**B**) and lateral X-rays **(D)**. The patient was discharged home at postoperative day 5.

3.4. Perioperative Outcomes

Perioperative variables are summarized in Table 2. The AP approach had longer operative time (553.9 ± 177.4 vs. 397.4 ± 129.0 min, $p < 0.001$), longer hospital length of stay (8.4 ± 10.7 vs. 7.0 ± 9.6 days, $p = 0.026$), and more interbodies placed (100% vs. 17.6%, $p < 0.001$). The AP group also had more mean total instrumented levels (11.4 ± 3.3 vs. 10.4 ± 3.1 levels), but this was not significantly different ($p = 0.065$). Both groups had similar rates of EBL (1285.1 ± 1147.3 vs. 1480.7 ± 1246.8 mL, $p = 0.194$) and discharge home vs. to other locations ($p = 0.967$). As a sub-analysis, we attempted to look at LOS in the AP group after the second stage to see if LOS was more similar when taking out time from the anterior stage. Comparing the LOS from the second stage of the AP group to the total LOS in the P-only group, no significant difference was seen (4.5 ± 1.6 vs. 6.9 ± 9.6 days, $p = 0.296$).

3.5. Radiographic Outcomes

No significant differences were found in postoperative radiographic parameters between the two groups (Table 3. However, regarding change in alignment, the combined AP group had a greater T1PA correction (13.4 ± 8.7° vs. 9.5 ± 8.6°, $p = 0.005$), greater improvement in L1-S1 lordosis (−14.3 ± 25.6° vs. −3.2 ± 20.2°, $p < 0.001$) and L4-S1 lordosis (−4.7 ± 16.4° vs. 3.2 ± 13.7°, $p = 0.008$), and a greater degree of SVA correction

(65.3 ± 44.8 vs. 44.8 ± 47.7 mm, $p = 0.007$). These outcomes remained statistically significant in multivariable analysis controlling for age, BMI, and previous fusion (Table 4).

Table 2. Intraoperative variables.

Variables	Total Cohort = 238	Combined N = 34	Posterior Only N = 204	*p*-Value
Intraoperative				
Total instrumented levels, mean ± SD	10.5 ± 3.2	11.4 ± 3.3	10.4 ± 3.1	0.065
Presence of interbody, mean ± SD	70 (29.4%)	34 (100%)	36 (17.6%)	<0.001
Number of interbody, *n* (%)				<0.001
0	168 (70.6%)	0	168 (82.4%)	
1	44 (18.5%)	15 (44.1%)	29 (14.2%)	
2	18 (7.6%)	14 (41.2%)	4 (2.0%)	
3	5 (2.1%)	3 (8.8%)	2 (1.0%)	
4	3 (1.3%)	2 (5.9%)	1 (0.5%)	
Operative time (min), mean ± SD	419.9 ± 147.2	553.9 ± 177.4	397.4 ± 129.0	<0.001
EBL, mean ± SD	1452.6 ± 1232.6	1285.1 ± 1147.3	1480.7 ± 1246.8	0.194
Discharge disposition, *n* (%)				0.967
Home, *n* (%)	112 (50.7%)	17 (51.5%)	95 (50.5%)	
IPR, *n* (%)	71 (32.1%)	10 (30.3%)	61 (32.4%)	
SNF, *n* (%)	38 (17.2%)	6 (18.2%)	32 (17.0%)	
Length of stay (days), mean ± SD	7.2 ± 9.8	8.4 ± 10.7	7.0 ± 9.6	0.026

Table 3. Postoperative radiographic measurements and radiographic correction.

Variables	Total Cohort = 238	Combined N = 34	Posterior Only N = 204	*p*-Value
Postop Radiographic Measurements				
PT, mean ± SD°	24.5 ± 10.7	27.8 ± 12.3	23.9 ± 10.3	0.060
T1PA, mean ± SD°	22.3 ± 12.1	24.2 ± 13.4	22.0 ± 11.9	0.364
L1-S1 lordosis, mean ± SD°	−24.6 ± 35.9	−28.3 ± 35.8	−23.9 ± 35.9	0.527
L4-S1 lordosis, mean ± SD°	−28.2 ± 12.6	−28.6 ± 15.9	−28.1 ± 11.9	0.853
CVA, mean ± SD (mm)	21.4 ± 21.3	24.5 ± 23.4	20.9 ± 21.0	0.459
PI, mean ± SD°	52.4 ± 14.1	56.4 ± 13.3	51.6 ± 14.2	0.115
SS, mean ± SD°	27.2 ± 10.0	29.3 ± 9.2	26.8 ± 10.1	0.202
cSVA, mean ± SD (mm)	31.3 ± 15.6	31.1 ± 14.6	31.4 ± 15.8	0.929
SVA, mean ± SD (mm)	50.5 ± 58.2	46.1 ± 50.6	51.3 ± 59.6	0.658
Postop Radiographic Correction				
PT, mean ± SD°	7.6 ± 7.2	8.7 ± 7.8	7.4 ± 7.1	0.217
T1PA, mean ± SD°	10.1 ± 8.7	13.4 ± 8.7	9.5 ± 8.6	0.005
L1-S1 lordosis, mean ± SD°	−5.0 ± 21.4	−14.3 ± 25.6	−3.2 ± 20.2	<0.001
L4-S1 lordosis, mean ± SD°	1.8 ± 14.5	−4.7 ± 16.4	3.2 ± 13.7	0.008
CVA, mean ± SD (mm)	31.4 ± 32.3	39.7 ± 39.3	29.9 ± 30.8	0.295
PI, mean ± SD°	10.6 ± 10.9	11.4 ± 11.7	10.4 ± 10.8	0.609
SS, mean ± SD°	8.5 ± 7.7	8.5 ± 7.9	8.5 ± 6.5	0.966
cSVA, mean ± SD (mm)	48.0 ± 47.7	65.3 ± 44.8	44.8 ± 47.7	0.007
SVA, mean ± SD (mm)	48.0 ± 47.7	65.3 ± 44.7	44.7 ± 47.6	0.005

Table 4. Multivariable linear regression, controlling for age, BMI, and previous fusion.

		Univariate		Multivariable	
Outcome	**Independent Variable**	**β (95%CI)**	***p*-Value**	**β (95%CI)**	***p*-Value**
T1PA correction	AP vs. P	3.94 (0.56–7.3)	0.022	3.72 (0.14–7.31)	0.041
L1-S1 correction		−11.1 (−19.2, −2.9)	0.008	−11.18 (−19.71, −2.65)	0.010
L4-S1 correction		−8.0 (−13.9, −2.1)	0.008	−7.26 (−13.65, −0.88)	0.026
SVA correction		20.5 (1.65–39.4)	0.033	20.49 (0.71–40.28)	0.042

Preoperatively, 23 (67.6%) patients had clinically significant pelvic retroversion in the AP group compared to 105 (52.0%) in the P-only group ($p = 0.097$). The mean PT in the AP group vs. P-only group was 29.6 ± 11.6 vs. 24.6 ± 11.4, respectively (0.037). Postoperatively, 14 (41.2%) patients had clinically meaningful pelvic retroversion in the AP group compared to 81 (39.7%) in the P-only group ($p > 0.999$).

Interestingly, patients undergoing the AP approach were significantly more likely to have pelvic tilt improvement by more than 5° compared to the P-only approach (50.0% vs. 27.5, $p = 0.043$). The association between the AP approach and improved pelvic tilt was also seen in the multivariable logistic regression controlling for the aforementioned variables (OR = 2.22, 95%CI = 1.01–4.95, $p = 0.049$).

3.6. Clinical and Patient-Reported Outcome Measures

Clinical measures and PROMs are summarized in Table 5. At 2-year follow-up, there were no significant differences in rates of pseudarthrosis (20.6% vs. 28.9%, $p = 0.315$), rod fracture (14.7% vs. 20.1%, $p = 0.461$), PJK (54.5% vs. 46.7%, $p = 0.404$), DJK (2.9% vs. 3.4%, $p > 0.999$), or reoperation rates for any reason (35.3% vs. 37.7%, $p = 0.784$). Similar non-significant findings were observed in the multivariate regression analysis.

Table 5. The impact of surgical approach on mechanical complications and patient-reported outcome measures.

		p		
Variables	**Total Cohort = 238**	**Combined N = 34**	**Posterior Only N = 204**	***p*-Value**
Postoperative Outcomes				
Mechanical complication	146 (61.3%)	22 (64.7%)	124 (60.8%)	0.664
Radiographic PJK	110 (47.8%)	18 (54.5%)	92 (46.7%)	0.404
Pseudarthrosis	66 (27.7%)	7 (20.6%)	59 (28.9%)	0.315
RF	46 (19.3%)	5 (14.7%)	41 (20.1%)	0.461
DJK	8 (3.4%)	1 (2.9%)	7 (3.4%)	>0.999
MCID ODI *	61 (54.0%)	5 (38.5%)	56 (56.0%)	0.233
MCID NRS Back *	58 (51.3%)	5 (38.5%)	53 (53.0%)	0.324
MCID NRS Leg *	67 (65.7%)	7 (53.8%)	60 (67.4%)	0.336
MCID EQ-5D *	67 (65.7%)	7 (53.8%)	60 (67.4%)	0.323

* missing values.

With regards to PROMs at 2 years, patients in the AP group reported higher ODI (42.5 ± 19.2 vs. 34.7 ± 19.4, $p = 0.208$), NRS-BP (5.9 ± 2.8 vs. 4.8 ± 2.9 $p = 0.202$), NRS-LP (3.5 ± 3.7 vs. 3.0 ± 3.2 $p = 0.601$), and lower EQ-5D (0.6 ± 0.2 vs. 0.7 ± 0.2 $p = 0.332$), but these were not significantly different. There was also no significant difference between the AP and P groups, respectively, in rates of achieving the MCID for ODI (38.5% vs. 56.0%,

p = 0.233), NRS-BP (38.5% vs. 53.0%, p = 0.324), NRS-LP (53.8% vs. 67.4%, p = 0.336), and EQ-5D (15.4% vs. 8.0%, p = 0.323).

4. Discussion

The present study evaluated outcomes in patients undergoing the combined AP vs. P-only approaches for ASD surgery. Patients undergoing the combined AP approach had greater preoperative sagittal malalignment with significantly higher preoperative PT and T1PA and lower L1-S1 and L4-S1 lordosis. Postoperatively, the combined AP approach provided better sagittal correction due to significantly greater change in postoperative T1PA correction, L1-S1 lordosis change, L4-S1 lordosis change, and SVA correction. There was no significant difference in mechanical complications or PROMs between the AP and P-only approaches. These findings support that the AP approach was chosen in cases of greater sagittal malalignment and, postoperatively, provided greater sagittal correction, with a similar profile of mechanical complications and PROMs.

The AP group had more sagittal malalignment preoperatively and also exhibited greater postoperative sagittal correction than the P-only group, specifically in the parameters of T1PA, L1-S1, L4-S1, and SVA. The powerful ability of the anterior approach to restore low lumbar lordosis has been well documented [7,21]. Haddad et al. [7] found a better SVA, PT, relative lumbar lordosis, and relative pelvic version in patients undergoing the AP vs. P-only approach. Similarly, Stephan et al. [21] reported a 5–15° segmental lordosis gain in the AP approach compared to the P-only approach at L4-L5 and L5-S1. Not only did our results corroborate these findings, but we also showed that rates of ALIFs being performed increased over time. As the field of ASD has evolved, surgeons have gained new appreciation for the importance of L4-S1 lordosis, evidenced by Roussouly and the Global Alignment and Proportion (GAP) score, and at our institution, our surgical approach has followed suit [19,22,23]. During an ALIF procedure, a larger interbody can typically be inserted, which has potentially far more lordosis correction compared to a posteriorly placed interbody, where additional carpentry and osteotomies are needed.

Despite the potent ability of an ALIF to improve low lumbar sagittal alignment, these results showed that the combined AP approach had a significantly longer operative time and LOS but were discharged home at similar rates. These findings are consistent with a study by Haddad et al. [7], who reported that combined approaches had significantly longer surgeries (548 vs. 283 min) and needed longer ICU stays (74 vs. 27 h). However, they had comparable complication rates and significantly fewer readmissions (9.1% vs. 38.1%) and reoperations (18.2% vs. 43.2%) at 2 years. Theologis et al. [11] compared patients undergoing multiple-level lateral interbody fusions at the apex of the coronal deformity with posterior fixation to a matched cohort of adult deformity patients treated with the posterior-only approach. All patients had an L5/S1 interbody fusion. Similar to our study, patients in the combined group had significantly more levels fused, longer operative times, and longer lengths of stay. Haddad et al. [7] also reported that patients undergoing the combined approach appeared to require more aggressive surgical intervention due to the inherent nature of their deformities, leading to an increased rate of fixation to the pelvis and a tendency toward more instrumented levels. In our cohort, we also saw that patients undergoing the combined AP approach had significantly more interbodies placed and more total instrumented levels. Our postoperative radiographic outcomes are similar to a report by Ming-Kai et al. [8] in which patients undergoing the combined approach with ALIF significantly improved sagittal and coronal correction compared to the posterior-only cohort. Theologis et al. [11] also found that the combined group had significant improvement in postoperative radiographic parameters such as PT, LL, and PI-LL.

The current study demonstrated no significant difference in mechanical complications or PROMs, signifying that either approach can lead to good outcomes. Patients also had no significant difference in MCID for postoperative PROMs such as ODI, NRS-BP, NR-LP, and EQ-5D. Similarly, Leveque et al. and Mundis et al. [24,25] compared patients undergoing anterior column realignment (ACR) with lateral graft placement and sectioning

of the anterior longitudinal ligament to posterior-only approaches and found similar clinical outcomes and similar rates of overall major complication. These two studies found no significant clinical differences other than in blood loss, which was significantly less in the ACR group compared to the posterior-only group. In comparison, Haddad et al. [7] reported that patients in the combined group had better clinical outcomes as measured by COMI and SRS-22, which can possibly be explained by their significantly lower readmissions and reoperations in the combined approach. Bae et al. [26] compared patients with a combined posterior approach with lateral lumbar interbody fusion (LLIF), and ALIF and posterior-only approaches and found lower rates of PJK and mechanical failure at the UIV and better ODI and SRS-22 scores in the posterior LLIF group only. Theologis et al. [11] found a significant improvement in ODI and visual analogue scale scores in patients undergoing a combined approach for ASD. Unlike our series, these advantages came at the expense of having significantly more major complications (56% vs. 13%) and postoperative leg weakness (31% vs. 6%) in the combined approach. Overall, our results show that regardless of the AP or P-only approach, similar mechanical complications and PROMs were seen.

Limitations

This study has several limitations warranting discussion. First, the AP cohort had a significantly higher rate of prior fusion, which could have influenced surgical approach and need for greater sagittal correction. Therefore, we accounted for prior fusion in our multivariable analysis and still found a significantly greater improvement in postoperative sagittal correction with the AP approach. Third, this is a retrospective, single-institution, multi-surgeon study and these findings may have limited generalizability. Fourth, determining the precise onset of ASD poses a significant challenge, as patients typically seek medical attention when symptoms become severe. Fifth, while we controlled for age, BMI, and previous fusion in our analysis, it was challenging to incorporate further covariates due to the small sample size. Lastly, the retrospective nature of our study posed added challenges to precisely determine the reasons behind the surgeon's chosen procedure. Future, prospective trials are encouraged to better control for these factors and elucidate the decision-making process regarding the surgical approach for each surgeon.

5. Conclusions

In patients undergoing ASD surgery, a combined anterior–posterior approach had higher preoperative rates of prior fusion, higher T1PA, lower L1-S1 and L4-S1 lordosis, and a higher PT compared to the posterior-only approach. Perioperatively, the combined anterior–posterior approach had increased operative time and length of stay but provided a better sagittal alignment correction without any difference in mechanical complications or PROMs.

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Data Availability Statement: For data inquiries, please contact Scott L. Zuckerman.

Conflicts of Interest: Zuckerman reports being an unaffiliated neurotrauma consultant for the National Football League. Stephens is a consultant for Nuvasive and receives institutional research support from Nuvasive and Stryker Spine. Abtahi receives institutional research support from Stryker Spine. No other perceived conflicts of interest by any of the listed authors are declared.

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Differences in Pubertal Curve Progression among Females with Adolescent Idiopathic Scoliosis Using Pregnenolone Therapy: A Retrospective Case-Controlled Series

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Abstract: Background: Differences in hormone metabolism have been observed in children with adolescent idiopathic scoliosis. These differences have been offered as underlying reasons for rapid curve progression during puberty. This study retrospectively compared two groups of females with a history of adolescent idiopathic scoliosis. They were seen for initial presentation prior to menarche, or within 2 months after menarche, and they were followed up 1 year after first menarche. **Methods**: All patients in both groups underwent baseline salivary hormone testing to identify any hormone imbalances. The control group was composed of females with curves between 10 and 25 degrees and maintained an observation-only management strategy. The treatment group showed baseline curve measurements ranging from 10 to 23 degrees, and additionally took pregnenolone daily for 12 months. **Results**: At one-year follow-up, the treatment group showed curve measurements ranging from 13 to 24 degrees, while the control group ranged from 16 to 29 degrees ($p < 0.05$). **Conclusions**: The study showed that adolescent females taking pregnenolone daily for low progesterone had reduced scoliosis curve progression over 1 year compared to controls.

Keywords: hormone; scoliosis; spine

1. Introduction

Adolescent idiopathic scoliosis refers to a condition marked by a spinal curvature measuring 10° or more, as determined by Cobb's angle on radiographic examination [1]. The prevalence of this condition is estimated to range from 0.47% to 5.2% among individuals aged 0–17 in the United States, with a subsequent increase to 8% in the adult population [1]. Treatment approaches for adolescent idiopathic scoliosis depend on the initial curvature magnitude, as outlined in the 2016 SOSORT treatment guidelines [1]. These guidelines recommend exercises for curves between 10 and 15 degrees, while curves ranging from 15 to 50 degrees should be managed with exercises and/or bracing, contingent on the patient's growth stage. Curves exceeding 50° typically warrant surgical interventions like spinal fusion surgery [2].

Despite these treatment guidelines addressing the spinal curvature, they do not encompass certain non-spinal comorbidities commonly associated with this condition, such as the differences in levels of hormones like vitamin D3 [3], leptin, ghrelin [4], FSH, LH, estrogen, progesterone [5], and melatonin [6]. These and other similar observations have contributed to a more comprehensive, hypothetical understanding of scoliosis etiopathogenesis [7].

Building upon these earlier observations in idiopathic scoliosis, the present study delves into specific hormone differences in individuals with scoliosis. Notably, progesterone exerts a significant influence on the motor memory centers of the brain, such as the hippocampus and thalamus, through synaptic plasticity [8]. Progesterone also serves to signal peak bone mass development, which may also contribute to the observed differences

in bone mineral density among adolescent idiopathic scoliosis patients [9]. Progesterone is derived from pregnenolone, which is also considered a neurotransmitter, acting centrally on N-methyl-D-aspartate (NMDA) receptors to modulate glutaminergic activity [10]. This pathway enables pregnenolone to exert positive influences on neuroplasticity, which may also be important in idiopathic scoliosis given the cerebellar/hindbrain component of scoliosis etiology [7].

This study reports the observations of scoliosis Cobb angle and salivary progesterone levels in scoliosis patients who were given pregnenolone for low progesterone, as compared to scoliosis patients who declined pregnenolone use or were otherwise not candidates. Pregnenolone is an immediate metabolic precursor to progesterone and is itself produced intrinsically from cholesterol. Pregnenolone has been shown to enhance locomotor activity, learning, and memory, and to promote neuron survival [11]. Considering the proposed neurological mechanisms involved in idiopathic scoliosis [12], as well as its ability to improve progesterone levels [13], the current study aims to retrospectively assess the data from a cohort of female patients who were prescribed pregnenolone for low salivary-progesterone values in relation to their scoliosis history.

2. Materials and Methods

2.1. Study Design

This research adhered to a retrospective case–control study design in line with the STROBE guidelines. The study aimed to observe any differences in the amount of pubertal curve progression in a cohort of patients with a history of idiopathic scoliosis if they concurrently took pregnenolone supplementation specifically for low progesterone levels. Historical data were considered.

2.2. Participants

A consecutive sampling method was employed, involving all patient records from a multidisciplinary medical clinic in Grand Blanc, MI, USA, from January 2019 to November 2022. Inclusion criteria for the present study were comprised of the following: (1) patients with a history of adolescent idiopathic scoliosis, (2) biological females, (3) either premenses or had their first menstrual period with the prior 2 months, and (4) completed a salivary hormone test and were subsequently given pregnenolone as part of their clinical management. A total of 14 patient files meeting these criteria were consecutively selected and included in the treatment group. A second group of scoliosis patient files were selected, using the same inclusion criteria except these patients did not start pregnenolone therapy. Consecutive sampling was also used until 13 files were collected. Data collection exclusively involved female patients for both groups to ensure consistency in reference progesterone levels, and males were excluded for homogeneity.

2.3. Variables

Non-identifying data for both groups included age, salivary progesterone levels, and radiographic Cobb angle measurements at baseline and 1 year. Cobb angle measurements were drawn from the superior endplate of the upper, most-tilted vertebra and the inferior endplate of the lowest, most-tilted vertebra. The measurement was derived from the angle created by the intersection of two lines drawn perpendicular from each endplate. Salivary progesterone levels were obtained through Labrix (St. Charles, IL, USA) (http://www.doctorsdata.com, accessed on 10 October 2023) due to its noninvasive nature, making it especially suitable for adolescent patients. Salivary progesterone has demonstrated a consistent correlation with serum progesterone values [14]; therefore, it was chosen for its ease of collection, particularly for younger patients. Salivary progesterone values are reported in picograms per milliliter. Confounding factors include patients within each group whose curves warranted participation in some type of physical treatment (i.e., scoliosis-specific exercises, bracing). A history of scoliosis also presents as a potential confounding variable, since the pregnenolone therapy was focused on treating low proges-

terone values, not idiopathic scoliosis. Patients who began pregnenolone supplementation were placed on either 10 mg, 20 mg, or 30 mg once every evening. This was administered orally in 10 mg tablets. The initial dose was based on baseline patient weight as well as the deficit in each patient's baseline progesterone value relative to the low end of the reference range published by the laboratory.

2.4. Bias

Given the retrospective nature of the current study, selection bias is of primary concern. If an effort to minimize this bias, matching criteria were applied to ensure comparability between cases and controls. The use of the primary outcome variables, radiographic Cobb angle measurements, and salivary progesterone levels also minimize the risk of recall bias and interviewer bias.

2.5. Statistical Analysis

Statistical analyses were conducted in R Studio [15], with additional data averages derived using Excel, to determine whether relationships existed for a multitude of variables. The first hypothesis tested whether the pregnenolone dosage had an impact on the change in progesterone levels between the treatment group and the control group. One-sample *t*-tests with 95% confidence intervals were used to look at the entire group of participants and then the treatment group only. *p*-values were used to determine whether the relationship was of statistical significance. Welch's *t*-test was used with a 95% confidence interval for the entire group's *t*-test. The dependent variable was the change in salivary progesterone levels. The independent variable was the dosage of pregnenolone or lack thereof. The alternative hypothesis postulated that there would be no difference in the average change in salivary progesterone levels between the groups. The relationship was then furthered to see if there was a dose–response relationship between the amount of pregnenolone administered and the change in progesterone levels upon one year of follow up. Dose–response analyses of the treatment group's dosages were performed along with another dose–response analysis with all the participants in R-Studio Version 4.2.1 using the drm() function [15]. A summary plot of the dose–response analysis was also made for both analyses. Log-logistic analyses under three parameters were used to determine the *p*-values for the dose–response relationship for the treatment group, and four parameters were used for the entire group of participants.

The second relationship tested was whether all participants, regardless of therapy, experienced a difference in curve progression based on their age. Scatterplots with age as the independent variable and change in curve progression were made in Excel. Three different graphs were made using Excel Version 2312 and R Studio Version 4.2.1 [15]: all participants, treatment group only, and control group only. Trendlines with their corresponding linear equations and R-squared values were made to visualize and quantify the potential relationship. Using R-Studio, a histogram of the change in Cobb angle was also made to determine if the variable was normally distributed amongst the participants. Correspondingly, in R-Studio, an asymptotic one-sample Kolmogorov–Smirnov test was used to test the normal distribution of the change in Cobb angle in all the participants. A scatterplot was also created in R-Studio with age as the independent variable and change in Cobb angle as the dependent variable. A linear regression analysis in R-Studio was performed on the graph to find the *p*-value, F-statistic, R-squared value, degrees of freedom, t-value of the slope, t-value of the intercept, standard error of the y-intercept, standard error or the slope, and formula for the linear regression line. The values were compared against the standard error and linear regression formula found in Excel to verify results.

Another relationship tested in R-Studio was whether the dosage of pregnenolone alters the course of curve progression within the treatment group. Dose–response analyses of the treatment group's dosages were performed along with another dose–response analysis with all the participants in R-Studio using the drm() function [15]. A summary plot of the dose–response analysis to the change in Cobb angle was also made for both analyses.

Log-logistic analyses under three parameters were used to determine the *p*-values for the dose–response relationship for the treatment group, and four parameters were used for the entire group of participants.

To test for the confounding variables of having scoliosis initially and initial progesterone levels, ANCOVA tests were performed using R-Studio for each of the variables separately [15]. ANOVA tests were first performed on the variables to determine if the co-variates of initial Cobb angle (the presence of scoliosis) and progesterone levels met the criteria for an ANCOVA test. The independent variable was the pregnenolone dosage, and *p*-values were used to determine if the variables were independent. Following the ANOVA tests, ANCOVA analyses were performed using the change in Cobb angle as the response variable, the pregnenolone dosage as the treatment variable, and the initial Cobb angle and progesterone levels as the covariates separately. A type III sum of squares was used for the analysis to obtain the *p*-values using R Studio [15].

3. Results

The mean age of the treatment group was 12.83 years, with a range of 10–15 years. The control group had a mean age of 12.42 years, and a range of 10–15 years. The average baseline Cobb angles for the experimental group and control group were 16.5 and 16.5 degrees, respectively, with 4.03 and 4.45 degrees of standard deviation for the treatment and control groups, respectively. The average baseline height was 154.71 cm for the treatment group and 148.46 cm for the control group. At 1 year, these values increased to 156.43 cm and 149.54 cm, respectively. Figure 1 shows a comparison of demographic and outcome data for age, initial and final Cobb angles, and initial and final serum progesterone levels between the groups.

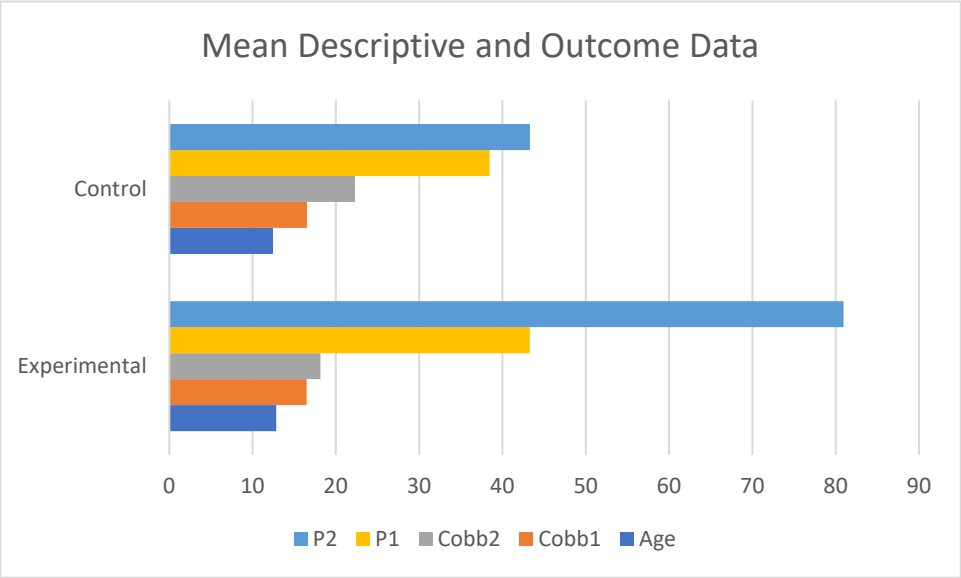

Figure 1. Mean descriptive and outcome data.

At 1-year follow-up, the treatment group's average Cobb angle was 18.14 degrees ±3.44, while the control group's average was 22.31 degrees ±4.32. The mean difference in Cobb angle at 1 year for the treatment group was 1.6 degrees, while the control group's mean difference was 5.8 degrees.

The baseline and 1-year salivary progesterone levels in the treatment group were averages of 43.3 pg/mL and 80.9 pg/mL, respectively. The averages for the control group were 38.5 pg/mL and 43.3 pg/mL. For the Welch's *t*-test analyzing whether there was a statistically significant effect on salivary progesterone levels depending on the usage of pregnenolone therapy, there was extremely strong evidence that the pregnenolone therapy influenced the salivary hormone levels with a *p*-value of 0.00004739. The 95% confidence

interval was between −46.19 and −19.40 to indicate that the mean between the groups was not equal to 0. The one-sample *t*-test of the treatment group based on dosage and its effects on salivary progesterone levels also showed extremely strong evidence that the pregnenolone therapy increased the salivary progesterone levels with a *p*-value of 0.0000121 and a 95% confidence interval between 25.73 and 49.55. As the mean change was much higher than 0 for this confidence interval while the other 95% confidence interval testing the means between the experimental and treatment groups was less than 0, this indicates that pregnenolone therapy did have a substantial impact on improving the salivary progesterone levels more so than not taking any pregnenolone at all. The histograms of the entire group of participants as well as the treatment group only with their respective changes in salivary progesterone levels are shown in Figures 2 and 3 below. Figure 4 details the mean and quartile ranges of the change in progesterone between the experimental and control group (note that the colors in Figure 4 bear no significant meaning).

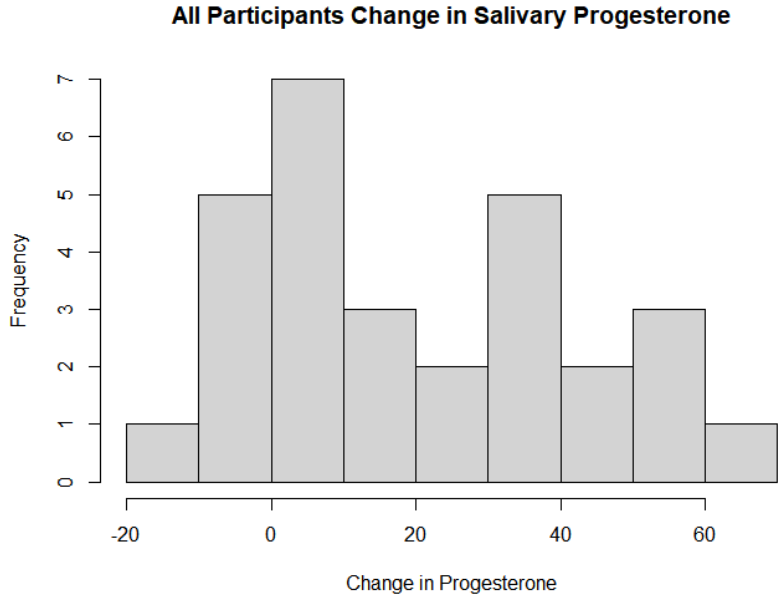

Figure 2. All participants change in salivary progesterone levels following pregnenolone therapy.

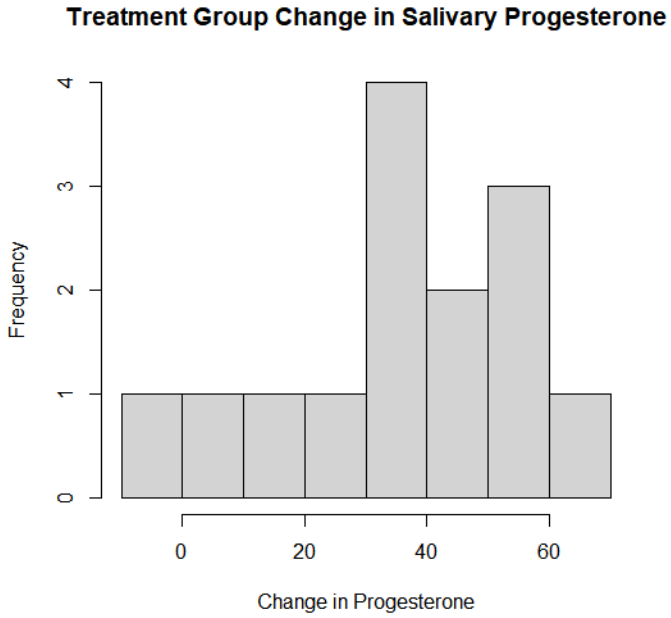

Figure 3. Treatment group change in salivary progesterone levels following pregnenolone therapy.

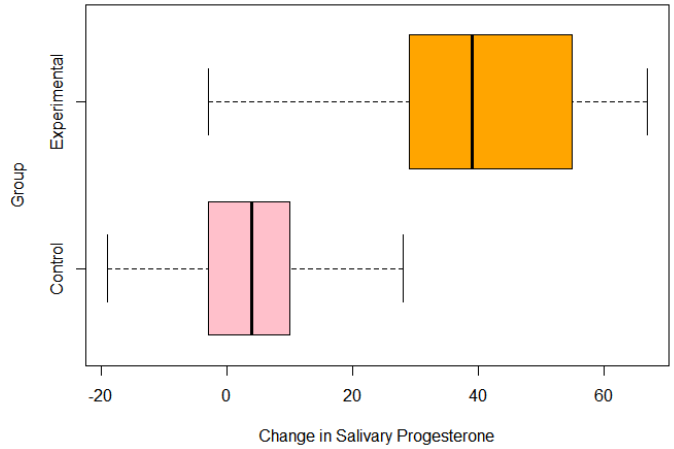

Figure 4. Boxplot of change in salivary progesterone across groups.

When determining whether the pregnenolone dosage showed a dose–response relationship with the amount of salivary progesterone change, there was an insignificant relationship between the dosage and the change based on the *p*-value alone; however, this may be due to the relationship between the treatment group participants only. When looking at the analysis of the entire group of participants, the *p*-values of the four parameters in the drm() test in R yielded values of 0.8300, 0.3259, 0.7877, and 0.9297. On initial conclusion, it would appear that the dosage had no effect on progesterone levels following treatment. However, when analyzing the graphs in Figures 5 and 6, and the *p*-values of the dose–response relationship in the treatment group alone, it would appear that the treatment group experienced a much larger increase in salivary progesterone compared to the control group. The control group showed an average change of 4.85, while each group's change in the treatment subsets was greater than 30 (34.80, 43.33, and 49, respectively). The highest change in the experiment group was 67, while the highest change in the control was 28 (a number lower than only three of the changes in the experimental group). When the dose–response relationship for the treatment group only was conducted using the drm() function in R Studio and a log-logistic function with three parameters, the *p*-values obtained were 0.8738, 0.9812, and 0.8832. These massive *p*-values show that the dosage of pregnenolone in the treatment group had no effect on the change in salivary progesterone levels. Any pregnenolone dosage was sufficient to cause a change in the salivary progesterone levels. Since the treatment group accounts for a little over half of the participants in the study (14 out of 27), the *p*-values analyzing the groups together are skewed to be larger. In this case, the argument for the dose–response relationship cannot be made based on *p*-values alone when comparing the groups simultaneously. The pregnenolone dosage did change the levels of salivary hormones of progesterone between the control group and inclusive subsets of the treatment groups.

Upon investigating whether the pregnenolone changed the development of the Cobb angle, one-sample *t*-tests for each group separately showed that the Cobb angle changes were of low statistical significance in the treatment group ($p = 0.05185$), but very statistically significant in the control group ($p = 0.0001949$). The *t*-test was set with mu = 0, the average change in the treatment group was 1.64 degrees, and the average change in the control group was 5.77 degrees. In looking at the *p*-values and the average changes, the treatment group showed a change that was not statistically significant from zero. In this instance, being closer to zero indicates a smaller curve progression (a more positive number from zero indicates that the curve has progressed). The control group showed an average change in Cobb angle of 5.77 degrees with a *p*-value of 0.0001949. This leads to the result that the control group had statistically significant evidence that the curves did progress beyond 0 to become worse without the pregnenolone therapy. The pregnenolone therapy resulted in a smaller curve progression compared to those not treated with the pregnenolone

therapy. From the Welch's *t*-test conducted in R-Studio to analyze the relationship between a difference in curve progression between the treatment and control groups, it was found that there was a statistically significant difference in curve angle progression based off the treatment of pregnenolone given to the two groups. When conducting a Welch's *t*-test across the groups, a *p*-value of 0.005378 was given for a 95% confidence interval of (1.355765–6.896982). Since the *p*-value of 0.005378 shows statistically significant results, the experimental group receiving the pregnenolone experienced a smaller progression of their Cobb angle following treatment. There is strong evidence to suggest that the experimental group exhibited a smaller progression in their Cobb angle from the treatment. As zero is not included in the 95% confidence interval, this strengthens the argument that the treatment caused a decreased curve progression compared to the control group. From the Excel and R Studio analyses, the following information was produced. The experimental group's mean difference in Cobb angle was 1.642 degrees. The control group's mean difference in Cobb angle was 5.769 degrees. The standard deviation in Cobb angle difference for the experimental group was 2.767 degrees. The standard deviation in Cobb angle difference for the control group was 3.786 degrees. The Welch's *t*-test t-value was 3.0899, which was positive because there was a smaller mean for the experimental group to indicate a smaller Cobb angle progression. Figure 7 highlights a boxplot of the mean outcomes of Cobb angle change between the two groups, with the experimental group having the lower average Cobb angle change and quartile range (note that colors bear not significant meaning).

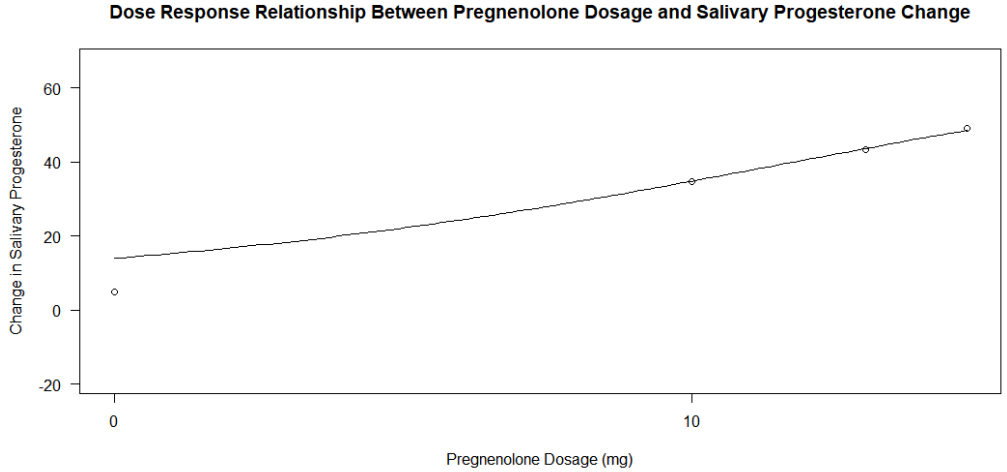

Figure 5. Dose–response relationship between pregnenolone dosage and salivary progesterone change.

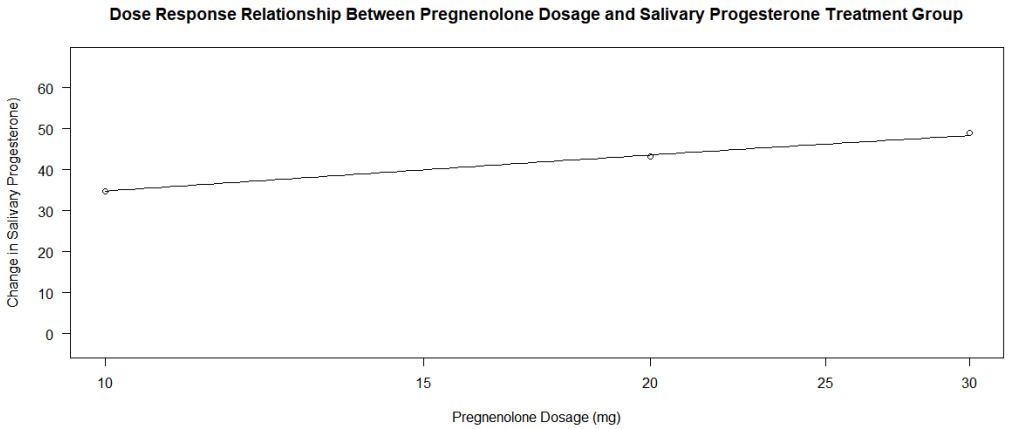

Figure 6. Dose–response relationship between pregnenolone dosage and salivary progesterone change in treatment group only.

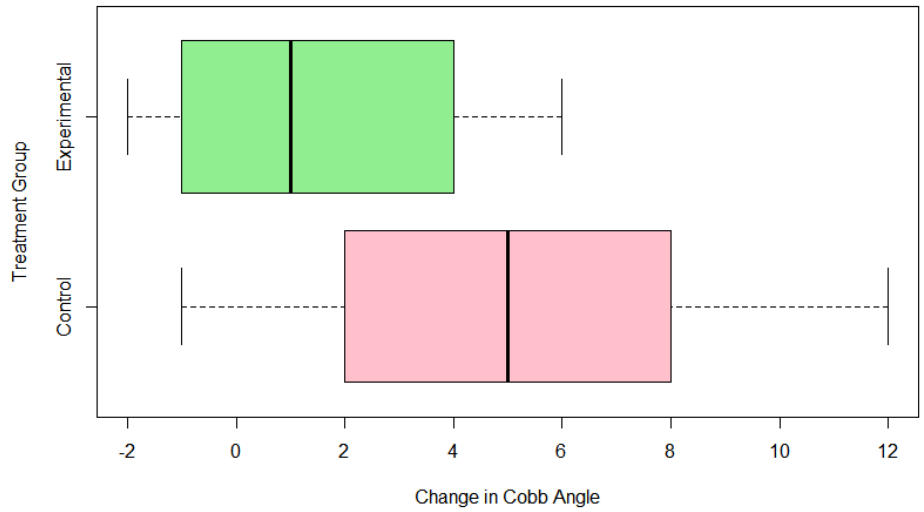

Figure 7. Boxplot of change in cobb angle across groups.

After comparing data for progesterone levels and Cobb angle measurements, we analyzed the potential relationship between age at baseline and amount of curve progression among both groups. It has been reported previously that younger ages of onset may be correlated with a higher risk of curve progression [1]. To evaluate this, scatterplots were created for each group as shown in Figures 8 and 9, as well as one for both groups combined as shown in Figure 10. When analyzing the trendline for the control group, the trendline had a negative slope of -0.7294 with an R squared value of 0.112. The treatment group had a negative trendline with a slope of -0.2329 with an R squared value of 0.0211, and the combined group showed a negative trendline with a slope of -0.6016 with an R squared value of 0.0727. It was found that both groups combined also had a p-value of 0.4496. Statistical analysis was completed in R Studio as well as Excel. After completing data analysis for age of onset and its relation to Cobb angle curve progression, the relationship is not statistically significant. Observing the scatterplots of all the groups, the graphs all exhibit negative slopes but critically low R squared values (0.0211, 0.112, and 0.0727, respectively). For the combined groups of all 27 participants, the curve progression (change in Cobb angle) tended to decrease as age increased; however, this was not the case for all of the points, as shown in Figure 10. There were some outliers in the young age group who had an increase in Cobb angle that was as high as that of the 15 year old group, but the trend tended to show no decreases in Cobb angle with younger participant ages upon diagnosis. As the age of onset increased in the treatment group (age 11 is the first instance of a decrease in Cobb angle), there was a greater likelihood of decreasing patient Cobb angle. This was not true in some cases, and this could be attributed to compliance with other aspects of treatment (physical therapy adherence, bracing, participating in different sports that might advance Cobb angle progression, etc.). When analyzing the trendline in the control group, the trendline did have a negative slope of -0.7294 and an R-squared value at 0.112. This indicates that there is the greatest relationship with age and change in Cobb angle progression, but even then the relationship is weak if it is there at all. Due to the small sizes of the sampling groups, the internal and external validity of the results and of the graphs from the small R squared values indicate an extremely minimal relationship, if any, with age to the Cobb angle progression.

