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Timing of Nephrectomy and Renal Transplantation in Patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD) in the Era of Living Kidney Donation

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Abstract: Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common hereditary disorders. Once progressed to end-stage renal disease, kidney transplantation may be needed. Whether and when to perform a (bilateral) native nephrectomy in case of end-stage renal failure are issues under debate. At our institution, with a growing number of living kidney donations, the general trend is to perform a native nephrectomy prior to transplantation. Our aim was to compare the outcomes of this approach to a nephrectomy during or after transplantation and to compare our findings to results reported in the literature. Data were prospectively collected from all ADPKD patients undergoing native nephrectomy and kidney transplantation at the Leiden University Medical Center between 2000–2017. A literature search was performed in the PubMed and Scopus databases. The clinical results were retrospectively reviewed and were stratified according to the timing of the nephrectomy. From the literature review, the most practiced approach was a combined unilateral nephrectomy and kidney transplantation. However, in our series, the favored approach was to perform a scheduled bilateral nephrectomy prior to kidney transplantation. A total of 114 patients underwent a native nephrectomy prior to (group 1, $n = 85$), during (group 2, $n = 5$), or after (group 3, $n = 24$) kidney transplantation. There were no statistically significant differences in postoperative morbidity after nephrectomy nor differences in kidney transplant outcome. Bilateral nephrectomy prior to kidney transplantation is a safe, controlled approach carrying minimal complication and mortality rates and facilitating a subsequent transplant procedure without mechanical or hemodynamic limitations for the graft.

Keywords: polycystic kidney; autosomal dominant; renal transplant; nephrectomy

1. Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common hereditary disorders and the leading genetic cause of end-stage renal disease accounting for 10% of patients with this disease [1]. ADPKD often has an asymptomatic course, with the first symptoms usually appearing in the third decade of life. It is caused by a mutation in the PKD1 (85%) or PKD2 (15%) gene and is manifested by the presence of multiple cysts in both kidneys, which cause kidney enlargement

and deformation, eventually leading to renal failure. Symptoms include lumbar pain, urinary tract infections, cyst bleedings, arterial hypertension, and renal colic due to cyst rupture or coexistent nephrolithiasis [2]. Also common are the presence of cysts in the liver and the formation of cerebral aneurysms [3,4].

The treatment of ADPKD is focused on managing symptoms. Treatment that stops the cysts from growing is not available and patients may die due to the consequences of uremia, hypertension, or rupture of intracranial aneurysms [5]. The treatment of choice in most end-stage renal failure patients is kidney transplantation. Due to the enlargement of the kidneys, patients may present with mechanical complaints and physical examination and imaging may reveal a lack of space for the future kidney graft. In these cases, it may be necessary to perform a native nephrectomy in addition to the kidney transplantation. The main indications for bilateral or unilateral native nephrectomy (BNN/UNN) include space creation for a kidney graft, pain relief, prevention of recurrent urinary tract infections, early satiety and weight loss, hematuria and resistant hypertension [6]. However, since the conservative management of ADPKD has progressed significantly with the introduction of better analgesics, antihypertensive medications and antibiotic therapies, there has been a reduction in the number of pre-transplant nephrectomies [7]. Consequently, there is discussion on whether a nephrectomy should be performed. If it is indicated, there is no widely accepted consensus on if it is best performed pre, during or post kidney transplantation.

In an effort to determine the preferred timing, patient characteristics and peri-operative data collected at our institution were compared to findings in literature. Traditionally, our preferred procedure was to perform the native nephrectomy concurrent with the kidney transplantation. However, because of an increase in living kidney donation, with the Netherlands having the highest living donation rates in Europe [8], performing a staged procedure has become a feasible option as well. It is well known that living kidney donation (LKD) results in superb graft survival compared to deceased kidney donation (DKD) [9]. A living donor kidney transplantation allows for a set timeframe for a patient to undergo a nephrectomy and be subjected to dialysis, i.e., to perform a staged procedure. In this study, we therefore aim to analyze if undergoing a native nephrectomy *prior* to kidney transplantation is a safe approach compared to carrying out the nephrectomy during or after the transplantation. Our patient population was divided into pre-transplantation nephrectomy (group 1), during transplantation nephrectomy (group 2) or post-transplantation nephrectomy (group 3) and was also stratified according to living kidney donation or deceased kidney donation.

