

Review

The Role of Artificial Intelligence in the Management of Pancreatic Cancer: Current Evidence and Future Perspectives

Afroditi Fotiadou ^{1,*}, Ioannis Margaritis ², Kyriacos Evangelou ³, Vasileios Zoubos ¹, Evangelos Kalaitzakis ⁴, Nikolaos Arkadopoulos ¹ and Ioannis Hatzaras ¹

¹ 4th Department of Surgery, ATTIKON University Hospital, National & Kapodistrian University of Athens, 12461 Athens, Greece; ihatzaras@med.uoa.gr (I.H.)

² Department of Surgery, Eugenideio Hospital, National & Kapodistrian University of Athens, 11528 Athens, Greece

³ School of Medicine, National & Kapodistrian University of Athens, 11527 Athens, Greece

⁴ Department of Gastroenterology, University Hospital of Heraklion, University of Crete, 71500 Heraklion, Greece

* Correspondence: agfotiadou@med.uoa.gr

Simple Summary

Pancreatic cancer is one of the most aggressive and lethal cancers, largely because it is often diagnosed at an advanced stage and responds poorly to current treatments. This study reviews how artificial intelligence can improve the management of this disease by analyzing complex medical data, including imaging, tissue samples, and clinical information. These technologies can help detect tumors earlier, support more accurate diagnosis, predict disease progression, and guide treatment decisions tailored to individual patients. This work aims to evaluate the current clinical applications of artificial intelligence in pancreatic cancer and assess its potential to enhance patient outcomes. While early results are promising, important challenges remain, including the need for validation in real-world settings. Overall, artificial intelligence has the potential to become a valuable tool in improving care for patients with pancreatic cancer.

Abstract

(1) Background: Pancreatic ductal adenocarcinoma remains one of the most lethal malignancies due to late diagnosis, aggressive tumor biology, and limited therapeutic options. Artificial intelligence has emerged as a promising tool to improve detection, risk stratification, and treatment planning. This study aims to review the current clinical applications of artificial intelligence in the management of pancreatic cancer and evaluate its translational potential. (2) Methods: A comprehensive literature search was conducted across major databases (PubMed/MEDLINE, Scopus, Web of science and Cochrane) for studies published between 2015 and 2026. Eligible studies included clinical investigations and systematic reviews reporting quantifiable outcomes related to diagnosis, staging, prognostication, and treatment response using artificial intelligence methods. (3) Results: A total of 24 studies were included, most of which were retrospective and utilized imaging, histopathology, and clinical datasets. Artificial intelligence demonstrated high diagnostic performance, particularly in imaging-based detection and lesion characterization, with several models achieving excellent accuracy. Applications in staging, surgical planning, and prognostication also showed promising results, although external validation and prospective data were limited. (4) Conclusions: Artificial intelligence has significant potential to enhance the management of pancreatic cancer, particularly as a decision-support tool. However, further prospective validation and integration into clinical workflows are required before widespread adoption.



Academic Editor: Hiroki Yokota

Received: 6 May 2026

Revised: 5 July 2026

Accepted: 9 July 2026

Published: 15 July 2026

Copyright: © 2026 by the authors.

Licensee MDPI, Basel, Switzerland.

This article is an open access article distributed under the terms and conditions of the [Creative Commons Attribution \(CC BY\)](https://creativecommons.org/licenses/by/4.0/) license.

Keywords: pancreatic ductal adenocarcinoma; artificial intelligence; deep learning

1. Introduction

Pancreatic ductal adenocarcinoma (PDAC) is predicted to become the third leading cause of cancer death by 2030, primarily due to late-stage diagnosis and a lack of effective treatment options. In fact, mortality from PDAC is rising by around 1% each year, and projections suggest that it could become the second leading cause of cancer-related death by 2030 [1]. The five-year overall survival rate for PDAC remains dismally low at 8–12%, depending on localization and staging at diagnosis [2,3]. Unlike other types of cancer, PDAC survival rates have not significantly improved over the years. Even with aggressive management, including surgical resection, adjuvant or neoadjuvant chemotherapy, and advanced supportive care, long-term survival remains poor, with virtually negligible 10-year survival rates in most patient cohorts [4]. Most patients present with unresectable or metastatic disease, and approximately 80–85% of PDAC cases are locally advanced at diagnosis [5,6]. Currently, only around 20% of patients are eligible for surgical resection, which remains the only potentially curative treatment option [7–9]. According to the American Joint Committee on Cancer (AJCC) staging system, operative management is generally only feasible in early-stage disease (Stages I–II), before major vascular involvement or distant metastasis develops [10]. This late presentation underscores the critical need for improved early detection strategies, more accurate prognostic and risk stratification, and personalized therapeutic approaches, including more precise treatment selection [11–13].

Beyond oncological staging and surgical eligibility, the contemporary management of PDAC relies on a highly coordinated, multidisciplinary approach designed to optimize outcomes despite the disease's aggressive biology. Current standards emphasize evaluation within specialized pancreatic cancer centers, where multidisciplinary tumor boards integrate expertise in radiology, endoscopy, surgical oncology, medical oncology, pathology, and palliative care [14]. High-quality cross-sectional imaging using a protocol specifically designed for the pancreas remains essential for assessing resectability, vascular involvement, and metastatic spread. Endoscopic ultrasound (EUS) with fine-needle aspiration/biopsy provides histological confirmation and enables molecular profiling when feasible [15]. Treatment pathways are increasingly shifting towards neoadjuvant therapy, even in cases of anatomically resectable disease. This approach aims to improve R0 resection rates, address micrometastatic disease early, and enhance patient selection for surgery [16]. Enhanced recovery protocols, structured nutritional support, and management of biliary obstruction or pancreatic exocrine and endocrine insufficiency are now routine components of perioperative care [17,18]. For advanced or borderline resectable PDAC, decision-making often incorporates systemic chemotherapy regimens such as modified FOLFIRINOX or gemcitabine/nab-paclitaxel. There is an increasing emphasis on biomarker-driven therapy, including BRCA-associated treatment strategies and targeted agents for rare molecular subtypes. Recent advances in genomic and molecular profiling have led to the identification of several distinct molecular subtypes of pancreatic cancer, paving the way for more personalized therapeutic strategies [19]. Upcoming liquid biopsy technologies and multiomics platforms are further expanding opportunities for precision oncology, enabling the integration of genomic, transcriptomic, proteomic, and metabolomic information into clinically actionable molecular signatures [20–22]. Emerging evidence suggests that between 12% and 25% of PDAC cases harbor actionable molecular alterations, providing opportunities for precision-based treatments that complement or refine conventional management approaches [23]. Despite these advances, real-world outcomes remain

limited, reinforcing the need for innovation in early detection, treatment personalization, and dynamic monitoring of treatment response and survival rates.

In the meantime, radiology, endoscopy, and pathology are generating rich, high-dimensional data conducive to AI. Over the last five years, machine learning (ML) and deep learning (DL) systems, as well as radiomics pipelines, have become increasingly investigated across the entire continuum of PDAC care, including early detection, diagnosis, risk stratification, treatment response prediction, and prognostication [24]. Beyond imaging, electronic health record (EHR) data and EHR-based models have been used to explore longitudinal risk and treatment forecasting [25,26]. Particular interest has focused on individuals with new-onset diabetes, which represents an emerging risk signal for occult PDAC and may enable targeted surveillance strategies through AI-assisted risk prediction models [27]. Furthermore, the integration of genomics, transcriptomics, proteomics, liquid biopsy biomarkers, and clinical data through multi-omics approaches is opening new opportunities for molecular subtyping and precision oncology [28].

Despite this rapid expansion, translation into routine clinical practice remains challenging. Many AI models have been developed retrospectively, frequently lack external validation, and are hindered by concerns regarding explainability, regulatory approval, cost-effectiveness, workflow integration, and implementation across different healthcare systems. Therefore, the present review aims to provide a comprehensive overview of the current applications of AI in PDAC management, summarizing the available evidence and quantitative performance metrics. We discuss current limitations, implementation challenges, and future directions necessary for the responsible integration of AI into pancreatic cancer care.

2. Methods

2.1. Search Strategy and Sources

A comprehensive search of the literature published from 2015 to 2026 was conducted up to 30 January 2026 in the following databases: PubMed/MEDLINE, Scopus, Web of Science, and Cochrane. Abstracts and titles were searched using keywords, MeSH terms and a combination of the following subject headings: ("pancreatic cancer" OR "pancreatic ductal adenocarcinoma" OR "PDAC") AND ("artificial intelligence" OR "AI" OR "machine learning" OR "ML" OR "deep learning" OR "DL" OR "radiomics" OR "neural network") AND ("CT" OR "MRI" OR "EUS" OR "pathology" OR "histology" OR "biopsy" OR "genomics" OR "multi-omics") AND ("management" OR "prediction" OR "prognosis" OR "staging" OR "surgery" OR "treatment response" OR "palliative" OR "surveillance"). We prioritized clinical and management-relevant studies. In addition, the references of relevant papers were hand searched, and their citations were examined using Google Scholar. Systematic reviews and meta-analyses were used to provide contextual background and to identify major AI application domains; however, they were not included in the final evidence synthesis, and some of them are yet to be discussed in Section 4. To avoid duplication and double-counting of evidence, only primary studies were included in the study tables and used for qualitative analysis. The search results are presented in Table 1 in Section 3.

2.2. Eligibility Criteria

Articles were screened for eligibility by the primary reviewer (AF). The inclusion criteria consisted of original human studies or systematic reviews/meta-analyses reporting quantifiable outcomes relevant to management (diagnosis aiding staging/treatment decisions; prediction of survival/recurrence/response; workflow triage; surveillance; or resource allocation). Eligible studies needed to evaluate AI-based methods such as ma-

chine learning, deep learning, radiomics, or multimodal algorithms, in at least one of the following domains: Diagnostic augmentation, including differentiation of malignant vs. benign peripancreatic structures or enhancement of staging accuracy, treatment-relevant decision support, such as resectability assessment, surgical planning, or workflow triage, prognostication, including models predicting survival, recurrence, or treatment response, surveillance and follow-up, or resource optimization, including workflow efficiency or case prioritization.

Studies were excluded if they focused exclusively on the technical development or validation of AI algorithms without presenting clinical endpoints, or if they involved single-case descriptions or single expert opinions. Furthermore, conference abstracts without full data and no response after an email request to the corresponding author, experimental animal or in vitro studies, or non-English studies were also excluded.

2.3. Data Extraction and Synthesis

We extracted the following information from the studies: cohort size; validation approach; primary endpoints (area under the curve (AUC), sensitivity/specificity, calibration); external validation status; and clinical utility indicators. The thematic categories of the included studies were developed a priori according to the principal clinical application of each AI model across the PDAC care pathway (e.g., early detection, diagnosis, staging, treatment planning, surgery, prognosis, and survival). Studies addressing similar clinical objectives were grouped to facilitate a clinically oriented narrative synthesis and to reflect the current translational landscape of AI in PDAC management. Within each category, the applications were analyzed further for innovation, translational potential, and scientific quality. Due to the limited amount of published literature (particularly original data) on this subject to date, as well as significant heterogeneity in sample size, modalities, endpoints, and thresholds, a narrative synthesis was performed. Although pre-defined search strategies, eligibility criteria, and quality appraisal methods were employed to enhance transparency and comprehensiveness, no formal systematic review methodology, pooled quantitative analysis, or meta-analysis was conducted. Consequently, the findings are presented descriptively and interpreted within the context of the available evidence. As critical appraisal of studies is strongly recommended when performing narrative reviews, the methodological strengths and limitations of the studies were independently assessed by two reviewers (KE and VZ) using the Critical Appraisal Skills Programme (CASP) qualitative checklist. The CASP checklist is a widely used tool for qualitative evidence synthesis and is recommended by the World Health Organization guidelines [29]. The authors acknowledge that more specialized tools, such as QUADAS-2, PRO-BAST(-AI), CLAIM, and TRIPOD-AI, may provide more detailed evaluations of a small group of specific study categories. In this study, the appropriateness of the study design, cohort adequacy, validation strategy, clinical relevance of the outcomes and applicability of the results were evaluated. Based on these criteria, the studies were classified as high, moderate or low quality (see Supplementary Materials, Table S1). No studies were excluded as a result of this quality assessment and no verification was performed. Any discrepancies between the two reviewers during study selection, data extraction, or quality assessment were resolved through discussion and consensus.