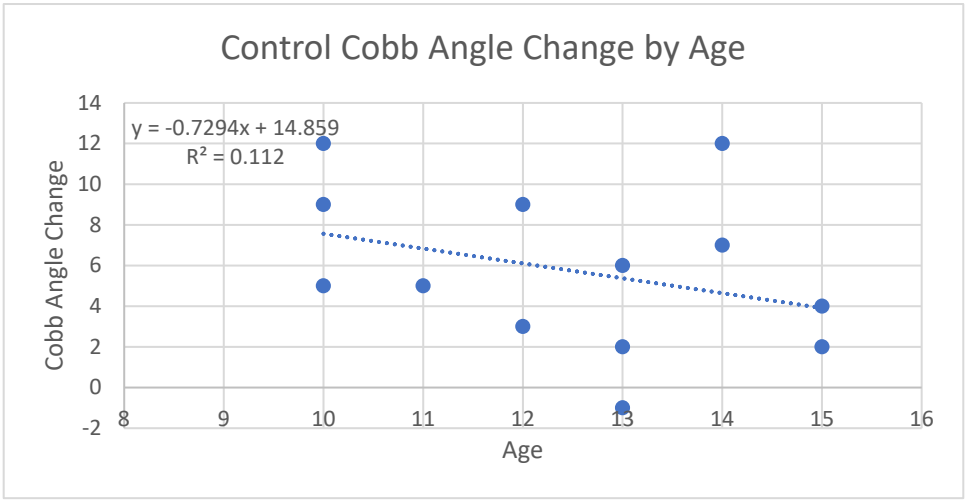

Figure 8. Control group cobb angle data.

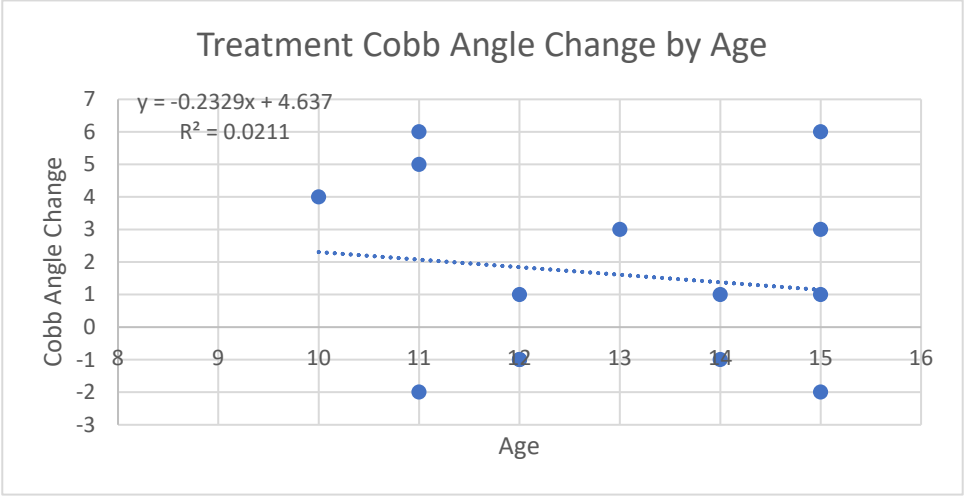

Figure 9. Treatment group cobb angle data.

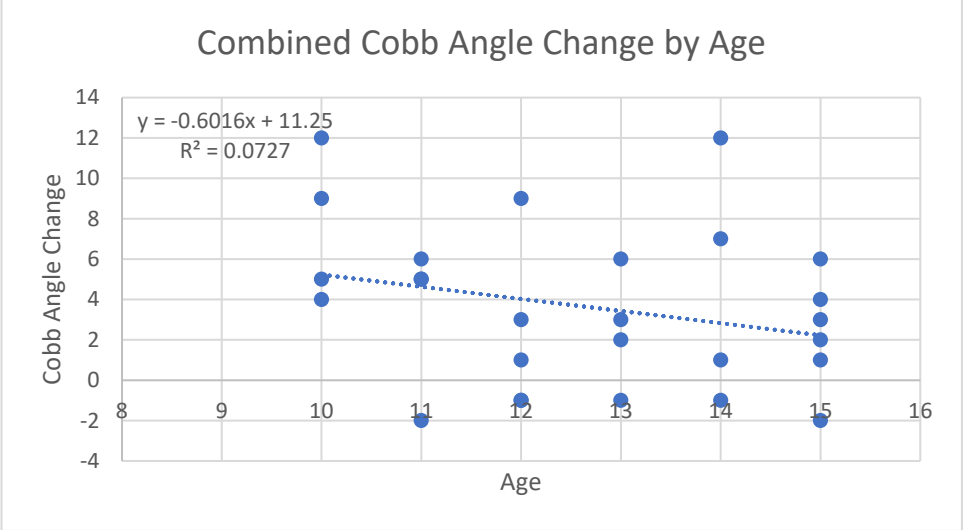

Figure 10. Intergroup cobb angle data comparison.

The pregnenolone dose among the patients in the treatment group also varied slightly, ranging from 10 mg daily to 30 mg daily. A total of nine patients were prescribed 10 mg, three were prescribed 20 mg, and one was prescribed 30 mg. A dose–response analysis of the treatment group's dosages found statistically insignificant *p*-values ranging between 0.7349, 0.9743, and 0.9555 when compared to differences in the Cobb angle measurements under three parameters. The dosage of the pregnenolone appeared to generally decrease the Cobb angle change, but the data points related to the 20 and 30 mg dosages did not show a significant difference. The small number of data points related to the higher dosages may contribute to the log-logistic analyses of the treatment groups under the three parameters giving high *p*-values. Figures 11 and 12 show the scatterplots of the treatment group's different dosages and their changes in Cobb angle using the averages of each dosage and each participant's data, respectively. While there was a decrease in the overall response from the pregnenolone dosage, there were still some in the 10 mg group that showed greater improvement than the one taking the 30 mg dose. Another analysis was performed with all of the participants under the four parameters. The *p*-value was 5.039×10^{-6}, with three of the parameters not giving information about the *p*-values. The statistically significant *p*-value gives extremely strong evidence that any form of pregnenolone treatment is beneficial to reducing or stabilizing Cobb angle change. However, as the dose in the treatment group alone did not produce significant *p*-values, this dose–response relationship is only upheld when the therapy is either not given at all or being given. In other words, there is extremely strong evidence for a statistically significant dose–response relationship when going from no pregnenolone supplementation compared to being treated with pregnenolone; however, this dose–response relationship is not seen between the different treatment groups. A difference was not found in Cobb angle progression between the 10 mg, 20 mg, and 30 mg treatment groups. As stated before, the small size of the treatment groups limits the internal comparison between the groups for a better understanding of dose–response relationship between groups taking the pregnenolone treatment. Further research is needed to uncover this relationship in greater detail. When taking the average change in Cobb angle in the different pregnenolone treatment dosages, the following values are obtained: 5.769 degrees for the 0 mg group, 2.100 degrees for the 10 mg group, 0.3333 degrees for the 20 mg group, and 1.000 degree for the 30 mg group. When looking superficially at the averages across the groups, it appears that any pregnenolone treatment does impact the curve progression in the participants.

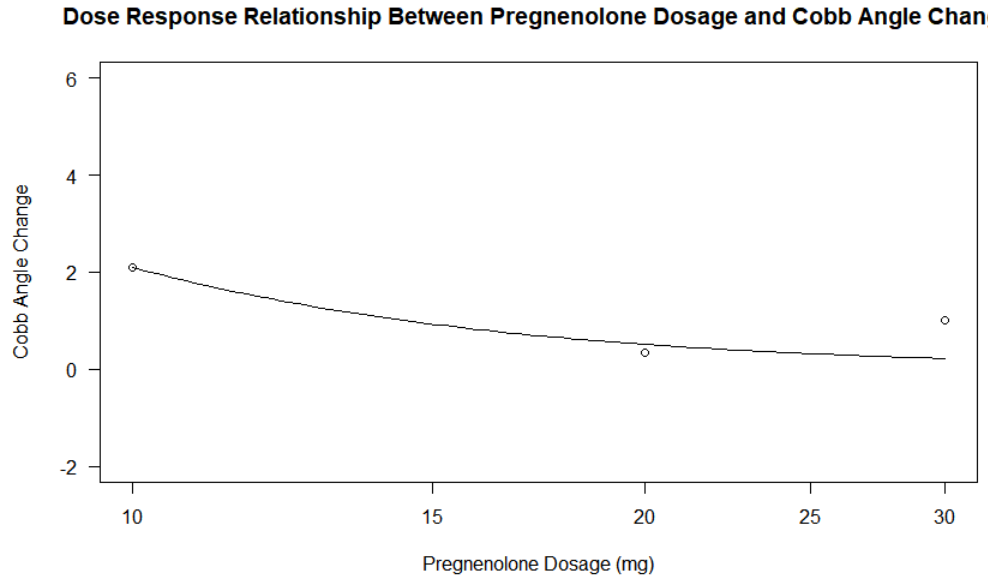

Figure 11. Dose–response relationship between pregnenolone dosage and cobb angle change treatment group only.

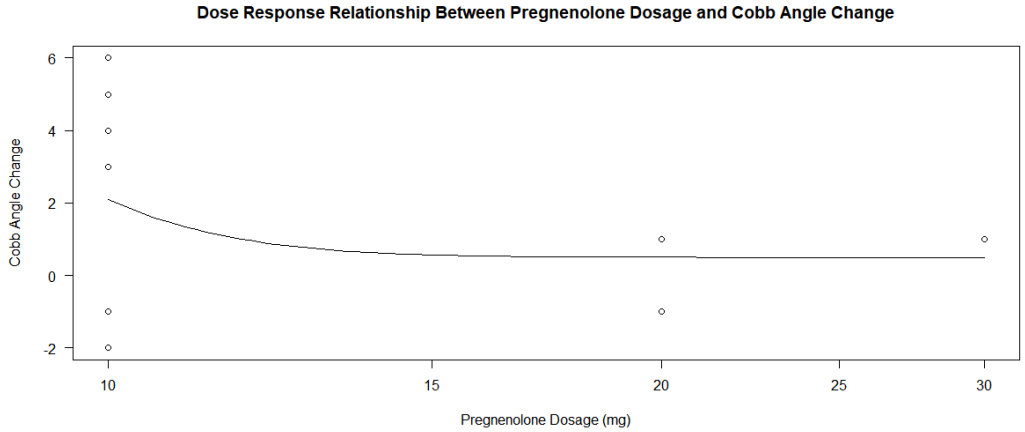

Figure 12. Dose–response relationship between pregnenolone dosage and cobb angle change treatment group only with all data points included.

From the ANCOVA tests run in R Studio to determine confounding variables, the presence of scoliosis at the start of the therapy was independent of the pregnenolone treatment, with a *p*-value of 0.414 [15]. Due to the high *p*-value, the impact that the initial curve had on the outcome was not related to the treatment of pregnenolone therapy. The ANCOVA type III test using the change in Cobb angle as the response variable, pregnenolone dosage as the treatment variable, and initial Cobb angle degree as the covariate yielded a *p*-value of 0.07074 for the pregnenolone dosage and 0.8560 for the initial Cobb angle. The initial Cobb angle is not statistically significant in this case while the dosage appears to have minimal effect on the change in Cobb angle with or without the initial Cobb angle degree. The initial Cobb angle's large *p*-value suggests that it has a smaller and possibly no effect on the change in Cobb angle compared to the pregnenolone dosage. Initial Cobb angle appeared to have no effect on the change in Cobb angle later with or without the treatment. The continuation of Cobb angle occurred most prominently due to the pregnenolone dosage in this case compared to the initial Cobb angle. However, this relationship has weak evidence due to the *p*-value of 0.07074 when compared to these standards. The progesterone dose has a weak effect on the change in Cobb angle when controlling for the variable of age at diagnosis.

In the ANCOVA tests for the possible confounding variable of initial progesterone level in saliva, the progesterone level at the start of the treatment was independent of the pregnenolone dosage, with a *p*-value of 0.656 from the ANOVA test between the variables. The subsequent ANCOVA type III test with the change in Cobb angle as the response variable, pregnenolone dosage as the treatment variable, and initial progesterone levels as the co-variate yielded good evidence from the statistically significant *p*-value for the pregnenolone dosage at 0.007193, while the initial progesterone dose had an insignificant *p*-value at 0.5662. The progesterone dose has a statistically significant effect on the change in Cobb angle when controlling for the variable of initial progesterone levels.

4. Discussion

Pregnenolone therapy and its response effect on progesterone levels between the experimental and the control groups shows promising effects on the ability to increase salivary progesterone levels regardless of dose. The *p*-value of 0.00004739 provides extremely strong evidence that there is a profound relationship between the pregnenolone therapy's ability to lead to a change in progesterone levels. As the average change was 37.64 after one year of treatment in the experimental group and 4.85 in the control group, the pregnenolone therapy led to a significant increase in salivary hormone levels in the patients. The 95% confidence interval in the treatment group's analysis based on the null hypothesis that there would be no change in progesterone level was 25.73 and 49.55 with a *p*-value of 0.0000121. This large increase in the interval from 0 with a small corresponding *p*-value indicate that

the treatment group showed extremely strong evidence that the pregnenolone therapy lead to an increase in salivary progesterone. The averages for the experimental groups across all dosages were much larger than that of the control group's (34.80, 43.33, and 49, respectively, for the 10 mg, 20 mg, and 30 mg dosages). As mentioned previously, the highest change in salivary progesterone in the control group was 28, which was only larger than 21% of the experimental group participants' individual numbers. While the *p*-values for the dose–response relationship for the pregnenolone therapy and the change in salivary progesterone were insignificant at 0.8300, 0.3259, 0.7877, and 0.9297, this was influenced by the fact that the dosage in the treatment group had no relationship. Through analysis of the two dose–response relationship graphs in Figures 5 and 6 along with the average changes for each dose, there does appear to be a dose–response relationship. However, it is hard to obtain statistically significant *p*-values when any dosage in pregnenolone appears to increase the salivary progesterone near the same amounts. Since the treatment group accounts for a little over half of the doses, the drm() function in R has difficulty detecting this relationship that seems to be all or nothing with the pregnenolone dosage. Obtaining large *p*-values when comparing all the participants does yield *p*-values that were smaller in some cases (0.8300, 0.3259, 0.7877, and 0.9297) than the treatment groups' *p*-values only (0.8738, 0.9812, and 0.8832). From the interpretation notwithstanding the *p*-values of the entire participant group, the conclusion that there is a relationship between pregnenolone therapy and its corresponding increase in salivary progesterone levels is obtained when analyzing the dose–response graphs of the entire group in Figure 5. However, the quantity of the dose has less overall impact on the change in progesterone levels compared to the relationship between not taking pregnenolone at all. From the results, a dosage of 10 mg appears to be almost as effective compared to the 20 mg and 30 mg dosages based on the large *p*-values alone. If seeking to increase salivary progesterone levels, a therapy of pregnenolone administered between 10 and 30 mg will yield increases in progesterone from the results above.

The analysis of two groups of consecutively selected scoliosis patient records showed that patients taking pregnenolone supplementation saw significantly less curve progression over 12 months when compared to scoliosis patients who did not take pregnenolone supplements as shown by Figures 13 and 14 below. The small *p*-value of 0.005378 provides statistically significant evidence that the treatment group receiving the pregnenolone therapy experienced a smaller progression in their Cobb angles. The 95% confidence interval did not include zero, strengthening the argument that the treatment experienced a decreased curve progression compared to the control group. The two groups also showed significantly different salivary progesterone levels after 12 months. The age of onset was not strongly correlated to decreased curve progression. The minimal correlation coefficients between the patients' Cobb angle change in relation to their age along with the large *p*-value of 0.4496 provides no evidence to support that the age of onset has an impact on the effectiveness of mitigating the change in Cobb angle. This holds true for both groups when analyzed separately as is shown in Figures 8–10 and 15. Figure 16 specifically highlights both groups on the same plot separately, with the red dots indicating the treatment group and the black dots denoting the control group. The spread of the data indicated little correlation to age and change in Cobb angle, as some young and old participants showed similar changes in Cobb angle even when the groups were analyzed separately. Each of the trendlines had R squared values close to zero, with the largest being 0.112 for the control group. For the combined groups of all 27 participants, the curve progression (change in Cobb angle) tended to decrease as age increased; however, this was not the case for all of the points as shown in Figures 10 and 15. There were some outliers for as high of an increase in Cobb angle in the 15 year old group, but the trend tended to show no decreases in Cobb angle depending on younger participant ages upon diagnosis. Compliance with other aspects of treatment (compliance with physical therapy routine, participating in different sports that might advance Cobb angle progression, etc.) may have also impacted the change in Cobb angle, which was not investigated in this study. When analyzing the

trendline for the control group, the trendline did have a negative slope at −0.7294 with an R squared value of 0.112. This indicates that there is little relationship between age and curve progression, which is similar to the treatment and control groups that had R squared values of 0.0211 and 0.0727 respectively. Due to the low number of participants in the treatment group, it is difficult to generalize the results and compile a strong relationship between the age and Cobb angle change between the groups.

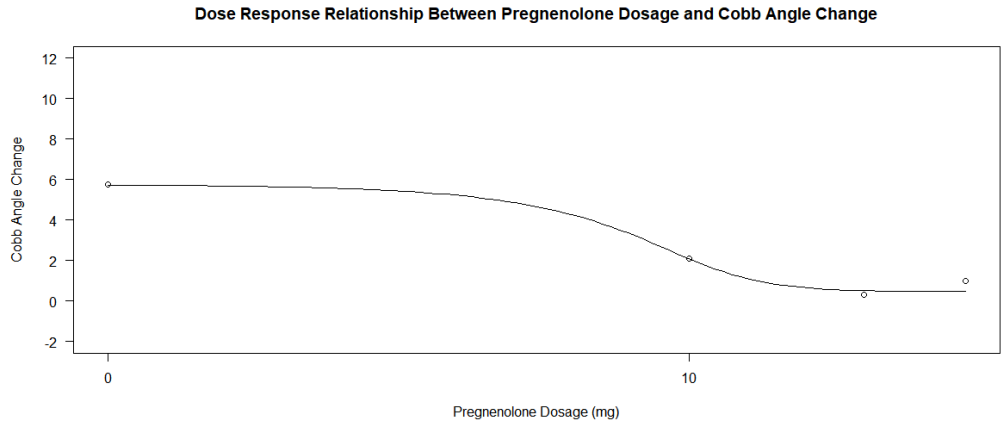

Figure 13. Dose–response relationship between pregnenolone dosage and cobb angle change across all participants.

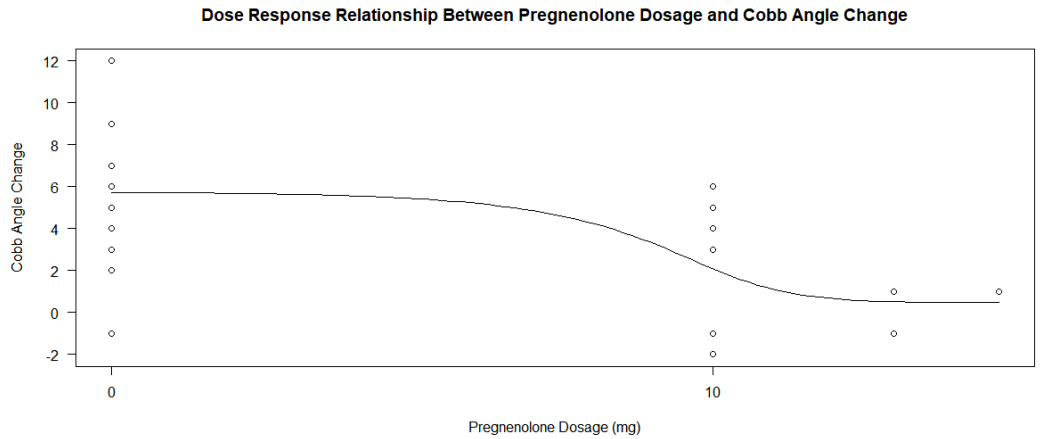

Figure 14. Dose–response relationship between pregnenolone dosage and cobb angle change across all participants with individual points.

In reviewing the patient data, there were three instances of reported side effects, one for a patient who started on 30 mg of pregnenolone, and two who started on 20 mg of pregnenolone. Specifically, the side effects reported were mild breast tenderness, insomnia, and irritability. All of these side effects had resolved by a maximum of 8 weeks after initiating the pregnenolone. There were no other reported side effects.

Although the relationship between progesterone and scoliosis is unclear, this study is consistent with previous findings that female patients with scoliosis show significantly different levels of salivary progesterone compared to non-scoliotic control patients [16]. In adolescence, the chief roles of progesterone are to influence the development of long-term memory, including central pattern generators within the central nervous system [17], as well as mediate the signaling of peak bone mass development as a child nears skeletal maturity [18]. Since disturbances in both functions are more common in idiopathic scoliosis [19–21], continued investigations into more detailed associations between progesterone and idiopathic scoliosis are reasonable and warranted. The dosage did appear to minimally influence the decrease in curve progression within the treatment group, as seen in Figures 11 and 12, but the small number of participants makes it difficult to extrapolate this

trend to a larger population. The large *p*-values of 0.7349, 0.9743, and 0.9555 also suggest that higher dosages did have a strong effect on the change in Cobb angle.

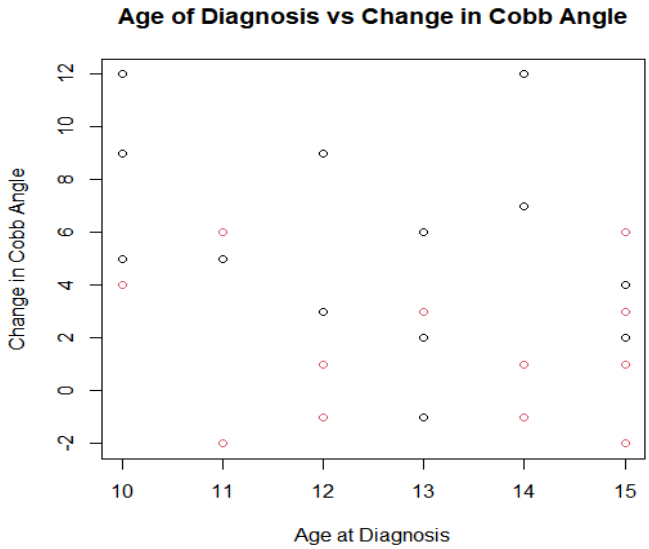

Figure 15. Age vs. change in cobb angle scatterplot (red dots indicate treatment group, black dots denote control group).

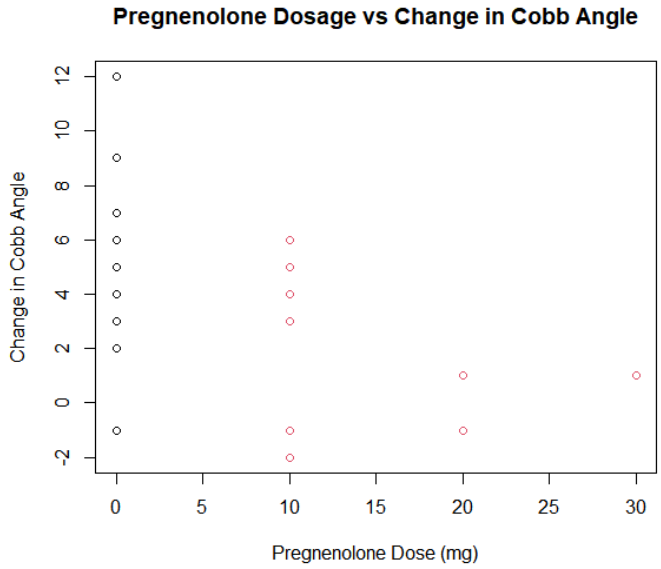

Figure 16. Pregnenolone dosage vs. change in cobb angle across all participants (red dots indicate treatment group and black dots indicate control group).

Limitations

Limitations inherent in the study design deserve consideration. While retrospective designs introduce the possibility of selection bias, this study aimed to mitigate this by inclusively selecting all patient records within a specific historical timeframe that met the inclusion criteria. However, it is crucial to note that male patients were excluded, thereby limiting the generalizability of the findings to females with a history of idiopathic scoliosis only.

The study involves a relatively small sample size, with only twenty-seven participants in total. If more data points or a stronger relationship could have been found, a more confident R-squared value could have potentially been calculated. From the results of this study, there is little evidence to support that there truly is a relationship between the age of

onset and the curve progression. In Figure 8 of the treatment group's graph, there are six points above the trendline, seven points below the trendline (two are at age 12 at −1), and one point on the trendline. In Figure 9 of the control group's graph, there are six points below the trendline, one point on the trendline, and six points above the trendline with a high standard deviation. Similar results are present in the combined group's trendline in Figure 10. There is a high standard error from the trendline, and a small R-squared equal to 0.0727. It is worth noting that the overall combined group experienced a negative slope at −0.6016. The graphs do not provide a strong relationship between the age of onset and the change in Cobb angle.

A further limitation to the study is the results from the normal distribution graph made in R-Studio. A histogram was used to plot the change in Cobb angle results as shown in Figure 17. The frequency was not normally distributed. Additionally, an asymptotic one-sample Kolmogorov–Smirnov test was used to analyze whether the change in Cobb angle was normally distributed. The *p*-value corresponding to the test was 0.00000000001253, indicating that the data are not normally distributed for the change in Cobb angle across all participants. From the linear analysis on the data, the following statistics are highlighted as follows. The formula for the linear regression (that corresponds with Excel's values) is y = −0.6016x +11.25. The residual standard error is 3.891 on 21 degrees of freedom. The R-squared statistic is 0.0727 (which matches with the value calculated in Excel). The F-statistic is 1.003 on 6 and 21 degrees of freedom. Most notably, the *p*-value is 0.4496. Due to the extremely large *p*-value, there is very little evidence to support that the age of onset/diagnosis of scoliosis has an impact on the change in Cobb angle.

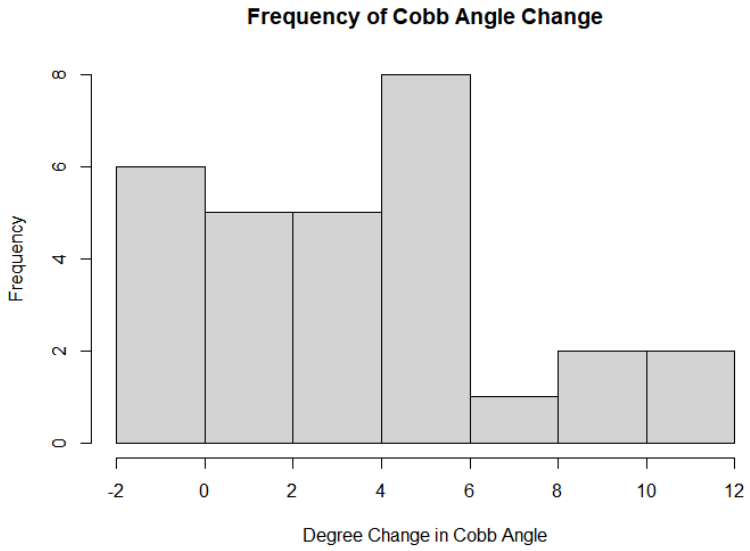

Figure 17. Histogram of change in cobb angle.

Concerning the observed Cobb angle differences, it is important to note that while the changes in Cobb angle were statistically significant, it is unknown based on the sample size and relatively small window of time as to whether these changes are clinically significant. Although the change may be within the margin of error for computerized Cobb angle measurements, it is possible that the magnitude of the Cobb angle change over a longer time period may show a larger Cobb angle change. This needs to be confirmed in future study.

Additionally, compliance with other scoliosis treatments like physical therapy exercises as well as how genetics influence the magnitude of curve development in each patient may have resulted in the outliers and weak correlation between age and Cobb angle development. Several patients in both groups were concurrently participating in some type of physical treatment for their curves. Some of the patients were prescribed bracing, some were performing a type of scoliosis-specific physiotherapy treatment like ScoliSMART, Schroth, or SEAS exercises, while others were on an observation plan. It is unknown how

the impacts of these physical treatments impacted the current results. However, patients in both groups were participating in physical treatment, not just one group or the other.

Although the different doses of pregnenolone did not appear to change the Cobb angle values in the treatment group only, this may have been due to the low sample size of patients taking 20 or 30 mg of pregnenolone compared to the number of patients taking 10 mg. Figures 11 and 12 show that there is a general decrease from the 10 mg to the 20 and 30 mg pregnenolone treatments, but the trend appears to plateau for the 20 and 30 mg pregnenolone therapy patients. When comparing the treatment group to the control group, they experienced overall a decrease in their Cobb angle change as shown in Figures 13, 14 and 16, with statistically significant *p*-values providing extremely strong evidence (0.000005039).

The insignificant *p*-values when comparing the treatment group to the dosage only do not show a relationship between pregnenolone dosage and Cobb angle change outcome, with *p*-values of 0.7349, 0.9743, and 0.9555 on log-logistic function with three parameters.

From the relationships analysis, clinical recommendations that can be extrapolated to female adolescent patients with low progesterone include to begin therapeutic treatment with pregnenolone. Recommendations for future studies include analysis of larger groups of patients within the pregnenolone treatment groups to provide a greater understanding of the dose–response relationship when therapy is administered.

It is also important to discuss the differences observed between Cobb angle progression among both groups. The treatment group progressed 1.64 degrees in one year, while the control group progressed 5.77 degrees. It is known that the risk of curve progression occurs chiefly between Risser stages 0–2, where bracing is typically recommended [1]. Morningstar also reported that scoliosis patients show lower salivary progesterone levels compared to non-scoliotic patients [16]. Progesterone serves to help regulate menstrual cycles, and perpetually lower progesterone can impact or delay menarche [22], which is a known risk factor for curve progression over a longer period of time [23]. From the results of this study, the administration of pregnenolone to patients resulted in increased salivary progesterone levels. Future research is needed to determine how the current results may be amplified if continued progression occurs over a longer time frame due to delayed skeletal maturation.

5. Conclusions

This study's results suggest that female patients with a history of adolescent idiopathic scoliosis may benefit from pregnenolone supplementation. Patients taking pregnenolone were shown to experience higher salivary progesterone levels and smaller scoliosis curve progression after 12 months. Both of these results were significantly different when compared to a scoliosis patient control group that did not participate in the pregnenolone therapy. It is unclear whether the progesterone increase was related to the rate of curve progression; nevertheless, these results warrant further prospective investigation into this topic.

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Systematic Review

Limited Intervention in Adult Scoliosis—A Systematic Review

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Abstract: Background/Objectives: Adult scoliosis is traditionally treated with long-segment fusion, which provides strong radiographic correction and significant improvements in health-related quality of life but comes at a high morbidity cost. This systematic review seeks to examine the literature behind limited interventions in adult scoliosis patients and examine the best approaches to treatment. Methods: This is a MEDLINE- and PubMed-based literature search that ultimately included 49 articles with a total of 21,836 subjects. Results: Our search found that long-segment interventions had strong radiographic corrections but also resulted in high perioperative morbidity. Limited interventions were best suited to patients with compensated deformity, with decompression best for neurologic symptoms and fusion needed to treat neurological symptoms secondary to up-down stenosis and to provide stability across unstable segments. Decompression can consist of discectomy, laminotomy, and/or foraminotomy, all of which are shown to provide symptomatic relief of neurologic pain. Short-segment fusion has been shown to provide improvements in patient outcomes, albeit with higher rates of adjacent segment disease and concerns for correctional loss. Interbody devices can provide decompression without posterior element manipulation. Future directions include short-segment fusion in uncompensated deformity and dynamic stabilization constructs. Conclusions: Limited interventions can provide symptomatic relief to adult spine deformity patients, with indications mostly in patients with balanced deformities and neurological pain.

Keywords: scoliosis; degenerative; deformity; limited intervention

1. Introduction

Degenerative lumbar scoliosis is a common spinal pathology estimated to have a prevalence of 35.5% in patients older than 60 and an incidence of 36.7% over 12 years [1]. While not all cases are symptomatic, they can present with complaints of chronic lumbar back pain and spinal stenosis, negatively impacting the quality of life for patients who suffer from scoliosis [1]. Multiple surgical approaches are possible for the treatment and correction of adult spinal deformities, along with the alleviation of associated symptoms such as back pain or radiculopathy. These range from decompressive procedures such as laminectomies or foraminotomies up to long spinal fusion constructs. Given the morbidity associated with long-level fusions and the associated exposures and recovery, limited approaches for the treatment of spinal deformity have become an attractive option for adult spinal deformity patients. In this systematic review, we examine the different approaches and surgical techniques utilized in the treatment of spinal deformity and associated symptoms, with an emphasis on limited approaches. We examine impacts on spinal alignments and patient-related outcomes, along with patient function following operative intervention.

2. Materials and Methods

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. This study does not have a registered protocol. We utilized PubMed and MEDLINE-indexed journals. We utilized the

search terms [(spine) AND ((deformity) NOT ((trauma) OR (fracture) OR (pediatric) OR (adolescent) OR (tumor) OR (metasta*))) AND (adult) AND ((((short-segment) OR (short)) AND (fusion)) OR (limited) OR ((laminectomy) OR (laminotomy) OR (foraminotomy)) OR (discectomy))]. Our initial search yielded 1085 results. We then proceeded to perform abstract screening with assessment of each record by a single reviewer, Z.J.M., with further record confirmation with reviewer S.T. Abstract screening excluded biomechanical studies, reviews, case reports, instructional courses, and expert opinions, in addition to studies examining congenital deformities, infectious etiologies (such as tuberculosis or pyogenic spondylodiscitis), rheumatological etiologies (such as ankylosing spondylitis), and cervical pathologies or instrumented fusion. Full-text screenings were used to exclude papers focusing solely on long-construct/segment spinal fusions. The screening process is summarized in Figure 1. After abstract and full-text screening, our final analysis consisted of 49 individual studies, with 1 Level II, 37 Level III, and 11 Level IV studies (Table 1).

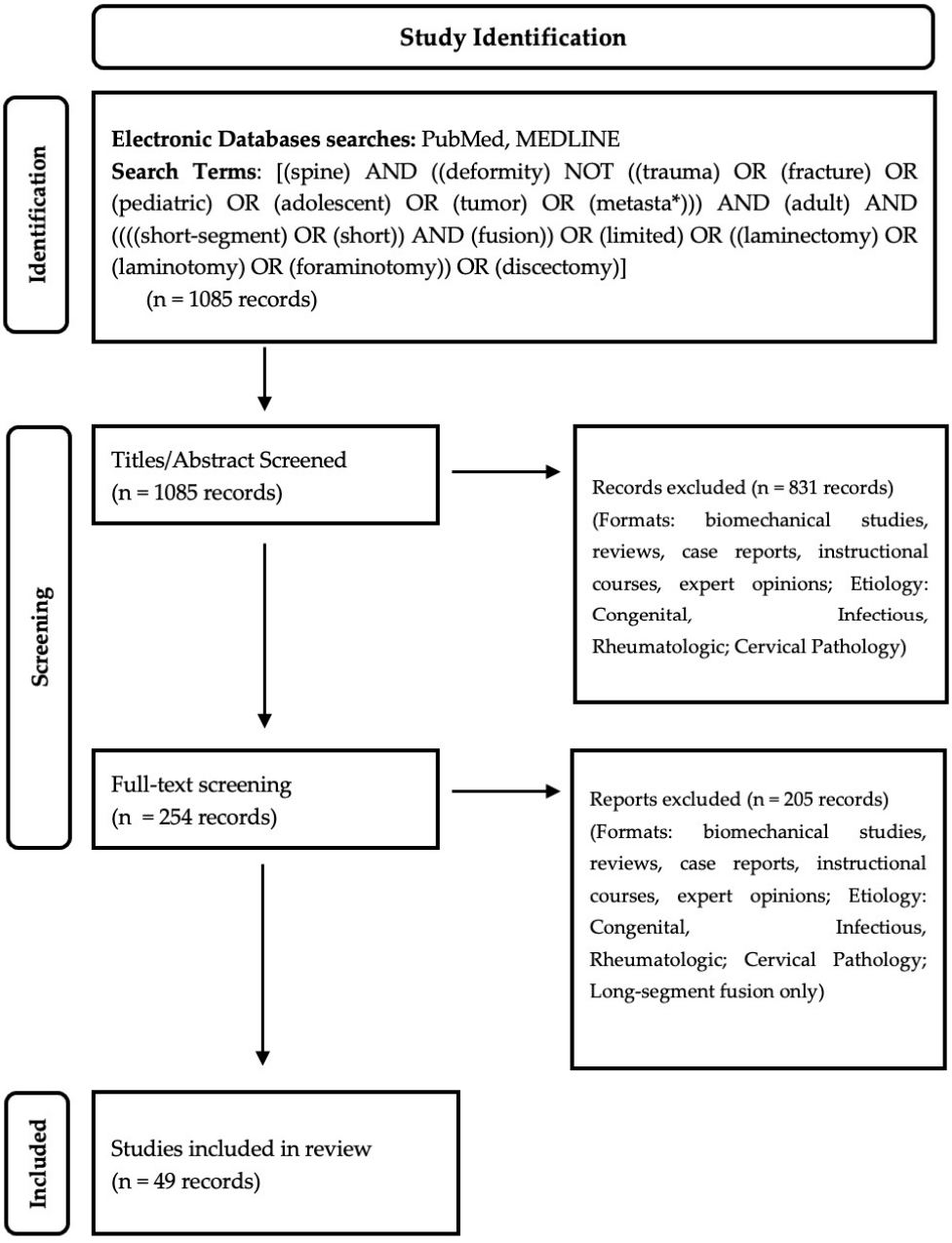

Figure 1. Systematic review flow diagram.

Table 1. List of included studies.

Author, Year	Study Design	*n*	Level of Evidence	Cohort	Intervention	Findings
Nakajima et al., 2022 [1]	Retrospective Cohort	26	III	Patients with adult spinal deformity	Three-level, Two-stage limited lumbar fusion	Significant improvements in coronal Cobb angle, C7 SVA, and PI-LL mismatch
Cho et al., 2008 [2]	Retrospective Cohort	50	III	Patients with degenerative lumbar scoliosis	Short fusion VERSUS Long fusion	Significantly better coronal Cobb correction, coronal imbalance, and lateral listhesis correction in long fusion cohort; higher rates of early complications in long fusion, adjacent segment disease in short fusion; no significant difference in post-operative ODI
Liu et al., 2009 [3]	Retrospective Cohort	112	III	Patients with degenerative lumbar scoliosis	Simple nerve decompression VERSUS short fusion and decompression VERSUS long fusion and decompression	Significantly greater improvement in lumbar scoliosis and lordosis in long fusion cohort over short fusion and simple decompression cohorts; significantly greater improvement in ODI in the long fusion cohort compared to the short fusion and simple decompression cohorts; increased rates of ASD in short fusion cohort—only 53.8% of patients symptomatic
Wang et al., 2016 [4]	Retrospective Cohort	108	III	Patients with degenerative lumbar scoliosis with associated lumbar stenosis	Simple nerve decompression VERSUS short fusion and decompression VERSUS long fusion and decompression	Significant differences between cohorts in post-operative coronal C7 plumb line, sagittal C7 plumb line, and rotational olisthesis; significant difference in post-operative final ODI between cohorts
Li et al., 2021 [5]	Retrospective Cohort	136	III	Patients with adult spinal deformity	Focal decompression VERSUS short-segment fusion VERSUS full scoliosis correction	Decompression and short fusion with significantly shorter surgical duration, less blood loss, shorter hospital stay; amongst MISDEF2 Class II patients, patients undergoing full correction had significantly higher rates of perioperative complications and revision surgery
Song et al., 2022 [6]	Retrospective Cohort	78	III	Patients with adult degenerative scoliosis	Short-segment limited fixation VERSUS long-segment radical fixation	No significant differences between cohorts in long-term complications and re-operations; long-segment group had significantly better coronal Cobb, lumbar lordosis, and sagittal balance; long-segment group had significantly higher implant-related complications

Table 1. *Cont.*

Author, Year	Study Design	*n*	Level of Evidence	Cohort	Intervention	Findings
Khalifé et al., 2023 [7]	Prospective Cohort	154	IV	Patients with scoliosis and lumbar stenosis	Lumbar decompression VERSUS short fusion and decompression VERSUS long fusion with deformity correction	Long fusion cohort with significant improvement in ODI, VAS, SF-12, SRS-30 scores at 2 years; significant increases noted in fractional curve Cobb in short fusion and C7 coronal tilt in decompression cohorts; long fusion had highest overall complication rates and revision rates
Schairer et al., 2013 [8]	Retrospective Cohort	836	III	Patients with adult spinal deformity	Spine fusion	Higher rates of readmission in patients with long fusion; risk factors for readmission were longer fusion length, higher illness severity, and medical comorbidities
Hart et al., 2013 [9]	Cross-Sectional	93	III	Patients who previously underwent lumbar spine fusion	Lumbar spine fusion	LSDI scores significantly different between 1-level and 5-level arthrodesis group; LSDI and ODI significantly correlated
Hart et al., 2014 [10]	Prospective Cohort	62	II	Patients with lumbar degenerative disease or spinal deformity	Lumbar spine fusion	All cohorts saw significant decreases in ODI following surgery; patients undergoing 1-level and 5+-level surgery saw significant improvements in physical composite score; patients with 1-level fusion saw significant decrease in LSDI; 3, 4, and 5+-level saw nonsignificant increase in LSDI
Isaacs et al., 2010 [11]	Prospective Cohort	107	IV	Patients with degenerative scoliosis	Extreme lateral interbody fusion ± posterior fixation	12.1% major complication rate, which compares favorably to previous literature
Pateder et al., 2008 [12]	Retrospective Cohort	361	III	Patients with spinal deformity	Deformity correction	Strong association between ASA score and mortality; no association between levels of fusion and mortality
Frazier et al., 1997 [13]	Prospective Cohort	90	IV	Patients with spinal deformity and spinal stenosis	Laminectomy	Pre-operative scoliosis is associated with decreased improvement in back pain following laminectomy
Minamide et al., 2017 [14]	Prospective Cohort	122	III	Patients with degenerative lumbar scoliosis with associated lumbar stenosis	Microendoscopic laminectomy or foraminotomy	Significant improvement in VAS-low back pain; clinical outcomes in foraminal stenosis related to pre-op Cobb angle and scoliosis progression
Aoki et al., 2015 [15]	Retrospective Cohort	52	III	Patients with degenerative lumbar disease	1 or 2 level TLIF	Significant correlation between post-operative PI-LL mismatch and VAS scores for low back pain, lower extremity pain, and numbness

Table 1. *Cont.*

Author, Year	Study Design	*n*	Level of Evidence	Cohort	Intervention	Findings
Bari et al., 2021 [16]	Retrospective Cohort	149	III	Patients with degenerative lumbar disease	Fusion surgery ≤ 4 levels	Hypolordotic group had increased odds of 1-year revision surgery; linear correlation between pre-operative pelvic incidence and post-operative lordosis distribution
Lugue et al., 2020 [17]	Retrospective Case-Control	119	III	Patients with degenerative lumbar disease	L4/L5 PLIF	Significant increase in local lordosis, correlated with increase in lumbar lordosis; high PI-LL and SVA cohorts had decreased clinical outcomes
Pugely et al., 2014 [18]	Prospective Cohort	15,668	III	Patients undergoing lumbar spine surgery	Lumbar spine surgery	Lowest risk of readmission with discectomy and highest risk with deformity surgery
Kapetanakis et al., 2017 [19]	Prospective Cohort	76	III	Patients with lumbar disc herniation	Percutaneous transforaminal endoscopic discectomy	Significant improvements seen in all domains of SF-36 scores
Kim et al., 2021 [20]	Retrospective Cohort	100	IV	Patients with lumbar disc herniation	transforaminal endoscopic lumbar foraminotomy and discectomy VERSUS interlaminar contralateral endoscopic lumbar foraminotomy and discectomy	Interlaminar approach associated with reduced rates of post-operative dysesthesia; both cohorts had favorable clinical outcomes
Bai et al., 2017 [21]	Prospective Cohort	39	III	Patients with lumbar disc herniation	Inter-vertebral approach VERSUS trans-iliac approach	No significant differences in operative time and post-operative VAS scores between the cohorts
Telfeian et al., 2018 [22]	Case Series	4	IV	Patients with lumbar disc herniation in setting of lateral lumbar listhesis	Percutaneous transforaminal endoscopic discectomy	Most patients saw improvements in ODI and VAS sustained for 1 year follow-up
Madhavan et al., 2016 [23]	Retrospective Cohort	16	III	Patients with scoliotic deformity and unilateral radicular pain secondary to foraminal stenosis	Endoscopic foraminal decompression surgery	Significant improvement in VAS for radicular leg pain post-operatively