2. Materials and Methods

2.1. Clinical Data

Data were prospectively collected from all ADPKD patients undergoing native nephrectomy and kidney transplantation at the Leiden University Medical Center between 2000–2017. The results were retrospectively reviewed and were stratified according to the timing of the nephrectomy and mainly focused on perioperative parameters.

2.2. Literature

A literature search was performed in the PubMed and Scopus databases. Please refer to Appendix A for the search strategy. The included articles were evaluated based on the research population, which had to consist of ADPKD patients either undergoing nephrectomy before, during or after transplantation or comparing either of those to patients who did not undergo a nephrectomy at all. Reasons for exclusion were articles published before 2000, which did not include a comparable population in terms of pathology, described the results of one specific surgical approach only or focused on the comparison of open versus laparoscopic approach instead of the timing of nephrectomy.

2.3. Physical Examination and Imaging

Physical examination included standard abdominal examination and, additionally, a hand fist was pressed in the iliac fossa to estimate the space needed for a graft kidney. Imaging included CT or MRI and whereby advancement of polycystic kidneys below the iliac crest was suggestive of a lack of space for the graft kidney.

2.4. Surgical Technique

With the exception of one patient who underwent a laparoscopic approach, all nephrectomies were carried out by either median or transverse laparotomy.

2.5. Statistics

Statistical analysis was carried out using IBM SPSS Statistics version 23. Continuous values are reported as means ± standard deviation and were compared between groups using a one-way ANOVA test. Categorical variables were compared between groups using generalized linear models.

We used the STROBE cross sectional checklist when writing our report [10].

3. Results

In a period of 17 years, 114 patients with ADPKD underwent native nephrectomy prior to (group 1), during (group 2) or after (group 3) kidney transplantation at our institution. Of the kidney transplants, 75 were a living donor procedure and 39 a deceased donor procedure. Demographics and preoperative characteristics are shown in Tables 1–3. Data were analyzed between groups 1–3 and also between LKD and DKD procedures (Table 4). Group 1 consisted of 51 males and 34 females, group 2 of 4 males and 1 female and group 3 of 14 males and 10 females. The mean age was 52.7 ± 9.8 years (group 1), 57.6 ± 9.8 years (group 2) and 58.1 ± 9.9 years (group 3). There were no significant differences in patient demographics between the groups. The majority of our patients (68.2%) received a kidney from a living donor, either related or unrelated. The highest percentage of LKD was found in the first group (68.2%) but was not statistically significant between groups.

Table 1. Demographics of patient population [1].

	Group 1 *n* = 85	**Group 2 *n* = 5**	**Group 3 *n* = 24**	**Total *n* = 114**	***p*-Value**
Sex					
- Male	51 (60.0%)	4 (80.0%)	14 (58.3%)	69 (60.5%)	0.673
- Female	34 (40.0%)	1 (20.0%)	10 (41.7%)	45 (39.5%)	
Age (SD)	52.7 (9.8)	57.6 (9.8)	58.1 (9.9)	54.1 (10.0)	0.035
BMI (SD)	25.5 (3.8)	27.7 (4.4)	25.2 (3.3)	25.6 (3.7)	0.351
Dialysis	53(62.4%)	5 (100%)	6 (25%)	64 (56.1%)	0.009
Nephrectomy					
- Unilateral	12 (14.1%)	4 (80.0%)	4 (16.7%)	20 (17.5%)	0.043
- Bilateral	73 (85.9%)	1 (20.0%)	20 (83.3%)	94 (82.5%)	
- Living donor	58 (68.2%)	2 (40.0%)	15 (62.5%)	75 (65.8%)	0.430
- Deceased donor	27 (31.8%)	3 (60.0%)	9 (37.5%)	39 (34.2%)	

[1] Demographics of patients undergoing native nephrectomy before kidney transplantation (group 1), during transplantation (group 2), and after transplantation (group 3).

