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Original Article

ORIGINAL ARTICLE

Kidney transplantation in patients with polycystic kidney disease: increased risk of infection does not compromise graft and patient survival

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ABSTRACT

Background. Patients with autosomal dominant polycystic kidney disease (ADPKD) represent >10% of patients awaiting kidney transplantation. These patients are prone to potentially severe urinary tract (UTI) and liver cyst infections after transplantation. Whether such infections compromise outcome is unclear.

Methods. Between 2000 and 2017 we performed 193 kidney transplantations in patients with ADPKD. In 189 patients, we assessed the occurrence, frequency, and severity of infection episodes requiring inpatient treatment and their impact on graft and patient outcomes compared with 189 matched controls. Risk factors were analyzed by uni- and multivariable analyses.

Results. During a mean observation period of 77 months UTIs occurred more frequently in ADPKD patients (39.1% vs. 26.7%, $P = .022$; 0.8 ± 1.4 vs. 0.5 ± 1.1 episodes, $P < .001$). Eight ADPKD patients suffered from 19 episodes of liver cyst infection. Steroid medication (RR 3.04; $P < .001$) and recipient age (RR 1.05; $P = .003$) increased the risk for UTI/urosepsis, while nephrectomy reduced it (unilateral, RR 0.60; $P = .088$; bilateral, RR 0.45; $P = .020$). Patient survival was similar in both groups. The risk of graft failure was lower in ADPKD patients [hazard ratio (HR) 0.67; $P = .047$] due to a lower risk of death-censored graft loss (HR 0.47; $P = .014$). Donor age (HR 1.34; $P = .002$) and rejection (HR 8.47; $P < .001$) were risk factors for death-censored graft loss.

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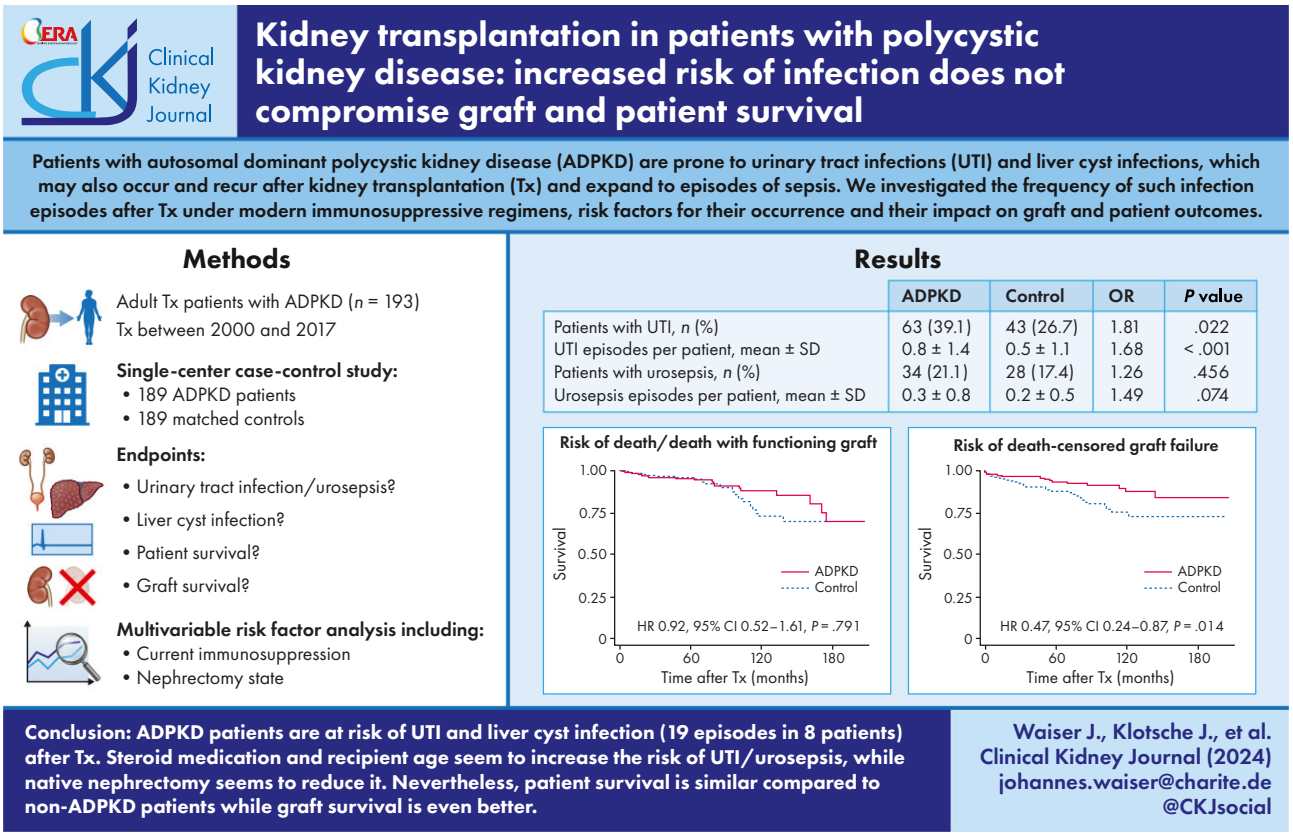
Conclusions. ADPKD patients are at increased risk of UTI and liver cyst infection after transplantation. Steroid medication and recipient age seem to increase the risk of UTI/urosepsis, while nephrectomy seems to reduce it. Nevertheless, patient survival was similar compared to non-ADPKD patients and death-censored graft survival even better.