3. Results

A literature search identified 1311 unique studies, which were then assessed for eligibility based on their titles and abstracts. After removing 37 duplicate articles, a further 64 articles were excluded as they were deemed irrelevant or inappropriate publication types (e.g., case reports, editorials, review articles, experimental studies, errata or congress

proceedings). A total of 1210 full-text articles were then assessed for eligibility. Of these, 1186 studies were excluded for the following reasons: lack of clinically relevant outcomes (276); absence of data (477); technical algorithm development without translational implications (265); non-English language (11); or unavailable full-text data (157). Following full-text screening, 24 studies were included in this review and analyzed. The characteristics of the included studies are summarized in Table 1. Most were retrospective in design and were either single- or multi-institutional studies with a variable number of participants ranging from 39 to 6239 patients.

The included studies comprised predominantly retrospective cohort investigations (22/24), whereas only two studies incorporated a prospective design. Both single-center and multicenter datasets were represented, together with nationwide and international cohorts, with study populations ranging from 39 to 6239 patients. In addition, one imaging study evaluated a broader abdominal imaging cohort of approximately 20,000 participants for automated organ segmentation and quality control. AI applications were evaluated across the entire clinical pathway of pancreatic ductal adenocarcinoma, including early detection and lesion characterization, automated segmentation, staging and resectability assessment, treatment planning, recurrence and treatment-response prediction, molecular subtyping, and histopathological analysis. Most studies were based on CT (11/24) and EUS imaging (6/24), while others utilized MRI data (2/24), whole-slide histopathology (4/24), or multimodal clinical datasets integrating radiomics and clinicopathological variables (e.g., tumor markers) (1/24). Internal validation was performed in most studies, whereas independent external validation was available in only a subset and prospective clinical validation remained uncommon. Overall, the current evidence reflects a rapidly evolving field with encouraging diagnostic performance, although most published models remain at the retrospective development stage. The following tables (Tables 1 and 2a,b) demonstrate the included studies, their design and their clinical applications.

Table 1. Summary of studies reporting the use of AI models and their validation approach in the management of PDAC, so as their clinical and outcome-related characteristics.

Author	Year	Study Design	Study Setting	Validation Approach	Clinical Application
Viriyasaranon et al. [30]	2023	Retrospective	Multicenter	Random hold-out split + independent EV	PDAC detection and classification on CT
Iwasa et al. [31]	2021	Prospective observational	Single center	4-fold CV (IV)	PDAC AS on CE-EUS
Chen et al. [32]	2022	Retrospective	Nationwide	Hold-out IV + multicenter (nationwide) EV	PDAC detection on CE-CT
Cao et al. [33]	2023	Retrospective	Multicenter	Independent IV + multicenter EV + real-world retrospective validation	PDAC detection and classification on non-contrast CT
Mukherjee et al. [34]	2022	Retrospective case-control	Multicenter	5-fold CV + independent hold-out test set + EV	PDAC prediagnostic detection on CE-CT
Alves et al. [35] (PANORAMA)	2026	Retrospective observational non-inferiority	International	Independent multicenter EV	PDAC detection on routine CT
Zhang et al. [36]	2020	Prospective multicenter	Multicenter	Hold-out IV + multicenter EV + prospective crossover	PDAC EUS training and quality control
Gu et al. [37]	2023	Retrospective	Single center	Hold-out IV + prospective temporal	PDAC EUS automatic detection

Table 1. *Cont.*

Author	Year	Study Design	Study Setting	Validation Approach	Clinical Application
Kuwahara et al. [38]	2023	Retrospective	Single center	Hold-out IV	PDAC vs. benign pancreatic lesions DD on EUS
Udriștoiu et al. [39]	2021	Retrospective	Single center	Random internal split (test also served as validation set)	PDAC vs. benign pancreatic lesions automatic detection DD on multiparametric EUS
Tang et al. [40]	2023	Prospective randomized	Multicenter	80/20 hold-out IV + prospective	PDAC vs. benign pancreatic lesions on EUS (+FNA real-time guide)
Mo et al. [41]	2024	Retrospective randomized	Single center	70/30 internal split + 10-fold CV (LASSO) + 5-fold CV (model development)	PDAC vs. PNET DD on EUS
Liang et al. [42]	2020	Retrospective	Single center	5-fold CV + independent hold-out test set	GTV PDAC AS on multiparametric MRI
Chen et al. [43]	2020	Retrospective	Single center	Internal hold-out validation (train/validation/split)	MRI radiotherapy treatment planning
Kart et al. [44]	2022	Retrospective	International (2 population cohorts)	Previous EV + large-scale expert visual quality control	AS of abdominal organs (incl. pancreas) on MRI
Bereska et al. [45]	2024	Retrospective	Single center (PREOPANC, LAPC, CONTROL datasets)	5-fold CV + independent hold-out test set (expert comparison)	PDAC vascular involvement (classification) and resectability plan on CT-LAP
Viviers et al. [46]	2026	Retrospective	Single center	3-fold bootstrapping with independent hold-out test set (70/15/15 train/validation/test split)	PDAC vascular involvement and resectability plan on pancreatic protocol CT
Guan et al. [47]	2025	Retrospective	Multicenter	Multicenter split-sample validation with independent internal test and EV cohorts	Prediction of PDAC early postoperative recurrence on CT
Fu et al. [48]	2021	Retrospective	Single center	Hold-out IV + EV (TCGA)	PDAC histopathologic diagnosis, AS to slide diagnosis and classification
Nimgaonkar et al. [49]	2023	Retrospective	Multicenter	Random internal split with independent EV and additional untreated external cohort	Adjuvant gemcitabine response prediction of PDAC
Yamaguchi et al. [50]	2024	Retrospective	Single center	NR (no EV)	PDAC recurrence prediction after resection and adjuvant therapy (S1) from histopathological images
Ahmadvand et al. [51]	2024	Retrospective randomized	Single center	10-fold CV + independent EV cohort	Prediction of molecular subtypes of PDAC from WSI (routine HE)

Table 1. *Cont.*

Author	Year	Study Design	Study Setting	Validation Approach	Clinical Application
Saillard et al. [52]	2023	Retrospective multicenter	International	Multicenter EV (4 independent cohorts) + spatially matched and unmatched	PDAC molecular subtype prediction and assessment of intratumoral heterogeneity
Janssen et al. [53]	2024	Retrospective	International	By-scanner IECV	Histopathological AS of residual PDAC after neoadjuvant therapy

IV = internal validation, EC = external validation, CV = k-fold cross-over validation, NR = not reported, AS = automated segmentation, CE = contrast-enhanced, DD = differential diagnosis, FNA = fine needle aspiration, LASSO = least absolute shrinkage and selection operator, PNET = pancreatic neuroendocrine tumor, GTV = gross tumor volume, LAP = late arterial phase, TCGA = the cancer genome atlas, S1 = tegafur/5-chloro-2,4-dihydropyridine/potassium oxonate, WSI = whole-slide imaging, HE = hematoxylin-eosin, IECV = internal and external cross-over validation.

Table 2. (a) Summary of studies reporting the AI applications in radiological and endoscopic imaging for PDAC. (b) Summary of studies reporting the AI applications in pathology and prognostic modeling for PDAC.

Author	Dataset Type	Patients (n)	AI Model	Performance IV	Performance EV	Key Findings
(a)						
Viriyasaranon et al., 2023 [30]	CT	IC: 4287 EC: 361	CE-CT self-supervised DL (PS integrated with CNN and transformer variants)	ACC _{CNN} = 94.3% SENS _{CNN} = 92.5% ACC _{DL} = 95.7% SENS _{DL} = 99.3% (both with PS)	ACC _{CNN} = 82.5% SENS _{CNN} = 81.7% ACC _{DL} = 87.8% SENS _{DL} = 86.5% (both with PS)	PS increased by ACC > 20.5% SENS > 37.0%
Iwasa et al., 2021 [31]	CE-EUS	IC: 100	DL AS CNN U-Net with 100 epochs	U-Net on EUS: median IoU = 0.77	NR	DL enabled AS of PDAC on CE-EUS, AI lesion delineation during EUS feasible
Chen et al., 2022 [32]	CE-CT	IC: 256 EC: 1473	DL CNN	SENS _{DL} = 89.9% SPEC _{DL} = 95.9% AUC = 0.96 p = 0.11	SENS _{DL} = 89.7% SPEC _{DL} = 92.8% AUC = 0.95 SENS _{DL} = 74.7% for Tu < 2 cm	PDAC accurate detection on CE-CT with reasonable SENS for Tu < 2 cm
Cao et al., 2023 [33]	non-contrast CT	IC: 3208 EC: 6239	DL (PANDA)	Detection Overall SENS = 97.2% Identification SENS = 92.6% SPEC = 97.3% AUC = 0.987	SENS = 92.9% SPEC = 99.9% AUC = 0.986–0.996	PANDA with non-contrast CT: non-inferiority to CE-CT in the DD of PDAC in a large-scale screening
Mukherjee et al., 2022 [34]	CE-CT	IC: 420 EC: 80	4 ML classifiers: KNN, SVM, RF, XGBoost	SENS _{SVM} = 95% SPEC _{SVM} = 90.3% F1 _{SVM} = 89.5% AUC _{SVM} = 0.98 ACC _{SVM} = 92.2% AUC _{KNN} = 0.95 AUC _{RF} = 0.95 AUC _{XGBoost} = 0.96 comparable	SENS _{SVM} = 96.4% SPEC _{SVM} = 87.2% F1 _{SVM} = 87.1% AUC _{SVM} = 0.97 ACC _{SVM} = 90.4%	Prediagnostic PDAC detected, median time till diagnosis: 386 d, superior performance to radiologists

Table 2. Cont.