Table 1. *Cont.*

Author, Year	Study Design	*n*	Level of Evidence	Cohort	Intervention	Findings
Brodke et al., 2013 [24]	Retrospective Cohort	90	III	Patients with lumbar stenosis in setting of spinal deformity	Interspinous spacer VERSUS laminectomy only VERSUS laminectomy and short-segment fusion	Significantly higher recurrence rate in interspinous spacer cohort; laminectomy alone cohort had highest 5-year survival on Kaplan-Meier analysis
Hasan et al., 2019 [25]	Prospective Cohort	45	III	Patients with degenerative spinal deformity with associated lumbar stenosis	Full-endoscopic VERSUS minimally invasive unilateral laminotomy for bilateral decompression	Endoscopic cohort had significantly shorter hospital stay, lower adverse events, and improved early ODI scores
Uribe et al., 2017 [26]	Retrospective Cohort	84	III	Patients undergoing adult spinal deformity correction	Minimally invasive VERSUS open approaches	MIS cohort had shorter construct lengths, lower blood loss, and shorter hospital length of stay
Deukmedjian et al., 2013 [27]	Retrospective Cohort	27	III	Patients who underwent surgical correction of adult degenerative scoliosis	Lumbar interbody fusion with augmentation dependent on deformity severity	Most cohorts showed improvements in radiographic and clinical outcomes; patients who were undertreated did not show significant improvements
Park et al., 2013 [28]	Retrospective Cohort	105	IV	Patients with adult lumbar degenerative scoliosis with a coronal Cobb angle of <40°	Decompression and instrumented fusion	Significant improvements noted in ODI, SF-36, and VAS scores post-operatively
Liang et al., 2020 [29]	Retrospective Cohort	58	III	Patients with adult degenerative scoliosis	Deformity correction surgery	Patients with limited correction in setting of sagittal imbalance had significantly worse radiographic outcomes but demonstrated no significant differences in coronal Cobb angles, ODI, or VAS
Amara et al., 2019 [30]	Retrospective Cohort	99	III	Patients with adult scoliosis	Fractional curve limited fusion VERSUS instrumentation to lower thoracic spine VERSUS instrumentation to upper thoracic spine	Fractional curve treatment with significantly lower rates of medical complications, lower blood loss, shorter hospital stays, and reduced discharge to acute rehab; Significantly increased risk of extension surgery

Table 1. *Cont.*

Author, Year	Study Design	*n*	Level of Evidence	Cohort	Intervention	Findings
Chou et al., 2018 [31]	Retrospective Cohort	118	III	Patients with adult scoliosis	Minimally invasive VERSUS open fractional curve correction	MIS approach with significantly less instrumented and decompressed levels; similar clinical outcomes in both cohorts
Kasliwal et al., 2012 [32]	Retrospective Cohort	60	III	Patients with previous short-segment fusion for adult scoliosis VERSUS patients undergoing initial operation	Scoliosis deformity correction	No significant differences in complications, perioperative morbidity/mortality, and clinical outcomes
Zurbriggen et al., 1999 [33]	Case series	40	IV	Patients with degenerative lumbar scoliosis	Posterior instrumentation and fusion	Improvements seen in radiographic and clinical outcomes following surgical intervention
Feng et al., 2015 [34]	Prospective Cohort	159	III	Patients with isthmic spondylolisthesis	Posterolateral fusion VERSUS Posterior lumbar interbody fusion	PLIF better at augmenting lumbar lordosis and aiding with the restoration of spinopelvic parameters
Johnson et al., 2013 [35]	Retrospective Cohort	22	III	Patients with degenerative lumbar disc disease	Extreme lateral interbody fusion	Significant improvements in segmental lordosis, scoliotic Cobb angle, and clinical outcomes
Anand et al., 2008 [36]	Retrospective Cohort	12	IV	Patients with degenerative lumbar scoliosis	Circumferential MIS fusion of deformity	Post-operative improvements seen in coronal Cobb angle, VAS score, and TIS score.
Hasegawa and Homma 2003 [37]	Case Series	23	IV	Patients with degenerative lumbar kyphoscoliosis	Multi-level posterior lumbar interbody fusion	Significant improvements in JOA score, Cobb angle, and torsional deformity noted post-operatively
Dakwar et al., 2010 [38]	Retrospective Cohort	25	IV	Patients with adult degenerative deformity	Lateral interbody fusion via transpsoas approach	VAS and ODI improvements seen post-operatively
Lee et al., 2016 [39]	Prospective Cohort	32	III	Patients with adult degenerative deformity	Lateral and Anterior lumbar interbody fusion with posterior fixation	ALIF levels with greater post-op segmental lordosis compared to LLIF levels; also noted greater increase in segmental lordosis; sagittal parameters all improved post-operatively; see worse parameters at follow-up, but still improved compared to pre-op

Table 1. *Cont.*

Author, Year	Study Design	*n*	Level of Evidence	Cohort	Intervention	Findings
Ahlquist et al., 2018 [40]	Retrospective Cohort	164	III	Patients undergoing lumbar fusion	Anterior VERSUS Lateral VERSUS transforaminal VERSUS posterior lumbar interbody fusion	ALIF and LLIF with significant improvements in segmental lordosis, anterior and posterior disc heights, and foraminal height; ALIF and LLIF outperformed PLIF in improvements seen post-op; ALIF only technique to significantly increase proportion of PI-LL < 10°
Anand et al., 2010 [41]	Retrospective Cohort	28	IV	Patients with adult scoliosis	Minimally invasive correction of deformity, 3+ levels	Improvements in VAS, TIS, ODI, and SF-36 scores; lower perioperative morbidity
Lo et al., 2015 [42]	Retrospective Cohort	973	III	Patients with adult degenerative deformity	Single-level fusion	Mini-Open and MIS with lower EBL, VAS, LOS, and infections; longer surgery time for both
Seng et al., 2013 [43]	Retrospective Cohort	80	III	Patients with adult degenerative deformity	Open VERSUS minimally invasive transforaminal lumbar interbody fusion	Perioperative variables—MIS had higher fluoroscopic time, less blood loss and morphine usage, and less time to ambulation and less LOS; all groups with significant improvements in patient-reported outcomes—no significant differences between groups; all groups with significant fusion by 5 years—open TLIF had nonsignificantly higher rates within 6 months and 2 years
Alimi et al., 2015 [44]	Retrospective Cohort	23	III	Patients with single-level unilateral vertical foraminal stenosis with radicular pain	Single-level extreme lateral interbody fusion	Significant increases in foraminal height and disc height; significant decrease in coronal Cobb, VAS-Leg, VAS-Buttock, and VAS-Back
Tani et al., 2022 [45]	Retrospective Cohort	36	III	Patients with adult spinal deformity	Anterior column reconstruction, lateral lumbar interbody fusion, and percutaneous pedicle screw fixation	Patients had significantly increased lumbar lordosis, thoracic kyphosis, and segmental disc angles after intervention; significantly decreased PI-LL and spino-vertebral angle; significant increases in disc heights, foraminal height, and cross-sectional area; decreases in ligamentum flavum thickness and disc bulge thickness; significant decrease in ODI
Elsamadicy et al., 2017 [46]	Retrospective cohort	874	III	Patients with adult spinal deformity	Spinal fusion alone VERSUS spinal fusion with laminectomy	Laminectomy cohort with increased blood loss, blood transfusions, and durotomies intra-op; higher rate of ICU post-op

Table 1. *Cont.*

Author, Year	Study Design	*n*	Level of Evidence	Cohort	Intervention	Findings
Kanayama et al., 2007 [47]	Retrospective cohort	56	III	Patients with adult spinal deformity	Graf ligamentoplasty	No significant differences in segmental lordosis—see a reduction in range of motion at the operative level; significant improvement in JOA scores from pre-op to follow-up. Unfavorable outcomes in degenerative scoliosis and lateral listhesis
Di Silvestre et al., 2010 [48]	Retrospective cohort	29	III	Patients with adult spinal deformity	Dynamic Stabilization without fusion	Significant improvements in ODI, RDQ, and VAS Back and Leg; significant improvements in scoliosis, Cobb angle, lateral listhesis, and anterior vertebral translation
Zhao et al., 2020 [49]	Retrospective cohort	16	III	Patients with adult lumbar degenerative scoliosis	Short-segment decompression and fusion WITH proximal segment stabilization	Significant changes seen in radiographic measures as well as in VAS Back + Leg and ODI

Data extraction was then performed by a single reviewer, Z.J.M. Data extracted for each study included study author, year of publication, study type, level of evidence, cohort size, patient population, intervention applied, and outcomes/findings. The main outcomes assessed in each study broadly included radiographic measurements (such as local and lumbar lordosis, sagittal vertebral alignment, spino-pelvic measurements including pelvic incidence, pelvic tilt, and sacral slope), symptomatic measures (such as the Visual Acuity Scale (VAS)), quality of life measures (such as the Oswestry Disability Index (ODI) or the Short Form assessments (SF-12/SF-36)), complications (such as proximal junctional kyphosis, instrument failure, and adjacent segment disease), and re-operation rates. Given the broad scope of this review and the varied patient populations covered therein, no meta-analysis of such data was able to be performed. A bias assessment of the included studies was performed using the Risk of Bias in Non-randomized Studies of Intervention (ROBINS-I) assessment tool (Supplementary Table S1).

Of note, this study focuses on limited interventions in adult spinal deformity; therefore, it becomes imperative to define what a limited intervention can look like. Cho and Kim propose a very succinct and apt definition: a limited/short intervention is one that remains confined to the deformity, not exceeding the deformity's upper affected vertebra or lower affected vertebra [2]. Thus, limited interventions can take multiple forms—from a single-level decompression or decompression and fusion to a multi-level decompression and fusion. While screening studies for inclusion in this analysis, we utilized an initial limit of 6 instrumented segments as an upper bound for a "short-segment" intervention and then further corroborated this with imaging to determine if the Intervention only spanned the affected vertebral levels.

3. Results

3.1. Long-Segment Fusion: Advantages and Drawbacks

Long-segment instrumented fusion, with constructs spanning the entire deformity length, has a few advantages when compared to more limited interventions. Such constructs are considered superior at radiographic correction, with multiple studies showing better post-operative radiographic outcomes in patients with long-segment fusion compared to more limited fusion. Cho et al. demonstrated that long-segment fusions (average 6.5 levels, range 4–9) had significantly greater changes in radiographic parameters, such as coronal Cobb angle, lumbar lordosis (LL), and sagittal balance (C7 plumb line), compared to more limited interventions (average 3.1 levels, range 1–5) [2]. Liu et al. found that long-segment constructs (>3 levels) resulted in significantly greater improvements in lumbar lordosis and coronal Cobb angles compared to more limited interventions ($\leq$3 levels) [3]. Wang et al. demonstrated that more invasive, long-segment fusions (average 4.9 $\pm$ 3.1 levels) had significantly higher improvements in post-operative sagittal and coronal balance [4]. More recently, Li et al. found that full correction (average 8.1 $\pm$ 3 levels) resulted in significantly increased Cobb angle correction compared to short-segment fusion and decompression (average 2.0 $\pm$ 1.1 levels) [5]. Song et al. found in a cohort followed for 4 years that Cobb angles, lumbar lordosis, sagittal balance, and coronal balance were all significantly better following long-segment fusion (average 7.9 $\pm$ 2.1 levels) [6]. Khalifé et al. noted that long-segment constructs were significantly better at fixing Cobb angles, fractional curves, lumbar lordosis, pelvic incidence-lumbar lordosis (PI-LL) mismatch, pelvic tilt (PT), and spinosacral angles (SSA) [7]. Overall, long-segment instrumented fusion is better at restoring coronal and sagittal balance, while limited interventions remain ill-equipped to restore spinal balance.

However, while long-segment fusion is well-equipped to improve coronal and sagittal balance, it comes at the cost of high perioperative morbidity and disability. Liu et al. noted that re-operation rates were higher in their long fusion cohort compared to shorter constructs, secondary to hardware failure [3]. Cho et al. expanded on these findings, demonstrating that long-segment constructs were associated with higher rates of non-union and implant-related complications, along with higher rates of re-operation secondary to [2].

Song et al. noted significantly higher rates of complications, including nonunion, in patients undergoing long-segment instrumented fusion, findings affirmed by Khalifé et al. [6,7]. Schairer et al. demonstrated a higher risk of readmission in patients who underwent long-segment fusion [8]. While examining patients within a single deformity class, Li et al. noted significantly increased rates of complications and re-operations with long-segment constructs, with long-segment constructs suffering primarily from implant failures and proximal junctional kyphosis [5]. Hart et al. authored two studies examining the impact of instrumented levels on lumbar stiffness, as measured through the Lumbar Stiffness Disability Index (LSDI) [9,10]. In a cross-sectional study, they noted significantly lower LSDI scores in patients who underwent 1-level arthrodesis versus those who underwent 5-level arthrodesis [9]. Their follow-up study demonstrated that patients who underwent 1-level arthrodesis saw a significant decrease in LSDI, while those in the 4- and 5-level cohorts saw nonsignificant increases in LSDI [10]. Isaacs et al. noted that an increase in instrumented segments was significantly correlated with an increase in complications [11]. Conversely, Pateder et al. noted no increase in mortality with increasing fusion length [12]. Overall, long-segment fusion is associated with increased perioperative morbidity in terms of post-operative complications, readmissions, re-operations, and lumbar stiffness-related disability. Thus, limited interventions, while unable to achieve as powerful a radiographic correction, are an attractive option due the lower associated perioperative morbidity.

3.2. Patient Selection

While limited interventions are inadequate to provide proper sagittal and coronal alignment, their lower associated perioperative morbidity and disability lend themselves well to consideration in certain patient populations. The primary means of stratification used to determine the appropriateness of limited surgical interventions is based on a patient's pre-operative radiographic alignment. Multiple studies have examined radiographic alignment in both limited decompressive and limited fusion procedures. In terms of decompression, Frazier et al. examined outcomes following laminectomy in patients with adult scoliosis, noting that increased pre-operative scoliosis was associated with lesser improvements in back pain upon follow-up [13]. Minamide et al. examined outcomes in patients undergoing endoscopic decompression, noting reduced symptomatic improvement in patients with a pre-operative Cobb angle of greater than 20°, along with an increasing pelvic incidence-lumbar lordosis (PI-LL) mismatch [14]. While patients still see symptomatic improvements, malalignment reduces the effects of surgery. These trends are also noted in limited fusions: Aoki et al. noted that increasing PI-LL mismatch was correlated with worse post-operative visual acuity (VAS) scores for low back pain (LBP), lower extremity pain, and lower extremity numbness [15]. Similarly, Bari et al. analyzed the impact of lordosis distribution, noting increased post-operative pelvic tilt and PI-LL mismatch, along with increased revision rates, in hypolordotic patients [16]. Bari also noted that increased pre-operative pelvic incidence was a risk factor for post-operative hypolordosis [16]. Lugue et al. noted that adult deformity patients with elevated PI-LL and sagittal vertebral axis (SVA) post-operatively had worse clinical outcomes, with lower Japanese Orthopaedic Association (JOA) and Short Form 36 (SF-36) scores [17]. Overall, patients with uncompensated or unbalanced deformities tend to not see as powerful symptomatic improvements as those with balanced deformities following limited interventions. Thus, such interventions are more appropriate for patients with balanced deformities.

In this review, we discuss two broad categories of interventions: decompressive procedures, including discectomy, laminectomy, and foraminotomy; and fusion procedures, including interbody fusions. These two procedures are best equipped for the treatment of differing deformity symptoms. Liang et al. mention the classification of patients based on their symptomatic complaints into two categories: neurogenic pain, resulting from central canal, lateral recess, and foraminal stenosis; and axial pain, resulting from muscle fatigue secondary to sagittal imbalances [4]. Treatment strategies for these two distinct problems differ. Patients with neurogenic symptoms often present with radicular or cauda

equina-like pain secondary to the central canal, lateral recess, and foraminal stenosis [3,4]. In such patients, decompressive procedures can be considered, with simple nerve root decompression reserved for purely radicular pain and posterior element manipulation reserved for cases with segmental canal stenosis [3]. Patients with axial pain present with low back pain secondary to muscle pain. Such symptoms can be divided into two separate types: primary imbalance due to malalignment and secondary imbalance due to stenosis, which leads to paraspinal muscular fatigue and loss of lumbar lordosis [4]. In patients with a primary, uncompensated deformity, long fusion is necessary for treatment of the deformity and restoration of spina alignment, which will result in the resolution of symptoms [3,4]. Wang et al. discuss treatment in patients with compensated deformities—such patients often suffer more from neurogenic symptoms than axial-based symptoms, and axial symptoms are often secondary to neurological deformity; thus, such patients can also undergo either decompression or fusion for symptomatic treatment, depending on the symptoms seen [4]. One other consideration to take note of is the presence of cephalad-caudad directional stenosis, colloquially referred to as "up-down stenosis" [30]. Such patients require fusion with interbody support for adequate decompression [30]. Based on the aforementioned considerations, we can begin to develop a treatment algorithm for spinal deformity—simple neurological complaints with radicular pain are more appropriately treated with decompressive procedures. In cases of compensated deformity and/or cephalad-caudad stenosis, then fusion becomes necessary for symptomatic treatment.

3.3. Decompression

Decompressive procedures are among the least-invasive procedures available for the surgical treatment of spinal deformities. Discectomy provides a minimally invasive technique to treat neurogenic symptoms secondary to disc herniation. Pugely et al. found that discectomy carries the lowest re-admission rates in spine surgery, in stark contrast with deformity correction [18]. Thus, discectomy presents an attractive option for limited intervention in adult deformities. The overwhelming majority of papers found in this analysis examined one specific approach to discectomy—percutaneous transforaminal endoscopic discectomy. Kapetanakis et al. demonstrated that this approach leads to significant improvements in patient-reported outcomes (PROs) such as the visual analog scale (VAS) and Oswestry Disability Index (ODI), with patients experiencing improved quality of life following discectomy [19]. Some studies have further expanded upon surgical techniques noted, devising novel approaches to discectomies, especially at the lumbosacral junction. Kim et al. proposed an interlaminar contralateral endoscopic discectomy with overall similar outcomes to transforaminal approaches, with lower rates of post-operative dysesthesia noted in the inter-laminar approach [20]. Meanwhile, Bai et al. demonstrated a trans-iliac approach for approaching such pathology, with similar outcomes noted to open approaches [21]. Telfeian et al. examined the applicability of discectomy in adult deformity in patients previously treated for lateral vertebral subluxation, a common finding in adult degenerative scoliosis, showing clinically significant improvements in both ODI and VAS scores [22]. Methods such as transforaminal endoscopic discectomy benefit from minimal disruption to the spinal posterior elements, utilizing a minimally invasive foraminotomy to access the affected disc, leaving the ligaments and musculature of the spine mostly intact [19,22]. While more studies are needed on the topic, discectomy is appropriate in patients with deformities who suffer from radicular symptoms due to herniated discs, and such treatment can provide symptomatic relief and clinical improvement in affected patients.

Discectomies are only a part of the spine surgeon's toolkits; surgeons can also perform more involved surgical procedures such as laminectomies and foraminotomies, with manipulation of the posterior spinal anatomy for further decompression of the spinal canal. Overall, such procedures are associated with symptomatic improvement, with a study by Madhavan et al. showing significant improvements in patient-reported outcomes, such as VAS, following foraminotomy [23]. Brodke et al. noted that compared to less invasive

modalities, such as interspinous spacers, laminectomies show better improvements in VAS, lower post-operative mortality, and recurrence, along with similar improvements in VAS for laminectomy and fusion patients [24]. Minamide et al. noted that patients undergoing endoscopic decompression had overall significant improvements in clinical outcomes, such as JOA scores [14]. Hasan et al. further expanded on the role of minimally invasive or endoscopic interventions in decompression, finding similar outcomes between both endoscopic and MIS interventions, albeit with lower complication rates in endoscopic interventions [25]. Decompressive procedures can provide symptomatic relief and clinical improvement in patients suffering from neurogenic pain, relieving pressure on neural structures. However, in some cases, especially secondary to deformity resulting in posterior element impingement of neural structures, realignment becomes necessary to fully decompress the spine.

3.4. Fusion

As previously mentioned, decompression is only appropriate for neurogenic symptoms resulting in cauda equina- or radicular-pattern pain [14,25]. However, axial pain resulting from mechanical instability will remain relatively unchanged as a result of decompressive procedures [14]. In such cases, spinal fusion, in addition to decompression, may become necessary. While decompressive procedures are well-equipped to provide some decompression of posterior neural elements, in certain cases, realignment becomes necessary for full neural decompression. In addition, in axial pain, which results from muscular fatigue from sagittal imbalances, fusion can provide some level of sagittal correction [4]. In cases of compensated deformity, where limited fusion constructs are most appropriate, fusion can stabilize decompression levels and prevent further deformity occurrence [3,4]. In comparison to purely decompressive interventions, decompression and fusion surgeries have a larger body of literature regarding their use. Fusion constructs often consist of interbody fusion and/or posterior spinal instrumentation, allowing for both the restoration of spinal radiographic parameters and rigid fixation of the deformity. This review focuses on limited interventions and thus will focus on short-segment fusions, which have been defined as spanning only the affected vertebral segments, with the upper instrumented vertebra and lower instrumented vertebra falling within or at the ends of the deformity [2]. Such segments need not span only the deformity—rather, they can also span symptomatic levels, with levels responsible for neurogenic or stenotic symptoms undergoing decompression and fusion as well.

3.4.1. Short-Segment Fusion: Does It Provide Relief?

As previously noted, long-segment fusion has been shown to have a stronger ability to provide both sagittal and coronal correction of spinal deformity compared to short-segment fusion and decompression constructs [2–7]. However, long-segment instrumented fusion has also been shown to carry a significant burden of post-operative morbidity and disability in comparison to more limited interventions [2,3,5–11]. Thus, in cases of compensated deformity, where given a balanced deformity, sagittal correction is not the primary aim of treatment, short-segment fusion and decompression can provide adequate symptomatic relief [4]. When juxtaposed with long-segment constructs in the setting of balanced deformities, short-segment constructs have been shown to provide similar clinical outcomes, both with regards to symptomatic improvement and functional outcomes. Numerous studies demonstrate similar functional and symptomatic outcomes between short-segment and long-segment instrumented fusion. Song et al. noted no significant differences in VAS-Back and VAS-Leg scores between a long-segment and short-segment cohort [6]. Khalifé et al. echoed these results: while they found a significantly lower VAS score for radicular pain with long fusion, they noted similar VAS-Back, ODI, and Scoliosis Research Society (SRS)-30 scores [7]. Liu et al. also noted similar outcomes in ODI following long-segment and short-segment fusions, albeit with greater improvement in ODI with long-segment fusions [3]. Wang et al. showed similar improvements in ODI

and SRS-22 scores, albeit between a compensated cohort receiving short-segment fusion and a decompensated cohort receiving long-segment fusion [4]. Uribe et al. showed that despite having short construct lengths, MIS techniques could result in similar clinical and radiographic outcomes to open surgery with lesser re-operation rates, blood loss, and hospital stay [26]. Deukmedjian et al. noted that in patients with compensated deformity, utilizing less invasive means and constructs led to significant improvements in ODI and VAS scores [27]. Cho et al. demonstrated that short- and long-segment fusion achieve similar changes in ODI post-operatively [2]. Park et al. demonstrated that short-segment fusion in patients with coronal Cobb angles of 40° or less leads to significant improvements in ODI, VAS, and SF-36 scores [28]. Nakajima et al. noted significant improvements in ODI, JOA score, and Numerical Rating (NRS) score following short-segment fusion [1]. Given the aforementioned body of evidence, short-segment instrumented fusion, while underpowered to provide radiographic realignment, shows equivalent and acceptable patient-related outcomes to long-segment fusion in patients with compensated deformities in adult scoliosis.

3.4.2. Role in Uncompensated Spinal Deformity?

We previously mentioned the concepts of spinal balance and its role in patient selection for limited intervention. The traditional literature has demonstrated that short-segment fusion. may not demonstrate adequate patient outcomes following intervention. Nakajima et al. found that while short-segment surgery saw overall improvements in PROs and radiographic outcomes, measurements such as PI-LL mismatch remained high, and patients who required re-operation often had pre-operative uncompensated deformities such as lumbar kyphosis [1]. Deukmedjian et al. noted that surgical undertreatment for larger deformities can lead to worsening sagittal balance [27]. Given the risks of progression and future re-operation, the traditional viewpoint has remained. Recently, some studies have examined outcomes in patients with decompensated deformities who underwent short-segment instrumented fusion. Liang et al. examined outcomes in deformity patients with limited sagittal alignment correction versus full correction and concluded that despite worse sagittal alignment in the limited correction group, clinical outcomes such as ODI and JOA scores did not differ significantly [29]. However, the literature supporting this view is novel and thus limited, so no conclusions can be drawn regarding short-segment constructs in uncompensated deformity. Thus, short-segment instrumented fusion in adult spinal deformity patients is currently most appropriate for non-neurogenic pain in a compensated/balanced spine, although future studies may clarify its use in uncompensated deformities.

3.4.3. Fractional Curve Treatment: A Means of Foraminal Decompression

Some specific approaches and variations to short-segment instrumented fusion exist in the literature. Traditional treatment of scoliosis focuses on correction of the primary curve, with instrumentation spanning the apex of the primary curve. One treatment approach surgeons can utilize is the correction of the fractional curve, which represents the secondary scoliotic curve at the lumbosacral junction and can be a source of neurogenic pain secondary to loss of foraminal height [29]. Amara et al. compared outcomes in adult scoliosis patients between fractional curve correction versus fusion to the lower or upper thoracic spine [30]. They found that while longer fusion constructs were better at providing radiographic correction, fractional curve treatment led to overall lower blood loss, length of hospital stay, medical complications, and non-extension revision operations [30]. A study by Chou et al. examined differences in approaches utilized in fractional curve correction, comparing an open approach versus a minimally invasive (MIS) approach [31]. Their findings indicated that overall, MIS approaches resulted in lower levels of blood loss and greater improvements in VAS Leg scores, which are impacted by neurogenic pain, despite fewer patients undergoing nerve root decompression [31]. Fractional curve treatment can provide symptomatic relief while reducing perioperative morbidity in comparison to traditional techniques.

3.4.4. Short-Segment Fusion: Potential Pitfalls?

While short-segment fusion has been shown to provide similar clinical outcomes to long-segment fusion with reduced perioperative morbidity, one of the most concerning complications of shorter constructs remains adjacent segment disease, with increased degeneration seen in the remaining curve [2]. Both Liu and Cho demonstrated that short-segment fusion had increased rates of adjacent segment disease, albeit not attaching any significant statistics to these findings [2,3]. Song et al. noted an increased rate of adjacent segment disease in short-fusion constructs, although this did not reach significance [6]. Interestingly, Khalifé et al. noted a higher rate of adjacent segment disease in the long fusion cohort, although no significance was able to be determined [7]. One item to note is the difference between radiographic and clinical adjacent segment disease. Song et al. noted that out of 14 patients with adjacent segment disease, only 4 (28.57%) had clinical symptoms [6]. Cho et al. noted only adjacent segment disease patients with clinical symptoms, noting only proximal disease in short fusions [2]. Liu et al. defined adjacent segment disease based on radiographic findings but noted that patients with radiographic findings had significant clinical complaints [3]. Overall, the evidence presented in this review remains mixed—while most studies show a higher incidence of adjacent segment disease, there are not much data on the significance of these findings and on whether radiographic disease leads to clinical findings. More data are needed to provide clarity on the matter.

One concern with short-segment fusion concerns the progression of deformity following fusion. Amongst the previously stated studies, those by Song, Liu, Khalifé, and Nakajima all contained data regarding differences in radiographic outcomes upon extended follow-up [1,3,6,7]. Liu et al. noted that patients undergoing short-segment fusion demonstrated a significant loss in lumbar lordosis at final follow-up compared to pre-operatively and some progression in Cobb angle as well, although there were approximately 6 and 5 years between the time points measured, respectively [3]. Nakajima et al. noted some correctional loss at follow-up but noted that the median loss was extremely small, in the single digits [1]. Song et al. noted some loss of radiographic correction in their cohort, while the long-segment fusion cohort better maintained correction over 5 years [6]. Most of the studies quoted show some progression of disease and loss of correction with time, thus raising concerns for future re-operations. However, Nakajima et al. note that the amount of Cobb angle progression seen after short-segment fusion is similar to natural progression, arguing that short-segment fusion does not lead to accelerated degeneration [1]. Moreover, Song et al.'s data demonstrated that correctional loss still resulted in better radiographic alignment in terms of Cobb angles and lumbar lordosis in short-segment fusion, albeit with loss of coronal and sagittal balance [6]. Overall, while studies do show loss of correction with short-segment fusion over time, the absolute loss over time remains in the single digits and often corresponds to the natural progression of the disease.

Given the potential for correction loss, one question that arises is the impact of short-segment constructs on future revisions. A study by Kasliwal et al. examined outcomes in patients with adult scoliosis following deformity correction, comparing patients undergoing re-operation with previous short-segment instrumented fusion with patients undergoing their first spinal procedure [32]. While patients with a previous operation had a near-significantly higher number of instrumented levels and higher blood loss, overall there were no significant differences between the two cohorts [32]. Both cohorts had similar outcomes in terms of both radiographic and clinical outcomes between the two cohorts. In addition, there was no significant difference in the post-operative complication rates between the re-operative and control cohorts [32]. Thus, while there are some differences in surgical parameters, re-operative patients have similar outcomes to first-time operative patients.

3.4.5. Interbody vs. Posterior Instrumentation Only

Historically, pedicle screw instrumentation was considered effective in the treatment of adult deformities—Zurbriggen et al. demonstrated that posterior instrumentation in

adult scoliotic deformities results in mostly good and excellent post-operative results, with correction of scoliotic Cobb angle and augmentation of lumbar lordosis [33]. However, more recent literature has shown interbody constructions, which augment pedicle screw constructs with interbody spaces, to have equivalent outcomes in deformity correction. Feng et al. examined outcomes in patients with isthmic spondylolisthesis undergoing posterior instrumentation versus posterior lumbar interbody fusion [34]. They noted similar radiographic correction and clinical outcomes in both cohorts, albeit with a lower incidence of pseudoarthrosis in the interbody cohort [34]. Other studies have examined the independent impacts of interbody-based constructs. Johnson et al. noted post-operative improvements in VAS, ODI, and SF-36, along with a significant increase in segmental lordosis and a significant decrease in coronal Cobb angles in patients with degenerative disc disease and degenerative scoliosis [35]. Anand et al. examined MIS approaches in interbody instrumented fusion and noted significant improvements in coronal Cobb angles, VAS scores, and Treatment Intensity (TIS) scores post-operatively [36]. Hasegawa and Homma showed that posterior lumbar interbody fusion could be used for sagittal and coronal deformity correction, with improvements in clinical outcomes based on JOA scores [37]. Dakwar et al. showed improvements in ODI and VAS with lateral lumbar interbody fusion for adult scoliosis patients [38]. In summary, interbody fusion is an effective means of providing symptomatic relief to patients with adult scoliotic deformities and should be utilized as appropriate.

In terms of interbody fusion, multiple approaches exist, including anterior (ALIF), lateral (LLIF), transforaminal (TLIF), and posterior (PLIF). Given the multitude of [39] approaches and constructs possible, surgeons have to consider the benefits and drawbacks of each interbody spacer type for their patients. A study by Ahlquist et al. examined radiographic measurements in patients undergoing single-level lumbar interbody fusion, and they demonstrated that ALIF and TLIF techniques were superior at restoration of segmental lordosis, lumbar lordosis, disc heights, and foraminal heights, with TLIF also able to aid in restoration of these parameters to a lesser extent [40]. Lee et al. examined the usage of different surgical approaches while performing ALIF in adult scoliosis patients and also noted a significant number of patients with post-operative restoration of normal PI-LL, along with improvements in lumbar lordosis, but they also noted that ALIF can potentially present with greater approach-related morbidity [39]. Given that LLIF and ALIF have been shown to provide better restoration of spinal alignment, they may be more appropriate interventions for the treatment of adult scoliosis. Of note, LLIF procedures cannot be performed at the L5-S1 junction given anatomical constraints, and thus cannot be used for treatment of the fractional curve at that specific level.

One technical note with regards to surgical approaches involves the use of minimally invasive techniques versus open approaches. The previously mentioned study by Lee et al. noted that open approaches, including those that utilize osteotomies, resulted in greater sagittal correction over a percutaneous approach, thus indicating that open approaches may be better equipped for sagittal restoration [39]. However, they also noted reduced intraoperative blood loss and blood transfusion in the percutaneous approach, along with similar improvements in ODI and VAS scores compared to other approaches [39]. Other papers have highlighted similar benefits of minimally invasive approaches. Anand et al. noted reduced intra-operative blood loss and morbidity in patients undergoing MIS LLIF, along with significant improvements in Treatment Intensity Score (TIS), VAS, ODI, SF-36 scores, and Cobb angle post-operatively [41]. Lo et al. examined mini-open and MIS TLIF approaches in single-level fusion for adult degenerative disorders and found improved post-operative VAS scores, reduced blood loss, and shorter hospital stays in the mini-open and MIS cohorts [42]. Seng et al. noted lesser blood loss, morphine usage, and shorter hospital stays in their MIS cohort, along with earlier ambulation and similar post-operative outcomes to open approaches [43]. Isaacs et al. noted that LLIF procedures that were entirely MIS had lower complication rates than procedures involving open posterior approaches [11]. Given the lower morbidity surrounding MIS surgeries, which have also

shown equivalent outcomes to open approaches, MIS approaches may present as a more appropriate approach in limited deformity correction.

3.4.6. Need for Decompression?

While the vast majority of constructs discussed thus far have utilized a combination of fusion and decompression, recent literature has raised an interesting question regarding the utility of decompression in the setting of interbody fusion. Given that interbody fusions can restore disc heights and foraminal heights, there is a possibility that interbody fusion alone is sufficient for the resolution of neurogenic symptoms. There are a few studies that have examined this hypothesis specifically. Alimi et al. examined unilateral stenosis in adult deformity patients and proposed treating it with a unilateral LLIF without decompression, noting significant increases post-operatively in both stenotic and contralateral formaminal and disc heights sustained on follow-up [44]. Similarly, they noted significant improvements in VAS-leg pain and buttock, which correlate with neurogenic symptoms, along with VAS-Back and ODI scores [44]. Tani et al. examined the impact of using anterior column realignment (ACR) in conjunction with LLIF and percutaneous pedicle screw instrumentation on neural anatomical elements, showing significant improvements in sagittal alignment, disc height, foraminal height, dural sac cross-sectional area, and ODI, along with decreased ligamentum flavum thickness and disc bulge thickness [45]. As previously mentioned, Chou et al. looked at the treatment of the fractional curve with interbody spacers and found similar outcomes to posterior open approaches, including improvements in VAS-Leg pain without surgical decompression [31]. Thus, interbody fusion can provide neurological decompression through the restoration of disc height and foraminal height.

While interbody spacers may restore disc and foraminal height and reduce neurological compression, what advantages do such procedures have over fusion and decompression combinations? Multiple studies have indicated that surgical decompression, when combined with fusion, can lead to increased post-operative complications. Elsamadicy et al., in a retrospective cohort of 874 spinal deformity patients, found that fusion procedures that incorporated laminectomies were associated with significantly higher rates of intraoperative blood loss, blood transfusions, and durotomies, along with increased intensive care unit admissions and rates of altered mental status, urinary tract infections, wound drainage, and instrumentation failure [46]. In another study design, Brodke et al. examined outcomes between laminectomies and fusions with laminectomies and found that the fusion cohort had significantly higher rates of early and late adjacent segment disease and significantly lower VAS-Leg and patient satisfaction [24]. Of note, avoiding decompressive procedures maintains posterior spinal anatomy by avoiding manipulation of the facet joints and posterior ligamentous structures, leading to improved overall spinal stability in patients post-operatively. Posterior element manipulation can lead to higher complication and revision rates in the setting of interbody fusion, thus providing some support to fusion-only constructs.

3.5. Dynamic Stabilization—A Potential Future Option?

While the aforementioned categories cover the vast majority of limited interventional treatments for adult spinal deformity, our literature search uncovered a few more techniques that did not quite fall into the aforementioned categories. Such approaches mostly utilize dynamic fixation and stabilization. Traditional instrumented fusion allows for the correction of sagittal and coronal deformities, helping restore spinopelvic parameters, but it also alters spine biomechanics, leading to an increased incidence of adjacent segment disease [47]. Dynamic fixation, utilizing ligament-and-screw constructs, can help preserve normal spinal biomechanics. Kanayama examined the use of Graf ligamentoplasty, consisting of pedicle screws and looped, braided polyester bands, to provide dynamic stability and found that Graf ligamentoplasty maintained segmental motion but was associated with poor clinical outcomes [47]. They concluded that Graf ligamentoplasty was inappropriate for the treatment of adult degenerative scoliosis and laterolisthesis [47]. Subsequently, Di

Silvestre et al. examined the usage of the Dynesys system in adult degenerative scoliosis, reporting statistically significant improvements in ODI, RMDQ, and VAS scores for leg pain and back pain, along with statistically significant corrections in scoliosis Cobb angle and anterior vertebral translation [48]. Zhao et al. examined short-segment instrumented fusion with proximal dynamic stabilization with the Wallis system, an interspinous spacer and a fixator and noted improvements in ODI and VAS scores along with no adjacent segment disease cephalad to fusion, but also noted limited radiographic correction [49]. Given the relatively small body of literature, with limitations in statistical power, regarding the usage of dynamic fixation in adult deformity, no concrete conclusions can be drawn regarding its efficacy. However, dynamic fixation remains a potential intervention for adult deformity, allowing for radiographic correction while maintaining segmental motion.

4. Discussion

This review delves into the different treatment options available for limited correction of adult spinal deformities. This field is ever-evolving, with new studies published yearly, further evolving our understanding of the field. Traditional deformity treatment relied heavily on long-segment constructs, which provided appropriate radiographic correction but were associated with significantly increased levels of post-operative morbidity and lumbar stiffness. Given these drawbacks, more limited interventions, when appropriate, can provide similar symptomatic and functional recovery without the associated morbidity of long-segment fusion. Such approaches are most appropriate in patients with compensated or balanced deformities, as limited interventions cannot provide significant improvements in radiographic parameters following surgical intervention. Thus, spinopelvic alignment, through the use of PI-LL, along with coronal deformity and sagittal deformity, should be considered when evaluating patient eligibility for limited interventions.

Given a compensated/balanced deformity, the next qualifier for intervention is based on the quality of pain and symptoms experienced by the patient. We previously categorized scoliotic pain into two categories—neurogenic and mechanical. Neurogenic pain occurs because of neurological compression, presenting with cauda equina- or radicular-like pain and deficits. In such patients, given the neurogenic etiology of their pain, decompression via discectomy or manipulation of the posterior spinal elements can provide symptomatic relief and is an appropriate first option for treatment. In patients with compensated deformity and low back pain, the underlying etiology of their pain relates muscular pain secondary to neural impingement. As such, short-segment fusion, which can provide a more powerful decompression, is a more appropriate option for patient treatment. Similarly, for patients with cephalad-caudad stenosis, decompression may not be enough to resolve symptoms, and fusion with interbody support will be necessary to provide relief.

While limited interventions may lack the ability of long-segment fusions to provide lasting sagittal re-alignment, they present immediate benefits in terms of perioperative morbidity, along with lesser stiffness-related disability following surgery. While radiographic outcomes in limited interventions are often significantly lesser than in long-segment interventions, functional and symptomatic outcomes—measured by patient-related outcomes such as ODI, VAS, JOA score, or SF-36—often show no significant differences in limited interventions when compared to long-segment fusions. Thus, they remain an appropriate option for compensated deformities. That being said, more recent literature argues for the efficacy of short-segment constructs in uncompensated deformities, noting that similar clinical outcomes are seen in such patients. However, more studies are needed to better understand the usage of short-segment instrumented fusion in uncompensated deformity. One specific short-segment construct looks at the treatment of the fractional curve, which presents at the lumbosacral junction—such constructs are well-suited to reduce pressure on neurological structures and improve neurogenic pain. Short-segment fusion also does not preclude future extension or operations—such constructs do not lead to increased morbidity in re-operative patients compared to treatment-naive patients.

Many papers today describe the usage of interbody constructs, which can provide improvements in patient outcomes while also reducing morbidity and operative complications due to more minimally invasive exposures. Interbody spacers lend themselves well to MIS constructs, which may not provide the same sagittal correction as open constructs but provide clinical improvements and reduce perioperative morbidity. In addition, interbody spacers help restore both disc and foraminal height, thus reducing pressure on the spinal cord and exiting nerves. Interbody spacers alone can provide adequate decompression without posterior element manipulation, which has been shown to increase complication rates compared to constructs that do not utilize decompression.

One of the more novel constructs being studied is dynamic fixation and stabilization, which use artificial bands and posterior instrumentation to provide stabilization of the spine while preserving movement. Some earlier constructs proved ineffective in scoliotic patients, but later constructs have shown promise both as a primary treatment and as an adjuvant to fusion to reduce adjacent segment disease incidence. However, there is a dearth of literature on this matter compared to other topics discussed, and this provides a future avenue for further work on the correction of scoliotic deformity.

Limitations

Our study is inherently limited by the evidence used for it. Given that the vast majority of the evidence we have compiled has a Level III level of evidence and a ROBINS-I score of moderate, most of the evidence we provide can help with drawing conclusions regarding treatment plans but does not consist of many randomized control trials, the golden standard of evidence. Our review process was also limited to MEDLINE-indexed journals, thus missing those indexed on SCOPUS, Web of Science, Google Scholar, and other indexing engines. Nonetheless, our paper provides a broad overview of considerations and practices for limited spine intervention in adult deformity patients.

5. Conclusions

Traditional adult scoliosis treatment has relied heavily on long-segment instrumented fusion, which provides sagittal realignment but comes at the cost of significant perioperative morbidity and spinal stiffness. In this review, we highlight the different limited treatment options available for scoliosis patients. Decompressive procedures such as discectomy or laminotomy/foraminotomy are best reserved for patients with neurogenic pain, while short-segment fusion is better suited for patients with neurologic symptoms secondary to compensated deformity, decompression of neural elements, stabilization of a short spinal segment, and relief of up-down stenosis. Such patients often see significant clinical improvement after surgical intervention. Interbody spacers can help provide restoration of normal spinal alignment and can potentially aid in the decompression of affected levels. Patients with an uncompensated deformity, as well as those with significant deformity-related symptoms and pain despite compensation, may be candidates for long-segment constructs. Future studies can examine short-segment fusion in uncompensated deformity and the potential for dynamic stabilization in adult scoliosis.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/jcm13041030/s1, Table S1: Risk of Bias Assessment.

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Review

Perioperative Blindness in Spine Surgery: A Scoping Literature Review

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Abstract: Perioperative vision loss (POVL) is a devastating surgical complication that impacts both the recovery from surgery and quality of life, most commonly occurring after spine surgery. With rates of spine surgery dramatically increasing, the prevalence of POVL will increase proportionately. This scoping review aims to aggregate the literature pertinent to POVL in spine surgery and consolidate recommendations and preventative measures to reduce the risk of POVL. There are several causes of POVL, and the main contribution following spine surgery is ischemic optic neuropathy (ION). Vision loss often manifests immediately following surgery and is irreversible and severe. Diffusion weighted imaging has recently surfaced as a diagnostic tool to identify ION. There are no effective treatments; therefore, risk stratification for counseling and prevention are vital. Patients undergoing prone surgery of long duration and/or with significant expected blood loss are at greatest risk. Future research is necessary to develop effective treatments.

Keywords: perioperative vision loss; spine surgery; complication; risk stratification; ischemic optic neuropathy; central retinal artery occlusion; cortical blindness

1. Introduction

Perioperative vision loss (POVL) is a rare yet incredibly disabling phenomenon, often leading to irreversible vision loss in an already vulnerable patient population. POVL commonly occurs after spine surgery, with rates ranging from 0.03% to 0.2% [1–4]. Visual acuity has been strongly correlated with physical activity levels, which has profound implications for the recovery process following spine surgery [5–7]. Dramatically increasing rates of spine surgery in the last 10 years suggest that the prevalence of POVL will increase proportionately, thus warranting research into this complication [8–10].

In the spine surgery patient population, POVL was originally reported in 1948 [11]. Several case reports in the early 1950s verified this finding of vision loss following surgery, hypothesizing pathophysiological contributions from systemic hypotension, malpositioning, and anesthetics [12–14]. More recent investigations describing POVL saw a shift from qualitative case reports to quantitative epidemiological studies. In 2009, Shen and colleagues analyzed 5.6 million patients from the Nationwide Inpatient Sample and found an increased incidence of POVL in patients undergoing spine and cardiac surgery at 0.09% and 0.03%, respectively [2]. These findings are corroborated by a population-based study from 2008 noting an incidence of visual disturbance following spine surgery of 0.094% and a retrospective review from 1997 describing loss of visual acuity in 0.20% of patients undergoing spine surgery [3,4]. In particular, patients undergoing scoliosis correction or posterior lumbar fusions were noted to have the highest rates of perioperative vision

impairment [3]. A recent comprehensive report of complications following adult deformity surgery found that three-column osteotomy procedures (3CO) have double the rate of visual acuity changes compared to non-3CO procedures, 0.4% and 0.2%, respectively [15].

Several studies have documented the existence of perioperative blindness following spine surgery; however, few reviews exist consolidating the known literature. Furthermore, the pathophysiological mechanisms underlying POVL have been studied in more detail in recent years; thus, a review of recent literature is warranted. This review will summarize existing case reports as well as aggregate conclusions from previous reviews to present a modern perspective on POVL as well as discuss preventative measures that may be taken to reduce the risk of vision loss in vulnerable populations undergoing spine surgery.