Table 2. Indications for native nephrectomy.

	Group 1 (*n* = 85)	**Group 2 (*n* = 5)**	**Group 3 (*n* = 24)**	**Total (*n* = 114)**
Lack of space	72.9%	100%	12.5%	61.4%
Infection	15.3%	0	37.5%	19.2%
Mobility	9.4%	0	45.8%	16.7%
Other	2.4%	0	4.2%	2.6%

Table 3. Perioperative data of patients undergoing native nephrectomy.

	Group 1 (n = 85)	**Group 2 (n = 5)**	**Group 3 (n = 24)**	**Missing (%)**	***p*-Value**
Weight native kidney (kg)				0	
- Left (SD)	2.5 (1.5)	2.8 (0.0)	1.9 (1.3)		0.205
- Right (SD)	2.5 (1.5)	3.6 (1.8)	1.7 (1.2)		0.010
Blood loss (L)	0.71 (0.63)	0.76 (0.47)	0.63(0.40)	10.5%	0.809
Blood transfusion units (SD)	1.06 (2.63)	0.60 (1.34)	1.67 (2.44)	0	0.510
Hospital stay in days (SD)	9.45 (7.17)	8.40 (2.51)	10.08 (7.03)	0	0.862
Hb				6.1%	
- pre (SD)	7.60 (1.18)	8.40 (0.95)	7.72 (1.47)		0.338
- post (SD)	5.74 (1.02)	6.22 (0.97)	6.29 (1.26)		0.089
Operation time in min (SD)	169 (48.1)	207 (25.8)	158 (173.8)	0	0.096
Diuresis (L/24 h)					
- before NN	1.53 (0.76)	1.14 (0.93)	1.59 (0.73)	0	0.494
- after UNN [1]	0.13 (0.36)	0.97 (1.01)	1.38 (0.88)	40.0%	0.000
Complications	36 (42.4%)	1 (20.0%)	7 (29.2%)	0	0.699
- hypotension	21	1	2		
- incisional hernia	4	0	1		
- shunt occlusion	4	0	0		
- other	7	0	4		

[1] Patients undergoing BNN were rendered anuric.

Most of our patients underwent native nephrectomy prior to kidney transplantation for the reasons listed in Table 2, the foremost being a lack of space for the graft kidney. Table 3 lists the perioperative data that were recorded with missing values in 10.5% of patients or less, depending on the item. The average weight of the explanted native kidney(s) was 2.3 kg ± 1.4 kg. The average blood loss during the procedures was found to be the highest in group 2 (0.76L ± 0.47, $p = 0.809$). Blood transfusion units were most often needed by patients in group 1 (mean 1.06 ± 2.63, $p = 0.510$). Hospital stay was the highest for group 3 (10.1 ± 7.0 days) but was not statistically significant compared to the other groups. Between the LKD and DKD groups, average blood loss (0.63 ± 0.42 L vs. 0.82 ± 0.78 L $p = 0.101$) and the amount of blood transfusion units required was highest in the DKD group (0.9 ± 2.4 vs. 1.6 ± 2.7, $p = 0.197$). Hospital stay was also longer in this group but did not reach statistical significance (9.1 ± 6.4 vs. 10.5 ± 7.9, $p = 0.302$).

In the current series, 94 (82.5%) patients underwent a bilateral nephrectomy, of which 73 (77.7%) were prior to transplantation, 3 (3.2%) were during transplantation and 20 (21.3%) were after transplantation. A total of seven (5.9%) patients went through two subsequent unilateral native nephrectomies prior to transplantation. A total of 20 (17.5%) patients underwent a unilateral nephrectomy prior to transplantation, of which three (17.6%) eventually needed a second nephrectomy after transplantation. A simultaneous bilateral native nephrectomy was carried out in two of three patients. A previous unilateral nephrectomy had already been carried out in the third patient some years before and the second native kidney was removed during the transplantation procedure. The last patient only required the removal of one native kidney during the procedure and retained the other native kidney.