Author	Dataset Type	Patients (n)	AI Model	Performance IV	Performance EV	Key Findings
(a)						
Alves et al., 2026 (PANORAMA) [35]	routine CT	IC: 2310 EC: 1130	Different DL models	$AUC_{AI} = 0.92$	$AUC_{AI} = 0.92$ $AUC_{RAD} = 0.88$	AI non-inferior ($p < 0.0001$) and superior ($p < 0.0001$) to radiologists on routine CT
Zhang et al., 2020 [36]	EUS	IC: 311 EC: 169	DL AS and station recognition on U/S (BP MASTER)	$ACC = 94.2\%$	$ACC = 82.4\%$	Expert-level EUS segmentation, improved trainee results ($ACC_{AI} = 78.4\%$ vs. $ACC = 67.2\%$, $p < 0.01$)
Gu et al., 2023 [37]	EUS	IC: 491	EUS based DLR (ResNet50)	$SENS_{DLR} = 0.831$ $SPEC_{DLR} = 0.904$ $ACC_{DLR} = 0.863$ $AUC_{DLR} = 0.936$	NR	Overall diagnostic performance to DD PDAC from CP improved, higher/comparable training performance
Kuwahara et al., 2023 [38]	EUS	IC: 933 *	DL CNN	$SENS_{DL} = 0.94$ $SPEC_{DL} = 0.82$ $ACC_{DL} = 0.91$ $AUC_{DL} = 0.9$	NR	Efficient PDAC differentiation (high ACC), and diagnostic potential
Udriștoiu et al., 2021 [39]	multi-parametric EUS	IC: 65	DL CNN-LSTM	$ACC_{DL} = 98.26\%$ $AUC_{DL} = 0.98$ $PPV_{PDAC} = 98.1\%$ $NPV_{PDAC} = 96.7\%$	NR	Automatic generation of real-time diagnosis (visual features' differentiation and dynamics' capture over time), clinical decision supporting system
Tang et al., 2023 [40]	EUS	IC: 39	Real-time CNN and RF (CH-EUS MASTER) M1: real-time capture and segmentation M2: DD benign vs. malignant Tu	Malignancy Identification $SENS_{CH} = 92.3\%$ $SPEC_{CH} = 92.3\%$ $ACC_{CH} = 92.3\%$ $PPV_{PDAC} = 96\%$ $NPV_{PDAC} = 85.7\%$ $p < 0.05$ EUS-FNA comparable with control group $p > 0.05$	NR	Significant superiority (ACC, SENS, SPEC) for PDAC diagnosis, may guide FNA in real time
Mo et al., 2024 [41]	EUS	IC: 231 *	Ultrasonics nomogram based on 8 ML algorithms (LR, LightGBM, MLP, RF, KNN, SVM, XGBoost)	RF superior Performance $AUC_{RF} = 0.999$ $SENS_{RF} = 0.946$ $SPEC_{RF} = 100\%$ $ACC_{RF} = 0.975$ $PPV_{RF} = 100\%$ $NPV_{RF} = 0.956$	NR	The highest level of diagnostic efficacy (test cohort $p = 0.1$)
Liang et al., 2020 [42]	MRI	IC: 40	Square window-based CNN	DSC: 0.73 HD = 8.11 mm MSD = 1.82 mm $p > 0.5$	NR	Model performance comparable to radiation oncologists, framework to incorporate MRI for GTV AS in MRgOART

Table 2. *Cont.*

Author	Dataset Type	Patients (n)	AI Model	Performance IV	Performance EV	Key Findings
(a)						
Chen et al., 2020 [43]	MRI	IC: 102 *	DL OARs segmentation multiscale feature fusion model (ALAMO)	ACC: 0.87–0.96 $p < 0.001$	NR	Full pancreas AS on MRI with high ACC and practical memory
Kart et al., 2022 [44]	MRI	IC: 20.000 * EC: >400	DL CNN (nnUNet)	AS error rate: 14.8%, 6.1% of datasets	NR	ACC~90% of data with no relevant segmentation errors, AS feasible
Bereska et al., 2024 [45]	CT-LAP	IC: 517	Semisupervised ML AS model (nnUNet)	Vascular Involvement 76% concurrence with radiologists $p = 10-35 < 0.05$ Resectability Classification 85%: resectable 80%: borderline resectable, 75% locally advanced	NR	AI quantifies vascular involvement and classifies resectability for PDAC
Viviers et al., 2026 [46]	pancreatic protocol CT	IC: 99	DL AS (nnU-Net, 3D U-Net, Probabilistic 3D U-Net)	SENS = 0.88 SPEC = 0.86 for tumor-vessel involvement Segmentation ACC _{vein} = 0.88 ACC _{artery} = 0.86 ACC _{Tu} = 0.86	NR	AS enables automated detection of Tu involvement and automated computation of the degree of tumor-vessel contact.
Guan et al., 2025 [47]	CT	IC: 493	CT-based AS < radiomics + DL + SVM/RF nomogram	AUC = 0.921 interfeature scores, significantly higher in patients with ER $p < 0.001$	NR	Nomogram combining CT features and clinical factors (CA19-9) predicted early recurrence risk
(b)						
Fu et al., 2021 [48]	WSI, HE pathology slides	IC: 231	Hierarchical DL CNN (patch-level U-Net, WSI with LightGBM)	ACC _{AP} = 95.3% ACC _{WSI} = 100% ACC = 90.38% classification with IVD	NR	PDAC detection on WSI, potential for digital pathology support, generalizable
Nimgaonkar et al., 2023 [49]	WSI	IC: 93 EC: 207	DL CNN histologic DSS signature	median DSS _{sig+} = 67.9 mo DSS _{sig-} = 16 mo $p = 0.01$ signature not associated with RNA-seq clusters	UPMC cohort: DSS _{VPG+} = 43.1 mo DSS _{VPG-} = 16 mo HR 0.41 $p = 0.02$	Gemcitabine benefit prediction, treatment specific also in EC
Yamaguchi et al., 2024 [50]	WSI, HE pathology slides	IC: 89	DL (autoencoder based feature extraction from WSI) + SVM classifier	AUC = 0.73 (histology only); AUC = 0.84 (histology + clinical data)	NR	Recurrence prediction, improved performance when combined with clinical data, poor Tu DD significantly associated with recurrence

Table 2. Cont.

Author	Dataset Type	Patients (n)	AI Model	Performance IV	Performance EV	Key Findings
(b)						
Ahmadvand et al., 2024 [51]	WSI, HE pathology slides	IC: 95 (TCGA) EC: 44	DL CNN on WSI (Vanilla, IDaRS, DeepMIL, VarMIL)	Tu Regions Identification ACC _{TCGA} = 89.13% Molecular Subtype Identification AUC _{TCGA} = 96.18% ACC _{VarMIL} = 97.5 ± 4.09% (best DL model)	Molecular Subtype Identification ACC _{EC} = 83.03%	Cost-effective and rapid PDAC molecular subtype classification, potentially replacing RNA-based classification
Saillard et al., 2023 [52]	WSI, HE pathology slides with molecular transcriptomics	IC: 202 EC: 396 (BJN_U, BJN_M, TCGA_PAAD, Liver_FNB)	Multi-step DL CNN histology model (PacpAInt)	High ACC for subtype classification (varies by cohort)	Validated in independent cohorts with consistent performance	Spatial intratumoral heterogeneity identification and molecular subtype prediction
Janssen et al., 2024 [53]	WSI, HE pathology slides	IC: 494/488/475/382 EC: 31/37/50/146 depending on model	DL CNN AS on HE images: ISGPP model (U-Net)	mean F1 = 0.78 High segmentation ASS, robust model performance	Lowest in Leica cases with mean F1 = 0.71	Accurate and reproducible AS of residual PDAC, can support objective assessment of treatment response

* = cohort not limited to PDAC patients, n = number, IC = internal cohort, EC = external cohort, NR = not reported, CE = contrast-enhanced, PS = pseudo-lesion segmentation, CNN = convolutional neural network, ACC = accuracy, SENS = sensitivity, IoU = intersection over union, SPEC = specificity, AUC = area under the curve, Tu = tumor, KNN = K-nearest neighbor, SVM = support vector machine, RF = random forest, XGBoost = extreme gradient boosting, RAD = radiologists, DLR = deep learning radiomics, DD = differential diagnosis, CP = chronic pancreatitis, PPV = positive predictive value, NPV = negative predictive value, LR = logistic regression, LightGBM = light gradient boosting machine, MLP = multilayer perceptron, OARs = organs at risk, AS = automated segmentation, LAP = late arterial phase. AP = automatic patch, WSI = whole-slide imaging, DSS = disease-specific survival, sig = signature patients, mo = months, VPG = visual pancreatic gemcitabine, S1 = tegafur/5-chloro-2,4-dihydroxypyridine/potassium oxonate, HE = hematoxylin-eosin, TCGA = the Cancer Genome Atlas.

4. Discussion

4.1. Fundamentals of AI in Clinical Medicine

AI encompasses computational methods capable of performing tasks that traditionally require human cognition, including pattern recognition, classification, prediction, and decision support [54]. In healthcare, AI has emerged as a powerful tool for extracting clinically meaningful information from increasingly complex and heterogeneous datasets. Unlike conventional statistical approaches, AI systems can integrate diverse sources of information, including imaging, histopathology, laboratory values, genomic profiles, and EHRs, allowing the identification of subtle relationships that may not be apparent through traditional analytical techniques [25,55].

ML, a major branch of AI, enables algorithms to learn from data and generate predictions without explicit programming. In medical research, AI and ML are often used interchangeably because most current clinical applications rely on machine-learning algorithms. ML methods have been widely applied to disease classification, risk stratification, prognostication, and treatment response prediction. Their ability to model nonlinear interactions and process high-dimensional datasets makes them particularly attractive for precision medicine and personalized oncology [56,57]. Typically, model development involves training and validation datasets, followed by independent testing and, ideally, external validation to assess generalizability and minimize overfitting. The greatest strength of ML lies in its ability to process and integrate vast datasets, linking observed inputs with predicted outputs in non-linear and highly interactive ways [55].

DL is a subset of machine learning that uses multi-layer neural networks to extract deeply hidden features. Deep learning enables machines to process raw data and automatically construct complex representations. Compared to shallow ML approaches and traditional analytical methods, DL models often achieve superior performance, particularly in fields involving large-scale, high-dimensional datasets, and they require minimal to no human intervention [58].

4.2. Adaptation of AI Technologies in Healthcare

The integration of artificial intelligence into the field of healthcare first occurred in the 1950s, during research into the Turing test. Significant innovations since 2000 include the introduction of deep learning and, subsequently, computer-aided detection (CAD) in endoscopy. This has been followed by the integration of AI technologies in robotic surgery and telemedicine [59–61].

In the context of precision medicine, AI now has the potential to support clinical decision-makers by swiftly converting large, complex datasets into concise, comprehensible outputs. This accelerates analysis, minimizes human errors inherent in manual review, enhances diagnostic accuracy, and enables continuous real-time predictive capabilities. ML and DL models can identify patterns linked to outcomes such as mortality, readmissions, and sepsis, even interpret unstructured notes using natural language processing (NLP) to support real-time decisions [62,63]. Beyond clinical prediction, AI-enhanced EHRs can streamline administrative tasks and improve operational efficiency. Emerging radiomic markers and advanced models—including Prov-GigaPath, Owkin’s systems, CHIEF, and Google DeepMind’s tools—further expand AI’s diagnostic potential. AI can also perform repetitive tasks very effectively, allowing physicians to focus on more complex and nuanced clinical decision-making. Furthermore, AI has the potential to drive innovation, sustainability, and equity in healthcare delivery on a global scale. However, challenges such as data interoperability, privacy, costs, and security remain significant barriers to their widespread adoption [59].

4.3. Adaptation of AI Technologies in the Management of PDAC

AI can be highly valuable in assessing PDAC, since clinical decision-making extends beyond simple diagnosis and encompasses risk stratification, identification of high-risk populations, early detection in high-risk or symptomatic patients, assessment of resectability and vascular involvement, molecular subtyping, treatment selection, prediction of therapeutic response, and longitudinal surveillance [11,19,23,25,27,57]. Furthermore, the increasing availability of multimodal data, including cross-sectional imaging, endoscopic ultrasound, histopathology, electronic health records, laboratory parameters, circulating biomarkers, and multi-omics datasets, creates opportunities but also poses major analytical challenges [25,27]. AI offers the ability to integrate these heterogeneous data sources, uncover complex patterns that may not be readily apparent to clinicians, and provide decision support across the entire continuum of care. Currently, AI models are being used to assist with diagnosis, grading, staging, outcomes prediction, therapeutic efficacy, and prospective clinical trial design.

The sequence of the following sections in the Discussion intentionally reflects increasing levels of complexity and decreasing levels of clinical maturity, moving from applications supported by stronger evidence to more exploratory domains.

4.4. Early Detection, Diagnosis, and Staging of PDAC

Although image quality is improving all the time, offering highly sensitive and advanced diagnostic techniques, diagnosing pancreatic cancer remains a significant challenge. AI is rapidly improving the early detection of pancreatic ductal adenocarcinoma (PDAC),

with several imaging-based and multimodal studies reporting high diagnostic performance. AI can contribute to multiple stages of imaging-based diagnosis, including image reconstruction, automated segmentation, lesion detection, and characterization or grading based on extracted radiological features. These methodologies can also be used to analyze digitized histopathology slides, enabling high-throughput and objective tissue evaluation [54]. So far, DL and ML methods, such as convolutional neural networks (CNNs) or support vector machines (SVMs), have been utilized to detect PDAC and have proved reasonably sensitive [30,31]. Overall, CT- and EUS-based AI models represent some of the most mature applications in PDAC, with several studies demonstrating multicenter validation and performance that approaches clinical implementation. Nevertheless, prospective validation and impact on patient outcomes remain limited.