2. Materials and Methods

We searched the PubMed database (Bethesda, MD, USA) for English-language studies relevant to POVL and spine surgery. A scoping review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) checklist [16]. A scoping review was selected instead of a systematic review due to the strengths of scoping reviews in both identifying knowledge gaps in the field and clarifying information [17]. The PubMed search strategy employed is described in the Appendix A and yielded 310 articles. Selected articles were included in this manuscript if blindness or vision loss manifested during or after spine surgery. Title and abstract screens excluded articles that did not address POVL in the setting of spine surgery. Non-English studies and non-human studies were excluded from the analysis. The references of the previously published reviews selected were also manually searched. A total of 78 articles were included in this scoping review. The most recent search was conducted on 8 December 2023.

3. Discussion

3.1. Historical Narrative of Blindness in the Literature

The first cases of POVL after spine surgery were documented in the late 1940s and significant progress in understanding both the pathology and risk factors has been made in the last 80 years. The main historical findings across various time periods are summarized in Table 1.

Table 1. Historical overview detailing POVL in spine surgery.

Time Period	Main Findings
1940–1990	First case reports describing patients with blindness after spine surgery; exam findings are consistent with CRAO. Blindness was also reported following cardiothoracic surgery and general surgery procedures.
1991–2000	Additional case reports were published and risk factors for POVL identified: hypotension and prolonged operating time. ION was suspected in conjunction with CRAO to underlie POVL.
2001–2005	Prone positioning was identified to increase IOP. Several reviews summarizing case reports documenting ION were published.
2006–2010	The American Society of Anesthesiologists Task Force published the first practice advisory on perioperative blindness in 2006. A large national population-based study was published describing visual complications following spine surgery.
2011–2019	The 2006 practice advisory was updated in 2012. Comprehensive reviews and case reports on POVL were conducted, with spine surgery noted as one of the most common causes of POVL. The 2012 practice advisory was updated for a second time in 2019.
2020–present	Various anesthetics are found to increase IOP, and IOP is noted to be greatest at the end of surgical cases. Additional case reports were published.

3.1.1. 1940–1990

Slocum, O'Neal, and Allen reported the first case of blindness after spine surgery in 1948 when a patient developed blindness after improper positioning using a Bailey headrest [11]. Givner and Jaffe reported an individual who developed blindness due to central retinal artery occlusion (CRAO) several hours following choledochojejunostomy for pancreatic carcinoma [12]. Gillan reported two patients in 1953 who developed unilateral blindness upon awakening from anesthesia, one from CRAO and the other of unknown origin, neither of whom recovered their vision [13]. The patient who developed CRAO was operated on due to pyelonephritis caused by a calculus impacting the right ureter and the other patient had hepatocellular carcinoma [13]. Hollenhorst reported eight patients who developed blindness following neurosurgical procedures and corroborates these findings in a series of studies using monkeys to further interrogate the pathophysiological mechanism [14]. Little, in 1955, reported 27,930 cases of deliberate hypotension during anesthesia procedures and describes three cases of retinal ischemia [18]. Bradish and Flowers reported a 12-year-old girl who underwent a two-stage spinal fusion for rapidly progressing scoliosis associated with osteogenesis imperfecta [19]. The operation was performed under permissive hypotension and the patient awoke with a visual acuity of counting fingers (CF) in one eye, which deteriorated to light perception within two days, attributed to CRAO of the eye [19]. Aldrich and colleagues, in 1987, examined 15 patients with cortical blindness, and an additional 10 patients' charts who previously presented with cortical blindness, to determine the causes of cortical blindness as well as the best techniques for diagnosing and managing the complication [20]. Shaw and colleagues sought to determine the etiology of postoperative neuro-ophthalmological complications using samples of individuals who underwent coronary artery bypass graft surgery and peripheral vascular surgery, consisting of 312 and 50 patients, respectively [21].

3.1.2. 1991–2000

Grossman and Ward, in 1993, reported a child who developed CRAO after scoliosis surgery where a horseshoe headrest was utilized [22]. Katzman et al., in 1994, described a patient who experienced blindness following significant hemorrhage during lumbar spine surgery and suggested this was the first report of amaurosis attributable to an orthopedic operative procedure [23]. Shapira and colleagues, in 1996, aimed to determine why the incidence of anterior ischemic optic neuropathy (ION) increased from less than 0.5% to 1.3% following open-heart procedures at their institution and described several perioperative risk factors: prolonged bypass time, low hematocrit, excess weight gain, and the use of epinephrine and amrinone [24]. Sys and colleagues, in 1996, published a case report of CRAO in an adult after a lumbar spinal fusion [25]. In 1997, Stevens et al. conducted a retrospective review of 3450 patients undergoing spinal surgery and observed 7 patients that experienced postoperative loss of visual acuity [4]. Myers and colleagues, in 1997, identified 37 patients that developed visual acuity loss following spine surgery, with complex instrumented fusions complicated by hypotension and prolonged operating time constituting a breadth of the cases [26]. Dilger described a case of ION in a diabetic, obese patient that underwent a lumbar spine fusion [27]. Alexandrakis and Lam, in 1999, described a 68-year-old woman that experienced bilateral ION after prone spine surgery, which they surmised was attributable to pressure to the periorbital region [28].

3.1.3. 2001–2005

Cheng et al. conducted an experiment recording intraocular pressure during various stages of prone spine surgery in 20 patients without eye disease and note that prone positioning is associated with an elevated intraocular pressure [29]. Lee and Lam, in 2001, reported a 58-year-old man undergoing posterior lumbar fusion without intraoperative complication who experienced unilateral vision loss diagnosed as posterior ION [30]. Roth and Barach published an Editorial View that accompanied Lee and Lam's 2001 case report which summarized the then current knowledge pertaining to POVL and described

additional work that would be necessary to better understand the complication [30,31]. Sadda et al., in 2001, conducted a retrospective review of patients with posterior ION and concluded that there are three main causes: perioperative, arteritic, and nonarteritic [32]. Dunker et al. compared 7 cases of posterior ION from their institution to 46 cases published in the literature, concluding that middle-aged males that underwent spine surgery with lengthy intraoperative hypotension, postoperative anemia, and facial swelling were at the greatest risk for developing posterior ION [33]. Deyo, Nachemson, and Mirza published in the New England Journal of Medicine a paper describing the increasing rates of spine-fusion surgery in the United States, and cited blindness as a complication of fusion surgery [8]. Halfon and colleagues, in 2004, presented two cases of complete ophthalmoplegia and CRAO following prone spine surgery [34]. Hayreh, in 2004, reports 42 patients with posterior ION, 3 of whom were classified as surgical-induced posterior ION, of which 1 underwent a posterior lumbar fusion [35]. Buono and Foroozan published a review in 2005 characterizing posterior ION, offering a comprehensive summary of the literature pertaining to spine surgery and posterior ION [36]. Ho et al. presented a review about POVL after spine surgery, with an emphasis on ION pathology [37]. Lee and colleagues described four patients treated in an intensive care unit that developed blindness secondary to ION (one patient who had both ION and traumatic optic neuropathy) and hypothesized that vasopressors may contribute to the loss of vision [38].

3.1.4. 2006–2010

Lee and colleagues, in 2006, retrospectively analyzed 93 cases of POVL after spine surgery and found that ION was the most common cause in 83 of the patients [39]. Leibovitch et al. published, in 2006, a case report of an 80-year-old man who experienced unilateral blindness due to ischemic orbital compartment syndrome after a lumbar decompressive laminectomy [40]. The American Society of Anesthesiologists Task Force published a practice advisory on perioperative blindness in 2006 summarizing the literature and describing risk factors [41]. Mobley et al. presented a literature review of concerns related to prone positioning during surgery [42]. Walick and colleagues, in 2007, conducted an experiment to determine whether intraocular pressure increases in the prone flat versus prone Trendelenburg position and found that intraocular pressure is elevated when patients are positioned in the prone Trendelenburg position [43]. Roth, Tung, and Ksiazek described a case of CRAO in a 53-year-old man undergoing posterior lumbar fusion with the use of eye protectors [44]. Baig et al., in 2007, presented a literature review on POVL by outlining its pathogenesis as well as current gaps in the existing knowledge [45]. Patil et al., in 2008, conducted a national population-based retrospective cohort study of all patients from 1993 to 2002 that experienced ION, CRAO, or other postsurgical visual impairments following spine surgery [3]. Yu et al., in 2008, documented a case of blindness due to ischemic orbital compartment syndrome following prone spine surgery [46]. St-Arnaud and Paquin elucidated safe positioning practices for patients undergoing neurosurgical procedures and indicated that blindness may result if excess pressure is placed on the eyes [47]. Reddy et al., in 2008, reported a 55-year-old gentleman who awoke from a prone lumbar laminectomy with a visual acuity of CF in the right eye and hand motion in the left eye [48]. The patient was diagnosed with posterior ION and, 4 weeks later, visual acuity subsequently resolved to 20/25 in the right eye and 20/20 in the left eye with restricted peripheral visual fields [48]. Shen, Drum, and Roth, in 2009, outlined the prevalence of POVL in spinal, orthopedic, cardiac, and general surgery throughout a 10-year period, demonstrating an increased risk for POVL in both cardiac and posterior spine fusion surgeries [2]. Hayreh, in 2009, characterized the various types of ION, indicating that there are several reports of posterior ION during prolonged surgical procedures, such as spine cases [49].

3.1.5. 2011–2019

Corda et al., in 2011, surveyed 437 patients (184 respondents) who underwent prone spine surgery and found that 80% of respondents would prefer full disclosure of POVL risk

prior to the procedure [50]. The American Society of Anesthesiologists Task Force updated their 2006 practice advisory with detailed statements pertaining to preoperative patient evaluation and preparation, intraoperative management, the staging of surgical procedures, and postoperative management [41,51]. Goni et al., in 2012, described a 38-year-old male that underwent posterior lumbar decompression and instrumentation who awoke with bilateral blindness found to have bilateral occipital lobe infarcts and diagnosed with cortical blindness [52]. Ooi et al., in 2013, documented a 22-year-old male who underwent prone surgery for resection of a cervical extradural hematoma and awoke with central blurring of the right eye, which was diagnosed as CRAO [53]. Nickels, Manlapaz, and Farag, in 2014, discussed and expanded upon the findings from the American Society of Anesthesiologists Task Force's practice advisory on POVL [54]. Sciubba et al., in 2015, aggregated 93 articles to present a thorough list of complications associated with adult spine deformity surgery, and 12 of 11,692 patients presented visual acuity changes [15]. Quddus et al., in 2015, discussed two cases of posterior ION that were not associated with spinal surgery, but acknowledged that prolonged surgical procedures, such as spine surgery, are common causes of posterior ION [55]. Kla and Lee, in 2016, offered an overview of POVL, indicating the spine surgery is one of the most common surgical causes of POVL [1]. Roth and Moss presented updated data describing perioperative ION epidemiology, presentation, and risk factors [56]. In 2019, the American Society of Anesthesiologists Task Force updated their 2012 practice advisory and included recommendations for management during the preoperative, intraoperative, and postoperative periods [41,51,57].

3.1.6. 2020–Present

Wang, Brewer, and Sadun, in 2020, presented a review summarizing the literature on perioperative posterior ION and an experiment to ascertain which risk factors most strongly contribute to its development [58]. Chang, Chien, and Wu, in 2020, reviewed studies published prior to 2019 to determine which anesthetics influence intraocular pressure and concluded that propofol-based total intravenous anesthesia ameliorates increased intraocular pressure better than volatile anesthetics; two of the sixteen studies analyzed consisted of patients undergoing prone spine surgery [59]. Singh et al., in 2021, reviewed ophthalmic complications associated with perioperative anesthesia, citing literature indicating that spinal fusion surgeries are associated with both ION and CRAO [60]. Oliver et al., in 2021, reported a 9-year-old boy who was diagnosed with posterior ION following supine craniotomy for an epidural abscess [61]. Mulukutla, Yelemarthy, and Vadpalli, in 2021, presented a 46-year-old female who underwent anterior cervical discectomy and fusion and developed bilateral loss of vision 9 h after the surgery, and was found to have cortical blindness [62]. Ramakrishnan et al., in 2021, described a 26-year-old male who underwent prone fusion and instrumentation from C5 to T2 and immediately upon awakening from surgery presented unilateral, left-sided vision loss, which was diagnosed as CRAO [63]. In 2021, Kaur et al. performed an experiment to monitor ocular pressure changes during prone spine surgery and found that ocular pressure was significantly elevated at the end of the case when compared to baseline pressures [64]. Danyel et al. described the use of diffusion-weighted MRI to diagnose ION in patients with giant cell arteritis [65].

3.2. Pathophysiology

ION and CRAO are the most common mechanisms underlying POVL following spine surgery. Relative to ION, CRAO occurs less frequently; one retrospective analysis of 93 POVL cases after spine surgery found ION to be the primary cause in 89% of patients, whereas CRAO was the cause in 11% [18,39]. Cortical blindness has also been reported, although this is more common when spine surgery is associated with cardiothoracic surgery due to hemodynamic manipulations and subsequent increased risk for emboli [66–68].

3.2.1. Ischemic Optic Neuropathy

ION is classified as anterior (AION) when affecting the optic disc and posterior (PION) when involving more proximal optic nerve and retrobulbar tissues [60]. Infarction of the small branches of the posterior ciliary arteries disrupting axoplasmic hemostasis is believed to underly AION [60,69–71]. PION describes intra-orbital infarction of the optic nerve, often stemming from hemodynamic complications or manual compression [60]. PION is the most common etiology of POVL in spine surgery [36]. Prone positioning has been shown to increase intraocular pressure (IOP) and may cause dependent pooling of fluid around the retina [29,42,46,47]. Subsequent large fluid boluses may increase orbital pressure and cause ischemic injury due to decreased perfusion to the optic nerve [37,40,43]. Orbital venous congestion similarly decreases arterial perfusion of the eye and has been observed in spine cases when patients have been in Trendelenburg [28]. Many studies have correlated anemia, hypotension, and hemodilution with ION, suggesting decreased ocular perfusion pressure inducing ischemic damage to the optic nerve [27,37]. The administration of vasopressors has also been correlated with ION, with one group reporting ION after lumbar fusion with constant phenylephrine infusion and other reports of associations concerning vasopressor infusion and ION [24,30,38].

3.2.2. Central Retinal Artery Occlusion

The pathophysiology of CRAO relates to vascular occlusion attributable to retinal emboli, atherosclerosis, inflammation, or vasospasm [60]. Inadvertent pressure to the orbits due to prone positioning directly modulates intraocular pressure (IOP) and orbital arteriovenous pressure, causing arterial and episcleral venous congestion [11,14,19,48]. The relief of pressure induces ischemic vasodilation, which is accompanied by transudate leaking from the vasculature into the tissue and subsequent pathologic retinal edema [14,34]. CRAO has been documented following the use of both horseshoe and rectangular headrests, and paradoxically eye protectors due to incidental traumatic compression of the eye [22,25,44]. Additionally, as blood loss can be significant in certain complex spine procedures, the use of hemostatic agents such as transexamic acid and other antifibrinolytic agents has become more common. These agents have the potential to become embolic and may be associated with an increased risk of vascular occlusion if they enter the systemic circulation, although no study has demonstrated a difference in thrombotic rate with tranexamic acid (TXA) [72–74].

3.2.3. Cortical Blindness

Cortical blindness, although rare, is attributable to hypoperfusion of the occipital cortex [2,20,75]. This may occur through ischemic or hemorrhagic events involving the posterior cerebral artery during the procedure.

While ION and CRAO are the most common causes of POVL after spine surgery, POVL has been documented across surgical domains. Recent investigation into the rates of POVL following non-ocular surgery found the incidence per 10,000 to be 8.64 for cardiac surgery, 3.09 for spinal fusion, 1.86 for hip/ femur treatment, 1.24 for colorectal resection, 1.08 for knee replacement, 0.86 for laminectomy without fusion, 0.66 for cholecystectomy, and 0.12 for appendectomy [2]. With respect to cardiac surgery, ION and CRAO remain the most common pathologies; however, the mechanisms often reflect cardiogenic or vascular processes such as aortic insufficiency, transient cerebral ischemia, carotid artery stenosis, embolic stroke, or atrial myxoma, and the risk is elevated with valve surgeries [76,77]. Few cases of POVL following colorectal procedures have been reported and the mechanism remains poorly understood [78,79].

3.3. Clinical Presentation

Symptoms generally occur upon awakening from anesthesia but may occur within 48 h of surgery, depending on when the patient becomes alert postoperatively [24,37,49]. Profound, painless central or peripheral vision loss is characteristic of POVL, often oc-

curring bilaterally [56]. Patients frequently present with visual acuity of CF or no light perception (NLP). Reports of NLP were as high as 40.8% in one study, and two additional works described vision of CFs or worse as 70% and 75.8% [32,36,58]. In cases of orbital compression, presentations may involve lid and orbital edema as well as proptosis [14].

4. Results

4.1. Assessment and Diagnosis

Fundoscopic exam and intracranial MRI are often implicated in the workup of POVL to rule out brain pathology. Orbital MRI is often warranted to assess for optic nerve pathology [56]. Exam findings vary depending on the pathogenesis of the POVL. Patients with ION will exhibit visual field deficits and sluggish pupils [37]. A swollen optic nerve can be visualized on fundoscopic exam for AION, while PION will not have these findings [32,37,80]. The presentation of PION will be consistent with optic neuropathy, but with an unremarkable fundoscopic exam [36]. While PION is often a diagnosis of exclusion, recent reports have argued for the use of diffusion weighted imaging (DWI) to diagnose the acute phase of PION [55,61,65]. DWI has been applied to AION and shows promise in detecting ischemic changes [81]. In the giant cell arteritis population, sensitivity and specificity for DWI in detecting aggregated AION and PION is 87% and 99%, respectively [65]. Fundoscopic exam for CRAO shows a pale and edematous retina coupled with a cherry red macula and the narrowing of arterioles [34,82,83]. Cortical blindness can be identified through a functional pupillary light reflex and unremarkable fundoscopic exam [20,75]. Postoperative MRI can confirm the occurrence of a posterior cerebral artery infarct [62].

4.2. Prognosis

Most cases of POVL lead to irreversible damage to the eye, although the prognosis can vary depending on the underlying cause. For patients with ION, prognosis is poor; the severe vision loss associated with PION is often irreparable [35,49,51]. Visual loss was temporary in patients with CRAO, with full recovery in those with retinal infarcts and minor visual disturbances in 50% of those with retinal emboli, albeit following coronary bypass surgery [21]. Cortical blindness may improve, but complete resolution of the visual disturbance is rare [54,63].

4.3. Treatment and Prevention

No treatments have demonstrated efficacy in managing POVL [56]. Corticosteroids have been implicated in reducing axonal inflammation, but the patients failed to improve clinically [23,84]. POVL is often irreversible; therefore, prophylactic measures are imperative. A recent meta-analysis of randomized control trials found that IOP was reduced when using propofol based anesthesia, recommending propofol-based total intravenous anesthesia for patients at risk of POVL [59]. A practice advisory in anesthesiology that was updated in 2012 reported that patients can be stratified based on risk [41,51]. High-risk patients were identified as patients undergoing prone spine surgery with preoperative anemia, anticipated long procedures (>6.5 h), or significant blood loss (>44.7% of estimated blood volume) [41,51]. Over 80% of patients undergoing prone spine surgery stated they would like to be informed of the risk of POVL [50]. The advisory suggests that physicians consider warning patients undergoing prolonged procedures or anticipated to have substantial blood loss, or both, that there is an unpredictable risk of POVL [51]. Several case reports indicate that patients with the following conditions are at an elevated risk of POVL: anemia, hypertension, coronary artery disease (CAD), diabetes, smoking history, and obesity [23,26,33,37,52,58,63,64] (Table 2).

Table 2. Patient-specific and procedure-specific risk factors for POVL in spine surgery.

Patient-Specific Factors	Procedure-Specific
Anemia [2,58,64]	Prone surgery [2,37,41,51,57,58,64]
Hypertension [2,35,58,63]	Long surgical duration [37,41,51,57,64]
CAD [2,26,35]	Large volume blood loss [30,41,51,57]
Diabetes [2,26,35,63]	Intraoperative hypotension [26,58]
Smoking history [2,26,62]	
Obesity [63,64]	

With respect to the rarer form of POVL caused by CRAO, the risk factors include hypotension, shock, anemia, longer duration of surgery, and bradycardia [34]. Due to the important role of positioning, some have advocated for the use of three-pin head fixation to eliminate potential orbital pressure [44,53,60,85]. Anatomic variants, such as hypoplasia of a vertebral artery, may increase the risk for cortical blindness, which some authors argue for preoperatively assessing via MR angiography [62]. Nevertheless, there is a paucity of research establishing causal links between POVL and various risk factors [45,51,63]. The strongest evidence for minimizing the risk of POVL involves ensuring no extrinsic orbital compression during positioning, avoiding intraoperative hypotension, minimizing procedural time, and optimizing anesthetic selection to avoid pathological rises in IOP [51,59,64] (Table 3).

Table 3. Preventative measures to reduce the risk of POVL in spine surgery patients.

Surgical Measures	Anesthesia Measures
Avoid orbital compression when positioning [64]	Management of intraoperative hypotension [41,51,57,64]
Minimize procedural time [41,51,57,64]	Optimize anesthetic selection relative to IOP [59]

5. Limitations and Future Directions

Due to the rare nature of POVL, there is a paucity of literature characterizing the complication. The majority of information comes from case reports, which inherently limits the generalizability of the conclusions. This work is a scoping review which offers value in identifying knowledge gaps in the literature but lacks the depth that a systematic review may offer. Furthermore, many of the risk factors described for POVL, such as increased length of procedure and significant blood loss, coincide with challenging, more complicated surgical cases. The stratification of patients by surgical indication, comorbidities, and intraoperative complications may help to eliminate confounding variables when analyzing POVL. Additional work using machine learning algorithms to develop better risk stratification protocols will enable clinicians to offer more informed counseling to patients. Imaging techniques to intraoperatively, or immediately postoperatively, monitor at-risk patients for ischemic ocular events may offer an avenue for detecting POVL prior to it causing devastating, permanent vision changes. While there are currently no treatments for POVL, innovative research focused on the mechanisms comprising POVL can potentially reveal therapeutic targets.

6. Conclusions

POVL is a rare and debilitating complication of spine surgery. Patients often show symptoms upon waking from surgery, but there have been reports of symptom onset within 48 h of anesthesia. Patients experience profound vision loss with visual acuity described as CF or HM. Workup for POVL involves a comprehensive fundoscopic exam as well as a brain MRI to assess for intracranial pathology. The pathophysiology underlying POVL is most commonly ION attributable to infarction of the arterial supply to the optic nerve; however, CRAO and cortical blindness also comprise a portion of POVL cases. Due to the ischemic nature of the injury, POVL is frequently associated with irreversible damage to

the eye. Risk stratification is vital to identify those most susceptible to POVL to temper expectations given the lack of effective treatments. Patients at the highest risk are those who are undergoing prone spine surgery with either preoperative anemia, a long duration of surgery, and significant blood loss during the case. As visual acuity is correlated with physical activity levels, POVL has significant implications for recovery following surgery. Further research is necessary to establish a robust risk stratification algorithm for POVL and develop effective treatments.

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Appendix A

Search Terms for Blindness or Vision Loss in Spine Surgery

((“spine” [MeSH Terms] OR “spine” [All Fields] OR “spines” [All Fields] OR “spine s” [All Fields] OR (“spinal” [All Fields] OR “spinalization” [All Fields] OR “spinalized” [All Fields] OR “spinally” [All Fields] OR “spinals” [All Fields])) AND (“surgery” [MeSH Subheading] OR “surgery” [All Fields] OR “surgical procedures, operative” [MeSH Terms] OR (“surgical” [All Fields] AND “procedures” [All Fields] AND “operative” [All Fields]) OR “operative surgical procedures” [All Fields] OR “general surgery” [MeSH Terms] OR (“general” [All Fields] AND “surgery” [All Fields]) OR “general surgery” [All Fields] OR “surgery s” [All Fields] OR “surgerys” [All Fields] OR “surgeries” [All Fields] OR “surg*” [All Fields]) AND (“complicances” [All Fields] OR “complicate” [All Fields] OR “complicated” [All Fields] OR “complicates” [All Fields] OR “complicating” [All Fields] OR “complication” [All Fields] OR “complication s” [All Fields] OR “complications” [MeSH Subheading] OR “complications” [All Fields]) AND (“blindness” [MeSH Terms] OR “blindness” [All Fields] OR “blindnesses” [All Fields] OR (“blindness” [MeSH Terms] OR “blindness” [All Fields] OR (“vision” [All Fields] AND “loss” [All Fields]) OR “vision loss” [All Fields]))) AND ((humans[Filter]) AND (english[Filter])).

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Spectrum of Surgical Site Infection Pathogens in Chronic Infectious Spondylitis Requiring Revision Surgery: A 5-Year Cohort Study

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Abstract: Background: Spectrum monitoring of the pathogen in spondylitis patients plays a key role in preventing infectious complications of spinal reconstructions in chronic spondylitis (CS) and in the treatment of surgical site infection (SSI). The aim of this study is to characterize the spectrum of SSI pathogens in CS requiring revision surgery. **Methods:** The primary cohort encompassed 569 surgical patients with infectious CS. In 99 patients (61 men and 38 women) requiring revision surgical interventions due to SSI, continuous microbiological monitoring of the pathogens was conducted. The average age of the patients was 63 ± 14 years. The vast majority of the patients underwent surgery on a set of multilevel (two or more spinal–motor segments) lesions. Lesions of the lumbar spine were more often noted, and lesions of the thoracic, thoracolumbar, and cervical spine sections were less often noted. This study included all patients operated on within the scope of revision spinal reconstructions in connection with the development of infection of the surgical area over the period from January 2018 to December 2022. Inclusion criteria were etiologically verified spondylitis, age of 18 years or older, and follow-up of 6 months or more. **Results:** The average rate of revision surgery due to SSI was 17.4%. Germ detection from the material of vertebral localization was noted in 48.3% and pathogen strains were isolated in urine in 60.8%, in decubital ulcers in 23.9%, and in hemoculture in 15.2% of all study patients. Aseptic, deep SSI was detected in 10.1%. Gram-positive, multidrug-resistant, and Gram-negative bacteria with extreme resistance prevailed in the microbiological landscape of late SSI, early, and delayed Gram-positive strains without drug resistance. **Conclusions:** Infectious etiology of spondylitis is associated with a significantly higher frequency of SSI. In the absence of a positive result from bacteriological examination of the vertebral localization material, it is advisable to conduct blood, decubital ulcer discharge, and urine sampling.

Keywords: chronic infectious spondylitis; surgical site infection; cohort study

1. Introduction

Chronic infectious spondylitis (CS) is an etiologically heterogeneous group of destructive infections characterized by the anterior spinal column [1–3]. The standard treatment for acute CS forms (disease duration of no more than 30 days) includes isolated etiotropic antibacterial therapy for types A1–B2 according to Pola et al. (2017) or surgical sanitation of the infectious process area combined with extrafocal instrument fixation and lengthy etiotropic antibacterial therapy [4]. The most important stage of preoperative verification

of spondylitis is percutaneous trepan biopsy from the vertebral lesion, followed by bacteriological, molecular genetic, and histological examination of the surgical material [5,6]. The frequency of verification of the pathogen through this method reaches 35–47% in acute infectious spondylitis, while the assignment of empirical antibacterial therapy at the first stage of treatment reduces the chances of detecting the pathogen microorganism to 14–21% [7–9].

When spondylitis becomes chronic (therapeutic pause lasts 3 months or more), not only is sanitation of the purulent focus necessary, but also three-column spinal reconstruction with correction of the sagittal balance parameters as a key criterion for ensuring the patient's quality of life in the post-surgical period [10,11]. Isolated autosteal grafts have long remained the gold standard for the reconstruction of the anterior column of the spine. However, the high frequency of pseudoarthrosis, the progression of kyphotic deformity, and the development of spinal instability over the long term have dictated the need for the use of non-biological titanium mesh cages filled with auto-fluid for anterior fusion [12,13]. At the same time, the use of multi-support posterior instrumentation has ensured reliable correction of the spine's sagittal profile and the preservation of the achieved parameters over the long term [14].

Despite the improvement of spinal instrumentation and technical instruments and the accumulation of surgical experience, such operations are associated with a high duration (from 5 to 7 h) and a significant volume of blood loss (from 800 mL to 2.1 L) [15,16]. Such operations are associated with high risks for developing deep surgical site infection (SSI) in the early (first 30 days after intervention) and late periods [17–19]. The use of various approaches is recommended depending on the timing of the postoperative complication. Thus, in conditions of early SSI in the field of surgical intervention stages, surgical site debridement, the imposition of negative-pressure wound therapy, and antibacterial therapy, taking into account the results of bacteriological research to preserve metal structures, are recommended. The development of delayed and late infection requires a more radical tactic—rehabilitation of the infection zone, the removal of implants, and a transition to non-focal osteosynthesis systems [20]. An important role is played by the localization of the infection, as the structure may be superficial or deep. The development of a deep infection in the field of surgical intervention requires the removal and replacement of metal structures as the main zone of the formation of microbial biofilms [21].

The progression of the infectious process often leads to the formation of two pathological conditions: loss of segmental stability with the development of pseudo-arthrosis and secondary vertebral canal stenosis with neurological disorders [22–25]. The main tasks to be solved during revision surgery include halting the signs of local and systemic inflammation, restoring vertebral stability, and decompressing intra-canal neural structures [26,27].

One of the causes of SSI is the high resistance of the microorganism strains to antibacterial drugs, which, according to different data, fluctuates from 1.1% to 7.4% [28–30]. Despite the optimized systems for perisurgical systemic antibacterial therapy in improved methods of SSI prevention (intra-wound use of vancomycin, irrigation of the surgical field with iodine-containing antiseptic solutions), the frequency of infectious complications developing after reconstructive surgery under chronic CS conditions reaches 21–29% [19,31,32].

The modern literature describes in detail the primary spinal reconstructions in chronic infectious spondylitis. At the same time, the specifics of conducting revision interventions, analyzing the microorganisms that cause infection in the surgical intervention area, and monitoring their drug resistance in chronic infectious spondylitis are poorly described.

Monitoring the SSI pathogen's microbiological spectrum plays a key role in preventing infectious complications in primary reconstructions during chronic CS and the treatment of SSI in patients requiring revision interventions.

The aim of this study is to characterize the spectrum of infection pathogens at the surgical intervention site in CS. To achieve this goal, we evaluated the pathogenic microorganism's characteristics depending on the period of SSI development. We also characterized the pathogen's drug resistance structure depending on the respective SSI development period.

2. Materials and Methods

The continuous monocentric cohort study, corresponding to class III, was conducted in the period from 10 January 2018 to 31 December 2022. All of the subjects gave their informed consent to inclusion before participating in the study. This study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the St. Petersburg Research Institute of Phthisiopulmonology (Project identification code—No. 358; date: 6 June 2018).

Patients were included in the study on the basis of the following criteria: CS at the time of the primary reconstructive surgery, the presence of SSI requiring revision surgery, a patient age of 18 years or older at the time of revision surgery, verification of wound cavity discharge with determination of the SSI pathogen drug resistance spectrum, verification of the pathogen from hemoculture (triple sampling at the height of fever), urine, subclavian catheters, and decubital ulcer superficial discharge during SSI, and follow-up tracked for 6 months or more. The exclusion criterion was no indications for revision surgical intervention.

During the analyzed period, 569 patients with chronic CS underwent surgery. Of these patients, 364 (63.9%) underwent primary reconstructions and 205 (36.1%) underwent surgery for revision surgical interventions (primary surgery was performed outside of the St. Petersburg Research Institute of Phthisiopulmonology). The final cohort consisted of 99 patients who, at different intervals during the postoperative period, had recorded SSI requiring repeat surgery. The study included all patients operated on within the scope of revision spinal reconstructions in connection with the development of infection of the surgical area. Inclusion criteria were etiologically verified spondylitis, age of 18 years or older, and follow-up of 6 months or more.

The data of 61 male and 38 female patients were analyzed. The average age of the patients at the time of revision surgery was 63 ± 14 years old. The assessment of patients' comorbidity was conducted using the Charlson index, which, in the study cohort, was 7.4 ± 1.2 points. Diabetes mellitus (32 patients, 32.3%), chronic viral hepatitis C (17 patients, 17.1%), and BMI ≥ 30 (12 patients, 12.1%) prevailed in the structure of predictors of the development of the surgical area's infection.

The vast majority of patients (74 cases) underwent surgery on a set of multilevel (2 or more spinal–motor segments) lesions. Lesions of the lumbar spine (56 cases) were more often noted, while lesions of the thoracic (23 cases), thoracolumbar (12 cases), and cervical (8 cases) spine sections were noted less often. The general characteristics of the patients included in the study are presented in Table 1.

Table 1. General characteristics of the patients.

Gender	Age	Localization/Extent of Destruction
Men, 61 patients; Women, 38 patients	63 ± 14 years	Polysigmental—74 patients; Monosigmental—25 patients; C (neck)—8 cases; Th (thoracic)—23 cases; Th/L (thoracolumbar)—12 cases; L (lumbar)—56 cases

Trepan biopsy under X-ray control was performed in all cases of deep infection of the surgical area at the stage of preparation for revision surgery. The criteria for the diagnosis of "infection in the area of surgical intervention" were visible inflammatory changes in soft tissues in the area of surgical intervention and the presence of a fistula communicating with the area of surgery. Superficial infection was limited to subcutaneous fat and muscle fascia. Deep infection was diagnosed in the event of communication with a metal structure. The development of the infectious process was also characterized by an increased level of Leu, ESR, and CRP proinflammatory markers in the blood and a 3-fold positive result of a bacteriological blood test against the backdrop of fever. Signs of infectious changes in the anterior or posterior fusion zone were revealed according to computed tomography and

magnetic resonance imaging data: pre-/paravertebral, epidural abscesses, peri-implant bone resorption, and Modic I type changes.

Bacteriological examination of the wound discharge was performed in all cases at the stage of preparation for revision surgery. The material was obtained through aspiration of the wound with superficial infection of the surgical area and with X-ray-navigated biopsy in the case of deep infection of the surgical area. Closed trepan biopsy was performed from the lesion under the control of an electron-optical converter during the establishment of the diagnosis "deep infection of the surgical intervention area". Trepan biopsy was performed by passing a Jamshidi needle along a transpedicular trajectory in the area of the cranial and caudal blocked segments (spongy bone tissue samples were taken), as well as through the Kambin triangle to take material from the intervertebral disc. Aspiration of the wound and the contents of the fistula was performed in all cases of a superficial infection of the surgical area. The obtained biological material was sent for bacteriological, molecular genetic, and histological (bone fragment) studies.

Bacteriological blood sterility testing was performed three times in all patients. The scope of the preoperative radiation examination included MRI and CT scans of the affected spine. Empirical antibacterial therapy was performed in 10 patients (10.1%) with negative results of the bacteriological examination of wound discharge, as well as in the case of negative blood and urine cultures.

The study plan is depicted in Figure 1.

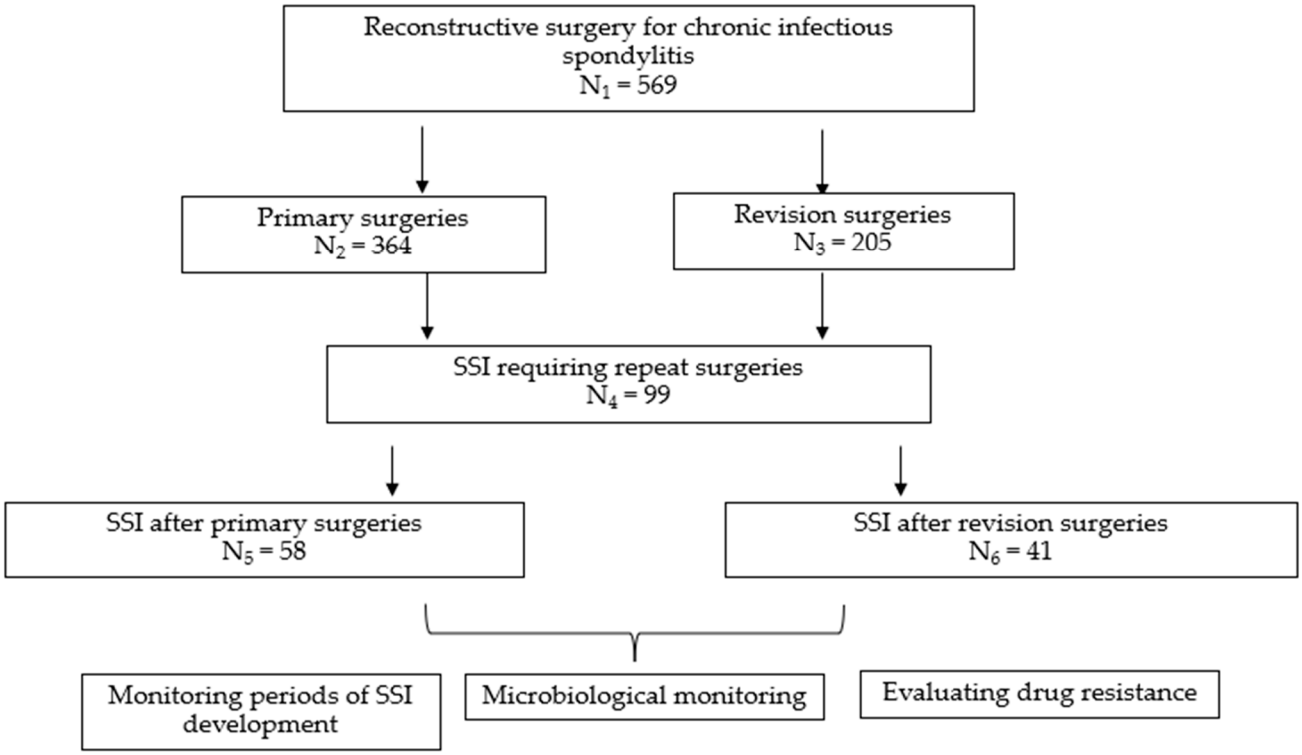

Figure 1. Study plan.

The following parameters were analyzed: type of SSI microorganism–pathogen, SSI microorganism–pathogen's drug resistance spectrum, and SSI development period according to the division into periods per Prinz V. et al. 2020 (early $\leq$ 6 weeks, delayed > 6 weeks, late > 12 months) [20]. Biological material was collected for bacteriological study before revision surgery from the wound discharge (if there was a fistulous process) and directly during the intervention (granulation, pus). If delayed and late SSI and an unstable rear metal structure were detected during removal of the support components, the implant's surfaces were given ultrasound treatment with subsequent bacteriological study.

Nonspecific microflora and *Mycobacterium* spp. were identified on the basis of inoculations on dense and liquid nutrient media, DNA detection of the mycobacterium tuberculosis complex, and amplification of the nucleotide sequence IS6110; a marker of the mycobacterium tuberculosis complex was conducted using the test system SPE DNA-Technology (DNA Technology, Moscow, Russia) through the PCR method in real time on the iCyclerQ, Bio-Rad analyzer (Bio-Rad Laboratories, Inc., Hercules, CA, USA). The threshold value for the colony-forming unit (CFU) of SSI microorganism–pathogens for inclusion in the study was adopted as $\geq 10^5$ (a lower CFU value was considered a version of sample contamination). In all instances, the bacteriological study of biomaterial for anaerobic and facultative–anaerobic microorganisms was supplemented by determination of the drug sensitivity of the SSI pathogens using the disc-diffusion method based on EUCAST (2020) recommendations. According to the recommendations from the Clinical Laboratory Standards Institute (CLSI), the European Committee on Antimicrobial Susceptibility Testing (EUCAST), and the US Food and Drug Administration (FDA), the structure of drug susceptibility revealed microorganisms with multi-resistance (resistance to one antibacterial drug in three or more drug groups), extreme resistance (resistance to one or more antibacterial drugs in all groups, with the exception of categories 1–2), and pan-resistance (resistance to all antibacterial drugs in all groups) [33]. A histological study was conducted based on an analysis of vertebral localization material obtained through paracentetic trepanobioposy.

A statistical analysis was conducted based on recommendations from the World Osteosynthesis Association and Falavigna A. et al. (2015) [34]. The software Statistical Package for the Social Sciences (SPSS), version 22.0 (SPSS Inc., Chicago, IL, USA) was used. The studied parameters were checked for normal distribution using the Kolmogorov–Smirnov criterion. The Kruskal–Wallis N-criterion was used to evaluate the significance of the differences in SSI development periods. The effect of spondylitis etiology on the drug sensitivity spectrum was verified using Pearson's x^2 criterion with the construction of conjugation tables. The differences were considered statistically reliable with two-sided $p < 0.05$.

3. Results

The greatest frequency in complications was noted in the late postoperative period, with 54 observations (54.5%); they were recorded less often in the early (31 patients) and delayed (14 patients) periods ($x^2 = 9.237$, $p = 0.009$). SSI pathogens were identified in 89 patients (89.8%); in this case, the microorganism was isolated from the vertebral localization material in 43 cases (48.3%). In cases of "culture negative" SSI, combined with clinical manifestations (fistulous process in the surgical area, elevated C-reactive protein level > 10 mg/L, and ESR > 30 mm/h) and with histological signs of inflammation, pathogen strains were isolated in the urine in 28 (60.8%), in decubital ulcers in 11 (23.9%), and in hemoculture in 7 (15.2%) of the patients, respectively. For 10 patients (10.1%) with clinical SSI signs, histological inflammation signs, and a negative result from the bacteriological material study of both vertebral and other localization, an SSI diagnosis was established with an unidentified pathogen; here, in all cases, it was identified in the late, postoperative period. Chronic spondylitis etiology had a significant impact on the frequency of SSI development; thus, postoperative complications under conditions of chronic non-specific spondylitis were noted in 67 cases (67.6%), while during tuberculous spondylitis they were noted in 32 (32.3%) of the cases ($x^2 = 21.345$, $p < 0.001$). Analysis of the microorganism types revealed significant differences. Multi-resistant Gram-positive and Gram-negative bacteria with extreme resistance were found more often in patients with late SSI, while pathogens of early and delayed SSI were more often Gram-positive bacteria without drug resistance ($x^2 = 17.516$, $p = 0.0032$). Two microorganisms were verified in 32 patients, and three were verified in 6 people.

The distribution of the detected vertebral localization isolates, depending on the SSI development period, is shown in Table 2.

Table 2. Presence of a certain type of microorganism, depending on the SSI development period.

	Total (abs. and %)	Early SSI (abs. and %)	Delayed SSI (abs. and %)	Late SSI (abs. and %)
Gram (+):	33/76.7%	8/18.6%	4/9.3%	11/25.5%
Including multi-resistant	10/30.3%	1/2.3%	1/2.3%	8/18.6% *
Gram (−):	10/23.2%	2/20%	1/10%	–
Including extremely resistant	6/60%	1/10%	1/10%	4/40% *
Pan-resistant	1/10%	–	–	1/10%

* Statistically significant differences were found across the groups of early, delayed, and late SSI using the Kruskal–Wallis N-criterion, $x^2 = 17.516$, $p = 0.0032$. abs.—absolute value.

In the evaluation of the drug resistance of pathogens obtained from vertebral localization, the specific weight of Gram-positive multi-resistant strains was 30.3%. Among them, *Staph. epidermidis* (MRSE) accounted for 63% and *Staph. aureus* (MRSA) accounted for 37%. The percentage of stable strains in the Gram-positive bacteria reached 80%. Among them, 87.5% of the isolates had extreme resistance (*Klebsiella* spp. and *Acinetobacter* spp.), while 12.5% had pan-resistance (*Pseud. aureginosa*).

4. Discussion

Revision surgery with spondylitis is one of the most complex challenges in spinal surgery, insofar as it is accompanied by a large number of infectious complications and the high economic costs associated with the rendering of specialized medical care [35,36]. Despite the increased number of publications in this field, there is virtually no information about the late results of revision interventions in patients with chronic CS, while data reflecting the results of microbiological monitoring in this patient cohort are only found in a few publications [1,4,16,17].

While predicting SSI development in spinal surgery is still relevant, a consensus opinion on the subject remains elusive. The risk factors for SSI development are both patient-associated (Charlson index, body mass index, comorbid rheumatological pathology, and others) and intervention-associated (primary/revision surgery, its duration, blood loss, and more) [19,31,37]. Mueller K. B. et al. (2022) suggested an SSI development risk scale after vertebral interventions that views the revisional nature of the surgery as one of the most significant predictors of infectious complications [22].

A study of late results in patients undergoing surgery for non-specific spondylodiscitis demonstrates the significant effect of the microorganism–pathogen type on mortality. According to Kehrer M. et al. (2015), mortality in the early and delayed post-surgical period is higher in patients with multi-resistant strains of *Staph. aureus*, while in the late period, muti-resistant Gram-positive microorganisms were found more often [36]. Our study identified similar results: one fatal outcome was recorded in patients with late, deep SSI associated with Gram-negative extremely resistant bacteria.

One of the methods for preventing SSI during initially "sterile" operations on the spine is the intra-wound use of vancomycin. A meta-analysis by Shan S. et al. (2020) indicates the significant effect of this method on the risk of developing infectious complications [38]. The nature of the microorganisms associated with SSI in the early post-surgical period is also noteworthy. Among them, 75% of the cases identified Gram-positive bacteria, which is a recommendation for the intra-wound use of vancomycin in this patient category as well.