Group 1 had the highest number of living kidney donations and most of these patients went through a nephrectomy in anticipation of the scheduled transplantation. A total of seven patients underwent bilateral native nephrectomy prior to DKD transplantation of which six died while being on the waiting list for a post-mortal donor organ. These patients had already been on dialysis for several years before the nephrectomy and underwent the nephrectomy because of mechanical complaints or in preparation of the transplantation. Four patients died in a time period of six months to three

years after the nephrectomy. One patient chose to remain on dialysis and refused transplantation. This patient was eventually lost to follow-up. One patient developed a pneumothorax and bacteremia after undergoing a bilateral nephrectomy, resulting in a total atelectasis, respiratory insufficiency, systemic inflammatory response syndrome (SIRS) and ventricular fibrillation after which the patient died 58 days postoperatively. One patient died 115 days postoperatively as a result of septic shock due to a streptococcus pneumonia infection. Upon retrospective data collection, two patients had been recorded deceased in their electronic patient file with no clear cause of death noted.

Diuresis before and after nephrectomy was recorded for most of the patients. Not surprisingly, diuresis was lowest in group 2 ($p = 0.494$) and in the DKD group ($p = 0.002$). Diuresis decreased after nephrectomy for all groups. For patients who had undergone a unilateral nephrectomy it ranged from 130–970 mL/24 h. It was found to be the least in group 1 ($p = 0.000$) and the DKD group ($p = 0.607$). Patients with a bilateral nephrectomy were rendered anuric.

A total of 64 patients (56.1%) required either hemodialysis (76.6%) or peritoneal dialysis (23.4%) before nephrectomy was carried out. These were 53 patients in group 1 (82.8%), of which 12 required peritoneal dialysis, 5 in group 2 (7.8%), of which one patient required peritoneal dialysis, and 6 in group 3 (9.4%), of which 2 required peritoneal dialysis. The number of patients requiring dialysis was considered the largest for group 2 ($p = 0.009$). In the LKD group, 40.0% of patients required dialysis versus 87.2% in the DKD group ($p = 0.000$).

Complications were recorded for all patients. More than half of patients in each group had an uneventful postoperative course after nephrectomy and were discharged without complications. The complication rates were not statistically significant between the three groups ($p = 0.699$) or the LKD and DKD group ($p = 0.430$). No patients died within 30 days after the procedure. The most recorded complication was hypotension following the procedure, which occurred most often in group 1 in 21 patients (24.7%), compared to one patient in group 2 (20.0%) and two in group 3 (8.3%). Correction of an incisional hernia was the second most recorded complication: four patients in group 1 (11.1%), one in group 3 (20.0%) and five patients in the LKD group (17.2%). Other recorded complications were AVF occlusion, fever, and gastro-intestinal complaints. No patients had a complication of gross hematuria recorded. Patient data were collected perioperatively until discharge from the hospital; therefore, no conclusions about graft function can be made since this would need to be assessed at least one year postoperatively.

None of the explanted kidneys showed malignant changes upon histology. However, there were three findings of chronic pyelonephritis, one finding of secondary focal segmental glomerulosclerosis, four findings of infected abscesses, one finding of a lipoma on the adrenal gland, one finding of nodular hyperplasia on the adrenal gland, one finding with reactive changes of the renal parenchyma, one finding of reactive changes in the urothelium, two findings of chronic inflammation, two findings of degenerative changes and one finding of type 1 localized papillary cystadenoma.

Table 5 summarizes our findings in the literature, which shows that the most reported approach seems to be concurrent nephrectomy and transplantation. Complication rates in our population ranged from 20.0% to 42.4% and varied greatly among reported studies as well. Finally, Table 6 offers a summary of advantages and disadvantages of each procedure.

Table 4. Patient data of recipients of living kidney donations (LKD) vs. deceased kidney donations (DKD).