4.4.1. CT-Based Deep Learning (Contrast and Non-Contrast)

In their retrospective study, Chen et al. developed and validated an end-to-end DL-based tool that combines a CNN segmentation model with an ensemble classifier on contrast-enhanced CT scans. They demonstrated that the tool's sensitivity for detecting tumors smaller than 2 cm significantly outperformed radiologist interpretation in both internal and nationwide real-world test sets, as analyzed using McNemar's test [32]. Although non-contrast CT is widely used for various clinical purposes, it has traditionally been considered unsuitable for detecting PDAC. However, its routine availability presents an attractive opportunity for large-scale screening. However, the pancreatic cancer detection with the artificial intelligence (PANDA) system, a deep-learning system created by the team of Cao et al. and trained on a dataset of 3208 single-center patients, achieved AUCs of 0.986–0.996 in multicenter validation. When applied to routine non-contrast CT, it demonstrated 92.9% sensitivity and 99.9% specificity in a real-world test set, outperforming the sensitivity of the average radiologist by 34.1% [33].

Radiomics-based machine-learning models have also identified PDAC changes on prediagnostic CT scans, even months to years before clinical diagnosis. Mukherjee et al. in their case-control study aiming to early detect PDAC using ML models and to compare performance against human radiologists reported that support vector machine (SVM) had the highest sensitivity (mean; 95% confidence interval) (95.5; 85.5–100.0), specificity (90.3; 84.3–91.5), AUC (0.98; 0.94–0.98), and accuracy (92.2%; 86.7–93.7) for classification of CTs into prediagnostic versus normal and classification accuracies in the low-to-mid 90s versus much lower radiologist performance [34]. Moreover, reviews of DL and radiomics approaches confirm that quantitative image features combined with CNN/SVM/ensemble classifiers substantially boost detection and risk-stratification compared to conventional reading. Beyond imaging, multimodal efforts that integrate blood-based biomarkers (ctDNA, exosomes, proteomic signatures) with clinical data and ML models are showing promise for screening and earlier diagnosis, though most remain investigational and require larger prospective validation.

Recent reviews have concluded that AI can function as a 'second reader' in pancreatic imaging, improving sensitivity, reducing time to diagnosis, and improving clinical outcomes. A brand new international, paired, non-inferiority, confirmatory, observational study (PANORAMA) by Alves et al. established an open-source benchmark to investigate AI systems for pancreatic ductal adenocarcinoma (PDAC) detection on CT scans, comparing their performance to that of radiologists at scale [35]. The study evaluated an AI system for PDAC detection on routine CT scans, involving over 3400 patients from nine tertiary centers across Europe and the USA. In a sequestered testing cohort, the AI system demonstrated high diagnostic accuracy (AUROC 0.92, 95% CI 0.89–0.94) and, in a multi-reader study involving 68 radiologists from 12 countries, it showed statistically

significant non-inferiority and superiority compared to human readers. The reference standard was based on histopathology and long-term clinical follow-up, thereby strengthening the reliability of the results.

4.4.2. EUS-Based AI for Lesion Characterization

EUS plays a pivotal role in evaluating solid pancreatic masses and guiding fine needle aspiration (FNA). Several AI systems (CNNs, radiomics, and handcrafted pipelines) can classify PDAC versus benign lesions using B-mode EUS or elastography. A meta-analysis of ten studies involving 1871 patients demonstrated that AI-assisted EUS has excellent diagnostic performance for pancreatic cancer. The pooled sensitivity and specificity were 0.92 (95% CI, 0.89–0.95) and 0.90 (95% CI, 0.83–0.94), respectively, reflecting high overall accuracy, as indicated by an AUC of 0.95 and a diagnostic odds ratio of 128.9 (95% CI, 71.2–233.8) [64]. A focused meta-analysis from 2023 similarly found high accuracy for AI-assisted EUS across detection, differentiation, and guidance for tissue sampling. This study emphasized the advantages of AI over conventional features alone, while calling for multi-center prospective validation and standardized reporting. This meta-analysis evaluated the diagnostic accuracy of AI applied to EUS images for pancreatic cancer, including seven studies with 1110 participants. AI demonstrated excellent performance, with a pooled sensitivity of 93%, a specificity of 90%, an AUC of 0.95, and a diagnostic odds ratio of 114, indicating reliable discrimination between malignant and benign lesions. Overall, these results suggest that AI-assisted EUS has the potential to reduce operator dependence and improve the early detection of pancreatic cancer [65]. Another illustrative example of how AI can assist with EUS training and quality control is a deep learning (DL)-based system named BP MASTER. This system demonstrated 90% accuracy in station classification and segmentation, performing comparably to expert endoscopists with a Dice similarity coefficient (DSC) of 0.77 and 0.81 in blood vessel and pancreas segmentation, respectively [36].

AI algorithms, particularly DL and CNNs, have demonstrated a high level of accuracy when it comes to differentiating between PDAC and chronic pancreatitis (CP), as well as other pancreatic lesions. For instance, DL radiomics achieved an AUC of 0.936 and enhanced the performance of junior endosonographers [37], while EfficientNet distinguished PDAC from other masses with an AUC of 0.9 [38]. Furthermore, a CNN-LSTM model attained 98.1% sensitivity, 96.7% specificity, and an AUC of 0.97 using multimodal EUS images. AI has also been used to differentiate between autoimmune pancreatitis and PDAC and CP, achieving sensitivities and specificities of up to 99% and 98%, respectively [39]. Real-time, AI-enhanced systems, such as CH-EUS MASTER, have improved diagnostic accuracy to 92.3% and first-pass EUS-FNA yield to 80% [40]. In terms of prognosis, ML models predicted the need for repeat EUS-guided celiac plexus neurolysis and pain relief with an AUC of up to 0.94. In the case of pancreatic neuroendocrine tumors (pNETs), AI was able to distinguish between pNETs and PDAC, as well as predict aggressiveness, with an AUC of 0.85 [41,55]. Different CNN models have achieved remarkable accuracy in differentiating mucinous from non-mucinous cysts (98.5%), predicting malignancy (94%), and stratifying low-grade vs. high-grade dysplasia (up to 99.6%), outperforming conventional guidelines [66].

4.4.3. MRI and Multi-Parametric Imaging

Although CT/EUS provides the strongest single-study evidence, MRI-based radiomics and DL tools are also emerging. Recent advances in magnetic resonance imaging combined with artificial intelligence have produced promising results in small-to-moderate patient groups for lesion detection and fibrosis/texture quantification, which could enhance staging

and resectability assessment. Deep learning and radiomics-based approaches, when applied to multiparametric MRI including diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC) maps, and contrast-enhanced sequences, enable the extraction of high-dimensional imaging features that cannot be identified through visual assessment. This improves lesion detection and classification [42].

Recent DL approaches have substantially improved the automated segmentation of the pancreas and other abdominal organs on MRI scans. CNN-based models such as U-Net and nnU-Net, as well as graph-based fusion methods, have achieved DSCs ranging from approximately 0.72 to 0.89 for the pancreas and exceeding 0.9 for larger organs such as the liver and kidneys [43,66]. Large-scale applications, including whole-body MRI segmentation using UK Biobank and German National Cohort datasets, have demonstrated robust generalisability. Specialized DL pipelines have also been developed for pancreatic cyst detection and segmentation using multisequence MRI, achieving clinically meaningful accuracy for lesions larger than 5 mm [44,67].

Several studies have demonstrated that AI-assisted MRI radiomics can distinguish PDAC from benign pancreatic lesions and chronic pancreatitis with high diagnostic accuracy, particularly in the case of early-stage or small tumors. Furthermore, machine learning models that integrate multiparametric MRI features have demonstrated the ability to predict biologically relevant tumor characteristics, such as the Ki-67 proliferation index and tumor grade. This offers a non-invasive means of achieving early risk stratification and facilitating more personalized treatment strategies [68]. Taken together, these findings emphasize the increasing importance of AI-enhanced MRI and multiparametric imaging as promising tools for the early detection and diagnosis of PDAC, although prospective validation and large multicenter datasets are still necessary before they can be routinely adopted in clinical practice.

4.5. Staging and Surgical Planning

Accurate staging and assessment of resectability are critical in the management of PDAC, yet conventional interpretation of imaging results shows significant interobserver variability, particularly when evaluating tumor vessel involvement. AI, particularly deep learning (DL) and radiomics, enhances objectivity by quantifying imaging features beyond human perception. Semisupervised AI models analyzing contrast-enhanced CT scans have achieved 75–85% agreement with expert radiologists in quantifying vascular involvement, offering standardized support for treatment selection [45].

Radiomics models can already predict margin positivity and lymph node metastases preoperatively with sensitivities of up to 64.8% and specificities of up to 77%, achieving an AUC of up to 0.92 and aiding decisions on neoadjuvant therapy versus upfront surgery [69,70]. AI-based segmentation also enables the automated assessment of tumor vessel contact and staging granularity, which correlates with pathological stage and guides surgical planning [45,46].

Intraoperative AI applications in minimally invasive pancreatic surgery use large amounts of surgical data to improve safety and outcomes. As we know, surgomics collects intraoperative features and combines them with preoperative data in order to predict postoperative morbidity and mortality, provide surgeons with feedback, and suggest actions based on peer practices [71]. AI integrated with augmented reality (AR), such as SmartLiver™, enables the real-time visualization of tumors and intra-parenchymal vascular structures from 2D images, thereby enhancing surgical guidance [72]. Furthermore, deep learning models applied to surgical videos can facilitate landmark detection, phase recognition, and ‘no fly zones’ during procedures such as laparoscopic cholecystectomy [73],

as well as assisting in the safe placement of trocars by identifying abdominal wall layers in real time for minimally invasive approaches [74,75].

4.6. Prognostication and Response Assessment

An increasing body of research shows that preoperative CT radiomics signatures can predict postoperative survival and early recurrence in pancreatic cancer. Integrated models that combine clinical, radiological, and radiomic features (CRR models) have demonstrated strong predictive performance for early recurrence (e.g., AUCs of up to ~0.92 in large cohorts) and outperform models based on clinical or radiomic data alone. This aids risk stratification and treatment selection prior to surgery [47]. An emerging body of research quantifying sarcopenia and adiposity from routine CT scans using radiomics also predicts recurrence-free survival, highlighting important tumor–host interactions that extend beyond tumor-centric imaging features [76].

Delta radiomics, which captures changes in radiomic features over time, has the potential to predict treatment response early on during neoadjuvant or palliative chemotherapy. Machine learning models that leverage longitudinal feature changes have achieved high predictive discrimination (AUC up to ~0.94) in differentiating responders from non-responders. This suggests that temporal texture dynamics may be powerful biomarkers of the effect of therapy [77]. However, recent reviews emphasize the necessity of anchoring delta radiomics signals to clinically meaningful endpoints, such as R0 resection rates, progression-free survival (PFS), and overall survival (OS), rather than relying solely on imaging surrogates.

Although prospective validation remains limited, early proof-of-concept AI systems that integrate routine laboratory time series (e.g., serial blood tests) with clinical data have been proposed to forecast near-term clinical evolution and potentially anticipate treatment tolerance or toxicity. Together, these AI-enabled prognostic models can inform critical management decisions, including choosing between neoadjuvant therapy and upfront surgery, the intensity of adjuvant therapy, personalized surveillance intervals, and shared decision-making with patients where the operative risk and expected benefit are balanced.