In the general cohort of SSI pathogens, the main strains were Gram-positive microorganisms identified in 76.7% of the cases. The leader among them is *Staphylococcus* spp. Representatives from *Enteococcus* spp., predominantly *E. faecalis* and *E. faecium*, were found in the nosocomial flora structure; here, the pathogen was detected in the urine and decubital

ulcer discharge. Multi-resistance to fluoroquinolones of the third and fourth generations was a feature of this microorganism group. Similar trends were detected during 6-year monitoring of the structure and resistance of the leading pathogens [39].

5. Conclusions

Microbiological monitoring of patients with chronic CS revealed the following. There is a predominance in the structure of SSI pathogens of Gram-positive bacteria with drug resistance. The development of late SSI is due to multi-resistant Gram-positive and extremely resistant Gram-negative microorganisms. The non-specific etiology of spondylitis is linked to the high development frequency of SSI. In the absence of a positive result from the bacteriological study of vertebral localization material, it is expedient to take a blood, decubital ulcer discharge, and urine sampling. The use of the obtained data will optimize the schemes of perioperative antibacterial prevention and help reduce the incidence of infection in the field of surgical intervention in patients with chronic infectious spondylitis.

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Institutional Review Board Statement: The protocol of this study was approved by the Ethics Committee of the St. Petersburg Research Institute of Phthisiopulmonology (Project identification code—No. 358; date: 6 June 2018).

Informed Consent Statement: All subjects gave their informed consent to inclusion before their participation in the study. This study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the St. Petersburg Research Institute of Phthisiopulmonology (Project identification code—No. 358; date: 6 June 2018).

Data Availability Statement: Data are contained within the article.

Conflicts of Interest: The authors declare no conflicts of interest.

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Preoperative Robotics Planning Facilitates Complex Construct Design in Robot-Assisted Minimally Invasive Adult Spinal Deformity Surgery—A Preliminary Experience

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Abstract: (1) **Background:** The correction of adult spinal deformity (ASD) can require long, complex constructs with multiple rods which traverse important biomechanical levels to achieve multi-pelvic fixation. Minimally invasive (MIS) placement of these constructs has historically been difficult. Advanced technologies such as spinal robotics platforms can facilitate the design and placement of these constructs and further enable these surgical approaches in MIS deformity surgery. (2) **Methods:** A retrospective study was performed on a series of ASD patients undergoing MIS deformity correction with ≥eight fusion levels to the lower thoracic spine with preoperative robotic construct planning and robot-assisted pedicle screw placement. (3) **Results:** There were 12 patients (10 female, mean age 68.6 years) with a diagnosis of either degenerative scoliosis (8 patients) or sagittal imbalance (4 patients). All underwent preoperative robotic planning to assist in MIS robot-assisted percutaneous or transfascial placement of pedicle and iliac screws with multiple-rod constructs. Mean operative values per patient were 9.9 levels instrumented (range 8–11), 3.9 interbody cages (range 2–6), 3.3 iliac fixation points (range 2–4), 3.3 rods (range 2–4), 18.7 screws (range 13–24), estimated blood loss 254 cc (range 150–350 cc), and operative time 347 min (range 242–442 min). All patients showed improvement in radiographic sagittal, and, if applicable, coronal parameters. Mean length of stay was 5.8 days with no ICU admissions. Ten patients ambulated on POD 1 or 2. Of 224 screws placed minimally invasively, four breaches were identified on intraoperative CT and repositioned (three lateral, one medial) for a robot-assisted screw accuracy of 98.2%. (4) **Conclusions:** Minimally invasive long-segment fixation for adult spinal deformity surgery has historically been considered laborious and technically intensive. Preoperative robotics planning facilitates the design and placement of even complex multi-rod multi-pelvic fixation for MIS deformity surgery.

Keywords: adult spinal deformity (ASD); minimally invasive surgery (MIS); spinal robotics; complex construct design; preoperative robotics planning; Mazor X Stealth Edition

1. Introduction

In adults aged 65 years and older, adult spinal deformity (ASD) may have a prevalence of up to 68%, and may lead to chronic back pain and neurologic deficits, in turn leading to disability [1]. Self-image, pain, and disability are found to be the most common drivers for patients to pursue surgical correction when conservative treatment measures have failed [2]. In a preoperative survey of adults planning to undergo ASD correction, 66% of patients anticipated a highly successful operation, with an average expected reduction in pain of 71% [3]. Surgeon expectations for deformity correction largely focus on functional improvement and radiographic correction to prevent future disability [4]. While there may be a mismatch in the primary expectations for surgical correction, there is a shared goal to achieve a robust functional outcome, reduce pain, and prevent future complications. As such, ASD correction strategies continue to evolve to maximize these benefits. More surgical procedures are carried out in a minimally invasive fashion when able, and there is

now Level 3 evidence which shows that patients have a positive perspective of minimally invasive surgery (MIS) in the spine, and prefer to have MIS spine surgery when able [5].

MIS techniques are well described in the treatment of degenerative disease, trauma, and ASD [6]. Compared to open procedures, MIS approaches reduce estimated blood loss (EBL), minimize tissue trauma, and shorten length of stay (LOS), while also restoring sagittal and coronal balance, promoting fusion, and decompressing the neural elements [7]. Patient-reported outcomes such as self-image, mental health, and satisfaction may also improve earlier in patients undergoing MIS compared to open ASD surgery [8]. These benefits have driven the creation of novel techniques for several contemporary open approaches, as surgical centers continue to bring more optimized outcomes to their patients.

As MIS approaches become further optimized and more familiar, these techniques may be applied to pathology not previously amenable to MIS, such as complex ASD. In these cases, effective and sustainable correction may require complex constructs. These advanced construct designs employ multiple rods and various loading distribution techniques to increase pillar support, bolster vulnerable osteotomy sites, enhance rigidity, and promote fusion in order to restore sagittal balance, improve load absorption, increase posterior column mobility, and restore lumbar lordosis (LL) [9–13]. Traditional open surgical techniques have previously required large incisions through the paraspinal fascia, with near total dissection of the paraspinal musculature to expose the posterior bony elements of the spine to implement these constructs. In MIS techniques, preservation of the posterior fascia and paraspinal muscles aims to reduce surgical trauma, but comes at the expense of the visualization of several landmarks when planning bony fixation, which in turn limits its applicability to larger and complex construct designs in ASD. A carefully planned preoperative design is therefore critical for desired postoperative correction [14]. This is especially important in MIS constructs where the spine is less exposed and the ability to see or modify these plans extemporaneously is reduced. The placement of long-segment MIS constructs can also be technically demanding, especially for surgeons less familiar with these techniques. In order to increase intraoperative confidence and reduce rates of "conversion to open" in MIS cases, a thorough and accurate preoperative plan for MIS correction in ASD may assist surgeons when offering MIS to patients with ASD. Barriers to adoption include concerns over appropriate tulip head alignment, minimally invasive tower management with collisions at the lumbosacral junction, and the minimally invasive passage of a long rod across multiple fixation levels. This report aims to describe a series of cases in which preoperative robotics planning software was used to address these points while designing complex constructs to correct ASD to be performed through an MIS approach.

A more recent advancement in the armamentarium of technology in ASD surgery is the inclusion of spinal robotic platforms. Robotic systems are now used in several spinal procedures, and were recently shown to provide a very high degree of screw accuracy and safety when compared to previous conventional techniques [15]. These systems not only include robotic arm and intraoperative navigation technology, but now also provide for simulation and planning software. The development of robotics systems with their requisite preoperative software planning enables comprehensive preoperative assessments and allows for not only straightforward minimally invasive placement of long-segment instrumentation but the design of complex construct designs that involve multi-rod and multi-pelvic fixation. We report here a case series of adult spinal deformity patients treated with robot-assisted minimally invasive surgical techniques and describe the feasibility of these techniques for wider adoption.

2. Methods

This study describes a retrospective series of patients at a single academic center who underwent minimally invasive correction of ASD with robotic assistance, with preoperative planning of complex constructs performed by a single attending neurosurgeon (M.H.P). In our series, ASD was defined as pelvic tilt (PT) > 25°, pelvic incidence minus lumbar

lordosis (PI-LL) > 10°, sagittal vertical axis (SVA) > 5 cm, or coronal Cobb angle > 20°. A complex construct was defined as ≥8 fusion levels with an upper instrumented level (UIV) into the lower thoracic spine. Data points collected included demographic characteristics, operative time, estimated blood loss (EBL), pedicle screw accuracy, radiographic alignment, inpatient stay metrics, and complications.

This study was reviewed and approved by the Institutional Review Board of the University of California San Diego (# 210617, approved on 23 January 2023), and all patients consented to participation in research prior to enrollment.

2.1. Preoperative Robotic Construct Design

A preoperative thin-cut CT scan is obtained and loaded into the planning software associated with the spinal robotics system (Mazor X Robotics Planning Software Version 5.0 with X-Align, Medtronic Sofamor Danek, Minneapolis, MN, USA) (Figure 1A). Interbody cages are then planned and simulated. Of note, the software assumes full movement of the chosen segment based on cage geometry and marked endplate surfaces, and under-correction of the simulation may oftentimes be needed due to rigid deformities or facet ankylosis and hypertrophy (Figures 1B and 2). With this correction provided, pedicle and iliac screws are then planned from the UIV to S2 and bilateral rods are simulated after each screw to confirm appropriate planar alignment (Figure 3). Adjustments to the trajectories of the pedicle screws can be made to ensure easy subfascial passage. Satellite accessory rods are planned using lateral-to-medial screw trajectories with positions outside of the main rod. While open surgical techniques allow for satellite rod placement with dual-headed screws or rod–rod domino connectors, the lack of direct visualization in MIS makes these strategies prohibitive and therefore satellite rods are usually not able to be directly connected to the main rod (Figure 4).

The extension towers from L4 to S2 need to be reviewed in detail because of their converging trajectories (Figure 5A), and minor adjustments can be made to the pedicle screw targeted positioning in the sagittal plane to avoid tower collisions at the skin level. If a patient-specific rod (PSR) is being used, screw planning can be performed to ensure rod geometries are appropriately similar and aligned after the simulated correction (Figure 5B).

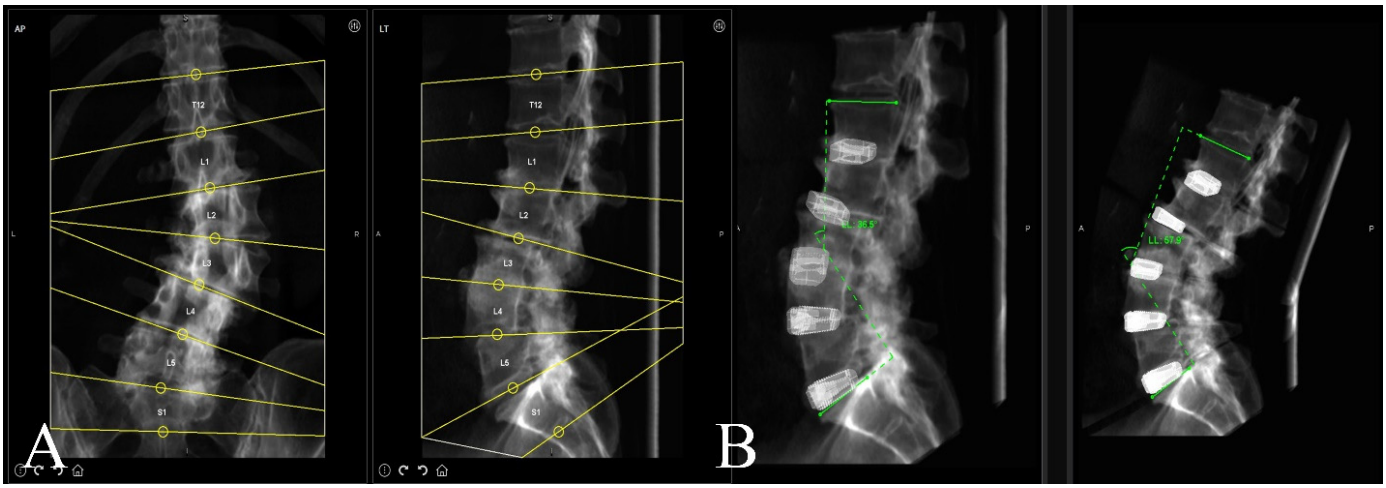

Figure 1. (**A**) Robotic software automatic segmentation of each vertebral level as a separate independent volume to allow for both screw fixation and interbody implant planning. (**B**) Sagittal simulation of interbody cage placement with movement of each individual vertebral segment to assess if appropriate sagittal correction can be achieved with minimally invasive placement of interbodies.

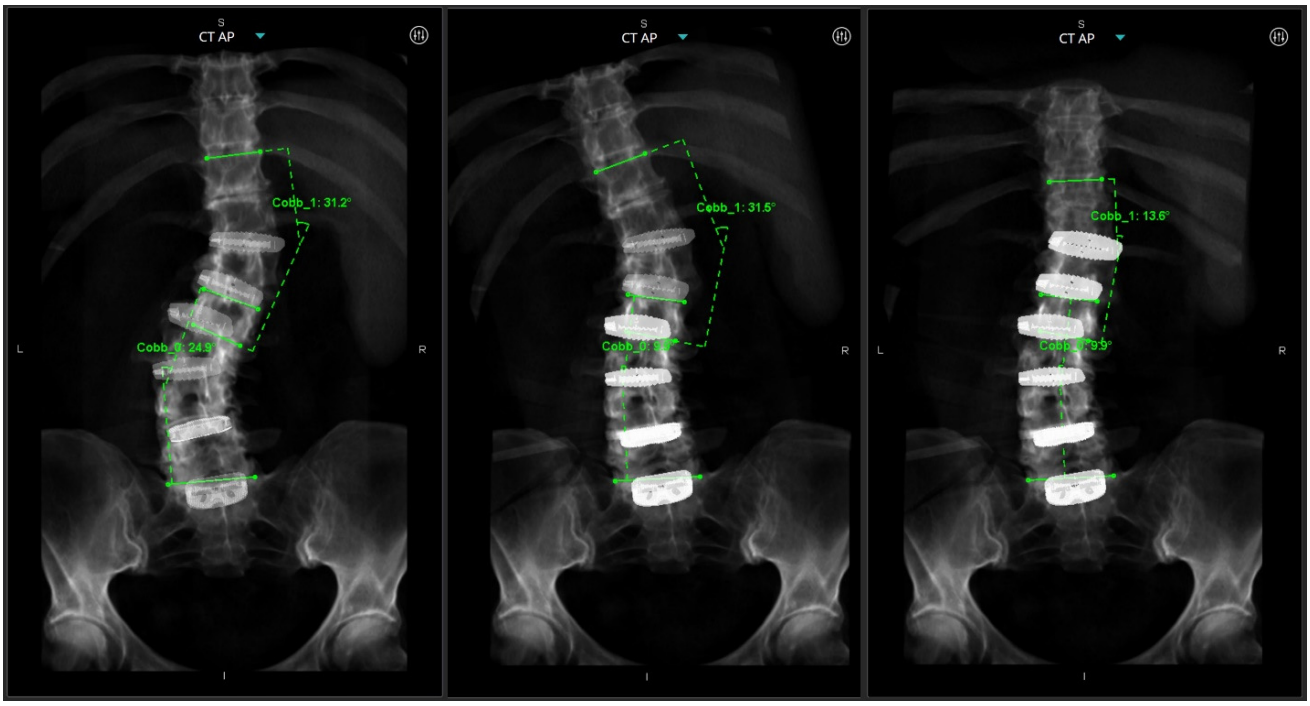

Figure 2. Coronal simulation of interbody cage placement to assess if minimally invasive placement of interbodies can effectively correct fractional and main coronal curve deformities through movement at each vertebral segment.

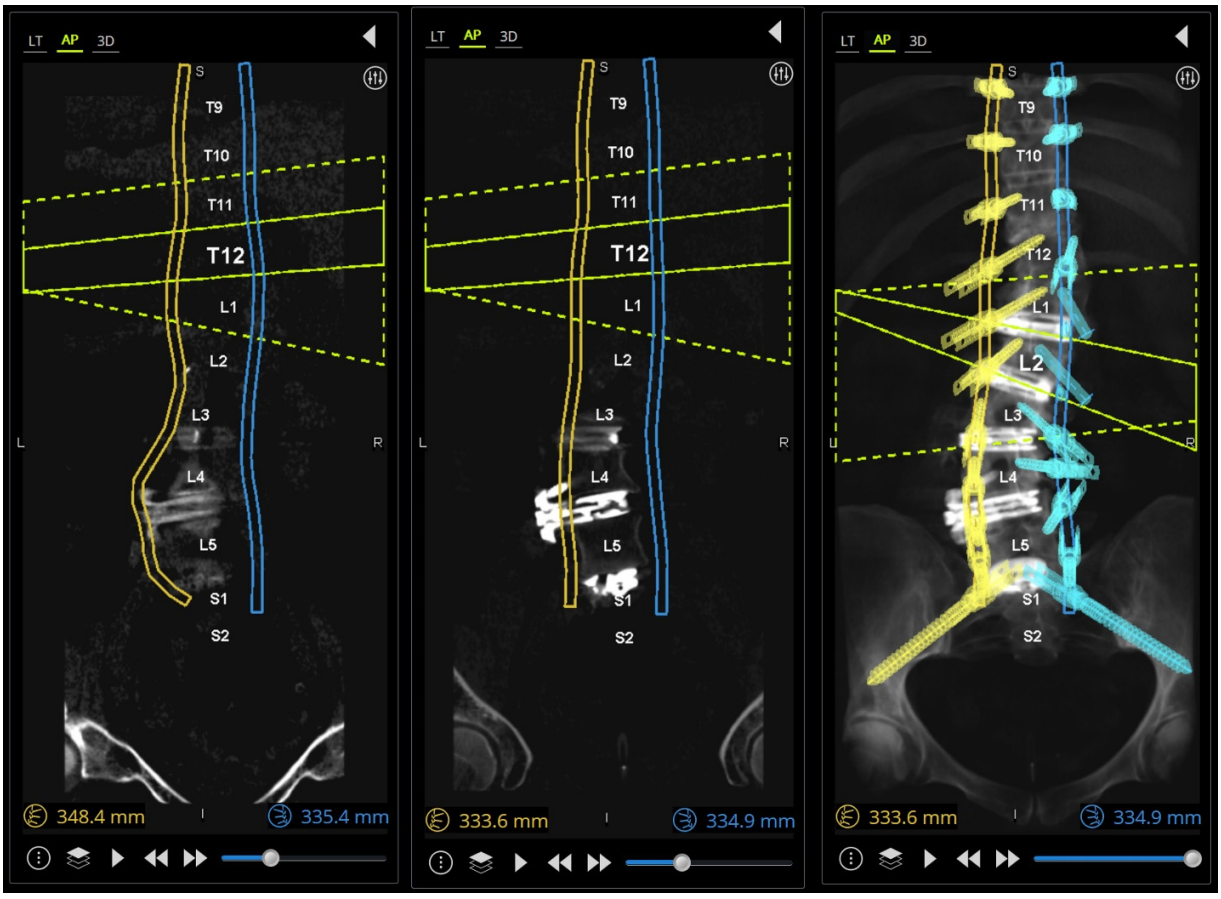

Figure 3. Rod simulation as each pedicle screw is placed in the software. (**left**) The yellow left-sided rod geometry is not amenable to planar cranial–caudal placement when screws are planned in "perfect

ideal" lateral-to-medial trajectories; (**middle**,**right**) the yellow left-sided rod geometry is now planar after adjusting screw trajectories to be straighter, treating pedicles more as bone for fixation in context of the entire construct, rather than individual perfect bone columns to maximally fill.

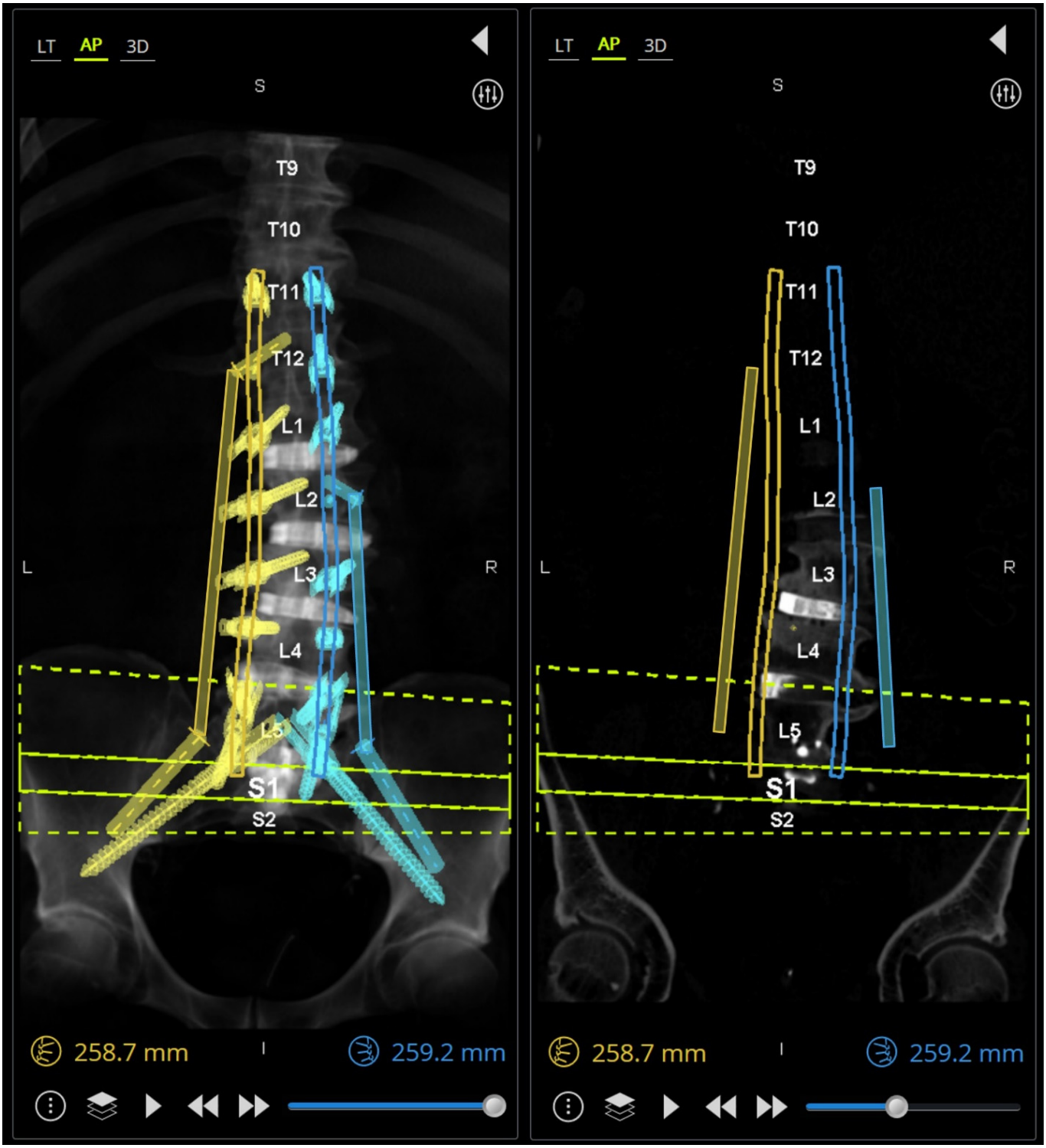

Figure 4. A multiple-rod construct with four iliac screws. Due to the limitations of dual-headed screws or dominos in MIS deformity techniques, satellite (accessory or kickstand) rods are currently designed to connect pedicle screws to traditional iliac screws without direct connection to the main rod.

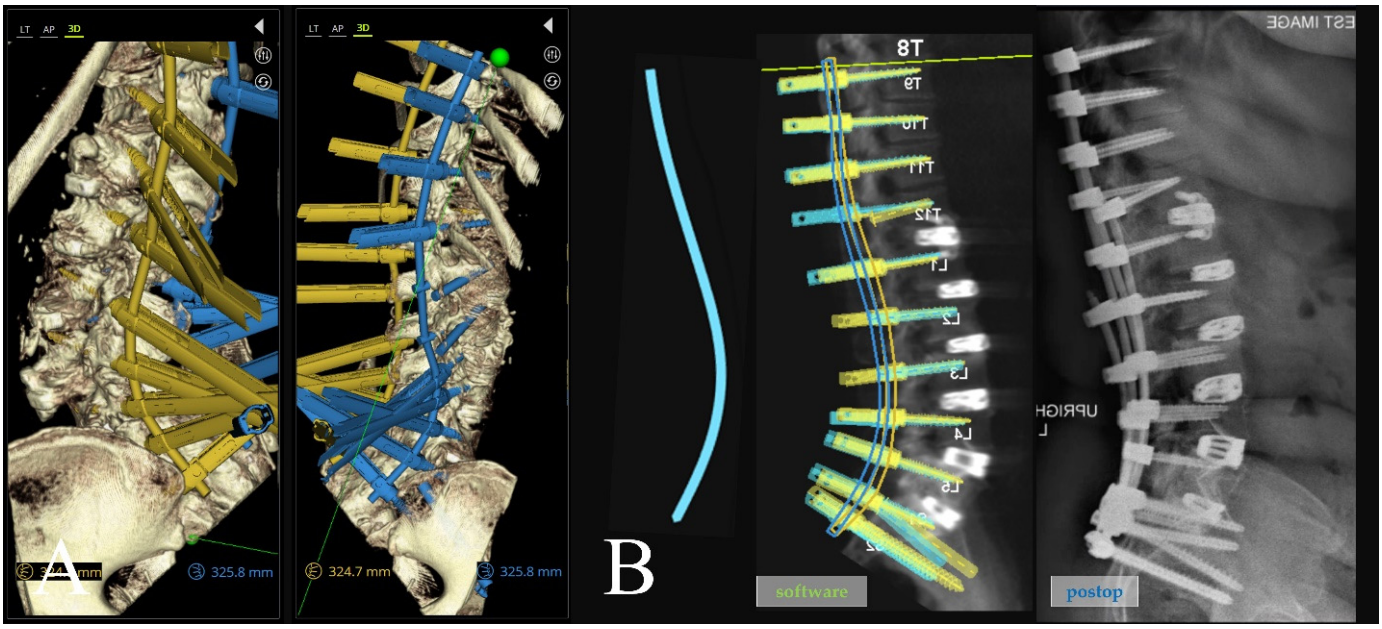

Figure 5. (**A**) Three-dimensional reconstruction of the simulated rod, pedicle screws, and minimally invasive extension towers. Note the focus at the L4–S2 levels where improper planning may lead to these respective screw towers colliding and potentially blocking subsequent screw placement. Small adjustments can be made in real time in this view to resolve potential collisions. (**B**) (**left**) A patient-specific rod geometry designed with predictive parameters; (**middle**) the robotic plan with screws in place aligned to the simulated correction; (**right**) postoperative standing lateral X-ray showing good apposition to rod geometry and plan.

2.2. Operative Technique

For Stage 1, placement of all interbody cages in this series was carried out using an anterior-to-psoas (ATP) technique also known as an oblique lumbar interbody fusion (OLIF) for levels above L5-S1, as well as a lateral anterior lumbar interbody fusion (ALIF) at L5-S1 as a first stage of surgery. The patient is first positioned in the right lateral decubitus position with the left side up. Because there may be a certain degree or rotational deformity that requires bed rotation, the patient is generously taped and secured to the bed. This also allows for the use of intraoperative navigation while minimizing inaccuracies of the navigation system. Incisions are then marked depending on the incisional access to the respective disc spaces; for multiple interbody placement, this may usually require 2–3 separate incisions, with each incorporating at least 2 interbody levels. For interbody levels above L5-S1, the retroperitoneal space is accessed after blunt dissection through the abdominal wall in line with the muscular fibers, and the disc space is palpated at the anterior border of the psoas. The peritoneal contents are carefully maintained in a forward and anterior position to avoid the great vessels based on knowledge of their position through evaluation on preoperative imaging. Minimally invasive retractor systems are then placed with discectomy, disc prep, and trialing to follow. If the anterior longitudinal ligament is released, then interbody fixation screws are placed. For the L5-S1 level, a retroperitoneal approach with access of the disc space between the great vessels is performed similar to the surgical corridor in a supine ALIF, but with the patient in lateral position. Once retractor blades are set with careful protection of the left common iliac vein (LCIV), discectomy and trialing proceed in a similar fashion with subsequent placement of an ALIF footprint cage. Usually, only one interfixated screw is placed to allow for further lordosis, realignment, or correction of the fractional curve from the posterior stage if needed.

Closure of the anterior stage of the procedure proceeds in the usual fashion. Following Stage 1, standing radiographs are taken to determine the degree of achieved correction, residual or new radiculopathy, and if additional coronal or sagittal balance is necessary

in the second stage of surgery. As such, this interval provides a secondary opportunity to adjust the preoperative planning design for the final construct.

Stage 2 of the procedure is next carried out on the second operative day with the patient in the prone position. To minimize the introduction of movement error that could affect robotic accuracy, we add circumferential tape during positioning at the best pad below the axilla and at the distal buttocks. Anesthesia also administers muscle relaxant after monitoring baselines to limit delayed sag or patient movement during instrumentation placement. The robotics system is registered to the patient and screws are placed transfascially through a single midline skin incision or percutaneously through multiple incisions if the patient has a high BMI (Figure 6). All techniques are performed using what we term "light-touch surgery", whereby all instruments pass down perfectly and smoothly coaxial to the robotic arm's end effector to minimize its deflection; any sticking is treated with irrigation and xeroform. Screws are placed in a sequence that is proximal (UIV) to distal (S1), and then all S2-alar-iliac (S2AI) or traditional iliac screws are placed last. This is to ensure maximum accuracy with the screws furthest away from the system most vulnerable to movement error, and because the placement of iliac screws generates an incredible amount of torque that can introduce error into the system. If there is any concern of error, robot and navigation checks are performed or the patient is re-registered with updated C-arm X-rays out of an abundance of caution.

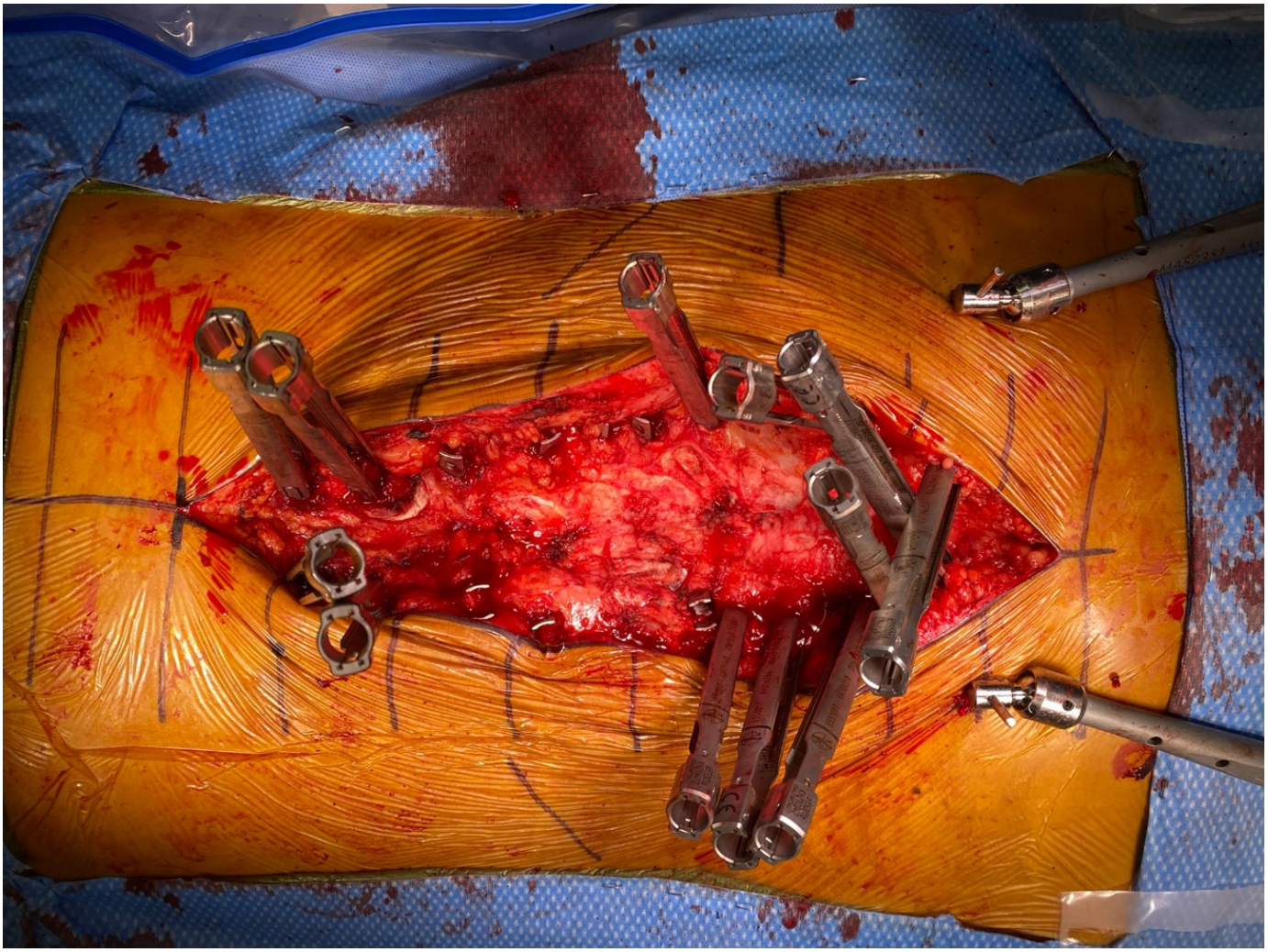

Figure 6. Intraoperative view showing a single skin incision with transfascial placement of all screws. Note extension towers were left off the L1-4 pedicle screws to facilitate visualization for subsequent mini-open posterior column osteotomies.

An intraoperative CT scan with a navigation frame attached to the patient is then obtained as a confirmation scan and to allow for navigated repositioning of any screws that are needed. A navigated burr is then used through the existing transfascial or percutaneous incisions to decorticate and drill out all facet joint levels that do not have anterior interbody fusions. These decorticated pockets are then packed with the bone graft of choice for the surgery. If needed, a mini-open exposure is performed for posterior column osteotomies (PCOs) to allow for further lordosis or scoliosis curve correction. Rods are then passed using a minimally invasive technique with rod passage inserters. While this historically has carried the possibility of great difficulty, the enabling technologies of planar screw planning has allowed this to proceed in very routine fashion. Satellite rods are first secured and locked into position so that their minimally invasive towers can be removed from the working airspace over the wound and any distractive techniques are completed if they are functional kickstand rods [16]. Placement of both main rods then follows. Acceptable alignment is then confirmed using a long film or a series of stitched X-rays (Figure 7). Closure proceeds in the usual fashion after all set screws are secured and towers removed.

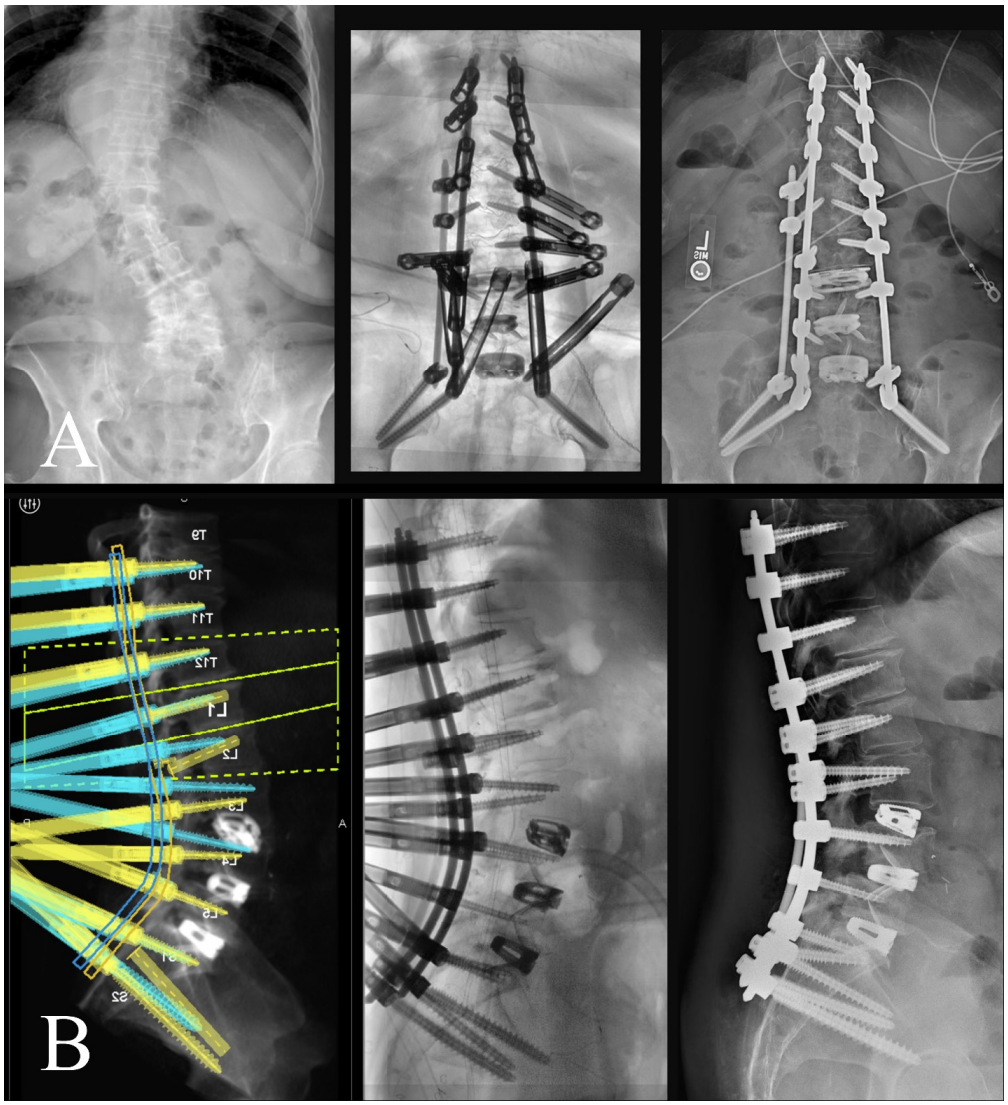

Figure 7. (**A**) (**left**) Preoperative AP X-ray; (**middle**) intraoperative AP long film showing appropriate coronal correction; (**right**) postoperative standing AP X-ray. (**B**) (**left**) Preoperative robotic plan with patient-specific rod geometry; (**middle**) intraoperative sagittal long film with appropriate sagittal correction; (**right**) postoperative standing lateral X-ray.

3. Results

There were 12 patients included in the study (10 female), with a mean age of 68.6 years (range 60–77) and either a diagnosis of degenerative scoliosis (8 patients) or sagittal imbalance (4 patients). All patients underwent minimally invasive robot-assisted percutaneous or transfascial placement of pedicle and iliac screws. Baseline demographic characteristics of the cohort are shown in Table 1. The operative parameters of the cohort are shown in Table 2 with radiographic correction shown in Table 3.

Mean operative values per patient were 9.9 levels instrumented (range 8–11), 3.9 interbody cages (range 2–6), 3.3 iliac fixation points (range 2–4), 3.3 rods (range 2–4), and 18.7 screws (range 13–24). Estimated blood loss was 254 cc (range 150–350 cc) with no patients requiring intraoperative blood transfusions. A total of 224 screws were placed minimally invasively with robotic assistance, with four breaches identified on intraoperative CT and repositioned (three lateral, one medial) for a screw accuracy of 98.2%.

Mean operative skin time for the Stage 2 robot-assisted posterior instrumentation was 347 min (range 242–442 min). Sub-analysis showed six patients who underwent minimally invasive placement of screw fixation only had mean operative times of 305 min, whereas the other six patients who also underwent mini-open laminectomies or posterior column osteotomies (mean 4 levels, range 3–6) had mean operative times of 374 min.

Mean improvement in spinopelvic alignment were sagittal vertical axis (SVA) −5.2 cm (range −20.3 to 4.5 cm), pelvic tilt (PT) 10.8° (range 1–23°), and pelvic incidence–lumbar lordosis (PI-LL) mismatch 21.9° (range −5° to 47°). Eight patients with scoliosis showed improvements in their coronal Cobb angles of 27.3° (range 19–43°). Ten patients ambulated within the first 2 postoperative days. The mean LOS was 5.8 days (range 4–10) and there were no ICU admissions.

Mean follow-up was 21.7 months (range 6–42). There were two reoperations for proximal junctional failure (PJF) (patients 2 and 3). One patient presented with early radiographic evidence of proximal junctional kyphosis (PJK) after a mechanical fall but is currently asymptomatic (patient 9). One patient suffered aspiration pneumonia between her first- and second-stage surgeries (patient 5), resulting in a prolonged hospital stay for respiratory recovery and persistent drug fevers. There were no instances in follow-up of surgical site infections, new neurologic deficits, pseudarthrosis, or implant failure.

Table 1. Summary of baseline characteristics of 12 patients included.

Sex	**Number (%)**
Male	2 (17)
Female	10 (83)
Age	68.6 (range 60–77)
BMI	28.1 (range 17.1–38.8)
Diagnosis	
Sagittal imbalance	4 (33)
Adult degenerative scoliosis	8 (67)
Fusion Extent	
Interbody cages	3.9 (range 2–6)
Levels instrumented	9.9 (range 8–11)
Pedicle screws *	18.7 (range 13–24)
Rods	3.3 (range 2–4)

* includes S2-alar-iliac and iliac screws.

Table 2. Data regarding patient demographics and treatment.

Pt	Age/ Sex	BMI	Procedure	Levels Fused	Rods/Iliac Fixation	Operative Time * (hh:mm)	Discharge	LOS (d)	Follow-Up (m)
1	71F	38.5	L3-S1 OLIF, T11-ilium PSF	9	3/3	4:02	Home	5	38
2	64F	18.8	L4-S1 OLIF, T10-ilium PSF	10	4/4	4:46	ARU	4	42
3	72F	32.3	L2-S1 OLIF, T10-ilium PSF	10	4/4	5:24	ARU	5	30
4	76M	22.7	T12-L4 OLIF, T9-ilium PSF	11	4/4	5:48	Home	6	31
5	60F	38.8	T12-S1 OLIF, T9-ilium PSF	11	4/4	6:22	Home	10 **	20
6	77F	17.1	L1-S1 OLIF, T12-ilium PSF	8	2/2	4:21	ARU	8	19
7	71F	23.8	T12-L1, L4-S1 OLIF, T10-ilium PSF	10	2/2	6:45	Home	5	19
8	71F	26.5	L3-S1 OLIF, T10-ilium PSF	10	3/3	5:42	Home	4	17
9	69F	28.5	L1-S1 OLIF, T9-ilium PSF	11	3/3	6:42	Home	6	17
10	71M	29.7	L1-S1 OLIF, T11-ilium PSF	9	4/4	5:38	ARU	7	13
11	56F	22.6	L4-S1 OLIF, T10-ilium PSF	10	3/3	6:38	Home	5	8
12	65F	37.6	L2-4 ACR, L5-S1 OLIF, T10-ilium	10	3/3	7:22	ARU	5	6

* Posterior stage for screw fixation. ** Due to aspiration pneumonia treatment and persistent drug fevers. Pt = patient; M = male; F = female; ACR = anterior column realignment; OLIF = oblique lumbar interbody fusion; PSF = posterior spinal fixation; LOS = length of stay; d = days; m = months; mm = millimeter; ARU = acute rehabilitation unit.

Table 3. Data regarding patient preoperative and postoperative radiographic parameters.

Pt	SVA (cm)		PT (°)		PI-LL (°)		Coronal Cobb (°)	
1	3.8	2.1	34	22	20	7	54	32
2	6.8	0.8	24	15	16	8	-	-
3	9.6	5.1	35	22	29	10	-	-
4	10.4	3.4	38	21	45	7	-	-
5	5.6	4.8	44	21	48	8	47	4
6	21	0.7	30	18	43	−4	37	15
7	−0.9	1.1	26	19	−12	−7	29	3
8	7.6	5.7	29	22	26	6	38	12
9	7.6	−2.9	19	18	10	−3	41	15
10	3.2	2.5	18	12	1	−7	32	13
11	−1.9	2.6	26	16	9	1	50	16
12	20.4	5.5	28	15	55	1	-	-

4. Discussion

While the benefits of MIS for degenerative spine surgery have been well studied, descriptions of its application in deformity correction have required a closer assessment of these techniques' effectiveness for instrumentation accuracy, achieved fusion, and improvement in coronal and sagittal balance when applied to ASD correction. Several retrospective reviews have suggested that MIS approaches for ASD provide comparable outcomes of

these parameters when compared to open surgery, with numerous other reported benefits consistent with an MIS profile [17–21]. Recognizing certain limitations of MIS approaches in severe or stiff deformities, treatment algorithms were also developed to guide decision making for patients who could benefit from minimally invasive techniques [22]. While this tool has been shown to be useful and reliable, these decision algorithms have not yet included the incorporation of preoperative robotics software for construct design and planning.