	LKD (n = 75)	DKD (n = 39)	Missing (%)	p-Value
Blood loss in L (SD)	0.63 (0.42)	0.82 (0.78)	10.5%	0.101
Blood transfusion units (SD)	0.95 (2.44)	1.59 (2.73)	0	0.197
Hospital stay in days (SD)	9.05 (6.43)	10.46 (7.92)	0	0.302
Hb - Pre (SD) - Post (SD)	 7.56 (1.28) 5.84 (1.10)	 7.82 (1.13) 5.94 (1.07)	6.1%	 0.295 0.648
Operation time in mins (SD)	168 (43.2)	170 (54.9)	0	0.841
Diuresis (L/24 h) [1] - Before - After	 1.68 (0.64) 0.35 (0.71)	 1.18 (0.89) 0.28 (0.52)	20.5%	 0.002 0.607
Dialysis	30 (40.0%)	34 (87.2%)	0	0.000
Complications - Hypotension - Incisional hernia - Shunt occlusion - Other	29 (38.7%) 17 5 1 6	15 (38.5%) 7 0 3 5	0	1.000

[1] Patients undergoing BNN were rendered anuric.

Table 5. Summary of published studies on peri-transplant nephrectomies.

Study	Years (No.)	Patients (No.)	Blood Loss (mL)	Blood Transfusions (units)	Hospital Stay (days)	OR Time (min)	Graft dysfunction [1] (No.)	Complication Rate [4,5]	Mortality (No.)
Kirkman [11]	6	35	-	-	-	-	2 (5.7%)		3 (8.6%)
- Pre		20 (57.1%)	-	0	-	-	0	35.0%	2 (10%)
- Sandwich [2]		3 (8.6%)	-	-	-	-	0	0	0
- Post		12 (34.3%)	-	-	-	-	2 (20%)	50.0%	1 (10%)
Sulikowski [5]	7	50	-	-	-	-	5 (10%)		1 (2%)
- Pre		25 (50%)	-	-	-	-	1 (20%)	56.5%	0
- Concurrent		4 (8%)	-	-	-	-	0	25.0%	0
- KT only		21 (42%)	-	-	-	-	4 (19%)	90.5%	1 (4.8%)
Wagner [12]	5	32	-	-	-	-	-		-
- Pre		15 (46.9%)	651	1.2	11.8	252	-	73.3%	-
- Concurrent		17 (53.1%)	617	2.2	6.9	430	-	70.6%	-

Table 5. *Cont.*

Study	Years (No.)	Patients (No.)	Blood Loss (mL)	Blood Transfusions (units)	Hospital Stay (days)	OR Time (min)	Graft dysfunction [1] (No.)	Complication Rate [4,5]	Mortality (No.)
Fuller [6]	10	32	-	-	-	-	-		1 (3.1%)
- Pre		7 (21.9%)	530	-	7	231	-	14.3%	0
- Concurrent		16 (50%)	570	2 [3]	8.6	370	-	0	0
- Pos		9 (28.1%)	520	-	6.3	208	-	11.1%	1 (11.1%)
Kramer [13]	4	20	724	3.3	7.2	391	0	20.0%	0
Nunes [7]	25	159	-	-	-	-	99 (62.3%)		-
- Concurrent		16 (10%)	-	1.81	16.5	254	12 (74.4%)	87.0%	-
- KT only		143 (90%)	-	1.05	12.7	181	87 (61.2%)	76.2%	-
Skauby [14]	19	157	-	-	-	-	2 (1.3%)		-
- Concurrent		78 (49.7%)	-	1.6	15.4	319.3	1 (1.3%)	30.8%	-
- KT only		79 (50.3%)	-	0.1	11.4	183.7	1 (1.3%)	26.6%	-
Ahmad [15]	10	118	-	-	-	-	12 (10.2%)		0
- Concurrent		66 (55.9%)	1251	3.4	6.6	381	4 (6.1%)	71.2%	0
- KT only		52 (44.1%)	425	0.46	4.8	204	8 (15.4%)	59.6%	0
Song [16]	9	63	-	-	-	-	10 (15.9%)		-
- Concurrent		31 (49.2%)	-	4.68	15.38	280	6 (19.4%)	80.6%	-
- KT only		32 (50.8%)	-	2.03	14.25	141	4 (12.5%)	53.1%	-
Glassman [17]	3	23	-	-	-	-	2 (8.7%)		0
- Pre		4 (17.4%)	650	0	13.3	403.8	1 (25%)	50.0%	0
- Concurrent		10 (43.5%)	1454.2	2.3	7.6	452.5	0	88.9%	0
- KT only		9 (39.1%)	344	1.0	7.1	295.6	1 (11.1%)	75.0%	0
Veroux [18]	15	145	-	-	-	-	49 (33.8%)		1 (0.7%)
- Pre		25 (17.2%)	421	-	15.4	421	11 (44%)	20.0%	0
- Concurrent		40 (27.5%)	300	-	13.3	300	10 (25%)	10.0%	0
- KT only		80 (55.2%)	522	-	16.5	522	28 (35%)	15.0%	1 (1.25%)
Current study	17	114	698	1.17	11.4	168.9	-		1 (0.9%)
- pre		85 (74.6%)	714	1.06	9.45	169.5	-	42.4%	0
- concurrent		5 (4.4%)	755	0.60	8.40	207.4	-	20.0%	0
- post		24 (21.1%)	628	1.67	10.1	158.6	-	29.2%	1 (4.2%)