4.7. Pathology and Biomarker Discovery

The application of AI to whole slide imaging (WSI) in histopathology is increasingly enabling the objective and high-throughput detection of tumors, the grading of surrogates, and the exploration of morpho-molecular signatures that correlate with clinical outcomes. Deep learning models have demonstrated very high performance in the automated detection and segmentation of PDAC on WSIs. Some architectures have achieved classification accuracies of over 95% at the patch level and around 100% at the slide level, illustrating their potential to support diagnostic workflows and reduce manual workload [48].

Beyond detection, AI can extract prognostic and predictive histological features that are not routinely evaluated by pathologists. For instance, an AI-derived histological signature has been identified that can predict disease-specific survival following adjuvant gemcitabine therapy in PDAC. External validation has confirmed its potential utility as a treatment response biomarker [49]. Additionally, the application of machine learning to WSI data combined with clinical variables (e.g., tumor markers) has been shown to improve the prediction of recurrence after resection compared to either domain alone, with AUCs increasing from ~0.73 to ~0.84 when clinical data were integrated [50].

AI has also been used to infer molecular subtypes directly from routine hematoxylin and eosin (H&E) slides, addressing a historically challenging task that has required costly genomic assays. Deep learning models have classified PDAC subtypes (classical vs. basal) with balanced accuracies of ~96% in the Cancer Genome Atlas (TCGA) cohorts and ~83%

in external cohorts, highlighting AI's potential to guide precision therapy from standard pathology specimens [51]. Advanced interpretable AI models, such as PACpAInt, have further elucidated intratumor heterogeneity. These models have shown that many tumors exist on a continuum between subtypes, which has important prognostic implications. They have also enabled the spatial phenotyping of tumor and stromal compartments related to therapy response [52].

Despite these advances, challenges remain, chiefly the need for large, multi-institutional annotated WSI datasets and regulatory-grade analytic pipelines to ensure robust model generalization across staining protocols and scanner platforms. Nevertheless, AI-enhanced histopathological analysis is evolving rapidly into a tool for improved diagnostics and biomarker discovery, as well as integration with genomics and liquid biopsy data, to support personalized management strategies in pancreatic cancer [78,79]. AI-based segmentation models, such as that developed by Janssen et al., enable the objective quantification of residual tumor burden following neoadjuvant therapy, which could improve pathological response assessment [53]. Overall, histopathology-based AI models demonstrate considerable potential for molecular subtyping and prognostication but currently remain primarily within the research setting.

4.8. Evidence Quality, Generalizability, and Implementation

Guidelines such as CONSORT-AI and SPIRIT-AI provide recommendations for the design and reporting of AI-based clinical trials, whereas emerging frameworks, including TRIPOD-AI and CLAIM, aim to standardize the development, validation, and reporting of predictive models and medical imaging studies [80–84]. However, there are several challenges that limit the current translation of AI into clinical practice. Dataset bias and drift arise from the reliance on single-center datasets with limited scanner and protocol diversity. Moreover, the majority of currently available AI models have been developed using retrospective datasets. In our presented studies, for instance, internal validation was commonly performed, whereas independent external validation was not always available, and prospective validation was rare. These differences are clinically important, as model performance obtained from internal cohorts may not generalize to other institutions, imaging protocols, patient populations, or workflows. Domain shifts and calibration drift can also threaten reliability. Reporting is inconsistent, and there is variable adherence to TRIPOD-AI/CONSORT-AI guidelines, as well as limited code and model sharing. Prospective clinical utility is rarely evaluated, with most studies only reporting diagnostic or predictive accuracy rather than patient-level outcomes. Workflow integration is most feasible in the form of a second reader, triage flag, or automated pre-screening tool. Explainability features, such as saliency maps and case-based reasoning, can enhance trust and encourage multidisciplinary adoption. The adoption of these standards, together with external validation and prospective multicenter studies, will reinforce the translation of AI in clinical practice.

4.9. Future Directions

AI has the potential to enable machines to analyze complex data and generate actionable insights. This offers opportunities to improve diagnostic accuracy, reduce errors, and support real-time clinical decision-making. In the case of PDAC, AI-based omics approaches are emerging as promising tools for the early discovery of biomarkers, molecular subtyping, the selection of treatments, and the prediction of survival and recurrence. These approaches have the potential to improve current poor outcomes. Despite major advances in this field, PDAC remains a significant global public health challenge, with five-year survival rates of around 15%, primarily due to late diagnosis, limited screening strategies,

and therapeutic resistance. Recent reviews emphasize the growing role of AI in transforming PDAC diagnosis and management, and highlight its potential to advance precision medicine in this lethal disease. Looking ahead, AI may enable comprehensive, whole-body cancer screening strategies rather than traditional organ-specific approaches [85].

AI currently appears to be most promising as an adjunctive ‘second reader’ in radiology and endoscopy, where it can improve the consistency of detection and reduce interobserver variability, particularly for small lesions or when the pancreas is not the main focus of the imaging. In EUS, AI can serve as an adjunct classifier to support malignancy discrimination and guide tissue sampling, thereby reducing variability related to operator experience. AI-driven risk triage using clinical and EHR data can prioritize high-risk patients for imaging and expedite referral pathways, building on evidence from multi-cancer deployments.

In terms of its emerging and promising applications, AI-based prognostic and early-recurrence radiomics may help to personalize neoadjuvant/adjuvant therapy and surveillance intervals. Meanwhile, delta-radiomics can provide early indicators of treatment response to guide adaptive therapy. In pathology, AI can extract morpho-molecular surrogates and automate quantification to maximize the information obtained from limited tissue samples. If integrated with confirmatory diagnostic pathways and outcome monitoring, opportunistic non-contrast CT screening offers potential for population-level early detection.

Successful adoption requires the integration of AI outputs into existing multidisciplinary team workflows, with human oversight and defined action thresholds (e.g., triggering a pancreas protocol CT or EUS-FNA). Models must undergo external, multicenter validation across diverse scanners, protocols, and populations, with ongoing monitoring for calibration drift. Equity and bias audits are essential to ensure consistent performance across age, sex, ethnicity, body habitus, and comorbid conditions. Explainability tools, such as heatmaps, similar-case retrieval, and confidence scoring, can reduce automation bias and encourage clinician trust.

Regulatory and research priorities include prospective trials measuring patient-centered endpoints such as time to diagnosis, R0 resection rates, progression-free survival, overall survival, and downstream resource utilization. High-risk surveillance programs (e.g., familial PDAC or germline mutation carriers) should evaluate AI-augmented MRI/EUS strategies with clearly defined, actionable thresholds. Trials of AI-guided treatment adaptation using delta-radiomics could test protocolised switching to optimize outcomes. Finally, transparent and shareable benchmarking, adherence to the TRI-POD-AI/CONSORT-AI reporting standards, and post-market monitoring are critical to ensuring reproducibility, safety, and equitable benefits across populations.

Equally important, successful translation into clinical practice will require explainable and externally validated models, prospective evaluation, regulatory oversight, health-economic assessment, and seamless integration into multidisciplinary workflows, ensuring that AI functions as a decision-support tool rather than a replacement for clinical expertise [24–26,86]. Future progress will depend less on the development of increasingly complex algorithms and more on the generation of robust multicenter prospective datasets, transparent reporting, external validation, regulatory approval, and seamless integration into multidisciplinary clinical workflows.

5. Limitations

5.1. Limitations of AI Applications

The effective and safe deployment of AI technology in pancreatic cancer care requires the resolution of several organizational, technical, and ethical challenges. Data storage, frequent information input, technical equipment, internet access, software updates, and

system maintenance are all vital to ensure the technology is used smoothly and without interruption [85]. Taking into account the universal nature of AI, interdisciplinary and international collaboration should also be considered as integral parts. The scarcity of high-quality, centralized datasets limits model performance and increases the risk of errors and bias. Several initiatives, such as the National Institutes of Health–National Cancer Institute (NIH–NCI EDRN), UK Biobank, Pancreatic Cancer Collective, Cancer Imaging Archive, and Global Cancer Observatory, aim to improve data availability while ensuring data security within each institution.

Furthermore, concerns about the quality of data and human biases embedded in algorithms during development and after clinical deployment can affect performance in real-world environments, which limits the safety and usefulness of AI in oncology clinical practice. The quality of AI algorithms depends entirely on the quality of the data and assumptions they are fed [86]. Consequently, an inadequate representation of patient populations and clinical scenarios in training datasets can lead to overfitting and produce unreliable or non-generalizable outputs in real-world settings. Therefore, it is essential to use diverse, representative data throughout model development, validation, and ongoing post-deployment monitoring.

Another important point to mention is familiarizing clinicians with AI use. A 2019 survey of Korean physicians found that, although 83.4% valued AI for medical diagnosis, only 5.9% were familiar with it and 29.3% noted its limitations in unexpected situations due to incomplete information [87]. Adoption is influenced by physician expertise, technological literacy, and age, while hesitancy often stems from a lack of explainability, unclear liability, and the cost of errors, as well as unfamiliarity with AI tools. Methods that quantify variable importance in model predictions can improve trust in AI and its integration into clinical workflows. However, an overreliance on AI at the expense of clinical judgment can lead to false positives or negatives being overlooked.

5.2. Limitations of the Current Study

Real-world clinical impact and cost-effectiveness data are scarce, which limits our ability to draw firm conclusions about the practical utility of AI applications in pancreatic cancer care. This review primarily focused on PDAC, only occasionally addressing cystic neoplasms and neuroendocrine tumors; therefore, the findings may not fully generalize to these other pancreatic neoplasms. The literature search was restricted to English-language publications and excluded proxy terms for resilience or alternative outcomes to maintain focus, which may have omitted relevant studies published in other languages or investigating related outcomes. The heterogeneity of AI models, datasets, imaging protocols, and outcome measures across the included studies limits the comparability and generalisability of the findings. Many studies relied on retrospective, case–control designs, or imbalanced single-center datasets with limited external validation, which reduces confidence in their broader applicability. In addition, some studies reported exceptionally high-performance metrics (e.g., AUC~1.0); they should be interpreted cautiously. Furthermore, the rapid pace of AI development means that newer models or applications may not have been included in the review. Finally, methodological variability, including differences in validation approaches, feature selection, and reporting standards, hinders reproducibility and precludes formal meta-analysis. Despite these limitations, the review took a theoretically informed narrative approach, conducting in-depth analyses using constructs of resilience and evidence quality to synthesize the current state of knowledge.

6. Conclusions

Modern AI systems are increasingly being integrated into pancreatic cancer research and show considerable promise across multiple domains, including imaging-based diagnosis, lesion characterization, prognostication, and biomarker discovery. Current evidence suggests that AI may serve as a valuable decision-support and augmentation tool (not an automation), particularly in enhancing diagnostic consistency and facilitating personalized treatment strategies. However, most available studies are retrospective and heterogeneous, with limited prospective validation. Therefore, AI should currently be regarded as a complementary technology rather than a replacement for clinical judgment. Future prospective, multicenter, and impact-oriented studies are essential to establish its clinical utility, safety, and cost-effectiveness before widespread implementation in routine pancreatic cancer care can be recommended. The next phase of AI research in pancreatic cancer should therefore focus on prospective clinical implementation studies rather than further retrospective model development.

Supplementary Materials: The following supporting information can be downloaded at <https://www.mdpi.com/article/10.3390/onco6030033/s1>, Table S1. Methodological Characteristics, Validation Status, and simplified CASP-Based Quality Assessment of Included Studies.

Author Contributions: Conceptualization, I.H., N.A., and A.F.; methodology, A.F. and K.E.; validation, I.H., I.M., and E.K.; formal analysis, A.F.; investigation, A.F.; resources, A.F.; data curation, K.E. and V.Z.; writing—original draft preparation, A.F. and V.Z.; writing—review and editing, I.H., N.A., and A.F.; supervision, N.A.; project administration, A.F. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: No original data were created or analyzed in this study. Data sharing is not applicable to this article.