This is an important adjunct to patient selection and operative planning, as the inclusion of these tools may increase the pool of patients in which MIS deformity correction may be considered. More recent reports have shown that in cases of even marked deformity, MIS techniques have shown to be quite effective while still benefiting from reduced complication profiles [23]. While these data may indicate that MIS approaches are feasible to correct ASD, they may not underscore the intraoperative limitations and challenges of applying such an approach. Anticipation of the challenges to applying MIS in ASD correction, such as tower collision, fixation of satellite rods, subfascial passage of rods, etc., is imperative for bringing these techniques into regular practice. Our report therefore advocates for preoperative planning of MIS constructs using robotic software to design these constructs in three-dimensional space, but also to modify screw and rod trajectories as intraoperative collisions and conflicts are anticipated. For example, Figure 7 illustrates a case in which two right-sided pedicle screws are preoperatively selected to affix to a satellite rod, rather than the main rod, with pre-adjusted trajectories of these screws allowing for easy intraoperative passage of right-sided rods. Loading pre-planned screw trajectories into the surgical robot ensures accurate and streamlined transfascial placement, accounting for previous components of the case during Stage 1 when interbody cages are placed. Also illustrated in Figure 7 is the omission of a of the left L5 pedicle screw, to avoid tower collision when lordosis correction is achieved. Tower collision at the lumbosacral junction is a common spatial limitation in the operative workspace and may be difficult to anticipate as lordosis correction is achieved during open surgery. This demonstrates how preoperative planning software may aid in anticipating intraoperative spatial limitations of the workflow and permits adjustments of the construct design to yield a surgical plan which achieves an optimal surgical correction but is also technically feasible through an MIS approach. Prior studies showing use of robotics in adult spinal deformity have mostly relied on accuracy of screws or placement of S2-alar-iliac pelvic fixation, which highlights the need to expand upon the benefits of robotics use specifically during this planning stage [24].

Other groups and institutions have implemented various techniques to improve the quality of the extent of preoperative planning in deformity correction to increase operative confidence, increase screw accuracy, and decrease intraoperative fluoroscopy time and surgical complications. One such adjunct is the use of 3D-printed anatomical models for preoperative planning. In a systematic review, these 3D-printed models were shown to increase screw accuracy and improve correction, though they could be associated with significant production costs and time [25]. Additionally, these models are generally used for planning in open surgical correction. Further, while these models may be quite useful in understanding preoperative deformity in order to plan instrumentation, they do not allow for a dynamic understanding of screw trajectory as the deformity parameters change intraoperatively. Again, our series here demonstrates that preoperative robotics software permits a continuous assessment of deformity correction as implants, screws, and rods are planned into the final construct.

Another method of preoperative planning used in ASD is machine learning software to generate patient-specific rods (PSR). This software analyzes the current deformity, then generates a rod with an appropriate length and contour to achieve the final desired correction. A series of 20 patients undergoing ASD correction with preoperative planning for PSRs showed that this software enabled accurate and feasible correction, though in open surgery [26]. Importantly, not all cases included two-stage correction with the use of anterior lumbar interbody fusion (ALIF) for interbody cages. Further, this series found that distal junctional failure was associated with the use of PSRs and was often related

to the absence of interbody grafts at the lumbosacral junction. This may emphasize the importance of preoperative planning software which simultaneously calculates and plans for necessary interbody graft inclusion and the anticipated contour of the final fixation rods. Use of these rods also requires careful and thoughtful prone positioning and the use of Smith-Peterson osteotomies during the case to achieve lordotic correction to allow fixation of the PSR. The preoperative planning workflow presented here instead includes more complex construct designs which include multiple interbody cages, often across important junctional levels, leading to deformity correction which takes place prior to rod placement. In turn, the workflow presented here may be more amenable to an MIS approach in which deformity correction prior to rod passage requires less posterior bony manipulation in order to fix the PSR into the final construct, and includes pre-planned interbody grafts to minimize the risk of junctional failure and reoperation.

In addition to the skillset of lateral access surgery which enables the majority of spinal deformity corrections in MIS surgery, a major barrier to the adoption of MIS deformity surgery is the subsequent requisite long-segment posterior fixation requiring multiple pedicle and iliac screws to be placed minimally invasively, followed by the passage of several long-segment rods. Three-dimensional navigation technologies have reduced these difficulties by providing real-time computer-aided visualization of anatomy in the operating room for placement of these implants [15,27]. We demonstrate here that robotics platforms, with their ability to preoperatively design constructs, can further reduce this barrier to adoption by providing the ability to preoperatively place pedicle and iliac screws for subsequent execution with the robotic arm in the operating room. This was shown to be feasible even for multiple rod placements with multiple iliac fixation points, with mean operating room times of 5 h and 47 min and a screw accuracy of 98.2% across a cohort with a mean of 9.9 levels fused to the lower thoracic spine. While the use of robotics systems has been described for the treatment of adult spinal deformity, the vast majority of these have been for open surgery or descriptions of S2-alar-iliac screw placement [24]. MIS placement of screws in short-segment degenerative pathologies has also been well reported [15,27,28], but their use for long-segment complex deformity correction has been described less frequently. Our series herein thereby serves to illustrate that long-segment constructs can be designed for MIS correction of ASD. The software here aids the design of screw numbers, trajectory, anticipated interbody grafts, and fixation rods. These designs are therefore created within the constraints of an MIS approach, and can be modified preoperatively to be tailored to each patient's anatomy and how each patient's anatomy is projected to change following correction. Placement interbody grafts, followed by pedicle screws and posterior column osteotomies, inherently adjust the spinopelvic parameters of the patient. In turn, this may complicate rod passage, and may limit further lordosis correction by rod bending once all rods are seated. Robot-assisted calculation of these changes with adjustments in construct design helps to ensure that all steps of posterior fixation are practically feasible, but also that fine manipulations to the final construct are allowed through the MIS approach to achieve the desired final result.

Our cohort's final radiographic parameters show the successful realignment of sagittal parameters as an endpoint even in cases of marked sagittal imbalance (patient 6, SVA 21.0 cm; patient 12, SVA 20.4 cm) and mean improvement in coronal Cobb measurements of 27.3° for patients with degenerative scoliosis, highlighting the success of MIS techniques in appropriately selected patients. While the success of open spinal deformity is well established [17–19], complication profiles can differ, and prior studies have demonstrated the benefits of minimally invasive approaches to reduce intraoperative and postoperative complications and hospital stay lengths [22]. Of note, there were no wound, neurologic, or implant-related complications in our series, which is consistent with these prior studies. Here, we achieved optimal radiographic correction outcomes, with similar complication profiles to that of the open literature. Again, these results emphasize that careful preoperative construct planning in select patients allows for comparable outcomes in ASD correction through an MIS approach when compared to open robotic-assisted techniques.

While the majority of MIS deformity correction in ASD relies on anterior realignment through the lateral placement of multiple interbody cages, subsequent long-segment posterior fixation and fusion is still needed. Due to the biomechanical stresses of correcting ASD, multiple rods with multi-pelvic fixation have been used to load-share across these complex constructs [29,30]. Robotics systems allow for the preoperative planning of these complex designs, which further allow for their subsequent execution in the operating room [16]. Ten of twelve patients underwent multi-rod and multi-pelvic fixation via an MIS approach which was only feasible through the ability to preoperatively design and plan these constructs. Our workflow yielded a minimally invasive screw placement accuracy of 98.2% with three lateral breaches and one medial breach identified on intraoperative CT that were subsequently repositioned without neurological deficits or other complications.

A purported benefit of MIS approaches for deformity correction is the preservation of the entirety of the proximal soft tissue envelope during placement of all instrumentation for the prevention of PJK and PJF. Still, we observed two patients who experienced PJF requiring reoperation and proximal extension of their constructs and one patient with radiographic PJK after a fall, highlighting the complex etiologies of this postoperative complication. The two patients who experienced PJF (patients 2 and 3) were early in our series, both of whom underwent transdiscal multilevel stabilization screws (MLSS) [31,32]. With early PJK and subsequent PJF requiring reoperation, we have since abandoned this technique. Ishihara et al. have demonstrated more promising results in PJK prevention, focusing on the proximal screws at the UIV by increasing the pedicle screw angle such that there is a more anatomic approach trajectory toward the anterior inferior vertebral body rather than parallel to the endplate [33]. In addition to longer screw length, this allowed for increased pullout strength at the UIV to prevent the screw from backing out and affecting the proximal disc space that could continue to propagate PJK. They also noted that further kyphosis contouring of the proximal rod to match postoperative reciprocal change in the thoracic spine showed a reduction in PJK and mechanical complications as well. Longer follow-up with a larger cohort over time will be needed to show if there are other mechanisms at play for the observed mechanical complications in our experience.

Lastly, because minimally invasive deformity correction relies on imaging and visualization of the anatomy, the ionizing radiation exposure of both surgeon and patient remains a concern [34]. Patients in our series inevitably underwent a total of three CT scans of their thoracolumbar to lumbosacral spine: (1) prior to surgery for preoperative planning and full understanding of the deformity, (2) between Stage 1 and Stage 2 after interbodies were placed for minimally invasive pedicle screw placement with the robotic software platform, and (3) an intraoperative confirmation CT scan during Stage 2 to confirm that all screws are in appropriate position. While risks of radiation-induced cancers vary substantially by age and gender at the time of exposure, with the risks being lowest in older patients that are usually the population requiring adult spinal deformity correction [35], this patient radiation exposure provides a significant caveat for minimally invasive surgeries as well as an opportunity for further technological development through improved software registration to obviate the need for an interstage CT and lower dose imaging for intraoperative confirmation scans.

We present here the first case series to our knowledge describing in detail the application of robotics systems for minimally invasive adult spinal deformity surgery with posterior instrumentation and fusion to the lower thoracic spine.

Limitations

Our study has several limitations known to retrospective case series, which include electronic charting errors, inaccuracies in radiographic measurements, and selection bias. This was also a single-center and single-surgeon study which precludes at this time a broader conclusion on its applicability across other clinical sites. Because many patients early in our series did not have preoperative patient-report outcome measures (PROMs), we were unable to discuss these results. As such, this paper relies on prior work showing that

realignment and correction of radiographic targets correlates with improved PROMs and clinical outcomes measures [36]. Given the preliminary initial experience of this technique, the described study cohort is small and further research is still needed with larger patient populations across multiple centers to demonstrate its external validity.

5. Conclusions

We present here our series of patients with robot-assisted MIS deformity correction for ASD with proximal instrumentation in the lower thoracic spine, the majority of which required multi-rod and multi-pelvic fixation. We demonstrate in this report that the preoperative design and optimization of these large constructs provided a practical intraoperative surgical workflow which yielded favorable radiologic correction parameters and complication profiles when compared to robot-assisted open techniques. Mean operative time was 5 h 47 min for a mean fusion length of 9.9 levels, highlighting the proficiency of robotic assistance. All patients showed improvements in radiographic parameters and benefited from a low perioperative complication profile consistent with MIS approaches. The present study, to our knowledge, is the first series describing in detail the use of robotics systems for long-segment minimally invasive adult spinal deformity surgery. The increased applicability of these techniques and approaches will elucidate technique variability among surgical centers, in an effort to expand MIS approaches to more patients with ASD.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

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Systematic Review

The Efficacy of Night Bracing in the Treatment of Adolescent İdiopathic Scoliosis: A Systematic Review

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Abstract: Background/Objectives: The effectiveness of night braces alone or in combination with other treatments for adolescent idiopathic scoliosis remains unclear. This systematic review study aimed to review and analyze the available literature to determine whether night braces are an effective treatment for idiopathic scoliosis. **Methods:** A total of 162 databases, including Cochrane Library (reviews, protocols, trials), Web of Science, PubMed, Medline, Scopus, PEDro, CINAHL (EBSCO), Ovid and Google Scholar, were searched for published articles from inception to February 2024. The available literature was screened by the following terms: "scoliosis and night-time brace", "scoliosis and night brace", "scoliosis and part-time bracing", "scoliosis and Providence" and "scoliosis and Charleston". **Results:** Twenty studies were included; only one study was a randomized controlled trial, and most of the studies were retrospectively designed. Providence, Charleston and Boston braces were used as night braces. The Cobb angle was evaluated in all studies, and Cobb angle change after treatment and surgical treatment rates were the parameters that were evaluated the most. In one study, the angle of trunk rotation, quality of life, perception of spinal appearance, and physical activity level were measured. In one study, sagittal plane assessments were performed in addition to the Cobb angle. **Conclusions:** The results of this review suggest that there is no evidence to support the use of night braces in the treatment of adolescent idiopathic scoliosis. Randomized controlled trials with a well-designed methodology are needed to determine the efficacy of night braces.

Keywords: adolescent; brace; scoliosis; spine

1. Introduction

High-quality data support the use of rigid full-time bracing in patients diagnosed with adolescent idiopathic scoliosis (AIS) prior to full skeletal maturation [1,2]. In the study of Weinstein et al. evaluating the effects of different thoracolumbar braces in the treatment of AIS, it was shown that brace treatment was effective with a success rate of 72% in patients who received brace treatment compared to patients who received only observation [2]. In the Gensingen brace, a CAD-based asymmetric brace, the success rate has been reported between 86 to 96% for curvatures between 25 and 40° as well as for curvatures exceeding 40° [3,4]. Also, a recent systematic review conducted by Babaee et al. provides evidence for the effectiveness of bracing in controlling the progression of AIS in curves greater than 40° [5].

Today, the use of a brace can be recommended to the patient as a full-time, part-time, or only at night treatment. Wearing a brace for 20 h or more is considered full time, while wearing one for 12 to 20 h is considered part time. Typically, night-time braces are worn for eight hours at a time [1,6]. For the effectiveness of brace treatment, full-time brace use and patient compliance are important, especially in periods of rapid growth and progression [1,7–11]. However, some authors nowadays suggest that using the brace only at night produces similar effects compared to full-time use [12,13].

The effectiveness of night braces has been assessed in some systematic reviews, and in some of them, it has been concluded that they are effective [14,15]. In contrast, Ruffilli et al. analyzed seven studies until 2020 and concluded that "The current available literature does not permit us to draw conclusions about night-time braces" [16]. Moreover, the study by Bretschneider et al. suggested that daytime or full-time Chêneau brace use was more effective in reducing curvature than the Charleston brace used only at night [17].

According to these contradicting suggestions, high-quality research is needed to comprehensively evaluate the efficacy and potential advantages and disadvantages of night bracing in the treatment of AIS. In particular, it should be taken into consideration that the main aim of bracing is to interfere with the asymmetrical loading by gravity during daytime activities and that the curve may naturally decrease at night due to the relaxation of muscles and ligaments while resting in horizontal positions.

Overall, the efficacy of night bracing in the treatment of adolescent idiopathic scoliosis remains a topic of ongoing research and debate. However, academically and clinically, it was observed that most of the studies included in these systematic reviews [14,15] had a retrospective design and were characterized by methodological deficits. This systematic review was designed with the hypothesis that night braces may be effective in the treatment of AIS when used alone or in combination with other treatments. The aim of this study was to reveal the efficacy of night braces in the treatment of adolescent idiopathic scoliosis by actually examining the content of existing studies, to conduct a systematic review, and to shed light on future studies.

2. Materials and Methods

2.1. Search Strategy

The search strategy was standardized using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist. Relevant published articles on the use of night braces for treating scoliosis and idiopathic scoliosis in adolescents were examined by three independent researchers. In this context, the Online Library System analyzed the electronic databases of Istanbul Bilgi, Marmara and Bandirma Onyedi Eylül Universities. These libraries have a total of 162 databases, including Cochrane Library (reviews, protocols, trials), Web of Science, PubMed, Medline, Scopus, PEDro, CINAHL (EBSCO), Ovid and Google Scholar. Regarding search terms, databases were searched for published articles from inception to April 2024. By reading the abstracts and titles, researchers independently filtered the search results. Initially, duplicate results were examined and excluded. Their inclusion was independently determined after obtaining the full texts of the possibly pertinent studies. The articles were discussed among the researchers in the event that there were disagreements among the authors.

2.2. Selection of the Studies

The available literature was screened using the terms "scoliosis and night-time brace," "scoliosis and night brace," "scoliosis and part-time bracing," "scoliosis and Providence," and "scoliosis and Charleston."

Only publications in English, Turkish and Spanish were considered. Studies that sampled participants with idiopathic scoliosis and diagnosed them with radiographic assessment included interventions, including night-time bracing and presenting objective treatment results such as Cobb angle, angle of rotation, or other outcome measurements. Studies that sampled participants with <10° Cobb angle, studies included patients who

used different braces during the day and night at the same time, studies that included only cases in which certain improvements were achieved in the brace, studies including soft braces, retracted studies, case reports, study protocols, conference abstracts and thesis studies were excluded.

The first and second reviewers independently evaluated the study designs and evidence levels in accordance with the Center of Evidence-Based Medicine in Oxford guidelines for therapeutic studies [18]. Level I was assigned to systematic reviews of randomized controlled trials (RCTs) and RCTs with narrow confidence intervals; Level II was assigned to prospective controlled studies and RCTs of lower quality; Level III was assigned to retrospective controlled studies; and Level IV was assigned to uncontrolled studies.

3. Results

3.1. Descriptive Data

After removing duplicate articles, a total of 89 articles were found between 1960 and February 2024. After abstract and full-text reviews, 20 studies (21 published articles) were included in our study (Figure 1) [13,19–38]. The two included articles were from the same randomized controlled trial. One included 6-month results from the same trial [33], and the other included the trial's full results [38].

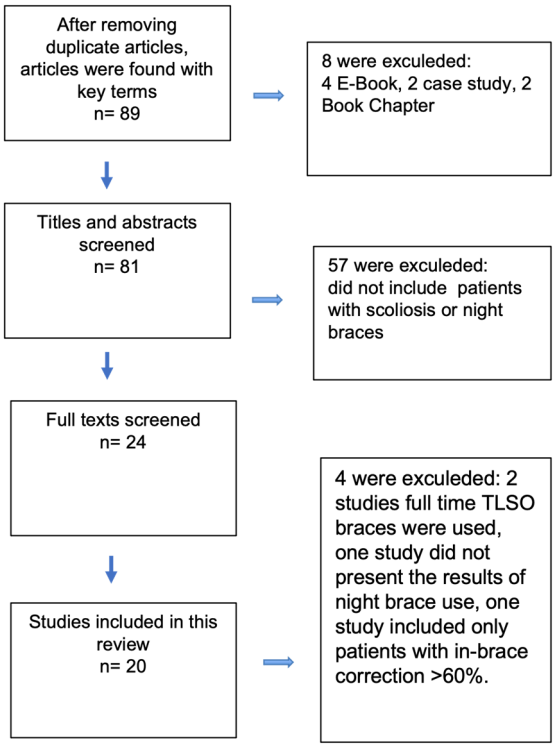

Figure 1. Flow chart of study evaluation and selection process.

The study characteristics are summarized in Table 1. The 20 studies that meet the inclusion criteria were published between 1997 and 2024 and were conducted in eight countries. Five studies are from Denmark [29,32,34,36,37], and five studies are from the USA [19,22,23,28,31] (Table 1). Most of the studies (14 studies) are retrospective studies with level IV evidence. Only one study from Sweden [33,38] is a randomized controlled study with level Ib evidence. In one study, the study design is not specified [12], and the others are uncontrolled prospective studies [13,20,23,25].

Table 1. Characteristics of the studies included in this review.

	Year/Country	Type of Brace/Intervention	Study Time/Sample Size	Gender	Skeletal Maturity/Age	Cobb Angle°	Outcome Measurements	Brace wearing Time	Follow-Up	Survival Rates
Katz et al. [19]	1997, Texas	Boston Charleston	Retrospective *n* = 153 *n* = 166	243 Females 25 Males	Risser 0–2, ≥10 years	25°–45°	Cobb Surgery rate Curve progression	Not specified	34 mos	41% for Charleston 61% for Boston
Price et al. [20]	1997, USA	Charleston	Prospective *n* = 98	90 Females 8 Males	Risser 0–2, ≥10 years	25°–49°	Cobb Curve Progression	Night-time	3.5 years	
Howard et al. [21]	1998, Canada	TLSO Charleston Milwaukee	Retrospective *n* = 45 *n* = 95 *n* = 35	NA	≥10 years		Cobb Surgery rate Curve Progression	Fulltime Night-time Fulltime	20 mos 16 mos 19 mos	55% for TLSO 48% for Charleston 35% for Milwaukee
Karol et al. [22]	2001, Texas	Milwaukee Charleston Boston	Retrospective and prospective *n* = 10 *n* = 53 *n* = 54	117 Males	Risser 0–3, ≥ 10 years	18°–45°	Cobb Curve Progression Surgery rate Compliance with Treatment	-	3.1 years	26% for all braces
D'Amato et al. [23]	2001, Rhode Island	Providence	Prospective *n* = 102	102 Females	Risser 0-2, >10 years	20°–42°	Cobb Curve Progression	8 h/night	>2 years	74%
Gepstein et al. [24]	2002, Israel	Charleston TLSO	Retrospective *n* = 87 *n* = 37	94 Females 28 Males	10–16 years	-	Cobb Curve Progression or Surgery rate	8 h/day 18–22 h/day	24 mos	81.2% for Charleston 82.1% for TLSO
Yrjonen et al. [25]	2006, Finland	Providence Boston	Prospective *n* = 36 *n* = 36	72 Females	Risser 0–3, 10–15 years	>25°	Cobb Curve progression	Night-time 23 h/day	1.8 years	68.6%
Janicki et al. [26]	2007, Canada	TLSO Providence	Retrospective *n* = 48 *n* = 35	83 Females	Risser 0–2, >10 years	25°–40°	Cobb Curve Progression Surgery rate	22 h/day 8–10 h/night	2 years	15% for TLSO 31% for Providence
Lee et al. [27]	2012, Korea	Charleston	Retrospective *n* =95	87 Females 8 Males	Risser 0–2, >10 years	25°–40°	Cobb Curve Progression Surgery rate	8 h/night	>2 years	77.9%
Bohl et al. [28]	2014, ABD	Providence	Retrospective *n* = 34	29 Females 5 Males	Risser 0–2, >10 years	25°–40°	Cobb Surgery rate Curve Progression	8 h/day	-	29%
Ohrt-Nissen et al. [29]	2016, Denmark	Providence	Retrospective *n* = 63	75 Females 2 Males	Risser 0–2, >10 years	25°–40°	Cobb Curve progression HRQOL	Night-time	2 years	57%
Thompson et al. [30]	2017, USA	TLSO Boston	Retrospective *n* = 168	NA	Risser 0–2, >10 years	25°–45°	Cobb Curve Progression Surgery rate	12.2–13.3 h/day	22 mos	64.2–84.6%
Davis et al. [31]	2018, USA	Providence	Retrospective *n* = 56	51 Females 5 Males	Risser 0–2, 10–18 years	25°–40°	Cobb Curve Progression Surgery rate	Night-time	2.21 years	57.1%
Ohrt-Nissen et al. [32]	2019, Denmark	Boston Providence	Retrospective *n* = 37 *n* = 40	75 Females 2 Males	Risser 0–2, >10 years	25°–40°	Cobb	>18 h/day 8 h/day	25 mos	65% for Boston 57% for Providence
Vicente et al. [13]	2021, Spain	Providence	Longitudinal study *n* = 108	94 Females 14 Males	Risser 0–3, 4–15 years	>25°	Cobb Surgery Rate	8–10 h/night	1 year	NA

Table 1. *Cont.*

	Year/Country	Type of Brace/Intervention	Study Time/Sample Size	Gender	Skeletal Maturity/Age	Cobb Angle°	Outcome Measurements	Brace wearing Time	Follow-Up	Survival Rates
Dufvenberg et al. [33]	2021, Sweden	Boston Specific exercises Physical activity	RCT *n* = 45 *n* = 45 *n* = 45	111 Females 24 Males	9–17 yr	25°–40°	Cobb ATR HRQoL, perception of spinal appearance Physical activity	Night-time	6 mos	NA
Heegaard et al. [34]	2023, Denmark	Providence	Retrospective *n* = 135	116 Females 19 Males	Risser 0–4, >10 years	25°–40°	Cobb Curve Progression Surgery rate	Night-time	13-39 mos	39% for Risser 0–2 63% for Risser3–4
Capek et al. [35]	2023, Sweden	Providence Boston	Retrospective *n* = 249 *n* = 109	314 Females 44 Males	Risser 0–3, >10 years	20°–40 °	Cobb Curve Progression Surgery rate Compliance with Treatment	Nightime 23 h	1.45 years	45% for Providence 54% for Boston
Heegaard et al. [36]	2024, Denmark	Providence	Retrospective *n* = 146	127 Females 19 Males	Risser 0–4	25°–45°	Cobb Curve Progression Surgery rate Sagital Plane	Night-time	1year after treatment	17%
Heegaard et al. [37]	2024, Denmark	Providence	Retrospective *n* = 299	271 Females 28 Males	Risser 0–4	25°–55°	Cobb Curve Progression Surgery rate	8 h/night	-	25% for >40° 62% for 40°>
Charalampidis et al. [38] (End results of the study by Dufvenberg et al.)	2024, Sweden	Boston Specific exercises Physical activity	RCT *n* =42 *n* =39 *n* = 41	111 Females 24 Males	Risser 0–4, 9–17 years	25°–40°	Curve Progression Surgery rate	8 h/night	12.9 mos 16.2 mos 16.1 mos	76% for Boston 53% for Exercise 58% for Physical activity

RCT: randomized controlled trial, h: hour, NA: not available.

A total of 2764 participants were included in the studies (Table 1). All patients included in the studies were diagnosed with idiopathic scoliosis. Overall, 1897 of these patients used a Providence or Charleston night brace. In a randomized controlled trial, 45 patients used a Boston brace at night [33,38]. In one study, a Boston brace was used in 168 patients, but it was reported that patients wore the brace for 12 to 13 h a day, but it is not clear at what time of day the brace was worn [30]. Most of the articles stated the duration of wearing the brace as 8 h per day. However, this time of use could have been objectively measured.

In several studies, the Boston brace [19,22,25,32,35] or TLSO brace [21,24,26] was used in studies with a control group, and the Milwaukee brace [21,22] was used as a third group in two studies that used the TLSO and Boston brace in the control group. In the only randomized controlled study, scoliosis-specific exercises and physical activity recommendations were applied in the control groups [33,38].

Two studies included 1850 females (66.9%), and gender characteristics were not presented in them [21,30]. Only male patients were included in the study by Karol et al. [22].

Although other studies reported the inclusion of patients diagnosed with adolescent idiopathic scoliosis (>10 years), one study [13] included patients aged between 4 and 15. Furthermore, the only available randomized controlled trial included patients aged 9 to 17 [33,38].

Studies generally included patients with a Risser value of 0–2. However, four studies included patients with Risser values between 0 and 3 [13,22,25,35]. Two studies, that by Hegard et al. [34,37] and a randomized controlled study [34,38], included patients with Risser values between 0 and 4. The lowest Cobb angle was 18 degrees, and the highest Cobb angle was 55 degrees in the patients included in the studies.

3.2. Outcome Measurements

When the studies' outcome measurements were reviewed, it was determined that all studies involved measuring the Cobb angle and the amount of change in Cobb angle; in other words, the curve progression rate was evaluated. In the studies, progression was defined as an increase in radiographic Cobb angle >5°, while a decrease in Cobb angle of more than 5° was defined as success.

In most of the studies, the rate of surgical treatment was also evaluated. Only Karol et al. and Capek et al. evaluated brace compliance [22,35]. Vicente et al. presented the results of POTSI (Posterior Trunk Symmetry Index) and deformity index evaluation at the beginning of their study but did not specify how these values changed after treatment [13]. This systematic review's only randomized controlled trial included assessments of Cobb angle, ATR (angle of trunk rotation), quality of life, perception of spinal appearance, and physical activity level [33]. However, in the other article in which the study results were published, these evaluations were not reported, and only the curve progression rate was presented [33,38]. A retrospective analysis of 146 patients by Heegaard et al. included sagittal plane assessment as well as Cobb angle change [36].

4. Discussion

The effectiveness of night braces alone or combined with other treatments for adolescent idiopathic scoliosis remains unclear. This systematic review study aimed to review and analyze the available literature to determine whether night braces are an effective treatment for idiopathic scoliosis at risk for being progressive. A total of twenty original research studies were included and analyzed. There was only one randomized controlled study, which two published articles were in reference to [33,38].

In patients with curves greater than 20° ± 5° Cobb, who are still growing (Risser 0 to 3), and who have deformity progression or an increased risk of worsening, bracing is advised unless a clinician with expertise in conservative treatment of spinal deformities determines otherwise [6,7]. All studies reported changes in Cobb angles, as a measure of deformity. Patients with Cobb angles ranging from 25 to 40 degrees of curvature were

included in ten of the studies. Among the patients included in the studies, the lowest Cobb angle was 18 degrees, and the highest Cobb angle was 55 degrees.

Although the mean baseline Cobb angle values differed in the studies, a 48–81.2% success rate was reported. Katz et al. and Howard et al. reported that Boston and TLSO braces worn full time were more effective than night braces [19,21]. Karol et al. and Gepstein et al. reported that night braces had similar effects to other brace types [22,24]. Howard et al. compared the effects of TLSO, Charleston and Milwakee braces and concluded that "The thoracolumbosacral orthosis was superior at preventing curve progression in adolescent idiopathic scoliosis." [21]. Yjonen and Janicki emphasized that night braces may be effective in small curves [25,26]. The only RCT that could be included in this systematic review reported that scoliosis-specific exercises, physical activity and night bracing had similar effects on Cobb angle improvement during the first six months of treatment [33]. In the end-result article of the same study but with a different first author, the success of the night brace was reported as 76% [38]. The article presenting the result did not present the results of the parameters evaluated, unlike the article presenting the results of the first six months [38]. The most important methodological problem in this randomized controlled trial is that the exercises or physical activity recommended to the patients must be controlled. The authors also did not present the Cobb angle values at the beginning and end of the treatment [33,38].

A study reporting that night braces are highly effective in the literature could not be included in this review [12]. Only patients with an initial in-brace Cobb angle correction greater than 60% were included by the authors [8]. Unsurprisingly, the results outperform those of other published cohorts when patients with the best possible in-brace correction are the only ones included and when X-rays are taken in the supine position [12]. The exclusive inclusion of patients with a correction effect of > 60% (X-rayed in horizontal position) disqualifies this study for any comparative analysis (selection bias). The paper by Simony et al. needs to include information regarding the results of patients whose correction effect was less than 60 degrees. Since the Risser sign has not been documented, the authors cannot confirm that each patient satisfies the SRS inclusion requirements (Risser 0–2) [12]. The different patient cohorts presented in this study had an average age exceeding 13 years, so we may assume the average patient from this study was at a Risser 2–3, which would represent a more mature sample. Within the BRAIST study by Weinstein and colleagues [2], as well as in other studies following the inclusion criteria for studies on bracing, the average age is about 12.6 years [29,39]. These facts, among others, were outlined in a letter to the editor from Potts [40].

Idiopathic scoliosis is called adolescent idiopathic scoliosis if a patient is diagnosed at the age of 10 years or older [6,7]. In the criteria recommended by the Scoliosis Research Society (SRS) to investigate the effectiveness of brace treatment, it was reported that the age of the patients should be older than 10 years [41]. In the majority of studies, patients with idiopathic scoliosis over the age of 10 years were included. One study included patients aged between 9 and 17 years [33,38]. In a single intervention-designed longitudinal study by Vicente et al., 108 participants aged 4–15 years with a main curve more significant than 25 degrees and a Risser 0–3 were examined. They reported that ISJ-3D night braces slowed the increase in angle values and progression of the curve. Female patients were followed up until Risser 4, and male patients were followed up until Risser 5. The mean follow-up period was reported as 2.78 years for males (SD $\pm$ 1.85) and 1.97 years for females (SD $\pm$ 1.19). An important problem here is that the mean age at the end of treatment was reported as 13.7 $\pm$ 1.1 years for males and 13.7 $\pm$ 1.2 years for females [13]. If treatment was completed at Risser 5 in males, the mean age should be expected to be older, such as 16 or 17 years [42], while another issue is that a patient who started treatment at the age of 4 years would be expected to have a mean follow-up time of about 10 years when followed up to Risser 4 or 5 values. Such situations seem contradictory in terms of interpreting the study results.

According to SRS standardization criteria, Risser values of patients included in bracing studies are recommended to be 0–2, which is a child's fastest growing period [41]. In the nine studies included in this systematic review, a Risser value of 0–2 was determined as the inclusion criterion. A Risser value between 0 and 3 was the inclusion criterion in 4 studies. The Risser value of 0–4 was approved as an inclusion criterion by Heegard et al. [34,36,37] in three retrospective studies and the end results study of a randomized controlled trial [38]. The risk of scoliosis progression in a child with a Risser value of 0 and a high growth potential cannot be the same as the risk of scoliosis progression in a child with a Risser value of 4 who has completed most of his/her maturation [7]. The fact that this difference will impact the study's findings should be taken into account. In the retrospective cohort study by Janicki et al., the authors reported that the Providence brace was more effective in preventing surgery and curve progression when initial curves were 35 degrees or less, according to the new SRS criteria. However, the authors' inclusion criteria and patient ages were not compatible. While the authors reported a Risser sign 0, 1, or 2 as inclusion criteria, it was reported that patients aged between 10.3 and 17.2 years were included in the TLSO group and patients aged between 10.5 and 14.9 years were included in the Providence group range [26].

In studies evaluating the effectiveness of brace treatment, follow-up for at least 2 years after maturation is completed is recommended [41]. Among the studies that could be included in this review, only the study by Lee et al. reported that patients were followed up for 2 years after maturation was completed. In the other studies, the mean follow-up period was short and ranged from 6 to 42 months.

Notably, relatively few pertinent studies were found during the analysis period (1997–2024), and the methodological quality was severely lacking. For example, Price et al. mention that using a night brace should be encouraged; however, the study was a prospective study only, and its methodological strength is weak to offer conclusions. The authors reported that 115 (83%) of the patients who participated in the study showed improvement. However, only 44 patients completed the treatment program. The 139 patients evaluated for inclusion in the study were reported to be between 10 and 16.6 years old, but the mean age of the patients included in the study was not presented. The mean follow-up period of the patients was reported to be one year and seven months. It was reported that brace treatment was followed up for 6–8 months after Risser 4 in female patients and 12–18 months after Risser 4 in male patients. Considering the follow-up period, it can be considered that the patients included in the study were older and the risk of progression was quite low [20].

In addition to the fact that the majority of the included studies were retrospective, one of the important methodological problems in the studies is that treatment compliance was not evaluated in most studies. Karol et al. reported unsuccessful results with low patient compliance (38%) in their study examining the efficacy of different types of braces in male patients [22]. In a retrospective study by Gepstein et al., patients with adolescent idiopathic scoliosis treated with the Charleston brace (85 patients) or TLSO brace (37 patients) were analyzed. The compliance was reported to be around 80%. However, although it was stated that the curvatures were measured at the beginning and end of the treatment, the degrees of curvature expected to be expressed as Cobb angle were not presented to give an idea in terms of any comparison or homogeneity of the groups, and the study methodology is weak in these respects and in terms of being retrospective [24]. Ten of the seventeen patients did not comply with their treatment, according to Bohl et al.'s report, and there was a correlation between the rate of surgery and treatment compliance [28]. Furthermore, Capek et al. reported that both the compliance and success of brace use were quite low in their study [35].

Another important point that draws attention in this review study is that in some studies, the efficacy of night braces was evaluated with supine X-rays, while the efficacy of the brace applied to the control group was evaluated with standing X-rays [22,25,31]. This creates a problem for comparing the efficacy of two different braces because it has been

reported in many studies that the angle of curvature is lower in supine imaging methods compared to standing imaging methods [43–46].

Considering the results of these studies, it is interesting to see that several systematic reviews have been conducted on night braces in the treatment of scoliosis, and some conclusions have been drawn from the literature [14,15]. Furthermore, statements that night brace use alone is effective in the treatment of idiopathic scoliosis were also presented, but it was emphasized that further studies including more sociodemographic data are needed [13]. A review of the literature on the subject shows that it is impossible to reach definitive conclusions on the effectiveness of the use of night braces alone in treatment due to methodological deficits, design problems, and other problems related to evaluations based on existing studies [47].

Costa et al. [47] highlight the insufficiency of randomized controlled trials to draw conclusive results on the effects of night-time braces. The study emphasizes the methodological limitations of existing research, which is predominantly retrospective, cautioning against recommending the use of night-time braces based on current evidence. Additionally, the study underscores the importance of considering the positioning of measurements when assessing the efficacy of wearing a night-time brace, indicating a gap in reflecting the true impact of such braces in a horizontal position. However, it is seen that Costa et al. did not examine the contents of the studies they included in their meta-analysis in detail. In their meta-analysis, they included the study of Simony et al. [12], which we did not include in our review study, and reported the success of rigid night braces as 52–89% [47]. Regarding this, a selective study with favorable inclusion criteria was conducted by Simony et al. The paper contains no information regarding the results of patients whose correction effect was less than 60 percent. Remarkably, neither the abstract nor the discussion go into further detail about this specific patient selection. Furthermore, the group of Simony et al. could not satisfy the SRS inclusion requirements for research involving braces [12].

The systematic review by Ruffili et al. published in 2021 evaluating the effect of night bracing in adolescent idiopathic scoliosis included seven studies [16]. The authors did not include some of the studies included in this study that were published before 2021 in their review [20,23,27–31]. A total of 20 studies published up to 2024 evaluating the efficacy of night bracing in patients with adolescent idiopathic scoliosis were included in this systematic review. Comparable to our findings, Ruffili et al. stated that there is not enough information in the literature at this time to allow us to make judgments regarding braces for use at night in the management of adolescent idiopathic scoliosis [16].

Generally, asymmetric techniques with strong corrective effects are applied in the treatment of scoliosis to reverse asymmetric loading on the vertebrae in both brace and exercise approaches, as well as in the control of activities of daily living [1,40,48–50]. Night braces are worn only during sleep and do not support the spine during daytime hours. This limited use can result in the spine not constantly receiving the necessary corrective forces. However, it is important to reverse the asymmetrical forces acting on the spine against gravity in daily living activities. A detailed review of the available studies in the literature shows that the results of these studies suggest that night braces may not provide the continuity needed to stop or correct the progression of AIS at risk for being progressive.

The strength of this systematic review study is its detailed examination of the articles' contents. This study has several limitations The review was limited to papers published in the English, Turkish and Spanish languages, so it is possible that other potentially relevant studies were omitted. The majority of the studies reviewed were retrospectively designed and only one was a randomized controlled trial. A meta-analysis study was not possible due to the lack of randomized controlled trials. Treatment outcomes may also be impacted by variations in the night brace types utilized in the Providence, Charleston, and Boston brace studies. Finally, it is challenging to reach a firm conclusion regarding the long-term effects of night bracing due to the lack of data on long-term outcomes.

5. Conclusions

According to the results of this systematic review, the number of randomized controlled trials is insufficient to draw conclusions about the effects of the use of night braces. Furthermore, the studies are controversial in terms of methodological quality, so it is inappropriate to recommend the use of night bracing in management of AIS based on the published research, which is almost all retrospective, and the assessment of the effectiveness of bracing in the horizontal position prevents comparability and a proper interpretation of the results. Additionally, it is seen that the follow-up periods of studies with night braces are too short to decide on the success rate. In order to optimize treatment outcomes in AIS, it is very important to take into account various factors such as patient compliance, additional exercises and the type of brace used, and the results could not be isolated in terms of the effects of these conditions.

Well-designed prospective RCT studies with comparable unselected samples are needed to clarify this subject's information and reach a definitive conclusion. In order to standardize studies, parameters such as age, Risser sign, Cobb angle, gender, treatment compliance and even progression factor estimation should be determined and optimal methods should be determined through studies with long-term follow-up and comparison of different treatment applications.

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The Optimal Lowest Instrumented Vertebra to Prevent the Distal Adding-On Phenomenon in Patients Undergoing Selective Thoracic Fusion for Adolescent Idiopathic Scoliosis with Lenke Type 1A and 1B Curves: Comparison of Nine Selection Criteria

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Abstract: Background/Objectives: There is no solid consensus regarding which lowest instrumented vertebra (LIV) selection criterion is best to prevent distal adding-on (DA) after adolescent idiopathic scoliosis (AIS) surgery. This study aims to search out the LIV selection criteria in the literature and to compare the ability of each LIV selection criterion to prevent DA in patients with AIS. **Methods**: Patients who underwent thoracic fusion for AIS of Lenke type 1A or 1B were included in this study. Nine criteria for LIV selection were found in a literature review. For each patient, whether the postoperative actual location of LIV was met with the suggested locations of the LIV was assessed. The preventive ability of nine criteria against DA was evaluated using logistic regression analysis. The patients who met the LIV selection criteria but developed DA were investigated. **Results**: The study cohort consisted of 145 consecutive patients with a mean age of 14.8 years. The criteria of Suk (OR = 0.267), Parisini (OR = 0.230), Wang (OR = 0.289), and Qin (OR = 0.210) showed a significantly decreased risk of DA if the LIV selection criterion was chosen at each suggested landmark. As the additional levels were fused, there was no statistically significant benefit in further reducing the risk of DA. Among the patients who met each criterion, the incidence of DA was lower in criteria by Takahashi (5.9%), Qin (7.1%), and King (7.4%) than the others. **Conclusions**: Qin's criterion, using the substantially touching vertebra concept, has the highest preventive ability against DA development. Extending the instrumentation further distal to this suggested LIV criterion did not add further benefit.

Keywords: adolescent idiopathic scoliosis; distal adding-on; lowest instrumented vertebra; selection of level; substantially touching vertebra

1. Introduction

Thoracic fusion is a common strategy used for surgical treatment for adolescent idiopathic scoliosis (AIS) with Lekne type 1A and 1B curves, with the goals of achieving surgical correction of thoracic curves while preserving as many lumbar motion segments as possible [1–6]. In thoracic fusion for these curves, the distal adding-on (DA) phenomenon, which is characterized as a progressive correction loss due to an increase in vertebral deviation or disc angulation below the lowest instrumented vertebra (LIV), has been a concern for a long time. Postoperative DA can negatively affect the clinical outcomes and sometimes necessitates revision surgery [7]. DA sometimes leads to increased coronal decompensation, which could lead to a bad appearance and degenerative changes later in life [5]. Numerous studies have demonstrated that improper location of the LIV is strongly

associated with DA development; therefore, proper selection of the LIV level is warranted to prevent DA [7–17].

With regard to LIV determination, several authors have proposed the optimal LIV location on the basis of diverse radiographic parameters such as the location within the stable zone, vertebral rotation, adjacent disc angulation, and curve flexibility [10–13,18,19]. Since King et al. first suggested that the optimal UIV level should be stable vertebra (SV), nine LIV selection criteria in Lenke type 1 curves have been proposed in the literature so far [7,10–16,18]. Although each criterion demonstrated its preventive ability against DA development in their original articles, they still require the external validation with regard to DA prevention. In addition, because each criterion was suggested by different radiographic findings, each criterion may provide different optimal LIV levels even for one patient. Therefore, we thought it necessary to comprehensively evaluate the preventive ability against DA development including all the current criteria for Lenke 1A and 1B curves.

Thus, this study primarily aims to compare the ability of each LIV selection criterion to prevent DA in patients with AIS of Lenke type 1A and 1B curves. We also investigated how the optimal LIV levels suggested by the nine criteria are agreeable with each other.

2. Materials and Methods

2.1. Study Cohort

This study was approved by the institutional review board at our institution (SMC 2022-08-128), and the need for informed consent was waived because of the retrospective nature of this study. The consecutive patients who underwent posterior thoracic fusion for AIS with Lenke type 1A or 1B curves between 2012 and 2020 were included. The minimum follow-up duration was two years. Exclusion criteria are as follows: patients with non-idiopathic scoliosis, patients undergoing anterior thoracic surgery, and patients with a follow-up loss within two years.

2.2. Surgical Protocol

Surgeries were performed by one of the two senior surgeons using conventional pedicle screw-based posterior instrumentation and fusion. The surgical techniques used to correct deformity were the same for all patients. After inserting pedicle screws, the rod was inserted on the concave side. The scoliosis was corrected, and thoracic kyphosis was created by rotating the rod counterclockwise. Direct vertebral rotation was performed at the 3–4 vertebrae of the apex, and then the screw caps were locked. A convex rod was inserted with underbending to press the thoracic hump, and segmental compression and distraction were performed around the UIV and LIV areas to correct the remnant vertebral tilt. The LIV was selected on a standing whole-spine radiograph considering various radiographic parameters such as SV, neutral vertebra (NV), end vertebra (EV), and their relationship to the center sacral vertical line (CSVL).