KT = Kidney transplantation. [1] I.e., delayed graft function, acute rejection, graft ex-plantation, chronic allograft dysfunction. [2] Native nephrectomies prior to, and following transplantation. [3] Two patients required blood transfusions: no. of units not specified. [4] Expressed as the total number of complications divided by the total number of patients in the respective group. [5] Different kinds of complications have been reported but most notably: surgical complications, acute rejection, reoperations, additional procedure.

Table 6. Summary of advantages and disadvantages to each approach.

	Advantage	**Disadvantage**
Pre-transplantation nephrectomy	Reduced risk of infection Reduced risk of malignancies Mechanical relief for patient Create space for graft kidney	Increased risk of graft rejection in case of transfusion Anuric state of patient Necessity for dialysis
Peri-transplantation nephrectomy	Single procedure No temporary hemodialysis No anuric state of patient	Longer procedure Possibly higher blood loss
Post-transplantation nephrectomy	Preservation of diuresis No temporary hemodialysis Preservation of diuresis	Increased risk of infection due to immunosuppression Increased risk of malignant developments Mechanical compression of graft kidney

4. Discussion

The timing and indication for native nephrectomy in the event of kidney transplantation in patients with ADPKD have given rise to much discussion. In the past, it was common to perform a nephrectomy before transplantation. This was partly because the conservative management of symptoms was less advanced than it is now, especially in the case of infected cyst-related complications [16]. Presently, different approaches can be distinguished: a native nephrectomy before, during or after kidney transplantation. In the literature review, we attempted to identify a general consensus and to compare that with our own observational findings. Only a limited number of studies comparing all three approaches were available. The focus was on comparing the approaches using the same type of surgery to compare groups (e.g., either open or laparoscopic). Advances have been made in laparoscopic native nephrectomy, however, with advantages such as decreased hospitalization time, decreased need for blood transfusions and lower and less severe rates of complications [19].

The most studied procedure is the concurrent approach compared with a staged procedure or post-transplantation nephrectomy, or with a group undergoing transplantation without nephrectomy. The combined operation could be favored by patients because it is limited to a single procedure without the necessity of temporary hemodialysis [6,20]. However, the findings from the current and other studies [17] suggest that it is not preferentially carried out in daily clinical practice.

According to Skauby et al. [14], specific advantages and disadvantages exist to the different timing of the nephrectomy. At our institution, staging a nephrectomy prior to transplantation is the favored approach. In our patient population, 72.9% of all nephrectomies occurred prior to transplantation due to a lack of space for the graft kidney. This is in line with what is reported in other studies [7,21]. Advantages to a staged procedure are a reduced risk of bleeding events, infectious complications during the transplantation, and development of malignancies. A serious consequence in the event of a blood loss and subsequent transfusion pre-transplantation is that the patient could be sensitized to human leukocyte antigens (HLA) which will increase the risk of future graft rejection, as described in one center that has, for this reason, shifted to post-transplant nephrectomies [19,22]. In our series, this was a low-frequency event with 38 patients needing transfusion and one patient with subsequent sensitization. We carried out a simultaneous approach in five patients, for whom we found a slightly larger amount of blood loss, more operating time but somewhat less need for transfusions and a shorter hospital stay. This is similar to findings reported in the literature (Table 5).