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

References

1. Mukund, A.; Afridi, M.A.; Karolak, A.; Park, M.A.; Permut, J.B.; Rasool, G. Pancreatic Ductal Adenocarcinoma (PDAC): A Review of Recent Advancements Enabled by Artificial Intelligence. *Cancers* **2024**, *16*, 2240. [CrossRef] [PubMed]
2. Sung, H.; Ferlay, J.; Siegel, R.L.; Laversanne, M.; Soerjomataram, I.; Jemal, A.; Bray, F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J. Clin.* **2021**, *71*, 209–249. [CrossRef] [PubMed]
3. Siegel, R.L.; Giaquinto, A.N.; Jemal, A. Cancer Statistics, 2024. *CA Cancer J. Clin.* **2024**, *74*, 12–49. Erratum in *CA Cancer J. Clin.* **2024**, *74*, 203. <https://doi.org/10.3322/caac.21820>. [CrossRef] [PubMed]
4. Rahib, L.; Wehner, M.R.; Matrisian, L.M.; Nead, K.T. Estimated Projection of US Cancer Incidence and Death to 2040. *JAMA Netw. Open* **2021**, *4*, e214708. [CrossRef] [PubMed]
5. Shi, C.; De, B.; Tran Cao, H.S.; Liu, S.; Florez, M.A.; Kouzy, R.; Grippin, A.J.; Katz, M.H.G.; Tzeng, C.D.; Ikoma, N.; et al. Escalated-Dose Radiotherapy for Unresected Locally Advanced Pancreatic Cancer: Patterns of Care and Survival in the United States. *Cancer Med.* **2024**, *13*, e7434. [CrossRef] [PubMed]
6. Yang, H.; Li, W.; Ren, L.; Yang, Y.; Zhang, Y.; Ge, B.; Li, S.; Zheng, X.; Liu, J.; Zhang, S.; et al. Progress on Diagnostic and Prognostic Markers of Pancreatic Cancer. *Oncol. Res.* **2023**, *31*, 83–99. [CrossRef] [PubMed]
7. Wei, K.; Hackert, T. Surgical Treatment of Pancreatic Ductal Adenocarcinoma. *Cancers* **2021**, *13*, 1971. [CrossRef] [PubMed]
8. Tarek, K.; Amine, T.M.; Rami, R.; Amal, A.; Francesca, G.; Stephane, S.; Tullio, P. Is There a Chance for Curative Treatment for Metastatic Pancreatic Adenocarcinoma? A Systematic Review with Meta-Analysis. *Langenbeck's Arch. Surg.* **2025**, *410*, 269. [CrossRef] [PubMed]

9. Ilic, I.; Ilic, M. International Patterns in Incidence and Mortality Trends of Pancreatic Cancer in the Last Three Decades: A Joinpoint Regression Analysis. *World J. Gastroenterol.* **2022**, *28*, 4698–4715. [[CrossRef](#)] [[PubMed](#)]
10. Shi, S.; Hua, J.; Liang, C.; Meng, Q.; Liang, D.; Xu, J.; Ni, Q.; Yu, X. Proposed Modification of the 8th Edition of the AJCC Staging System for Pancreatic Ductal Adenocarcinoma. *Ann. Surg.* **2019**, *269*, 944–950. [[CrossRef](#)] [[PubMed](#)]
11. Neoptolemos, J.P.; Hu, K.; Bailey, P.; Springfield, C.; Cai, B.; Miao, Y.; Michalski, C.; Carvalho, C.; Hackert, T.; Büchler, M.W. Personalized Treatment in Localized Pancreatic Cancer. *Eur. Surg.* **2024**, *56*, 93–109. [[CrossRef](#)]
12. Ilic, M.; Ilic, I. Epidemiology of Pancreatic Cancer. *World J. Gastroenterol.* **2016**, *22*, 9694–9705. [[CrossRef](#)] [[PubMed](#)]
13. König, A.K.; Gros, H.; Hinz, U.; Hank, T.; Kaiser, J.; Hackert, T.; Bergmann, F.; Büchler, M.W.; Strobel, O. Refined Prognostic Staging for Resected Pancreatic Cancer by Modified Stage Grouping and Addition of Tumour Grade. *Eur. J. Surg. Oncol.* **2022**, *48*, 113–120. [[CrossRef](#)] [[PubMed](#)]
14. Tempero, M.A.; Pelzer, U.; O'Reilly, E.M.; Winter, J.; Oh, D.-Y.; Li, C.-P.; Tortora, G.; Chang, H.-M.; Lopez, C.D.; Bekaii-Saab, T.; et al. Adjuvant nab-Paclitaxel + Gemcitabine in Resected Pancreatic Ductal Adenocarcinoma: Results from a Randomized, Open-Label, Phase III Trial. *J. Clin. Oncol.* **2023**, *41*, 2007–2019. [[CrossRef](#)] [[PubMed](#)]
15. Shetty, N.S.; Agarwal, U.; Choudhary, A.; Gupta, A.; PG, N.; Bhandare, M.; Gala, K.; Chandra, D.; Ramaswamy, A.; Ostwal, V.; et al. Imaging Recommendations for Diagnosis, Staging, and Management of Pancreatic Cancer. *Indian J. Med. Paediatr. Oncol.* **2023**, *44*, 77–83. [[CrossRef](#)]
16. Versteijne, E.; Suker, M.; Groothuis, K.; Akkermans-Vogelaar, J.M.; Besselink, M.G.; Bonsing, B.A.; Buijsen, J.; Busch, O.R.; Creemers, G.M.; van Dam, R.M.; et al. Preoperative Chemoradiotherapy Versus Immediate Surgery for Resectable and Borderline Resectable Pancreatic Cancer: Results of the Dutch Randomized Phase III PREOPANC Trial. *J. Clin. Oncol.* **2020**, *38*, 1763–1773. [[CrossRef](#)] [[PubMed](#)]
17. Lassen, K.; Coolsen, M.M.; Slim, K.; Carli, F.; de Aguilar-Nascimento, J.E.; Schäfer, M.; Parks, R.W.; Fearon, K.C.; Lobo, D.N.; Demartines, N.; et al. Guidelines for Perioperative Care for Pancreaticoduodenectomy: Enhanced Recovery After Surgery (ERAS®) Society Recommendations. *Clin. Nutr.* **2012**, *31*, 817–830. [[CrossRef](#)] [[PubMed](#)]
18. Dominguez-Muñoz, J.E.; Vujasinovic, M.; de la Iglesia, D.; Cahen, D.; Capurso, G.; Gubergrits, N.; Hegyi, P.; Hungin, P.; Ockenga, J.; Paiella, S.; et al. European Guidelines for the Diagnosis and Treatment of Pancreatic Exocrine Insufficiency: UEG, EPC, EDS, ESPEN, ESPGHAN, ESDO, and ESPCG Evidence-Based Recommendations. *United Eur. Gastroenterol. J.* **2025**, *13*, 125–172. [[CrossRef](#)] [[PubMed](#)]
19. Duseti, N.; Bachet, J.B.; Chanez, B.; Neuzillet, C.; de Mestier, L.; Williet, N.; Frauhoffer, N.; Nicolle, R.; Boilève, A.; Turpin, A.; et al. Medical Management of Pancreatic Cancer: From Personalization to Broadening Treatment Strategies. *Cancer Treat. Rev.* **2025**, *138*, 102973. [[CrossRef](#)] [[PubMed](#)]
20. Bardol, T.; Dujon, A.M.; Taly, V.; Dunyach-Remy, C.; Lavigne, J.P.; Costa-Silva, B.; Kurma, K.; Eslami-S, Z.; Cayrefourcq, L.; Canivet, C.; et al. Early Detection of Pancreatic Cancer by Liquid Biopsy “PANLIPSY”: A French Nation-Wide Study Project. *BMC Cancer* **2024**, *24*, 709. [[CrossRef](#)] [[PubMed](#)]
21. Zobolas, J.; George, A.-M.; López, A.; Fischer, S.; Becker, M.; Aittokallio, T. Prognostic Biomarker Discovery in Pancreatic Cancer through Hybrid Ensemble Feature Selection and Multi-Omics Data. *BioData Min.* **2026**, *19*, 43. [[CrossRef](#)] [[PubMed](#)]
22. Reese, K.-L.; Pantel, K.; Smit, D.J. Multibiomarker Panels in Liquid Biopsy for Early Detection of Pancreatic Cancer—A Comprehensive Review. *J. Exp. Clin. Cancer Res.* **2024**, *43*, 250. [[CrossRef](#)] [[PubMed](#)]
23. Hayashi, H.; Higashi, T.; Miyata, T.; Yamashita, Y.I.; Baba, H. Recent Advances in Precision Medicine for Pancreatic Ductal Adenocarcinoma. *Ann. Gastroenterol. Surg.* **2021**, *5*, 457–466. [[CrossRef](#)] [[PubMed](#)]
24. Daemi, A.; Kalami, S.; Tahiraga, R.G.; Ghanbarpour, O.; Barghani, M.R.R.; Hooshier, M.H.; Özbolat, G.; Yönden, Z. Revolutionizing Personalized Medicine Using Artificial Intelligence: A Meta-Analysis of Predictive Diagnostics and Their Impacts on Drug Development. *Clin. Exp. Med.* **2025**, *25*, 255. [[CrossRef](#)] [[PubMed](#)]
25. Mishra, A.K.; Chong, B.; Arunachalam, S.P.; Oberg, A.L.; Majumder, S. Machine Learning Models for Pancreatic Cancer Risk Prediction Using Electronic Health Record Data—A Systematic Review and Assessment. *Am. J. Gastroenterol.* **2024**, *119*, 1466–1482. [[CrossRef](#)] [[PubMed](#)]
26. Rajkomar, A.; Dean, J.; Kohane, I. Machine Learning in Medicine. *N. Engl. J. Med.* **2019**, *380*, 1347–1358. [[CrossRef](#)] [[PubMed](#)]
27. Murray, K.; Oldfield, L.; Stefanova, I.; Gentiluomo, M.; Aretini, P.; O'Sullivan, R.; Greenhalf, W.; Paiella, S.; Aoki, M.N.; Pastore, A.; et al. Biomarkers, Omics and Artificial Intelligence for Early Detection of Pancreatic Cancer. *Semin. Cancer Biol.* **2025**, *111*, 76–88. [[CrossRef](#)] [[PubMed](#)]
28. Farinella, R.; Felici, A.; Peduzzi, G.; Testoni, S.G.G.; Costello, E.; Aretini, P.; Blazquez-Encinas, R.; Oz, E.; Pastore, A.; Tacelli, M.; et al. From Classical Approaches to Artificial Intelligence, Old and New Tools for PDAC Risk Stratification and Prediction. *Semin. Cancer Biol.* **2025**, *112*, 71–92. [[CrossRef](#)] [[PubMed](#)]