2.3. Searching for the LIV Selection Criteria

Published clinical studies and review articles dealing with the selection of LIV in AIS for surgical treatment were included for this study. PubMed, Scopus, Web of Science, and Google Scholar were used to search relevant studies. The following key words were searched in the databases: “adolescent idiopathic scoliosis”, “fusion level”, “lowest instrumented vertebra”, “adding-on”, “Lenke type 1”, “Lenke type 1A or 1B”, and various combinations of these terms. A total of 57 studies were identified. Finally, nine articles suggested LIV selection criteria for Lenke type 1 curves [7,10–16,18]. The nine criteria of LIV selection are summarized in Table 1.

Table 1. Summary of the nine LIV selection criteria.

Study	Curve Type	No. of Patients	Mean Age (Years)	Mean FU (Years)	Suggestion
King et al. (1983) [18]	King 3, 4, 5	405	14.8	4.0	SV
Suk et al. (2003) [10]	King 3, 4	42	15.5	4.2	Diff. between NV and EV: $\leq$1 levels $\rightarrow$ NV $\geq$2 level $\rightarrow$ NV-1
Parisini et al. (2009) [11]	Lenke 1A	31	16.3	Min. 2	Direction of rotation at LEV+1 is equal to that of thoracic curve and diff. between SV and EV is $\geq$3 level $\rightarrow$ L2 or L3. Otherwise $\rightarrow$ SV-2 or SV-3
Wang et al. (2011) [7]	Lenke 1A	45	-	3.6	1st vertebrae >10 mm from CSVL
Sarlak et al. (2011) [12]	Lenke 1A	36	15.8	4.3	L3 tilt (−) $\rightarrow$ LEV-1 L3 tilt (+) $\rightarrow$ LEV
Takahashi et al. (2011) [13]	Lenke 1B, 1C, 3C	172	14	2	SV+1
Matsumoto et al. (2013) [14]	Lenke 1A	112	16.1	3.6	LTV
Qin et al. (2016) [16]	Lenke 1A	104	14.5	Min. 2	LSTV or nSTV+1
Fischer et al. (2018) [15]	Lenke 1, 2	544	14.7	4.1	LTV within NV-2

SV indicates stable vertebra; NV, neutral vertebra; EV, end vertebra; Diff., difference; Min., minimum; LEV, lower end vertebra; CSVL, center sacral vertical line; LIV, lower instrumented vertebra; LTV, last touched vertebra; LSTV, last substantially touched vertebra; nSTV, non-substantially touched vertebra.

2.4. Radiographic Measurements

For all patients, whole-spine standing posteroanterior, lateral, and fulcrum bending radiographs were taken preoperatively. After surgery, standing posteroanterior and lateral whole-spine radiographs were performed at six weeks, three months, six months, and then annually as part of a routine evaluation of all scoliosis cases. First, we designated radiographic parameters such as EV, NV, and SV on a preoperative whole-spine AP radiograph (Figure 1). The last touching vertebra (LTV) and last substantially touching vertebra (LSTV) were measured using CSVL. On the same radiograph, the nine suggested LIVs according to the selection criteria were separately recorded. Then, we compared the location of suggested LIVs and the actual LIV, and evaluated whether the actual LIV was the same, proximal, or distal relative to the suggested LIV. DA was defined as a progressive increase in the number of vertebrae included within the distal curve, with either an increase of more than 5 mm in the deviation of the first vertebra below the instrumentation from the CSVL or an increase of more than 5° in the angulation of the first disc below the instrumentation [7]. Finally, the preoperative Cobb's angle (CA) of the main thoracic curve (MTC), flexibility of the MTC, postoperative CA of the MTC, and correction rate of the MTC were measured.

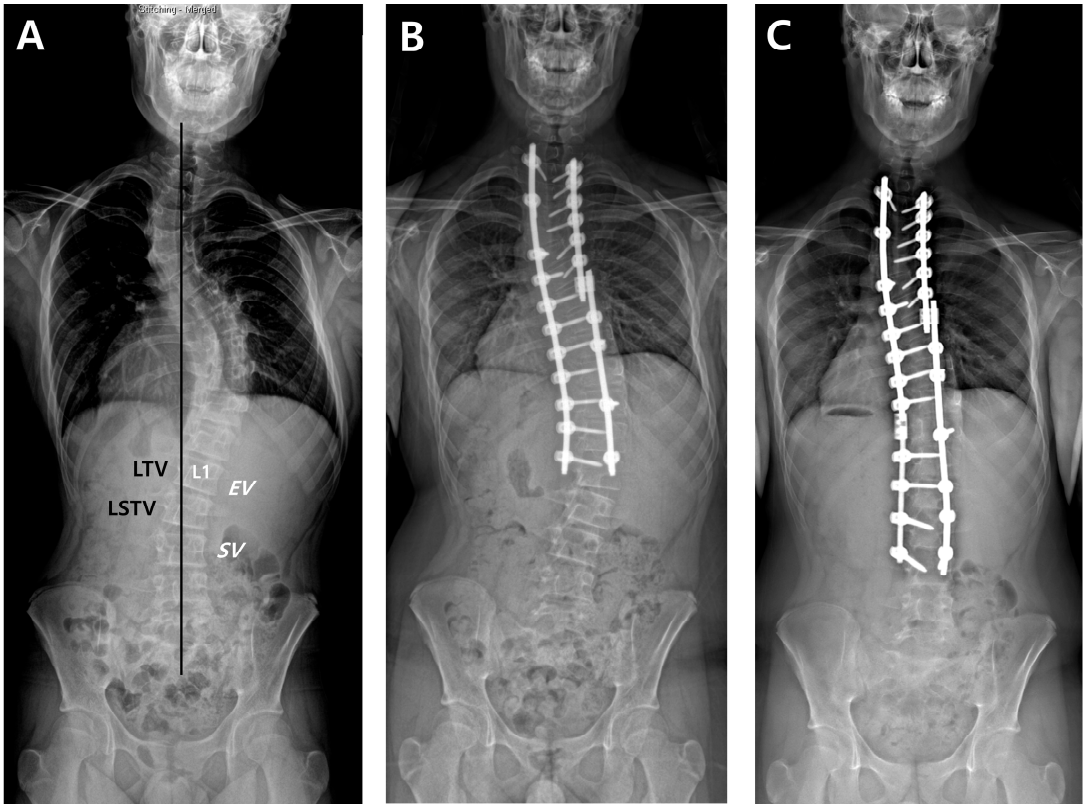

Figure 1. A thirteen-year-old male underwent posterior fusion from T1 to L1 for AIS of Lenke type 2A curves (**A**,**B**). Revision surgery with fusion extension to L3 was carried out due to the development and progression of DA (**C**). According to the nine LIV selection criteria, the postoperative actual LIV (L1) met the criteria by Wang, Sarlak, Matsumoto, and Fischer. The location of the postoperative LIV was proximal to the suggested LIVs by King (L3), Suk (L3), Parisini (L2), Takahashi (L4), and Qin (L2).

2.5. Outcomes Measures

We calculated the mean level and distribution of the suggested LIVs according to the nine criteria. For describing LIV location, vertebral bodies were numbered as follows: 9 as T9, 10 as T10, 11 as T11, 12 as T12, 13 as L1, 14 as L2, 15 as L3, and 16 as L4. Then, we evaluated the preventive capability against DA separately when the actual LIV was proximal to the suggested LIV location and when the actual LIV was distal to the suggested LIV location. We also analyzed the degree of agreement among the nine criteria of LIV selection in pairs. Finally, we investigated the patients who met the LIV selection criteria but developed DA in each criterion.

2.6. Statistical Analysis

Data were presented as frequencies with percentages for categorical variables and means with standard deviations for continuous variables. The Chi-square test or Fisher's exact test were performed to compare the categorical variables and analysis of variance (ANOVA) for continuous variables among groups. Logistic regression analysis was performed to determine the preventive capability of DA. The results were expressed as the odds ratio (OR) with a 95% confidence interval (CI). Agreement among the nine criteria was evaluated using the intra-class correlation (ICC) test. ICC values are interpreted as follows: >0.8 denotes very good; 0.6~0.8, good; 0.4~0.6, moderate; 0.2~0.4, fair; and <0.2, poor. Statistical analyses were performed by professional statisticians using SPSS (version 27.0.0; IBM Corp., Armonk, NY, USA). A p value of < 0.05 was considered statistically significant.

3. Results

3.1. Baseline Data

The study cohort consisted of 145 consecutive AIS patients (26 males and 119 females). The mean age at the time of surgery was 14.8 ± 2.6 years. There were 117 patients with Lenke type 1A and 28 with type 2A. Preoperative CA of the MTC was 55.1 ± 10.3°, and flexibility of the MTC was 52.7 ± 17.2%. Postoperative CA of the MTC improved to 52.7 ± 17.2° with a correction rate of 65.1 ± 13.3%. There were 54 patients who met the criteria by King, 109 by Suk, 118 by Parisini, 117 by Wang, 136 by Sarlack, 17 by Takahashi, 109 by Matsumoto, 84 by Qin, and 112 by Fischer (Table 2). There were no significant differences with regard to female sex, age, Lenke type, preoperative CA of the MTC, flexibility of the MTC, postoperative CA of the MTC, and correction rate among the patients who met the nine criteria (Table 2).

Table 2. Comparison of characteristics in patients who met each LIV criterion.

	King	Suk	Parisini	Wang	Sarlak	Takahashi	Matsumoto	Qin	Fischer	*p*
No. of patients	54	109	118	117	136	17	109	84	112	-
Female (%)	83.3%	80.7%	82.2%	82.9%	82.4%	88.2%	81.7%	82.1%	83.9%	0.999
Age (years)	14.5	14.9	14.7	14.7	14.9	13.2	14.7	14.6	14.6	0.536
Lenke 1A (%)	81.5%	79.8%	79.7%	79.5%	80.1%	85.1%	78.9%	77.4%	78.6%	0.770
Pre CA (°)	54.8°	56.1°	56.4°	55.5°	56.0°	52.9°	55.3°	54.9°	55.1°	0.913
Flexibility (%)	53.0%	51.6%	50.7%	51.9%	51.8%	53.9%	52.4%	52.3%	52.7%	0.993
Post CA (°)	19.2°	20.2°	20.6°	19.9°	19.8°	15.1°	19.8°	20.0°	19.5°	0.653
Correction rate (%)	65.3%	64.5%	63.9%	64.7%	65.2%	71.1%	64.7%	64.0%	65.1%	0.775

Numbers are presented as the mean value. LIV indicates lowest instrumented vertebra; pre, preoperative; CA, Cobb's angle; post, postoperative.

3.2. Suggested LIV Location According to the Criteria

The suggested location of LIV was the most proximal in Parisini's criteria (mean level of 11.4), while the LIV location suggested by Takashahi was the most distal (mean level of 14.1) (Table 3). The LIVs suggested by the criteria were most frequent in T12, followed by T11 and L1. The detailed distributions of LIV suggested by each criterion are also presented in Figure 2. The actual location of LIV was the mean level of 12.3 ± 1.1; the mean level of EV was 11.7 ± 1.0, NV was 12.3 ± 1.6, and SV was 13.1 ± 1.7 (Table 3). The mean actual LIV level of the current study population was approximately similar to the NV level and was located between the EV and SV levels.

Table 3. Summary of suggested LIV location according to the nine criteria.

	Mean ± SD	Minimum	Maximum
Nine criteria			
King	13.1 ± 1.7	9.0	16.0
Suk	12.1 ± 1.4	9.0	15.0
Parisini	11.4 ± 1.9	7.0	14.0
Wang	12.1 ± 1.4	8.0	15.0
Sarlak	11.7 ± 1.0	8.0	14.0
Takahashi	14.1 ± 1.7	10.0	17.0
Matsumoto	12.0 ± 1.6	8.0	16.0
Qin	12.6 ± 1.6	9.0	16.0
Fischer	12.1 ± 1.6	8.0	16.0

Table 3. *Cont.*

	Mean ± SD	Minimum	Maximum
Current Study population			
EV	11.7 ± 1.0	8.0	14.0
NV	12.3 ± 1.6	9.0	16.0
SV	13.1 ± 1.7	9.0	16.0
Postoperative actual LIV	12.3 ± 1.1	9.0	14.0

7 indicates T7; 8, T8; 9, T9; 10, T10; 11, T11; 12, T12; 13, L1; 14, L2; 15, L3; 16, L4; 17, L5; SD, standard deviation; LIV, lowest instrumented vertebra; EV, end vertebra; NV, neutral vertebra; SV, stable vertebra.

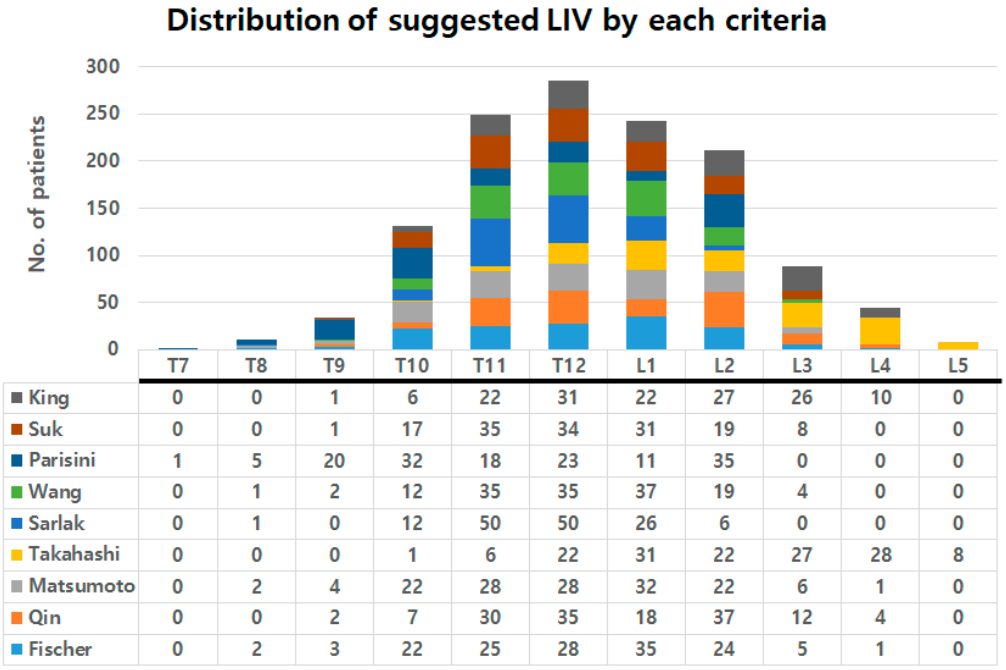

Figure 2. Graph showing distribution of suggested LIV by each criterion.

3.3. Comparison of Preventive Ability against DA by Odds Ratio

During a mean follow-up duration of 82.4 ± 58.6 months, a total 24 of 145 patients (16.6%) developed DA. The rates of DA did not differ according to the LIV ($p = 0.241$). In logistic regression analysis, when the actual LIV location is same as the LIV suggested by the criteria of Suk, Parisini, Wang, and Qin, the risk of DA significantly decreased compared to cases with stopping at a proximal level to the suggested LIVs (OR = 0.267, $p = 0.010$ for Suk; OR = 0.230, $p = 0.045$ for Parisini; OR = 0.289, $p = 0.020$ for Wang; and OR = 0.210, $p = 0.004$ for Qin) (Table 4). The data also showed that even if levels were fused for longer than the suggested LIV location, there was no statistically significant benefit in further reducing the risk of DA except for Fischer's criteria. In the case of Fischer's criteria, the risk of DA was reduced when selecting a level distal to rather than at the suggested LIV level (OR = 0.221, $p = 0.025$).

Table 4. Prevention of distal adding-on according to the nine LIV selection criteria.

	B	S.E	Wald	*p*	Odds Ratio	95% CI
King						
Proximal to LIV vs. at LIV	−1.190	0.653	3.323	0.068	0.304	0.085–1.094
At LIV vs. distal to LIV	−0.251	1.195	0.044	0.833	0.778	0.075–8.095

Table 4. *Cont.*

	B	S.E	Wald	*p*	Odds Ratio	95% CI
Suk						
Proximal to LIV vs. at LIV	−1.319	0.513	6.608	**0.010**	0.267	0.098–0.731
At LIV vs. distal to LIV	−1.487	0.816	3.324	0.068	0.226	0.046–1.118
Parisini						
Proximal to LIV vs. at LIV	−1.471	0.734	4.012	**0.045**	0.230	0.054–0.969
At LIV vs. distal to LIV	−0.306	0.705	0.188	0.665	0.736	0.185–2.935
Wang						
Proximal to LIV vs. at LIV	−1.240	0.533	5.407	**0.020**	0.289	0.102–0.823
At LIV vs. distal to LIV	−0.413	0.592	0.486	0.486	0.662	0.208–2.111
Sarlak						
Proximal to LIV vs. at LIV	−1.463	0.754	3.766	0.052	0.231	0.053–1.015
At LIV vs. distal to LIV	−0.138	0.484	0.081	0.775	0.871	0.337–2.251
Takahashi						
Proximal to LIV vs. at LIV	−0.784	1.704	0.533	0.465	0.457	0.056–3.745
At LIV vs. distal to LIV	−1.131	0.229	1.487	0.222	−0.323	0.052–1.985
Matsumoto						
Proximal to LIV vs. at LIV	−0.768	0.501	2.348	0.125	0.464	0.174–1.239
At LIV vs. distal to LIV	−1.162	0.689	2.844	0.092	0.313	0.081–1.207
Qin						
Proximal to LIV vs. at LIV	−1.563	0.544	8.241	**0.004**	0.210	0.072–0.609
At LIV vs. distal to LIV	−0.611	1.125	0.295	0.587	0.543	0.060–4.922
Fischer						
Proximal to LIV vs. at LIV	−0.135	0.507	0.071	0.790	1.145	0.424–3.092
At LIV vs. distal to LIV	−1.511	0.674	5.020	**0.025**	0.221	0.059–0.828

Bold *p* values mean statistical significance. LIV indicates lowest instrumented vertebra; CI indicates confidential interval.

3.4. Agreement of LIV among the Nine LIV Selection Criteria

All criteria of LIV selection showed various degrees of correlation in pairs with different agreement powers (Table 5). King and Takahashi (ICC = 0.850), King and Qin (ICC = 0.916), Parisini and Matsumoto (ICC = 0.827), Wang and Matsumoto (ICC = 0.872), Wang and Qin (ICC = 0.833), Wang and Fischer (ICC = 0.851), Matsumoto and Qin (ICC = 0.885), Matsumoto and Fischer (ICC = 0.960), and Qin and Fischer (ICC = 0.871) showed very good agreement.

Table 5. Agreement of LIV among the nine LIV selection criteria.

	King	Suk	Parisini	Wang	Sarlak	Takahashi	Matsumoto	Qin	Fischer
King	1	0.614	0.621	0.727	0.487	**0.850**	0.789	**0.916**	0.776
Suk		1	0.604	0.710	0.678	0.406	0.710	0.690	0.778
Parisini			1	0.698	0.561	0.422	**0.827**	0.673	0.786
Wang				1	0.720	0.477	**0.872**	**0.833**	**0.851**

Table 5. *Cont.*

	King	Suk	Parisini	Wang	Sarlak	Takahashi	Matsumoto	Qin	Fischer
Sarlak					1	0.295	0.706	0.611	0.681
Takahashi						1	0.534	0.682	0.527
Matsumoto							1	**0.885**	**0.960**
Qin								1	**0.871**
Fischer									1

Values of mean ICC (intra-class correlation coefficient). Bold *p* values indicate very good agreement among two criteria. Interpretation of ICC value: >0.8 (very good), 0.6~0.8 (good), 0.4~0.6 (moderate), 0.2~0.4 (fair), and <0.2 (poor).

3.5. Development of DA despite Suggested LIV Criteria Being Met

The number of patients who developed DA despite the suggested LIV criteria being met were evaluated. There were 7.4% of such patients (4/54) for King, 9.2% (10/109) for Suk, 11.0% (13/118) for Parisini, 12.0% (14/117) for Wang, 14.7% (20/136) for Sarlak, 5.9% (1/17) for Takahashi, 11.9% (13/109) for Matsumoto, 7.1% (6/84) for Qin, and 11.6% (13/112) for Fischer (Figure 3).

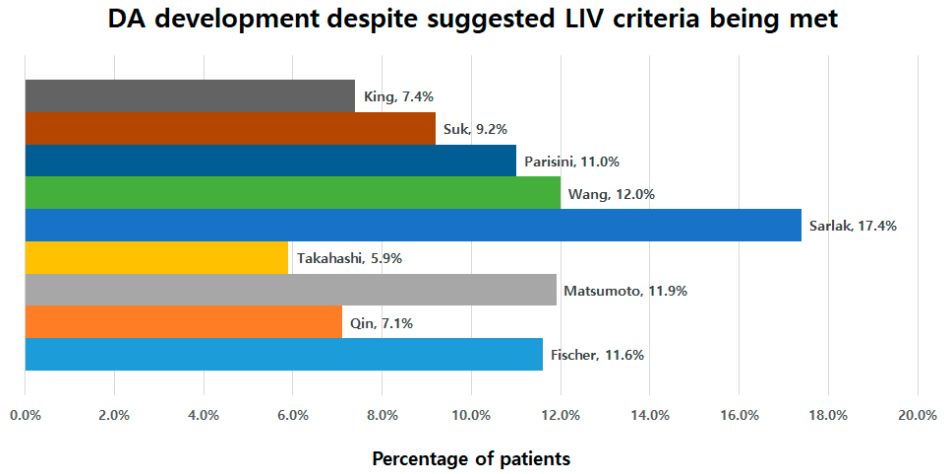

Figure 3. The incidence of DA despite the suggested LIV criteria being met.

4. Discussion

The ultimate goal for AIS correction is to achieve a globally balanced spine in both the coronal and sagittal planes while maintaining as many motion segments as possible. Despite promising results after fusion surgery for AIS, there is always a trade-off between curve correction and loss of mobility. Therefore, we believe that it is necessary to address mobility loss. Helenius et al. [20]. studied the spinal mobility and functional outcomes in 78 patients who underwent fusion surgery using Harrington instrumentation. With use of a goniometer, they found decreased lumbar flexion in 18 patients (23%), decreased lumbar extension in 22 patients (28%), and decreased trunk side-bending in 46 patients (59%). However, they concluded that patients could perform, on average, as well as the reference population in nondynamometric trunk strength tests, including sit-ups, arch-ups, and squatting. Sanchez et al. [21]. performed a similar study on trunk flexibility using a dual digital inclinometer. They divided patients into three groups based on the LIV level: group 1 (T12, L1, or L2), group 2 (L3), and group 3 (L4, L5, or S1). They observed that group 3 showed a significantly decreased trunk flexibility compared with the other groups. Despite a few reports comparing the quality of life according to fusion levels, these two studies indirectly support the plausible advantages of short fusion on a better quality of life.

Although deformity correction seems to be easy in Lenke type 1A or 2A curves, there has been a major concern of DA. It is well known that determination of the spinal fusion level plays an important role in preventing DA. Despite the importance of LIV selection, there is no universally accepted method for determining the LIV for AIS correction. In the present study, we found nine criteria for the determination of LIV to prevent the DA phenomenon (Table 1).

In this study, we compared the relations of LIV location between the nine criteria and the current study population (Table 3). The LIVs suggested by the criteria were most frequent in T12, followed by T11 and L1. This seems to be mainly where thoracic fusion was conducted for the cases of Lenke 1A or 2A curves. In our study, the mean LIV was 12.3 ± 1.1, which was approximately similar to the NV level, and between the EV and SV levels. The suggested LIVs somewhat differ according to the nine criteria. The LIVs suggested by King and Takahashi et al. were more distal than the others. On the other hand, Parisini and Sarlak's criteria suggested a more proximal level than the others. That may be because King and Takahashi's criteria are based on the SV and Parisini and Sarlak's criteria are based on the EV [11–13,18].

Among the nine criteria, we found four criteria (by Suk, Parisini, Wang, and Qin) that showed a statistically significant preventive ability when compared to the case of short fusion relative to the suggested LIVs (Table 4). Initially, in 2003, Suk et al. suggested that the curve should be fused down to the NV when the preoperative NV and EN showed no more than two level gap differences. When the gap was more than two levels, fusion down to NV-1 was recommended [10]. In 2009, Parisini et al. recommended that if the rotation of the first vertebra just below the EV is in the same direction as the thoracic curve, and if the SV and EV have a difference of >2 levels, fusion should extended to L2 or L3. Otherwise, SV-2 or SV-3 can be selected as the LIV. These two criteria were significantly preventive against DA development, with an OR of 0.267 for Suk's criteria and 0.230 for Parisini's criteria. Although the EV, NV, and SV have been the traditional guide for LIV selection, the recent literatures have pointed out the low measurement reliability for locating these levels, which limits the application of these parameters chosen to be the LIV [7,14,16,22]. To overcome the inconsistencies of using EV, NV, and SV as methods of LIV selection, several authors have demonstrated that using the last touching vertebra (LTV) and substantially touched vertebrae (STV) are more reliable methods of LIV selection for Lenke 1 and 2 curves [7,14–16]. Therefore, Wang et al. recommended choosing the first vertebra cranially that deviates from the CSVL >10 mm as the LIV [7]. In the present study, Wang's criteria significantly prevented against DA, with an OR of 0.289. In 2013, the concept of LTV was first introduced by Matsumoto et al., which is defined as the last cephalad vertebra touched by the CSVL. They suggested choosing the LIV as at least level to the LTV to avoid postoperative DA [14]. However, in our study results we found that using the LTV as the LIV, which is one of the commonly used landmarks for AIS correction, did not significantly prevent DA. In 2016, Qin et al. developed and subdivided the LTV concept because they realized that the original LIV concept was insufficient to predict the DA phenomenon. They defined the STV as the vertebra where the CSVL was between the pedicles or touching the pedicle and the non-substantially touched vertebrae (nSTV) as the vertebra where the CSVL was only touching the corner of the vertebra lateral to the pedicle. The authors recommended choosing the STV or nSTV+1 as the LIV for patients with Lenke type 1A curves [16]. Our data showed that Qin's criteria had the ability to prevent the occurrence of DA, with an OR of 0.210, which was the lowest OR among the four statistically significant criteria. On the other hand, it is interesting that fusion beyond the suggested LIV did not provide a further statistically significant risk reduction in DA in all criteria except for Fischer's criterion. In the case of Fischer's criterion, a more distal fusion than suggested was statistically significant in preventing DA (OR = 0.221). In other words, it seemed that Fischer's criteria suggesting LTV within NV-2 is too short to prevent DA.

Because all criteria have been introduced using different landmarks for the one goal of preventing DA, it is necessary to assess how each LIV suggested by the nine criteria matches each other. We found that all criteria had a various degree of agreement in pairs (Table 5). King and Takahashi (ICC = 0.850) and King and Qin (ICC = 0.916), based on a similar concept of SV or bisecting vertebra bodies, had very good agreement. Also, Wang, Matsumoto, Qin, and Fischer all had very good agreement with each other (ICC > 0.8). This is because these four criteria are based on a concept similar to LTV.

Finally, it is necessary to determine which criterion is best in LIV selection against the development of DA. For being the ideal criteria, the following conditions would be met: (1) a statistically proven ability to prevent DA, (2) a not-too-distal location of suggested LIV, and (3) less patients who developed DA when the suggested LIV criteria are met. In a logistic regression analysis, Qin's criteria (OR = 0.210) had the highest prevention rate in reducing the DA among the four significant criteria (Table 4). The suggested location of LIV in most criteria was similar around T12, except for King and Takahashi's criteria, which suggest a more distal location of LIV (Table 3). In terms of DA development despite the suggested LIV criteria being met, the incidence rate of those patients was lower for the criteria by Takahashi (5.9%), Qin (7.1%), and King (7.4%) compared to other criteria (Figure 3). When these results are taken into account, we can suggest that Qin's criterion would be the best one because it showed the lowest prevention rate, with a not-too-distal location and a low incidence rate of DA despite the suggested LIV criteria being met.

We have to acknowledge a few limitations. First, a small sample size in a single institution and the retrospective nature of this study are inherent limitations. Second, not all criteria may be applied to every case, likely rendering comparison difficult. However, that point, in turn, means that different criteria can be applied even for a single patient. In addition, there might be confounding factors between groups with different LIV selection criteria, such as different Cobb's angles, potentially leading to bias in the current findings. Third, we did not consider the sagittal plane in radiographs, although the importance of the sagittal plane has been reported in AIS patients recently [23–30]. Therefore, the relation between the development of DA and the sagittal plane needs further research. Finally, our findings could be biased by the relatively small number of patients with DA. Multicenter study is warranted for a sound conclusion.

5. Conclusions

Nine LIV selection criteria were compared in terms of their preventive ability against DA. Qin's criterion using the STV or nSTV+1 has the highest preventive ability against DA development. Extending the instrumentation further distal to this landmark may not be necessary.

Author Contributions: Study design, S.-J.P. and C.-S.L.; data acquisition, D.-H.K.; data interpretation, S.-J.P., J.-S.P., D.-H.K. and C.-S.L.; writing—original draft preparation, S.-J.P.; writing—review and editing, J.-S.P., D.-H.K. and C.-S.L. All authors have read and agreed to the published version of this manuscript.

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Institutional Review Board Statement: The study protocol was approved by the Institutional Review Board (IRB) of Samsung Medical Center (Seoul, Republic of Korea; approval no. SMC 2022-08-128; Approval date: 1 August 2022) and the IRB of NHIS approved this study protocol. This study was performed in accordance with the relevant guidelines and regulations and the principles of the Declaration of Helsinki.

Informed Consent Statement: An informed consent exemption was granted by the board.

Data Availability Statement: Data used in this study can be shared upon the reasonable request from the journal. However, it can be limited due to patient privacy and ethical restriction.

Conflicts of Interest: The authors declare no conflicts of interest.

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Evaluation of Mis-Selection of End Vertebrae and Its Effect on Measuring Cobb Angle and Curve Length in Adolescent Idiopathic Scoliosis

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Abstract: Background: The Cobb angle is critical in assessing adolescent idiopathic scoliosis (AIS) patients. This study aimed to evaluate the error in selecting the upper- and lower-end vertebrae on AIS digital X-rays by experienced and novice observers and its correlation with the error in measuring the Cobb angle and determining the length of the scoliotic curves. **Methods:** Using the TraumaMeter v.873 software, eight raters independently evaluated 68 scoliotic curves. **Results:** The error percentage in the upper-end vertebra selection was higher than for the lower-end vertebra (44.7%, CI95% 41.05–48.3 compared to 35%, CI95% 29.7–40.4). The mean bias error (MBE) was 0.45 (CI95% 0.38–0.52) for the upper-end vertebra and 0.35 (CI% 0.69–0.91) for the lower-end vertebra. The percentage of errors in the choice of the end vertebrae was lower for the experienced than for the novices. There was a positive correlation (r = 0.673, p = 0.000) between the error in selecting the end vertebrae and determining the length of the scoliotic curves. **Conclusions:** We can conclude that errors in selecting end vertebrae are common among experienced and novice observers, with a greater error frequency for the upper-end vertebrae. Contrary to the consensus, the accuracy of determining the length of the scoliotic curve is limited by the Cobb method's reliance on the correct selection of the end vertebrae.

Keywords: adolescent idiopathic scoliosis; Cobb angle; measurement errors; radiographic assessment; spine curvature

1. Introduction

Adolescent idiopathic scoliosis (AIS) is a complex three-dimensional misalignment of the spine consisting of a coronal curve of more than 10°, vertebral rotation [1] and altered sagittal curvature [2–4], with no congenital or neuromuscular abnormal findings [5]. AIS can progress over the years if untreated, especially during growth, and can cause significant musculoskeletal problems, pain in adulthood, pulmonary impairment and psychological problems [6–9]. Measuring the Cobb angle on a standing posteroanterior full-length spine X-ray is the gold standard for diagnosing AIS, assessing its severity, monitoring its changes

and making decisions about its treatment [10–14]. The selection of the end vertebrae plays a pivotal role in determining the Cobb angle and accurately describing the curve's length, which is crucial for defining appropriate treatment strategies. For instance, if a scoliotic curve exceeds 50°, posterior spinal fusion can be the most appropriate treatment in some cases, which irreversibly alters the biomechanical function of the spine [15–17]. In this surgical procedure, selecting the appropriate end vertebrae determines the curve length to be fused, affecting the biomechanical stability achieved and reducing the incidence of post-surgical complications [18,19]. Conversely, there is a consensus in the literature that selecting the end vertebrae in the Cobb angle measurement method in AIS X-ray is a significant source of intrinsic error [20–23] or the primary source of intrinsic error [24–27]. The literature on the accuracy and precision of the Cobb method in AIS X-ray indicates that potential sources of intrinsic error in traditional manual measurement include the erroneous choice of vertebral endplates, inaccurate drawing of lines along the vertebral endplates, imprecise drawing of perpendicular lines and inaccurate angle measurement itself [22,25–29]. Within the random error of the measurement method, we can differentiate the extrinsic and the intrinsic error. The intrinsic error is the part of the random, aleatory or unpredictable error attributable to the measuring instruments, the equipment or the procedure itself.

This study aims to evaluate the error in selecting the upper- and lower-end vertebrae on AIS X-ray images by experienced and novice observers. Additionally, it aims to explore the correlation between the error in selecting the end vertebrae and the error in measuring the Cobb angle and the correlation between the error in selecting the end vertebrae and the error in quantifying the length of scoliotic curves.

2. Materials and Methods

2.1. Measurement Tool

The software Traumameter v.873 [Hurtado-Avilés and Santonja-Medina, registration number 08/2021/374, Murcia, Spain] was employed to identify the end vertebrae, measure the Cobb angle and quantify the length of the scoliotic curves. This software replicates the manual Cobb angle measurement method observed in AIS X-rays, enabling measurements with high intra- and inter-observer accuracy and precision (MBE = 1.8°, SD = 0.65°, CI95% 1.58°–2.02° and MBE = 1.82°, SD = 0.59°, CI95% 1.62°–2.02°, respectively) [30]. The software eliminates the intrinsic error due to inaccurate drawing of perpendicular lines and inaccurate angle measurement. On the other hand, it reduces the error due to the wrong choice of the end vertebrae and inaccurate line drawing along the vertebral endplates through tools such as the ability to zoom in on the regions of interest and to vary the contrast (fractional difference in the optical density of brightness between two regions of an image) of the digital X-ray image. The software allows the observer to draw lines along the vertebral endplates of various upper- and lower-end vertebrae and selects the steepest ones, returning the Cobb angle result in degrees (Figure 1). Our group has published research on the software's accuracy in previous studies [30].

2.2. Study Design and Measurement Protocol

A prospective and observational study was conducted on 68 scoliotic curves in 42 standing frontal full-length spine X-rays of patients with AIS. The X-ray images were selected retrospectively from an image repository during routine medical care of patients with AIS. Our study adhered to the World Medical Association Declaration of Helsinki's ethical standards, as revised in 2013. This study was exempted from the requirement for ethical approval since the complete and irreversible anonymisation of the images did not involve data processing. The X-ray sample was homogeneous, had equivalent image quality and was without defects. The X-ray images were obtained natively in digital format (in DICOM, with a resolution of 283.46 pixels/mm).

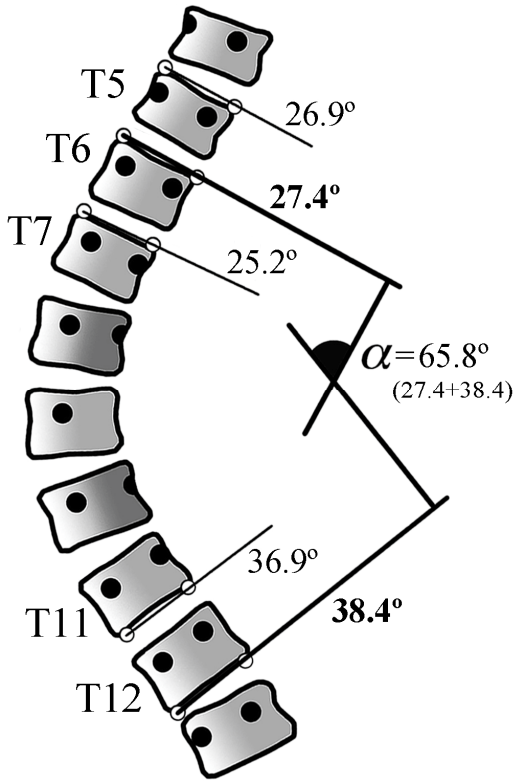

Figure 1. Schematic description of the end vertebrae selection with the software Traumameter v.873. Lines along the several vertebral endplates can be drawn when there is doubt about which ones are more tilted. The software will automatically choose the vertebrae that are most inclined to the horizontal (in this example, T6 (27.4°) and T12 (38.4°)). α: Cobb angle.

According to the angular classification proposed by the International Society on Scoliosis Orthopaedic and Rehabilitation Treatment [31], the selected X-rays showed asymmetry in 2 cases (curves between 0° and 10°), low scoliosis in 17 cases (curves between 11° and 20°), moderate scoliosis in 25 cases (curves between 21° and 35°), moderate-to-severe scoliosis in 9 cases (curves between 36° and 40°), severe scoliosis in 11 cases (curves between 41° and 50°), severe-to-very-severe scoliosis in 1 cases (curves between 51° and 55°) and very severe scoliosis in 3 cases (curves with 56° or more). Of the upper-end vertebrae, 66 (97.1%) were thoracic and 2 (2.9%) were lumbar. Of the lower-end vertebrae, 35 (51.5%) were thoracic and 33 (48.5%) were lumbar.

Hopkins absolute reliability criteria [32,33] were employed to assess validity and reliability. These criteria stipulate that a minimum of 30 cases must be included, at least six blinded observers must act as assessors and at least three tests must be conducted per observer, with a minimum of two-week intervals between tests. A specialist in orthopaedics and traumatology and a specialist in physical medicine and rehabilitation, with over 35 years of professional experience each in the field of the spine, were engaged in a joint and simultaneous measurement of all scoliotic curves on the same computer to establish a gold standard for the Cobb angles, the end vertebrae and the length of each curve.

Both experienced observers measured each radiograph three times on the same computer using the TraumaMeter v.873 software. These two specialists also have extensive experience with the software (one of them has participated in its development as a consultant). The accuracy and precision of their measurements were examined with the software and found to be less than 1° for the Cobb angle measurements. Using the method explained above, it is possible to control the internal consistency and temporal stability of the measurements obtained, which determine the random error in establishing the final vertebrae. This resolution is not affected by significant variations in reliability or accuracy. On the other hand, the systematic error or bias in the estimation will also be reduced when the

measurements are made jointly by the two experienced observers (i.e., the results have a consensus that avoids tendencies to overestimate or underestimate the measurements).

The research was conducted with eight independent evaluators with varying experience levels in measuring Cobb angles. Four observers, designated as "Experienced", were one orthopaedic specialist and three physical therapy and rehabilitation specialists with more than 20 years of experience in the routine measurement of radiographs of scoliotic patients in their daily practice, but who had not determined their intra-observer error. Despite their theoretical knowledge of X-ray measurement techniques for the spine, the four "Novice" observers from various health sciences disciplines (without being orthopaedic surgeons) had never applied Cobb's method in practice. Prior to the commencement of the measurements, a five-hour briefing was held, during which comprehensive information was provided on the study and training in the use of the Traumameter v.873 software. In each X-ray, each observer identified the curves, measured Cobb's angle on them with the software and recorded the resulting measurement and the uppermost and lowest vertebrae of each scoliotic curve in an Excel table. The observers conducted the measurements on three occasions, with a one-month interval between each measurement. A total of 1632 curves were evaluated for this study (204 curves by each observer). The study coordinator randomly assigned the sequence in which the radiographic images were presented in each test to avoid bias, keeping the randomisation key confidential.

2.3. Statistics

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 25 for Windows (SPSS, Inc., Chicago, IL, USA). The values of the variable "Cobb angle error" (eCobb) were obtained in degrees with one decimal place due to the scale of the software measuring tool. The values of the variables "error in the choice of the upper or cranial end vertebra" (eCr), "error in the choice of the lower or caudal end vertebra" (eCa) and "error in the quantification of the length of the scoliotic curve" (eLC), were obtained in the unit "number of vertebrae per curve" with one decimal place. The eCobb, eCr, eCa and eLC values for each scoliotic curve were obtained from the distribution of the 24 scoliotic curve measurements (8 observers in the three tests). In the measurement distributions of each curve, values lower than Q1 − (1.5xIQR) and higher than Q3 + (1.5xIQR) (where IQR is the interquartile range) were identified. These values were considered outliers and eliminated from each distribution (1.96% of eCobb; 0.12% of eCr; 0.06% of eCa; 0% of eLC). The percentage error of each observer in the choice of the upper- and lower-end vertebrae was used to obtain four distributions, namely "percentage of upper and lower end vertebrae wrongly chosen by experienced and novices, respectively". These distributions did not contain any outliers. The Shapiro–Wilk test was employed to ascertain that the p-values of the data from these distributions were above the significance level of 0.05, with the null hypothesis that the data fit a normal distribution being accepted. In all cases, $p \geq 0.34$. All variables were reported as Mean Bias Error (MBE), Standard Deviation (SD), Standard Error of the Mean (SEM) and Confidence Interval of 95%. A Student's t-test was employed to ascertain whether the differences in MBE values between each pair of measurements were statistically significant. Two-sided p values and the CI95% were reported, and significance was accepted at $p < 0.05$. Pearson correlation was obtained between the distributions eCr + Ca (sum of the distributions eCr and eCa) and eCobb and between the distributions eCr + Ca and eLC.

3. Results

Table S1a,b (Supplementary Material) show the gold standard and observer-recorded data for the Cobb angle and end vertebrae, respectively. Table S2 (Supplementary Material) shows the outliers removed. Table 1 shows the data for the error selection of the end vertebrae, the measurement of the Cobb angle and the quantification of the length of the scoliotic curves for the total set of measurements.

Table 1. Statistical values of each error distribution for the total set of measurements.

	eCr	eCa	eCr + eCa	eCobb	eLC
MBE	0.45	0.35	0.80	1.53	0.43
SD	0.28	0.27	0.47	0.44	0.34
n	68	68	68	65	66
SEM	0.03	0.03	0.06	0.05	0.04
IC95%	0.38–0.52	0.29–0.42	0.69–0.91	1.42–1.63	0.35–0.51

The values of eCobb (Cobb angle error) are given in degrees, and those of eCr (error in the choice of the upper or cranial end vertebra), eCa (error in the choice of the lower or caudal end vertebra), eCr + eCa and eLC (error in the quantification of the length of the scoliotic curve) are given in the number of vertebrae per scoliotic curve. MBE is Mean Bias Error. SD is Standard Deviation. SEM is Standard Error of the Mean. IC95% is Confidence Interval of 95%.

The error rate in the choice of the upper-end vertebrae is higher than for lower-end vertebrae (44.7%, CI95% 41.05–48.3 compared to 35%, CI95% 29.7–40.4). This difference is statistically significant ($p = 0.008$) (Figure 2). The error percentage in the choice of the end vertebrae is lower in the experienced than in the novices, with a statistically significant difference ($p = 0.009$ between upper-end vertebrae, $p = 0.000$ between lower-end vertebrae) (Figure 2). The percentage of erroneous choices made by the experienced evaluators was 37.99% (CI95% 33.96–42), while that of novices was 51.35% (CI95% 48.77–53.97). Experienced evaluators incorrectly identified the lower-end vertebra in 26.35% (CI95% 21.45–31.25) of the measurements, while novices incorrectly identified it in 43.75% (CI95% 37.06–50.44).

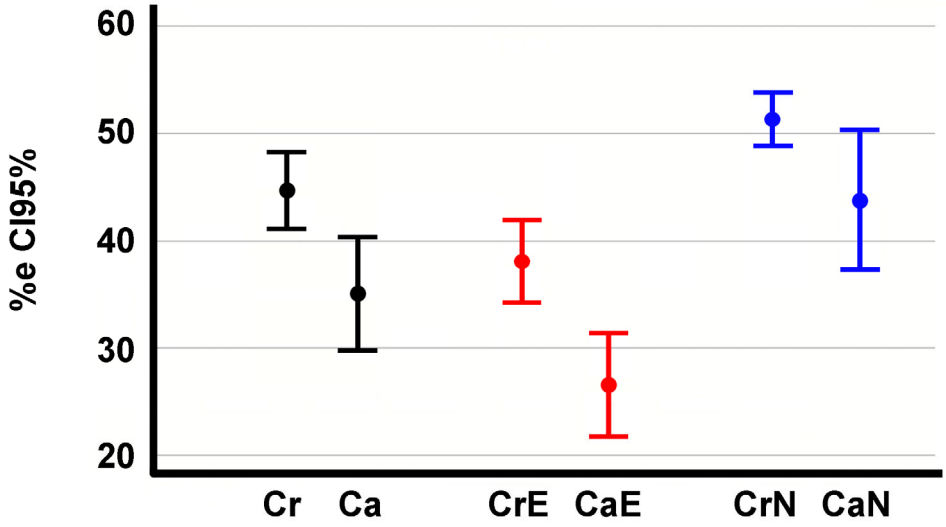

Figure 2. 95% confidence intervals of the percentage error in the choice of upper or cranial and lower or caudal end vertebrae by Experienced observers (CrE, CaE, respectively) and upper- or cranial- and lower- or caudal-end vertebrae by Novice observers (CrN, CaN, respectively).