Regarding malignancies, ADPKD significantly alters the anatomy and function of the native kidneys and it may be more difficult to detect malignancies [11]. Hajj et al. [23] have compared the prevalence of renal cell carcinomas in APKD versus chronic renal failure patients undergoing nephrectomies and have concluded that it was two to three times higher in APKD patients.

More obvious reasons for nephrectomies are mechanical relief for the patient and, as mentioned before, space creation. A disadvantage is that it causes patients to be anephric and anuric when a BNN is performed. Consequently, patients will be dialysis dependent and will have a fluid restriction. When no living donor is available, dialysis dependency could last for a period of months or even years, significantly lowering the quality of life and being associated with a higher mortality [24,25]. Fortunately, because ADPKD patients are often younger and have fewer comorbidities than patients with other causes of end-stage renal failure requiring transplantation they are twice as likely to receive a new kidney [26].

A more suitable approach for pre-transplantation nephrectomy in the absence of a living donor is to perform a unilateral nephrectomy. When the least functional kidney (as assessed by radioisotope renography, for example) is being removed, space has been created for a future kidney transplant while diuresis has been preserved. Although this is beneficial for the recipient's quality of life, it also carries the risk of a future contralateral native nephrectomy due to mechanical complaints or cyst infection that may pose a kidney graft at greater risk [5]. Patel et al. [27] reviewed 157 cases of APDK patients who underwent kidney transplantation of which 20% required a native completion nephrectomy due to recurrent infections and pain or space creation for combined pancreas kidney transplantation (n = 1). In our population seven patients had underwent a prior unilateral nephrectomy in the past due to cyst infections or mechanical complaints which were also reasons to remove the second native kidney at a later stage. Three patients needed a second unilateral nephrectomy after transplantation due to mechanical complaints. Thus, in our series, the chance of needing an additional nephrectomy (n = 10) after unilateral nephrectomy (n = 20) was 50.0%.

Bilateral nephrectomy before transplantation in the absence of a living donor should be reserved for patients with severe mechanical or infectious complaints, as the majority of the patients in the current study died before receiving a transplantation, with one death being related to the nephrectomy. Although native bilateral nephrectomy prior to deceased kidney transplantation is now an uncommon approach at our institution, the procedure was still performed if (1) the kidney size surpassed the pelvic crest on a computerized tomography (CT) or magnetic resonance imaging (MRI) scan and (2) during physical examination the space below the enlarged kidney in the iliac fossa was less than fist sized.

Furthermore, in our clinical experience, bilateral nephrectomy is accompanied by perioperative decrease in blood pressure that may jeopardize graft function in case of synchronous transplantation. Hypotension was observed after nephrectomy mostly in patients in group 1, which required extra monitoring in the post-anesthesia care unit and administration of inotropics. This hypotension can be significant as four arteriovenous dialysis fistulas in group 1 occluded following the procedure. One may argue that the deregulatory effect of a bilateral nephrectomy may be reversed to some extent by kidney transplantation, but, in our opinion, the risk of potential hazards of hypotensive periods during transplantation should be prevented.

An alternative to nephrectomy might be selective embolization of the renal artery. Essentially, this will cause the affected kidney to shrink, which could theoretically reduce symptoms of mechanical origin and could negate the need for a native nephrectomy. It could be used as an alternative to create space for a graft kidney. Cornelis et al. [28] have carried out a transcatheter arterial embolization (TAE) in 25 ADPKD patients with end-stage renal failure as an alternative to native nephrectomy before transplantation, achieving a significant reduction in kidney volume sizes. Suwabe et al. [29] have performed a bilateral TAE in 188 ADPKD patients and have reported a reduction in symptoms and positive results on quality of life. Renal TAE could be a safe, minimally invasive first-step procedure that could have a place in the management of future patients with enlarged polycystic kidneys [24]. However, Versteeg et al. [24] reported possible issues with this procedure. Most notably, the amount of time it takes to reduce the kidney volume to alleviate symptoms and create space for the kidney graft is about six months. For patients receiving a kidney transplantation, especially from a living kidney donation, a native nephrectomy might be a more time-efficient option.