29. Noyes, J.; Booth, A.; Flemming, K.; Garside, R.; Harden, A.; Lewin, S.; Pantoja, T.; Hannes, K.; Cargo, M.; Thomas, J. Cochrane Qualitative and Implementation Methods Group Guidance Series—Paper 3: Methods for Assessing Methodological Limitations, Data Extraction and Synthesis, and Confidence in Synthesized Qualitative Findings. *J. Clin. Epidemiol.* **2018**, *97*, 49–58. [[CrossRef](#)] [[PubMed](#)]
30. Viriyasaranon, T.; Chun, J.W.; Koh, Y.H.; Cho, J.H.; Jung, M.K.; Kim, S.-H.; Kim, H.J.; Lee, W.J.; Choi, J.-H.; Woo, S.M. Annotation-Efficient Deep Learning Model for Pancreatic Cancer Diagnosis and Classification Using CT Images: A Retrospective Diagnostic Study. *Cancers* **2023**, *15*, 3392. [[CrossRef](#)] [[PubMed](#)]
31. Iwasa, Y.; Iwashita, T.; Takeuchi, Y.; Ichikawa, H.; Mita, N.; Uemura, S.; Shimizu, M.; Kuo, Y.-T.; Wang, H.-P.; Hara, T. Automatic Segmentation of Pancreatic Tumors Using Deep Learning on a Video Image of Contrast-Enhanced Endoscopic Ultrasound. *J. Clin. Med.* **2021**, *10*, 3589. [[CrossRef](#)] [[PubMed](#)]
32. Chen, P.T.; Wu, T.; Wang, P.; Chang, D.; Liu, K.L.; Wu, M.S.; Roth, H.R.; Lee, P.C.; Liao, W.C.; Wang, W. Pancreatic Cancer Detection on CT Scans with Deep Learning: A Nationwide Population-Based Study. *Radiology* **2022**, *304*, 91–99. [[CrossRef](#)] [[PubMed](#)]
33. Cao, K.; Xia, Y.; Yao, J.; Han, X.; Lambert, L.; Zhang, T.; Tang, W.; Jin, G.; Jiang, H.; Fang, X.; et al. Large-Scale Pancreatic Cancer Detection via Non-Contrast CT and Deep Learning. *Nat. Med.* **2023**, *29*, 3033–3043. [[CrossRef](#)] [[PubMed](#)]
34. Mukherjee, S.; Patra, A.; Khasawneh, H.; Korfiatis, P.; Rajamohan, N.; Suman, G.; Majumder, S.; Panda, A.; Johnson, M.P.; Larson, N.B.; et al. Radiomics-Based Machine-Learning Models Can Detect Pancreatic Cancer on Prediagnostic Computed Tomography Scans at a Substantial Lead Time Before Clinical Diagnosis. *Gastroenterology* **2022**, *163*, 1435–1446.e3. [[CrossRef](#)] [[PubMed](#)]
35. Alves, N.; Schuurmans, M.; Rutkowski, D.; Saha, A.; Vendittelli, P.; Obuchowski, N.; Liedenbaum, M.H.; Haldorsen, I.S.; Molven, A.; Yakar, D.; et al. Artificial Intelligence and Radiologists in Pancreatic Cancer Detection Using Standard-of-Care CT Scans (PANORAMA): An International, Paired, Non-Inferiority, Confirmatory, Observational Study. *Lancet Oncol.* **2026**, *27*, 116–124. [[CrossRef](#)] [[PubMed](#)]
36. Zhang, J.; Zhu, L.; Yao, L.; Ding, X.; Chen, D.; Wu, H.; Lu, Z.H.; Zhou, W.; Zhang, L.; An, P.; et al. Deep Learning-Based Pancreas Segmentation and Station Recognition System in EUS: Development and Validation of a Useful Training Tool (with Video). *Gastrointest. Endosc.* **2020**, *92*, 874–885.e3. [[CrossRef](#)] [[PubMed](#)]
37. Gu, J.; Pan, J.; Hu, J.; Dai, L.; Zhang, K.; Wang, B.; He, M.; Zhao, Q.; Jiang, T. Prospective Assessment of Pancreatic Ductal Adenocarcinoma Diagnosis from Endoscopic Ultrasonography Images with the Assistance of Deep Learning. *Cancer* **2023**, *129*, 2214–2223. [[CrossRef](#)] [[PubMed](#)]
38. Kuwahara, T.; Hara, K.; Mizuno, N.; Haba, S.; Okuno, N.; Kuraishi, Y.; Fumihara, D.; Yanaidani, T.; Ishikawa, S.; Yasuda, T.; et al. Artificial Intelligence Using Deep Learning Analysis of Endoscopic Ultrasonography Images for the Differential Diagnosis of Pancreatic Masses. *Endoscopy* **2023**, *55*, 140–149. [[CrossRef](#)] [[PubMed](#)]
39. Udristoiu, A.L.; Cazacu, I.M.; Gruionu, L.G.; Gruionu, G.; Iacob, A.V.; Burtea, D.E.; Ungureanu, B.S.; Costache, M.I.; Constantin, A.; Popescu, C.F.; et al. Real-Time Computer-Aided Diagnosis of Focal Pancreatic Masses from Endoscopic Ultrasound Imaging Based on a Hybrid Convolutional and Long Short-Term Memory Neural Network Model. *PLoS ONE* **2021**, *16*, e0251701. [[CrossRef](#)] [[PubMed](#)]
40. Tang, A.; Tian, L.; Gao, K.; Liu, R.; Hu, S.; Liu, J.; Xu, J.; Fu, T.; Zhang, Z.; Wang, W.; et al. Contrast-Enhanced Harmonic Endoscopic Ultrasound (CH-EUS) MASTER: A Novel Deep Learning-Based System in Pancreatic Mass Diagnosis. *Cancer Med.* **2023**, *12*, 7962–7973. [[CrossRef](#)] [[PubMed](#)]
41. Mo, S.; Huang, C.; Wang, Y.; Zhao, H.; Wei, H.; Qin, H.; Jiang, H.; Qin, S. Construction and Validation of an Endoscopic Ultrasonography-Based Ultrasomics Nomogram for Differentiating Pancreatic Neuroendocrine Tumors from Pancreatic Cancer. *Front. Oncol.* **2024**, *14*, 1359364. [[CrossRef](#)] [[PubMed](#)]
42. Liang, Y.; Schott, D.; Zhang, Y.; Wang, Z.; Nasief, H.; Paulson, E.; Hall, W.; Knechtges, P.; Erickson, B.; Li, X.A. Auto-Segmentation of Pancreatic Tumor in Multi-Parametric MRI Using Deep Convolutional Neural Networks. *Radiother. Oncol.* **2020**, *145*, 193–200. [[CrossRef](#)] [[PubMed](#)]
43. Chen, Y.; Ruan, D.; Xiao, J.; Wang, L.; Sun, B.; Saouaf, R.; Yang, W.; Li, D.; Fan, Z. Fully Automated Multiorgan Segmentation in Abdominal Magnetic Resonance Imaging with Deep Neural Networks. *Med. Phys.* **2020**, *47*, 4971–4982. [[CrossRef](#)] [[PubMed](#)]
44. Kart, T.; Fischer, M.; Winzeck, S.; Glocker, B.; Bai, W.; Bülow, R.; Emmel, C.; Friedrich, L.; Kauczor, H.-U.; Keil, T.; et al. Automated imaging-based abdominal organ segmentation and quality control in 20,000 participants of the UK Biobank and German National Cohort Studies. *Sci. Rep.* **2022**, *12*, 18733. [[CrossRef](#)] [[PubMed](#)]
45. Bereska, J.I.; Janssen, B.V.; Nio, C.Y.; Kop, M.P.M.; Kazemier, G.; Busch, O.R.; Struik, F.; Marquering, H.A.; Stoker, J.; Besselink, M.G.; et al. Artificial Intelligence for Assessment of Vascular Involvement and Tumor Resectability on CT in Patients with Pancreatic Cancer. *Eur. Radiol. Exp.* **2024**, *8*, 18. [[CrossRef](#)] [[PubMed](#)]

46. Viviers, C.; Ramaekers, M.; Valiuddin, A.; Hellström, T.; Tasios, N.; Van Der Ven, J.; Jacobs, I.; Ewals, L.; Nederend, J.; De With, P.; et al. Segmentation-Based Assessment of Tumor-Vessel Involvement for Surgical Resectability Prediction of Pancreatic Ductal Adenocarcinoma. In Proceedings of the IEEE/CVF International Conference on Computer Vision Workshops (ICCVW), Paris, France, 2–6 October 2023. Available online: https://openaccess.thecvf.com/content/ICCV2023W/CVAMD/papers/Viviers_Segmentation-Based_Assessment_of_Tumor-Vessel_Involvement_for_Surgical_Resectability_Prediction_of_ICCVW_2023_paper.pdf (accessed on 8 July 2026).
47. Guan, X.; Liu, J.; Xu, L.; Jiang, W.; Wang, C. A CT-Based Deep Learning Radiomics Nomogram for Early Recurrence Prediction in Pancreatic Cancer: A Multicenter Study. *Ann. Surg. Oncol.* **2025**, *32*, 7567–7576. [[CrossRef](#)] [[PubMed](#)]
48. Fu, H.; Mi, W.; Pan, B.; Guo, Y.; Li, J.; Xu, R.; Zheng, J.; Zou, C.; Zhang, T.; Liang, Z.; et al. Automatic Pancreatic Ductal Adenocarcinoma Detection in Whole Slide Images Using Deep Convolutional Neural Networks. *Front. Oncol.* **2021**, *11*, 665929. [[CrossRef](#)] [[PubMed](#)]
49. Nimgaonkar, V.; Krishna, V.; Krishna, V.; Tiu, E.; Joshi, A.; Vrabac, D.; Bhambhani, H.; Smith, K.; Johansen, J.S.; Makawita, S.; et al. Development of an Artificial Intelligence-Derived Histologic Signature Associated with Adjuvant Gemcitabine Treatment Outcomes in Pancreatic Cancer. *Cell Rep. Med.* **2023**, *4*, 101013. [[CrossRef](#)] [[PubMed](#)]
50. Yamaguchi, R.; Morikawa, H.; Akatsuka, J.; Numata, Y.; Noguchi, A.; Kokumai, T.; Ishida, M.; Mizuma, M.; Nakagawa, K.; Unno, M.; et al. Machine Learning of Histopathological Images Predicts Recurrences of Resected Pancreatic Ductal Adenocarcinoma With Adjuvant Treatment. *Pancreas* **2024**, *53*, e199–e204. [[CrossRef](#)] [[PubMed](#)]
51. Ahmadvand, P.; Farahani, H.; Farnell, D.; Darbandsari, A.; Topham, J.; Karasinska, J.; Nelson, J.; Naso, J.; Jones, S.J.M.; Renouf, D.; et al. A Deep Learning Approach for the Identification of the Molecular Subtypes of Pancreatic Ductal Adenocarcinoma Based on Whole Slide Pathology Images. *Am. J. Pathol.* **2024**, *194*, 2302–2312. [[CrossRef](#)] [[PubMed](#)]
52. Saillard, C.; Delecourt, F.; Schmauch, B.; Moindrot, O.; Svrcek, M.; Bardier-Dupas, A.; Emile, J.F.; Ayadi, M.; Rebours, V.; de Mestier, L.; et al. Pacpaint: A Histology-Based Deep Learning Model Uncovers the Extensive Intratumor Molecular Heterogeneity of Pancreatic Adenocarcinoma. *Nat. Commun.* **2023**, *14*, 3459. [[CrossRef](#)] [[PubMed](#)]
53. Janssen, B.V.; Oteman, B.; Ali, M.; Valkema, P.A.; Adsay, V.; Basturk, O.; Chatterjee, D.; Chou, A.; Crobach, S.; Doukas, M.; et al. Artificial Intelligence-Based Segmentation of Residual Pancreatic Cancer in Resection Specimens Following Neoadjuvant Treatment (ISGPP-2): International Improvement and Validation Study. *Am. J. Surg. Pathol.* **2024**, *48*, 1108–1116. [[CrossRef](#)] [[PubMed](#)]
54. Huang, S.-C.; Chaudhari, A.S.; Langlotz, C.P.; Shah, N.; Yeung, S.; Lungren, M.P. Developing Medical Imaging AI for Emerging Infectious Diseases. *Nat. Commun.* **2022**, *13*, 7060. [[CrossRef](#)] [[PubMed](#)]
55. Sarker, M. Reinventing Wellness: How Machine Learning Transforms Healthcare. *J. Artif. Intell. Gen. Sci.* **2024**, *3*, 116–131. [[CrossRef](#)]
56. Mejza, M.; Bajer, A.; Wanibuchi, S.; Malecka-Wojcieszko, E. Can AI Be Useful in the Early Detection of Pancreatic Cancer in Patients with New-Onset Diabetes? *Biomedicines* **2025**, *13*, 836. [[CrossRef](#)] [[PubMed](#)]
57. Mobarak, M.H.; Mimona, M.A.; Islam, M.A.; Hossain, N.; Zohura, F.T.; Imtiaz, I.; Rimon, M.I.H. Scope of Machine Learning in Materials Research—A Review. *Appl. Surf. Sci. Adv.* **2023**, *18*, 100523. [[CrossRef](#)]
58. Fahim, Y.A.; Hasani, I.W.; Kabba, S.; Ragab, W.M. Artificial Intelligence in Healthcare and Medicine: Clinical Applications, Therapeutic Advances, and Future Perspectives. *Eur. J. Med. Res.* **2025**, *30*, 848. [[CrossRef](#)] [[PubMed](#)]
59. Petropoulou, T.; Simoens, J.; Polydorou, A.; De Backer, P.; Mottrie, A. World’s First Live AI-Assisted Augmented Reality (AR) Robotic Colon Surgery with Instrument Deocclusion: Navigating the Future of Surgery. *Colorectal Dis.* **2025**, *27*, e70296. [[CrossRef](#)] [[PubMed](#)]
60. Patel, V.; Saikali, S.; Moschovas, M.C. Robotics, Artificial Intelligence, Telepresence, and Telesurgery: The Future of Urology. *Asian J. Urol.* **2025**, *12*, 131–133. [[CrossRef](#)] [[PubMed](#)]
61. Friedman, C.; Rindfleisch, T.C.; Corn, M. Natural Language Processing: State of the Art and Prospects for Significant Progress, a Workshop Sponsored by the National Library of Medicine. *J. Biomed. Inform.* **2013**, *46*, 765–773. [[CrossRef](#)] [[PubMed](#)]
62. Rajkomar, A.; Oren, E.; Chen, K.; Dai, A.M.; Hajaj, N.; Hardt, M.; Liu, P.J.; Liu, X.; Marcus, J.; Sun, M.; et al. Scalable and Accurate Deep Learning with Electronic Health Records. *npj Digit. Med.* **2018**, *1*, 18. [[CrossRef](#)] [[PubMed](#)]
63. Sarvamangala, D.R.; Kulkarni, R.V. Convolutional Neural Networks in Medical Image Understanding: A Survey. *Evol. Intell.* **2022**, *15*, 1–22. [[CrossRef](#)] [[PubMed](#)]
64. Dumitrescu, E.A.; Ungureanu, B.S.; Cazacu, I.M.; Florescu, L.M.; Streba, L.; Croitoru, V.M.; Sur, D.; Croitoru, A.; Turcu-Stiolica, A.; Lungulescu, C.V. Diagnostic Value of Artificial Intelligence-Assisted Endoscopic Ultrasound for Pancreatic Cancer: A Systematic Review and Meta-Analysis. *Diagnostics* **2022**, *12*, 309. [[CrossRef](#)] [[PubMed](#)]
65. Yin, H.; Yang, X.; Sun, L.; Pan, P.; Peng, L.; Li, K.; Zhang, D.; Cui, F.; Xia, C.; Huang, H.; et al. The Value of Artificial Intelligence Techniques in Predicting Pancreatic Ductal Adenocarcinoma with EUS Images: A Meta-Analysis and Systematic Review. *Endosc. Ultrasound* **2023**, *12*, 50–58. [[CrossRef](#)] [[PubMed](#)]