Experienced evaluators incorrectly identified one end vertebra in 36.6% (274) of the scoliotic curves, while in 15.4% (126) of the cases, they incorrectly identified two end vertebrae. By contrast, novices incorrectly identified one end vertebra in 34.7% (278) of the scoliotic curves, while in 30.39% (248) of the cases, they incorrectly identified two end vertebrae.

Table S3 (Supplementary Material) presents the number of incorrectly selected end vertebrae and the error in the Cobb angle for each measurement. It demonstrates that the

error in the Cobb angle measurements for each scoliotic curve is randomly distributed and unrelated to the number of incorrectly selected end vertebrae.

Further analysis was performed on the distribution of Cobb angle measurements for each scoliotic curve to identify the 50% of measurements closest to the gold standard value. This analysis showed that 44.6% (365) of these measurements were carried out with the two end vertebrae correctly identified. By contrast, 33.9% (278) were obtained with one of the end vertebrae incorrectly identified, and 21.5% (176) were obtained with both end vertebrae incorrectly identified.

The correlation between the error in the choice of the end vertebrae and the error in the Cobb angle measurements is not statistically significant ($r = 0.198$, $r^2 = 0.039$, $p = 0.111$) (Figure 3). The correlation between the error in the choice of the end vertebrae and the error in the determination of the length of the scoliotic curves is statistically significant ($r = 0.673$, $r^2 = 0.453$, $p = 0.000$) and positive (Figure 4). The linear equation forced to the origin of coordinates describing the correlation is $eCr + eCa = 1.243 \cdot eLC$ ($r = 0.610$).

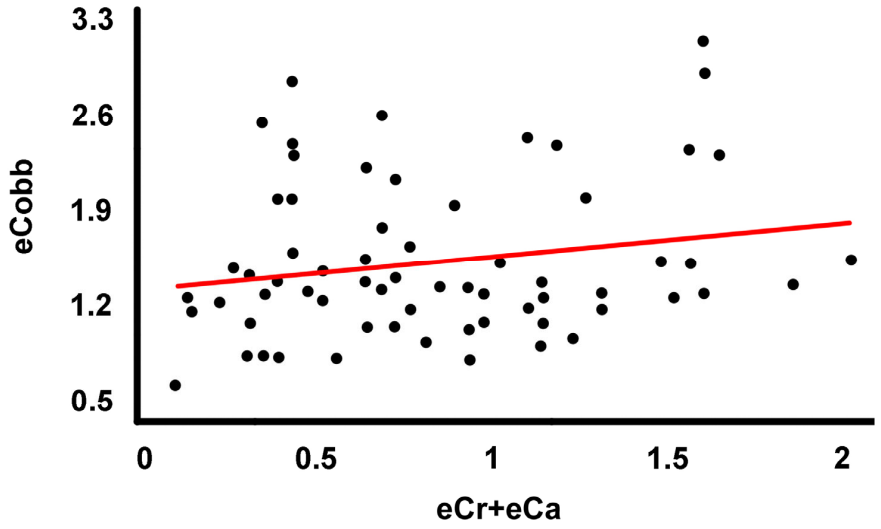

Figure 3. Regression line fitted to the point cloud corresponding to the variables "number of end vertebrae incorrectly selected in a scoliotic curve" (eCr + eCa) and "error in measurement of the Cobb angle" (eCobb) in each curve.

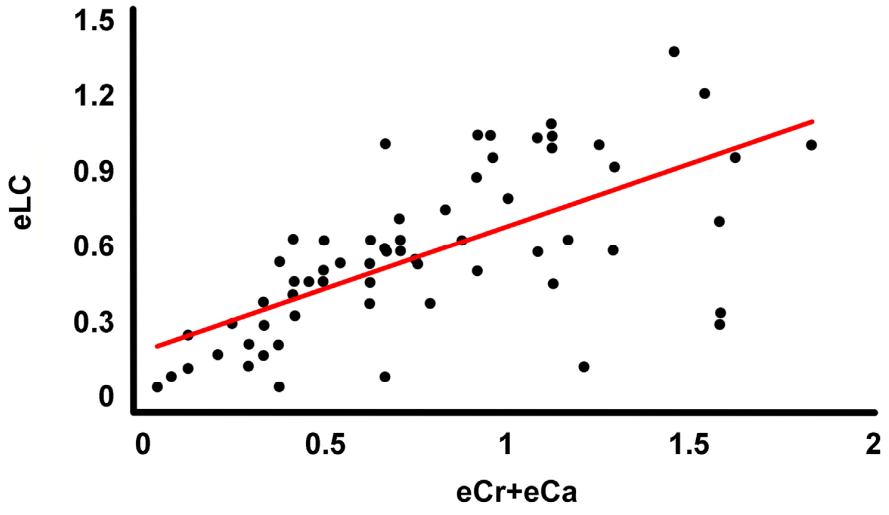

Figure 4. Regression line fitted to the point cloud corresponding to the variables "number of incorrectly selected end vertebrae in the curve" (eCr + eCa) and "error in determining the length of the scoliotic curve" (eLC).

4. Discussion

The most important finding of this study was that errors in selecting end vertebrae are common among both experienced and novice observers, with a greater frequency of error in the upper-end vertebrae. Likewise, the lack of dependence between the end vertebrae error and the Cobb angle error is also relevant.

In AIS, the error in selecting the uppermost and the lowest vertebrae when measuring the Cobb angle can be relevant to the correct decision on treatment (observation, physiotherapy, orthosis, surgery) and its characteristics [10,11,13,34]. For example, if the applicable treatment for a scoliotic curve is instrumented arthrodesis, a longer-than-necessary fusion means sacrificing too many segments of motion and, therefore, function [34–37], increased risk of neurological complications and infection and increased cost. There is consensus that the incorrect selection of the end vertebrae is a significant source of intrinsic error in measuring the Cobb angle on AIS X-rays [22,23,27]. However, in studies of Cobb angle inaccuracy where the error is measured using preselected end vertebrae, the erratum is not significantly improved, with intra-observer MBE in such studies ranging from 3° to 9.04° [25,26,28,29,37].

Artificial intelligence will likely play an essential role in Cobb angle measurement in the coming years. There is a growing number of publications on deep learning methods for Cobb angle measurement [38]. Not all of the proposed systems are more accurate than human operators [39], but there is a trend towards a progressive increase in the accuracy of such systems [40,41].

Our study's absolute error in the Cobb angle mean was MBE = 1.53°, CI95% 1.42°–1.63°. With this accuracy and precision, we found that the error in the Cobb angle measurements was not related to the correct choice of the end vertebrae ($p = 0.111$). Of the 50% of Cobb angle measurements closest to the actual value, 55.4% (454) were obtained by incorrectly selecting at least one end vertebrae. In summary, the erroneous choice of the end vertebrae is not a source of intrinsic error in the Cobb method but a consequence of the inaccurate drawing of the lines along the vertebral endplates.

The error in selecting the end vertebrae and the error in measuring the Cobb angle have the exact cause when using the Traumameter v.873 software. When using the manual Cobb method, the sources of error are many, but with our software, they are reduced to one; the inaccuracy in drawing the straight line parallel to the upper and lower surface of the end vertebrae is greater than the difference in inclination of the vertebrae adjacent to the end vertebrae and the end vertebrae. Due to the high accuracy and precision of the TraumaMeter v.873 software, the error in the choice of the end vertebrae results in a minimal error in determining the Cobb angle, as the difference in inclination between the correct and incorrectly chosen end vertebrae is tiniest. Our study found that the error rate in choosing the end vertebrae is higher in upper-end vertebrae (44.7%) than in lower-end vertebrae (35%), which is statistically significant. The fact that upper-end vertebrae tend to appear in the thoracic region, with the overlapping of different organs and structures on X-ray, or better visibility of the lower region of the endplate architecture [42], could justify the more significant error in their choice.

The error rate in choosing end vertebrae was statistically significantly higher in novice observers than in experienced observers. Experienced observers wrongly chose at least one of the end vertebrae in 52% of the measurements (400) and novices in 65.1% (526). This aspect can be explained by the lower Cobb angle measurement error shown by experienced measurers [30] when measuring with the TraumaMeter v.873 software and manually traditionally. Our results show a significant positive correlation between the error in choosing end vertebrae and the error in determining the length of the scoliotic curves. From the regression line obtained from the correlation, we can predict an increase in the error in scoliotic curve length determination of 0.805 vertebrae for each incorrectly chosen end vertebra. The error in determining the end vertebrae is due to a limitation of the Cobb method itself. Its systematic error is, in many cases, greater than that required to select the end vertebrae correctly.

This study is not without its limitations. Firstly, we did not consider the computer equipment of each observer (e.g., visible image size, display resolution, luminance, contrast ratio or the characteristics of the mouse or touchpad), which may have influenced the accuracy of the measurements. Secondly, the outliers removed from the distribution used in the study could be due not only to imperfect measurement but also to errors in recording the value of the measurements in the database provided by each observer. Thirdly, we lacked the necessary radiographic projections to present the curve patterns according to, for example, Lenke's classification [43], which may have helped explain the significant error in selecting the upper-end vertebra. Despite these limitations, the authors believe that the study results are valuable. One of the strengths of our study is that its design meets the Hopkins criteria (minimum of 30 cases, at least six blinded observers and at least three tests per observer, separated by at least two weeks) [32,33]. Also, we established training sessions for the observers to avoid measurement bias.

The clinical importance cannot be overstated, as the correct determination of the end vertebrae can significantly influence therapeutic decisions, such as the length of the arthrodesis in the surgical treatment of AIS. It is crucial to note that the error usually made by observers in misidentifying the cranial and caudal end vertebrae on AIS X-ray does not change the value of the Cobb angle measurements in a statistically significant way. However, such an error leads to the misjudgement of the length of the scoliotic curves, which has clinical implications.

5. Conclusions

Errors in selecting end vertebrae are common among experienced and novice observers, with a greater frequency of error in the upper-end vertebrae. There is no correlation between the error in selecting the end vertebrae and the Cobb angle error. Inappropriate choice of end vertebrae leads to an estimated error in determining the length of the scoliotic curves of 0.805 vertebrae for each end vertebra chosen incorrectly.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/jcm13154562/s1, Table S1a: gold standard and observer-recorded data for the Cobb angle. Table S1b: gold standard and observer-recorded data for end vertebrae. Table S2: outliers removed. Table S3: number of incorrectly selected end vertebrae and the error in the Cobb angle for each measurement.

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Review

Bone Health Optimization in Adult Spinal Deformity Patients: A Narrative Review

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Abstract: Osteoporosis and low bone mineral density (BMD) pose significant challenges in adult spinal deformity surgery, increasing the risks of complications such as vertebral compression fractures, hardware failure, proximal junctional kyphosis/failure, and pseudoarthrosis. This narrative review examines the current evidence on bone health optimization strategies for spinal deformity patients. Preoperative screening and medical optimization are crucial, with vitamin D supplementation showing particular benefit. Among the pharmacologic agents, bisphosphonates demonstrate efficacy in improving fusion rates and reducing hardware-related complications, though the effects may be delayed. Teriparatide, a parathyroid hormone analog, shows promise in accelerating fusion and enhancing pedicle screw fixation. Newer anabolic agents like abaloparatide and romosozumab require further study but show potential. Romosozumab, in particular, has demonstrated significant improvements in lumbar spine BMD over a shorter duration compared to other treatments. Surgical techniques like cement augmentation and the use of larger interbody cages can mitigate the risks in osteoporotic patients. Overall, a multifaceted approach incorporating medical optimization, appropriate pharmacologic treatment, and tailored surgical techniques is recommended to improve outcomes in adult spinal deformity patients with compromised bone quality. Future research should focus on optimizing the treatment protocols, assessing the long-term outcomes of newer agents in the spine surgery population, and developing cost-effective strategies to improve access to these promising therapies.

Keywords: osteoporosis; scoliosis; kyphosis; compression fracture; spinal fracture; diphosphonates; denosumab; teriparatide

1. Introduction

Spinal deformities are one of the most common medical disorders with significant impact on the patients' quality of life. With a significant burden on healthcare costs, it is estimated that 27.5 million elderly patients suffer from some form of spinal deformity [1]. Spinal deformity is a heterogenous spectrum of disorders defined as the malalignment or malrotation of the spine in the axial, coronal, and/or sagittal plane. Specific subtypes of spinal deformities include scoliosis, kyphosis, sagittal malalignment, spondylolisthesis, axial plane deformity, and rotary subluxation [2,3]. The prevalence of different types of spinal deformities differs depending on various factors such as age, genetics, comorbidities, and lifestyle. Scoliosis, for example, is prevalent in childhood and adolescent populations, with the most common subtype being idiopathic scoliosis accounting for 80% of spinal deformities in pediatric patients [4]. The progression of adolescent spinal deformities into adulthood, degenerative changes associated with age, and iatrogenic deformities post-surgery impose a huge risk for the development of de novo spinal deformities in adult and elderly populations [1–3]. Among the most cited factor in the development of spinal deformity or the progression of deformity post-surgery is low bone mineral

density-related conditions. Suboptimal management of this can lead to poorer outcomes and therefore requires close attention in the preoperative optimization of patients planned for reconstruction surgery [5–7].

This narrative review aims to explore how different pharmacological agents affect fusion rates and hardware-related complications in adult spinal deformity patients with osteoporosis, as well as the most effective preoperative bone health optimization strategies for improving surgical outcomes in adult spinal deformity patients with low bone mineral density.

2. Osteoporosis and Osteopenia

While there are several factors implicated in the pathogenesis of spinal deformities, smoking, weight, core muscle strengthening, as well as general lifestyle, career and activity choices are among those that can be modified to improve quality of life and outcomes from surgery [8–10]. In terms of comorbid modifiable medical conditions, osteoporosis is a disorder of the bone whereby decreased bone mass is coupled with increased risk of fragility fractures [11,12]. A significant public health concern, consistently cited as the most common bone disease in humans, osteoporosis was shown in a meta-analysis to be prevalent in 18.3% of the global population and 23.1% of women [13,14]. On a broad basis, osteoporosis is one of many bone demineralizing diseases that falls under the umbrella term osteopenia [15]. Now recognized as a variable decrease in the bone mineral density but not low enough for the diagnosis of osteoporosis, osteopenia is more common in men and postmenopausal women than osteoporosis, with more than half of postmenopausal women in the US developing osteopenia [12,16–18]. Among the lifestyle choices that affect the development of osteoporosis and osteopenia and the maintenance of bone health are included nutrition (specifically calcium and vitamin D), smoking, exercise, alcohol use, body mass index (BMI) (low BMI or body weight is usually associated with an increased risk of osteopenia and osteoporosis), occupation, recreational/sport activities, and caffeine consumption [11,12,15–17,19,20]. Other risk factors include inflammatory conditions, recurrent infections, HIV, malabsorptive diseases, diabetes mellitus, and certain medications [11,12,15–17]. Risk factors such as age, ethnicity and sex are also heavily involved in the pathogenesis of primary osteoporosis while the other risk factors, most of which are modifiable, are involved in the pathogenesis of secondary osteoporosis [11,21]

3. Risks and Complications in Osteoporotic Patients

Osteoporosis is an essential parameter for surgeons, as many patients undergoing spinal surgery have compromised bone quality [22,23] and adverse outcomes are directly proportional to the complexity of the deformity [24,25]. The incidence of osteoporosis in patients undergoing spine surgery who are older than 50 years is reported to be 14.5% of men and 51.3% of women [26,27]. This interrelation warrants attention, as adult spinal deformity in the United States has increased 3.4-fold in the past decade [28,29]. Both osteoporosis and osteopenia are associated with vertebral fractures after instrumentation, hardware failure, proximal junction kyphosis, and pseudoarthrosis [22,23,27,30,31]. and carry an increased risk of revision surgery and surgical complications within two years of the procedure [32] (Figure 1). Gupta et al. found that of 399 adult spinal deformity patients, 131 of whom had osteoporosis, 40% needed revision surgery, which is 1.45 times more likely than those without osteoporosis [32]. With degenerative scoliosis affecting 69% of the elderly population, it is apparent that bone mineral density, advanced age, and spinal deformity are associated characteristics that warrant careful surgical planning before surgical intervention is conducted [33,34]. Below are the commonly cited complications presented in osteoporotic and osteopenic patients undergoing spinal surgery.

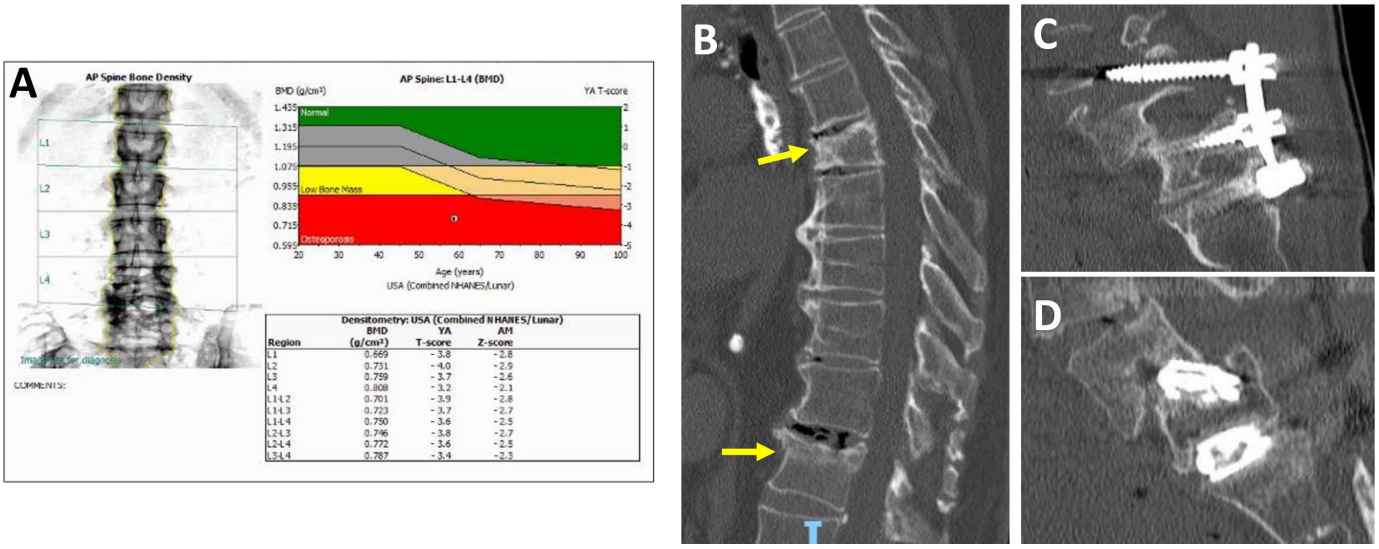

Figure 1. Spinal pathology due to osteoporosis. (**A**) Bone densitometry scan (DEXA) demonstrating a postmenopausal woman with osteoporosis of the lumbar spine, defined as a T-score (comparison with healthy adults) less −2.5 and a Z-score (comparison with similar peer group) less than −1.5, Green is normal bone density, yellow is low bone mass, and red is osteoporosis. (**B**) Acute vertebral compression fractures (yellow arrows). (**C**) Hardware failure with pedicle screw loosening, osteolysis, and migration. (**D**) Interbody cage subsidence, nonunion, and resultant spondylolisthesis.

3.1. Vertebral Compression Fractures

Vertebral compression fractures (VCF) compromise the anterior column of the spine, placing excessive strain on the anterior portion of the vertebra and the anterior longitudinal ligament [35]. The most common fractures due to osteoporosis are within the vertebrae, as osteoporosis in the aging spine significantly increases the risk of vertebral compression fractures and proper fixation [27,36]. Although widely under-reported, as many VCFs go undetected, VCFs comprise approximately 700,000 of the total 1.5 million annual osteoporotic fractures in the USA [31,37,38].

VCF presentation is highly variable, ranging from severe pain causing hospital admission to minor to no symptoms, and is incidentally found on imaging [31,35]. Symptomatic presentation tends to consist of severe focal back pain, functional disability, and progressive kyphosis of the thoracic spine that ultimately results in decreased appetite, poor nutrition, and impaired pulmonary function [35,38,39]. Neurologic symptoms may arise due to spinal cord or cauda equina compression, including increased kyphosis, hyporeflexia, hyperreflexia, sensory loss, urinary retention, and sphincter dysfunction [35,38,39]. Irrespective of clinical presentation, VCFs are key clinical markers for skeletal fragility, as one VCF increases the risk of a future, potentially more harmful, fracture by 5-fold [31,35,36,39]. With respect to spinal deformities, VCFs can cause the progression of pre-existing curvature abnormalities [24,38]. The loss of height that results from a compression fracture may lead to the worsening of kyphotic deformity of the spine. This is especially true for multiple compression fractures where significant height loss is a concern. Management can range from conservative pharmacologic analgesia, bracing, percutaneous vertebroplasty or kyphoplasty, and corrective surgeries with instrumentation and interbody grafts [35,38,40] (Figure 2A).

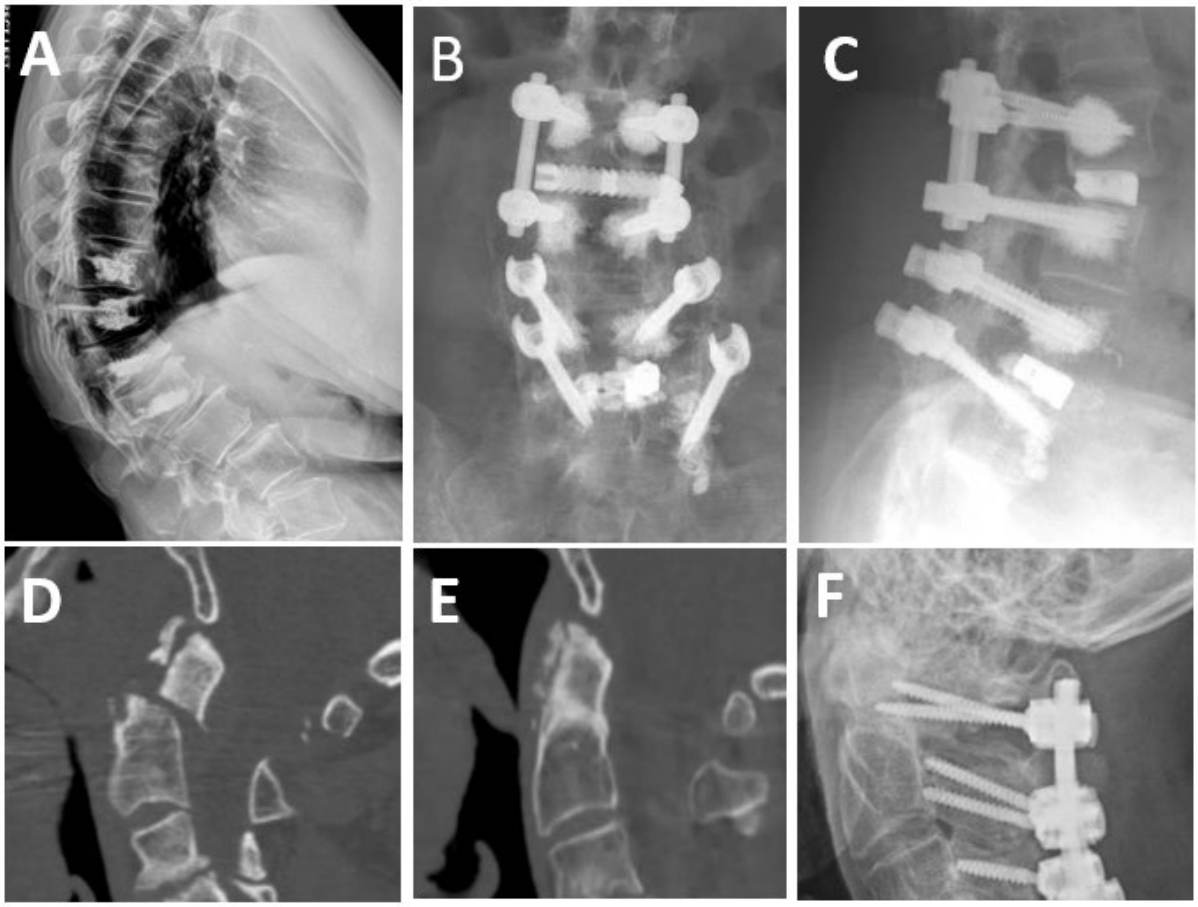

Figure 2. Surgical treatment options for patients with osteoporosis. (**A**) Four-level kyphoplasty in an elderly woman with multiple thoracic vertebral compression fractures and thoracic hyperkyphosis. (**B**,**C**) AP and lateral X-rays from a hardware revision and fusion extension in a patient with osteoporosis and adjacent segment disease (ASD) at L2/3 following solid arthrodesis from previous L3–5 fusion. Note the new screws at L2 and L3 with cement augmentation through fenestrated screws. Larger interbody cages, such as those that can be inserted from an anterolateral approach, rest on the apophyseal ring of the vertebrae and thus provide stronger anterior column support and higher fusion rates. (**D**) Preoperative sagittal CT scan of a patient with advanced osteoporosis and a type II traumatic odontoid fracture. (**E**,**F**) Postoperative sagittal CT and lateral X-rays of the same patient 6 months following surgical stabilization and teriparatide treatment, demonstrating reduction and healing of the fracture.

3.2. Hardware Failure

Osteoporotic bone is known to exhibit decreased pullout strength and insertional torque [41,42]. This characteristic makes patients more vulnerable to screw toggling, loosening, and eventual pullout [25,32,41,43]. These complications are compounded with multilevel adult spinal deformity constructs, as even stronger forces are placed on the patient's bone to maintain substantial correction and withstand the forces of daily living activities [32]. Bone mineral density (BMD) has been cited as one of the most important factors to consider when assessing the risk of screw pullout and bone-screw interface failure [22,30]. In a recent systematic review and meta-analysis by Ogiri et al., consisting of 133,000 patients, 12% of which had osteoporosis, those with compromised bone quality were 2.59 times more likely to have screw loosening and 1.65 times more likely to need revision surgery compared with those with standard bone quality [22]. Similarly, Rometsch et al. found that in their systematic literature review of the incidence of screw loosening in osteoporotic spines, pedicle screw loosening rates were twice as high as in patients with regular bone density when the screws were placed in a nonaugmented fashion [42].

To prevent hardware malfunctions, some papers have cited that a spine with poor bone mineral density may require multiple fixation points, including adjunct fixation and augmentation of pedicle screws, and the use of larger interbody cages [24,42] (Figure 2B,C). Additionally, large-diameter, long pedicle screws with or without fenestrations for cement augmentation can structurally fill more of the pedicle, maintaining the integrity of a solid construct in osteoporotic patients [32,41]. Cement augmentation in vertebroplasty and kyphoplasty provides significant pain relief and vertebral height restoration with minimal invasiveness, but it carries risks of bone cement implantation syndrome (BCIS), which can result in severe complications such as hypoxia, hypotension, and cardiovascular collapse, potentially leading to fatal outcomes [44,45]. Several other risks exist like cement leakage, adjacent fractures, and other surgical complications; however, risk mitigation can be performed through medical intervention with agents such as bisphosphonates, calcitonin, abaloparatide, and teriparatide [32,44,45].

3.3. Proximal Junctional Kyphosis and Failure

Proximal junctional kyphosis (PJK) is a radiographic phenomenon that demonstrates kyphosis in which the proximal junction angle (the sagittal Cobb angle between the inferior endplate of the upper instrumented vertebra and the superior endplate of the vertebra two levels above) becomes more than 10 degrees [23,46–48]. PJK is often diagnosed when spinal deformity patients return for follow-up with unremitting pain at the top of the construct [49]. Patients with either osteoporosis or osteopenia undergoing lumbar fusions have an elevated risk for PJ [30,41,43]. This risk is compounded within patients with adult spinal deformity [29,47,48]. Proximal junctional failure arises upon symptom onset, vertebral collapse, or instrumentation failure and carries a substantial risk of sudden paralysis [46,48]. Retrospective studies have shown that pre-existing low BMD is an independent risk factor for proximal junctional failure (PJF), with a 2% incidence rate [46].

In a recent systematic review and meta-analysis by Ogiri et al., consisting of 133,000 patients, 12% of whom had osteoporosis, the risks of PJK/PJF were 1.89 higher in those with poor bone quality than in those with healthy bone [22]. Similar associations were found in the lens of adult spinal surgery, as Kuo et al. found that in their retrospective chart review of 116 patients who had received ASD surgery, a vertebral bone quality score of 2.85 or higher was independently associated with PJK/PJF occurrence with a 94.3% predictive accuracy [29]. Another study of 113 patients surgically treated for spinal deformity were grouped as having either mildly low to normal BMD (T-score > -1.5) or significantly low BMD (T-score < -1.5) and found that the incidence of PJF was significantly higher in the patient group with significantly low BMD (33% occurrence) when compared with patients with normal BMD (8% occurrence) [46].

To prevent PJK, techniques such as ligament augmentation, vertebroplasty, transverse process hooks, flexible rods, sublaminar tape, and multilevel stabilization screws have been used [48,50]. In their systematic review of studies assessing PJK prevention in ASD surgeries, Doodkorte et al. found that the laminar or sublaminar use of polymeric cable systems showed particularly significant efficacy in PJK prevention in the osteopenic ASD patient population [50]. This corroborates previous studies' findings indicating that resistance to failure in laminar hook and sublaminar wire fixation was not correlated to overall bone mineral density, which benefits a vulnerable BMD population [51]. Additionally, laminar bone mineral density is relatively higher than other places of fixation, such as the pedicles and transverse processes, which further supports its use in osteopenic ASD patients [52].

4. Osteoporosis Treatment and Optimization for Spine Surgery

The appropriate management of the risk factors for osteoporosis and osteopenia, and by extension, spinal deformities, can dramatically reduce the risk of fractures and surgical intervention [11,12,15–18,32,53]. Both pharmacological and nonpharmacological interventions can also improve pre- and post-surgical bone health optimization thereby minimizing the previously mentioned surgical complications [32]. There are many modalities

in which osteoporosis can be treated and they can be classified as nonpharmacological and pharmacological interventions. Nonpharmacological interventions include supplements (particularly calcium and vitamin D), exercise (the nature of which involves biomechanical stress to promote bone remodeling), reduction/optimization of modifiable risk factors (occupational hazards, recreational/sport activities, alcohol consumption, smoking cessation, caffeine consumption) and the appropriate management of medical conditions (diabetes mellitus, recurring infections, inflammatory conditions, HIV, malabsorptive diseases, etc.) [11,12,15,16,19–21,54,55]. On the other hand, pharmacological interventions include the use of antiresorptive agents (bisphosphonates, denosumab), parathyroid hormone analogues (teriparatide, abaloparatide), hormonal therapies (estrogen agonists/antagonists, estrogen-progestin therapy, testosterone therapy, calcitonin), and novel therapies and drugs [21,56,57] (Table 1).

Table 1. Pharmacologic treatment options for bone health optimization.

Class	Agent	Brand Name	Mechanism of Action
Vitamin and mineral supplements	Calcium	N/A	The main mineral component of bone. Forms calcium salts (mostly calcium phosphate) by osteoblasts which harden cartilaginous bone matrices and thus bone building
	Vitamin D	N/A	Activates intestinal absorption of calcium and maintaining calcium homeostasis
Antiresorptive agents	Bisphosphonates	Reclast, Boniva, Fosamax, Zoneta, Actonel Aclasta	Inhibits osteoclast function, thus allowing osteoblasts to more efficiently build bone mass
Anabolic agents	Denosumab	Prolia	Monoclonal antibody that inhibits receptor activator of nuclear factor kappa-B ligand (RANKL), resulting in decreased osteoclast development
	Romosozumab	Evenity	Monoclonal antibody that binds and inhibits sclerostin, a protein secreted by osteocytes that inhibits osteoblast function increases RANKL which activates osteoclasts (PMID: 30775535). Thus, romosozumab is unique in that it increases bone formation and decreases bone resorption
Parathyroid hormone (PTH) analogs	Teriparatide	Forteo	Regulates calcium and phosphate metabolism in bone and the kidneys. Counterintuitively increases bone resorption, thus resulting in increased serum calcium levels. However, low-dose and intermittent exposure (i.e., once daily) disproportionately activate osteoblasts with increased serum calcium more than osteoclast function, thus having a net effect of increased bone mineral density
	Abaloparatide	Tymlos	Similar to teriparatide, but with different pharmacokinetics that may confer some advantages in bone mineral density improvements

4.1. Vitamin and Mineral Supplementation

Some of the literature has investigated the use of nonpharmacologic interventions for osteoporosis in improving outcomes following spine surgery. In a study in rats, Cho et al. found that dietary calcium improved the volume and overall mechanical strength of lumbar fusions [58]. However, there are no clinical studies in humans to corroborate these results and support calcium supplementation in spinal surgery. There is more evidence that indicates the use of vitamin D supplementation in spinal surgery. In vivo, Metzger et al. found that rats given higher doses of vitamin D were correlated with higher fusion rates,

biomechanical stiffness, and bone density following posterolateral fusion [59]. Several studies in human patients who underwent spinal fusion have shown that vitamin D deficiency, compared to normal or elevated vitamin D levels, is correlated with worse post-operative scores for disability, pain, and quality of life [60,61]. Additionally, vitamin D supplementation improves or even resolves chronic back pain, particularly in patients with failed back surgery [62–64].

In a recent randomized controlled trial, Hu et al. found that patients given vitamin D supplements exhibited shorter time to fusion, improved spine function, and decreased pain scores following spinal fusion surgery [65]. A second randomized control study by Krasowska et al. found that the decreased pain experienced by patients with vitamin D supplementation was correlated with lower levels of serum markers for systemic inflammation [66]. Based on this review, substantial evidence supports the use of vitamin D supplements to improve outcomes in patients undergoing spinal fusion surgery. However, there is a clear deficit in and a dire need to increase the number of studies analyzing calcium supplementation in these patients.

4.2. Antiresorptive Agents

Bisphosphonates

Bisphosphonates are a group of medications that inhibit osteoclast function, thus allowing osteoblasts to more efficiently build bone mass. These include zoledronic acid, ibandronate, alendronate, and risedronate. In a randomized controlled trial, Nagahama et al. found that patients given alendronate following posterior lumbar interbody fusion had a significantly higher incidence of solid fusions, and a lower incidence of cage subsidence and subsequent vertebral fractures [67]. Notably, alendronate was associated with a decrease in bone resorption and formation, suggesting impaired healing of spinal fusion, but the authors argued that the mechanical benefits of alendronate outweighed its deficits in healing [67]. Similarly, a retrospective analysis by Tu et al. found that patients administered with zoledronic acid before lumbar interbody fusion had decreased incidence of vertebral compression fracture, pedicle screw loosening, and cage subsidence, which corroborated with results from a clinical trial [68,69]. As an initial characterization of the temporal nature of the benefits of bisphosphonates, a comparative study reported that fusion rates at 6 months post-surgery were lower in patients that took bisphosphonates but were substantially higher for those patients after 2 years [70].

Several systematic reviews and meta-analyses have attempted to synthesize the results of bisphosphonate use across randomized controlled trials, prospective studies, and retrospective cohort analyses. Meta-analyses by Govindarajan et al. and Liu et al. found that the use of bisphosphonates following spinal fusion increased the odds of successful fusion, decreased the likelihood of postoperative vertebral compression fracture, and significantly reduced the scores for disability and pain [71,72]. Liu et al. and Mei et al. found that patients administered bisphosphonates were significantly less likely to exhibit pedicle screw loosening and cage subsidence, like the findings in a review by Buerba et al. analyzing bisphosphonate use after thoracolumbar spinal fusion [72–74]. However, Liu et al. saw no benefits of bisphosphonates in reducing the likelihood of implant fixation failure [72].

Some systematic reviews and meta-analyses in the current literature, however, report conflicting results. For example, meta-analyses by Buerba et al., Cheng et al. and Mei et al. found that bisphosphonate therapy does not improve fusion rate following spinal fusion surgery [73–75]. Many reviews also document that bisphosphonate use does not change the rate of screw loosening or improve disability scores [71,73–76]. However, the specific meta-analyses for these parameters in these reviews are relatively underpowered, excluding papers that are present in other recent analyses and, thus, weakening the reliability of these results.

In general, the current literature surrounding bisphosphonate use in spinal fusion surgery is positive. Individual and pooled analyses both show that bisphosphonates in-

crease the mechanical strength of the fusion, which minimizes post-operative complications and improves patient outcomes.

4.3. Anabolic Agents

4.3.1. Denosumab

Denosumab is a human monoclonal antibody that inhibits the receptor activator of nuclear factor kappa-B ligand (RANKL), resulting in a reduction in osteoclast development. Some studies have analyzed the combination of denosumab and teriparatide in patients undergoing spinal fusion [75,77]. The pooled analyses in Cheng et al. show that patients with both teriparatide and denosumab therapy experienced higher fusion rates compared to placebo controls [75]. In a randomized controlled trial examining patients who underwent posterior lumbar interbody fusion, Ide et al. found that patients treated with a combination of teriparatide and denosumab experienced accelerated fusion rates than with teriparatide alone, which correlated with heightened measures of bone formation [77]. This suggests that the two medications administered together have a heightened effect compared to teriparatide alone.

A recent study by Tani et al. showed that denosumab treatment alone strengthened pedicle screw fixation—with stronger compression force and pullout strength—and increased BMD around the pedicle screw placement [78]. However, these outcomes were not based on analyses after spine surgery but rather on finite element analysis, a computer model generated from measured patient characteristics to simulate vertebral properties [78]. Future investigation with clinical studies analyzing the effects of denosumab therapy on outcomes following spine surgery is required.

4.3.2. Romosozumab

Romosozumab is a monoclonal antibody that binds and inhibits sclerostin, a protein secreted by osteocytes that inhibits osteoblast function and increases RANKL which activates osteoclasts [79]. Thus, romosozumab is unique in that it increases bone formation and decreases bone resorption. Studies in rat models of lumbar fusion had demonstrated increased fusion rates and increased trabecular bone area in animals treated in a dose–response fashion with romosozumab after twice weekly injections for 8 weeks [80]. Mikula et al. found a significant improvement in CT-scan-based Hounsfield units of the lumbar spine by 26% after treatment with romosozumab for a mean length of 10.5 months [81]. When compared with patients treated with teriparatide, denosumab, and alendronate, romosozumab were able to achieve a more substantial improvement in bone density in a shorter duration of time. While many groups have advocated for this use in the spinal deformity population based on anecdotal experience, long-term outcome data are not yet published, but studies are currently ongoing [82–84].

4.4. Parathyroid Hormone (PTH) Analogs

4.4.1. Teriparatide

PTH analogs regulate the calcium and phosphate metabolism in bone and the kidneys. Counterintuitively, PTH increases bone resorption, thus resulting in increased serum calcium levels. However, low-dose and intermittent exposure (i.e., once daily) disproportionately activate osteoblasts with increased serum calcium more than osteoclast function, thus having a net effect of increased bone mineral density. In a multi-center, prospective randomized study by Ebata et al., 6 months of weekly teriparatide injections significantly increased the rate of bone fusion following posterior or transforaminal lumbar interbody fusion compared to non-treated controls [85]. A retrospective study with patients who underwent posterolateral fusion surgery found that the benefits of teriparatide on bone fusion were significantly greater for periods of treatment longer than 6 months [86]. These results are consistent with systematic reviews and meta-analyses where pooled analysis showed that patients with teriparatide treatment experienced higher fusion rates compared to placebo controls [75,87]. A meta-analysis and retrospective study found that

teriparatide-treated patients had decreased subsequent vertebral fractures compared to non-teriparatide-treated patients [87,88].

In a clinical trial, the incidence of pedicle screw loosening was significantly less in patients administered with teriparatide prior to lumbar spinal fusion surgery compared to those with no therapy [76]. Teriparatide administration prior to fusion surgery in osteoporotic postmenopausal patients increased the insertional torque of pedicle screws during surgery, suggesting greater purchase of the screws to the bone [89]. However, conflicting evidence in a recent study shows no significant difference in pedicle screw loosening in teriparatide-treated patients [90]. Additionally, pooled analysis by Fatima et al. found a trend towards a reduced likelihood of pedicle screw loosening in the teriparatide group, but this was not significant [87].

The mechanical benefits of teriparatide after spinal fusion are consistent with improvements in radiographical measures, as evidenced by decreased sagittal misalignment and a mean loss of correction in the local kyphosis angle in patients treated with teriparatide [87,90]. In terms of clinical outcomes, results from meta-analyses show that patients receiving teriparatide following spinal fusion were less likely to experience pain, despite a minimal effect on disability scores, compared to non-teriparatide patients [71,75,87].

Studies have also compared teriparatide to bisphosphonate treatment following spine surgery. A study by Seki et al. found that patients with teriparatide treatment before surgical correction for adult spinal deformity had significantly higher rates of fusion than those treated with bisphosphonates [91]. Similarly, a prospective study by Ohtori et al. showed that the incidence of fusion was larger and the duration until fusion was shorter in patients with teriparatide compared to bisphosphates following posterolateral fusion [92]. These results are consistent with several systematic reviews and meta-analyses showing that teriparatide usage significantly increases the likelihood of fusion compared to bisphosphonates [72,73,87].

In a clinical trial by Ohtori et al., the incidence of pedicle screw loosening was significantly lower in patients administered with teriparatide prior to lumbar spinal fusion surgery compared to those with bisphosphonates [76]. A single-institution study found that by one-year post-surgery, the incidence of pedicle screw loosening was reduced in patients with teriparatide compared to the bisphosphonate group following transforaminal interbody fusion [93]. Regarding clinical outcomes, based on a retrospective study and a prospective clinical trial, patients undergoing spinal fusion did not have differing pain scores depending on if they were given teriparatide or bisphosphonates [92,93].

Together, there is a substantial amount of literature promoting the use of teriparatide in spine surgery to improve the success and strength of fusion. Additionally, there is compelling evidence suggesting a greater mechanical benefit from teriparatide than bisphosphonates in osteoporosis patients undergoing spinal fusion, although there are minimal differences in pain and disability scores (Figure 2D–F). Based on a systematic review, the College of Neurological Surgeons provides an evidence-based guideline recommending teriparatide treatment in osteoporotic patients undergoing spine surgery because it increases BMD, results in earlier and more robust fusion, and improves patient outcomes [94]. Similarly, an expert consensus study among 18 panelists suggests a best practice guideline supporting anabolic agents, including teriparatide, as a first-line treatment for patients with increased risk of fracture undergoing spinal reconstruction, due to their bone-building properties [95].

4.4.2. Abaloparatide

Most studies on parathyroid hormone analogs pertain to teriparatide. However, preliminary evidence suggests that abaloparatide may be beneficial in reducing complications following spine surgery. One study by Arlt et al. found that abaloparatide increased the levels of bone fusion markers in rats that underwent posterolateral fusion [96]. At 28 days post-surgery, 50% of the abaloparatide-treated rats exhibited bilateral fusion compared to only 25% of the controls [96]. While there is limited data evaluating the efficacy of

abaloparatide in spine-deformity outcomes, other high-quality studies have demonstrated significant benefit in subsets of patients. Matsumatoto et al. found a statistically significant 12.5% increase in lumbar spine BMD in a randomized, double-blind, placebo-controlled study of postmenopausal women and men with osteoporosis receiving daily injections of 90 micrograms of abaloparatide for 78 weeks [97]. Miller et al. performed a phase 3 double blind RCT in postmenopausal women with osteoporosis and found morphometric vertebral fractures occurred less frequently in the active treatment groups vs. placebo, with greater BMD increases [98]. As this medication has gained more widespread use, ongoing and future studies will more accurately describe the efficacy of this medication in the spinal deformity population.

5. Future Research Plans

Optimizing the treatment protocols for adult spinal deformity patients, particularly focusing on the long-term outcomes of newer anabolic agents like abaloparatide and romosozumab is an imperative next step. Additionally, studies could explore the cost-effectiveness and accessibility of these therapies. Research could also investigate the combination of various pharmacological agents with surgical techniques, such as cement augmentation or the use of larger interbody cages, to determine the best strategies for improving surgical outcomes in patients with compromised bone quality. Further studies might aim to assess the effectiveness of preoperative bone health optimization, particularly in high-risk populations, and develop standardized guidelines for bone health management in spinal deformity surgeries.

6. Conclusions

Several pharmacological and surgical solutions have been proposed to optimize bone health in patients with spinal deformity requiring nonoperative and operative management. Prevention remains the mainstay, with emphasis on lifestyle, nutrition, weight-bearing activity, and routine age-appropriate screening. In addition to the longstanding efficacy of vitamin and mineral supplements, bisphosphonates, and PTH-analogs, newer anabolic agents and monoclonal antibody treatments show great promise, with ongoing studies to demonstrate their short- and long-term value in reducing complications after spinal deformity surgery. Cost remains a significant hurdle, since despite their known efficacy, access and insurance coverage remains highly variable from patient to patient. Focus on cost-effective strategies will no doubt be a major contributor to the future utilization and outcome measures for these medications.

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