Moreover, next to the risks associated with any surgical procedure, a risk of failure is also involved, meaning that patients undergoing a TAE might need a subsequent nephrectomy.

Another approach might be decortication of the cysts percutaneously, laparoscopically or by open surgery. In a review published by Millar et al. [30], this tactic seems effective to combat pain complaints but does not show clear benefits in blood pressure regulation or improvements in renal function. Pharmacologically, vasopressin receptor antagonists have shown to reduce the total growth in kidney volume and overall decrease in kidney function as shown in a trial by Torres et al. [31]. However, this study was limited by the fact that patients were asked to keep hydrated—this led to some developing hypertension at baseline. The effects of the vasopressor used could therefore not be completely trusted to have effects on hypertension. Finally, among newly emerging techniques in performing nephrectomies in ADPKD patients are robot-assisted procedures, which have been proven to be safe and effective with no major complications and lower estimated blood loss [32].

Although the current retrospective series include the largest cohort of operated ADPKD patients to date, it is limited by an unequal amount of patients in every group. This may lead to differences being statistically insignificant, while it may be clinically relevant. Another limitation is the collective data on both the nephrectomy and transplantation in group 2, hampering interpretation on the sole influence of the nephrectomy. Differences in outcomes were not statistically significant but may be interpreted as clinically relevant.

5. Conclusions

In conclusion, (bilateral) native nephrectomy prior to kidney transplantation in case of a living donor is a safe and controlled approach carrying minimal complication and mortality rates and facilitating a subsequent transplant procedure without mechanical limitations for the graft to be placed. When patients are on the waiting list for a deceased donor kidney, nephrectomy may best be postponed to be conducted synchronously.

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Appendix A Search Strategy

Table A1. Search components.

Component	PICO
Patient/Population	Patient with autosomal dominant polycystic kidney disease (ADPKD)
Intervention	native nephrectomy AND renal transplantation
Comparison/Control	no nephrectomy AND renal transplantation
Outcome	graft survival, complications

Component 1: ("Polycystic Kidney Diseases"[MeSH] OR "autosomal dominant polycystic kidney"[Tw])

Component 2: (nephrectomy[MeSH] OR "native nephrectomy"[TiAb] OR "nephrectomy"[Tw] OR "native nephrectomy"[Tw])

Component 3: ("Kidney Transplantation"[MeSH] OR "renal transplantation"[TiAb])

Component 4: ("Postoperative Complications"[MeSH] OR "graft survival"[TiAb] OR "complications"[TiAb])

Combined strategy 1: ("Polycystic Kidney Diseases"[MeSH] OR "autosomal dominant polycystic kidney"[Tw]) AND ("nephrectomy"[MeSH] OR native nephrectomy[TiAb]) AND ("Kidney Transplantation"[MeSH] OR "renal transplantation"[TiAb]) AND ("Postoperative Complications"[MeSH] OR "graft survival"[TiAb] OR "complications"[TiAb])

Combined strategy 2: ("Polycystic Kidney Diseases"[MeSH] OR "autosomal dominant polycystic kidney"[Tw]) AND ("nephrectomy"[MeSH] OR native nephrectomy[TiAb]) AND ("Kidney Transplantation"[MeSH] OR "renal transplantation"[TiAb]) AND ("Postoperative Complications"[MeSH] OR "graft survival"[TiAb] OR "complications"[TiAb]) NOT ("laparoscopic"[TiAb] OR (("laparoscopy"[MeSH] OR "laparoscopy"[Tw] OR "laparoscopic"[Tw])

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