66. Podină, N.; Gheorghe, E.C.; Constantin, A.; Cazacu, I.; Croitoru, V.; Gheorghe, C.; Balaban, D.V.; Jinga, M.; Tieranu, C.G.; Săftoiu, A. Artificial Intelligence in Pancreatic Imaging: A Systematic Review. *United Eur. Gastroenterol. J.* **2025**, *13*, 55–77. [[CrossRef](#)] [[PubMed](#)]
67. Mazor, N.; Dar, G.; Lederman, R.; Lev-Cohain, N.; Sosna, J.; Joskowicz, L. MC3DU-Net: A Multisequence Cascaded Pipeline for the Detection and Segmentation of Pancreatic Cysts in MRI. *Int. J. Comput. Assist. Radiol. Surg.* **2024**, *19*, 423–432. [[CrossRef](#)] [[PubMed](#)]
68. Li, K.; Li, J.; Liu, X.; Chen, J.; Chen, W. Multi-Parametric MRI Diffusion Models Combined with Clinical Information for Predicting Ki-67 Expression in Pancreatic Ductal Adenocarcinoma: A Prospective Cohort Study. *Abdom. Radiol.* **2025**, *51*, 1668–1679. [[CrossRef](#)] [[PubMed](#)]
69. Zhu, L.; Zhao, B.; Xia, T.; Chang, D.; Xia, C.; Liu, M.; Li, R.; Cao, B.; Qiu, Y.; Yu, Y.; et al. A Radiomics-Based Model for Predicting Lymph Node Metastasis of Pancreatic Ductal Adenocarcinoma: A Multicenter Study. *Insights Imaging* **2025**, *16*, 141. [[CrossRef](#)] [[PubMed](#)]
70. Ren, S.; Zhao, R.; Cui, W.; Qiu, W.; Guo, K.; Cao, Y.; Duan, S.; Wang, Z.; Chen, R. Computed Tomography-Based Radiomics Signature for the Preoperative Differentiation of Pancreatic Adenosquamous Carcinoma from Pancreatic Ductal Adenocarcinoma. *Front. Oncol.* **2020**, *10*, 1618. [[CrossRef](#)] [[PubMed](#)]
71. Wagner, M.; Brandenburg, J.M.; Bodenstedt, S.; Schulze, A.; Jenke, A.C.; Stern, A.; Daum, M.T.J.; Mündermann, L.; Kolbinger, F.R.; Bhasker, N.; et al. Surgomics: Personalized Prediction of Morbidity, Mortality and Long-Term Outcome in Surgery Using Machine Learning on Multimodal Data. *Surg. Endosc.* **2022**, *36*, 8568–8591. [[CrossRef](#)] [[PubMed](#)]
72. Ramalhinho, J.; Yoo, S.; Dowrick, T.; Koo, B.; Somasundaram, M.; Gurusamy, K.; Hawkes, D.J.; Davidson, B.; Blandford, A.; Clarkson, M.J. The Value of Augmented Reality in Surgery—A Usability Study on Laparoscopic Liver Surgery. *Med. Image Anal.* **2023**, *90*, 102943. [[CrossRef](#)] [[PubMed](#)]
73. Fujinaga, A.; Endo, Y.; Etoh, T.; Kawamura, M.; Nakanuma, H.; Kawasaki, T.; Masuda, T.; Hirashita, T.; Kimura, M.; Matsunobu, Y.; et al. Development of a cross-artificial intelligence system for identifying intraoperative anatomical landmarks and surgical phases during laparoscopic cholecystectomy. *Surg. Endosc.* **2023**, *37*, 6118–6128. [[CrossRef](#)] [[PubMed](#)]
74. Ducas, A.; Mangano, A.; Borgioli, L.; Cassiani, J.; Lopez, P.; Giulianotti, P.C. The Role of Artificial Intelligence in Pancreatic Surgery: Current and Future Perspectives. *Ann. Hepato-Biliary-Pancreat. Surg.* **2025**, *29*, 1–4. [[CrossRef](#)] [[PubMed](#)]
75. Jearanai, S.; Wangkulangkul, P.; Sae-Lim, W.; Cheewatanakornkul, S. Development of a Deep Learning Model for Safe Direct Optical Trocar Insertion in Minimally Invasive Surgery: An Innovative Method to Prevent Trocar Injuries. *Surg. Endosc.* **2023**, *37*, 7295–7304. [[CrossRef](#)] [[PubMed](#)]
76. Gu, Q.; Liu, P.; Hu, X.; Liu, J.; He, Y. Development and validation of a CT-measured body composition radiomics model for prognostic assessment in resected pancreatic adenocarcinoma. *Sci. Rep.* **2025**, *15*, 28722. [[CrossRef](#)] [[PubMed](#)]
77. Nasief, H.; Zheng, C.; Schott, D.; Hall, W.; Tsai, S.; Erickson, B.; Li, X.A. A machine learning based delta-radiomics process for early prediction of treatment response of pancreatic cancer. *npj Precis. Oncol.* **2019**, *3*, 25. [[CrossRef](#)] [[PubMed](#)]
78. Kim, D.; Thrall, M.J.; Michelow, P.; Schmitt, F.C.; Vielh, P.R.; Siddiqui, M.T.; Sundling, K.E.; Virk, R.; Alperstein, S.; Bui, M.M.; et al. The Current State of Digital Cytology and Artificial Intelligence (AI): Global Survey Results from the American Society of Cytopathology Digital Cytology Task Force. *J. Am. Soc. Cytopathol.* **2024**, *13*, 319–328. [[CrossRef](#)] [[PubMed](#)]
79. Weselá, P.; Eid, M.; Moravčík, P.; Vlažný, J.; Hlavsa, J.; Procházka, V.; Kala, Z.; Vaňhara, P. Artificial Intelligence in Pancreatic Cancer Histopathology and Diagnostics—Implications for Clinical Decisions and Biomarker Discovery. *Cell Div.* **2025**, *20*, 15. [[CrossRef](#)] [[PubMed](#)]
80. Collins, G.S.; Moons, K.G.M.; Dhiman, P.; Riley, R.D.; Beam, A.L.; Van Calster, B.; Ghassemi, M.; Liu, X.; Reitsma, J.B.; van Smeden, M.; et al. TRIPOD+AI statement: Updated guidance for reporting clinical prediction models that use regression or machine learning methods. *BMJ* **2024**, *385*, e078378. Correction in *BMJ* **2024**, *385*, q902. <https://doi.org/10.1136/bmj-2023-078378>. [[CrossRef](#)] [[PubMed](#)]
81. Sijithra, P.C.; Santhi, N.; Ramasamy, N. A Review Study on Early Detection of Pancreatic Ductal Adenocarcinoma Using Artificial Intelligence-Assisted Diagnostic Methods. *Eur. J. Radiol.* **2023**, *166*, 110972. [[CrossRef](#)] [[PubMed](#)]
82. Liu, X.; Cruz Rivera, S.; Moher, D.; Calvert, M.J.; Denniston, A.K. SPIRIT-AI and CONSORT-AI Working Group. Reporting Guidelines for Clinical Trial Reports for Interventions Involving Artificial Intelligence: The CONSORT-AI Extension. *Nat. Med.* **2020**, *26*, 1364–1374. [[CrossRef](#)] [[PubMed](#)]
83. Cruz Rivera, S.; Liu, X.; Chan, A.-W.; Denniston, A.K.; Calvert, M.J. SPIRIT-AI and CONSORT-AI Working Group. Guidelines for Clinical Trial Protocols for Interventions Involving Artificial Intelligence: The SPIRIT-AI Extension. *Nat. Med.* **2020**, *26*, 1351–1363. [[CrossRef](#)] [[PubMed](#)]
84. Mongan, J.; Moy, L.; Kahn, C.E., Jr. Checklist for Artificial Intelligence in Medical Imaging (CLAIM): A Guide for Authors and Reviewers. *Radiol. Artif. Intell.* **2020**, *2*, e200029. [[CrossRef](#)] [[PubMed](#)]
85. Ozsahin, D.U.; Usanase, N.; Ozsahin, I. Advancing Pancreatic Cancer Management: The Role of Artificial Intelligence in Diagnosis and Therapy. *Beni-Suef Univ. J. Basic Appl. Sci.* **2025**, *14*, 32. [[CrossRef](#)]

-
86. Kolla, L.; Parikh, R.B. Uses and Limitations of Artificial Intelligence for Oncology. *Cancer* **2024**, *130*, 2101–2107. [[CrossRef](#)] [[PubMed](#)]
 87. Oh, S.; Kim, J.H.; Choi, S.W.; Lee, H.J.; Hong, J.; Kwon, S.H. Physician Confidence in Artificial Intelligence: An Online Mobile Survey. *J. Med. Internet Res.* **2019**, *21*, e12422. [[CrossRef](#)] [[PubMed](#)]

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.