GRAPHICAL ABSTRACT



Keywords: infection, kidney transplantation, polycystic kidney disease, risk factors, survival

KEY LEARNING POINTS

What was known:

- Patients with autosomal dominant polycystic kidney disease (ADPKD) are prone to urinary tract infections and liver cyst infections, which may also occur and recur after kidney transplantation. However, the frequency of such infection episodes after transplantation under modern immunosuppressive regimens, risk factors for their occurrence and their impact on graft and patient outcomes are unclear.

This study adds:

- In this single-center study comparing 189 ADPKD patients with an equal number of matched controls, we found that significantly more patients (OR 1.81) experienced significantly more episodes (OR 1.68) of urinary tract infection requiring inpatient treatment and that liver cyst infections occurred in 4% of patients. Nevertheless, patient survival was similar and graft survival, especially death-censored graft survival even better. Recipient age and steroid treatment seem to increase the risk of infection while nephrectomy of the native kidneys seems to reduced it.

Potential impact:

- The observation of similar survival rates and lower rates of graft loss despite an increased risk of infection is reassuring for ADPKD patients considering kidney transplantation. Awareness of the increased infection risk may facilitate early diagnosis and treatment. Our findings suggest that a reduction in infection risk should be weight into risk benefit assessments for nephrectomy and that steroid sparing immunosuppressive regimes may mitigate infection risk.

INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary kidney disease and the fourth leading cause of kidney failure accounting for ~10% of patients requiring kidney replacement therapy [1–4]. For patients with ADPKD and kidney failure kidney transplantation (Tx) is the preferred treatment option [5]. In 2021, >16% of all patients, who were added to the Eurotransplant waiting list in Germany suffered from ADPKD [6]. After Tx, these patients may experience episodes of urinary tract infection (UTI) and cyst infection of their native kidneys and liver. These episodes may recur and expand to episodes of sepsis. In this case-control study, we compared the occurrence, frequency, and severity of UTIs and liver cyst infections in a cohort of hospitalized ADPKD patients, who had received a kidney transplant at our center, with a cohort of matched control kidney transplant patients, who suffered from other causes of kidney failure. In addition, we analyzed patient survival, graft survival and graft function. Risk factors for the respective endpoints were analyzed by uni- and multivariable analysis.

MATERIALS AND METHODS

In 2017, we searched our electronic database system 'Tbase' [7] for patients who had received a kidney allograft between 1 January 2000 and 31 October 2017. We found 1478 Tx events during this period. In 272 cases the individual chart contained the term *cyst*, *zyst*, *ADPKD*, or the ICD-10 code *Q61*. We excluded 37 cases, in which Tx was performed under the age of 18 years, and 42 cases in which the diagnosis could not be confirmed by either family history, pathology or imaging [8]. This resulted in a group of 193 Tx events. Patients with any other cause of kidney failure were matched with the ADPKD cohort using the following criteria: donor type (living or deceased donor), recipient gender, recipient age (±5 years), and date of Tx (±1 year). Hereby, we were able to identify 189 matched pairs.

Notably, only patients without current and historical, preformed donor-specific HLA antibodies (2000–2008: ELISA, Lambda Antigen Tray LAT, One Lambda; since 2008: Luminex Single Antigen Bead Assay, One Lambda) and negative preoperative complement-dependent cytotoxicity crossmatch using isolated donor-derived T and B lymphocytes were accepted for transplantation. Because the immunological risk in all patients was considered low, thymoglobulin induction was not used.

Both groups were compared concerning the following endpoints: UTI, urosepsis, liver cyst infection, death, overall graft failure, death-censored graft failure, and renal function measured as serum creatinine-based estimated glomerular filtration rate ($eGFR_{cr}$) calculated according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [9]. Patients were censored at the time of graft failure. Risk factors for the previously mentioned endpoints were calculated by univariable and multivariable analyses. In the analysis of UTI and urosepsis patients were censored from the time at which both native kidneys had been removed.

A diagnosis of UTI was made in patients with typical signs and symptoms of UTI including blood tests and a positive urine culture. We did not distinguish between lower and upper UTI, because in our experience such a differentiation is generally difficult in renal allograft recipients. A diagnosis of urosepsis was based on the sepsis-2 criteria including positive urine and blood cultures [10]. Liver cyst infection was diagnosed by magnetic resonance imaging or positron-emission computed tomography [11] in combination with blood tests and blood cultures. Only infection episodes requiring hospitalization were recorded. The necessity of inpatient treatment was caused by either the severity of disease or the necessity of intravenous (IV) antibiotic treatment or both.

The Charlson Comorbidity Index (CCI) was calculated at the time of Tx. The CCI is a common, validated and widely accepted instrument used to predict 10-year mortality [12]. The CCI was further adapted in kidney failure patients [13] and kidney transplant recipients [14, 15]. Kidney failure as comorbid condition was considered present in all patients, irrespective of graft function. Serious ongoing conditions such as dementia, acquired immunodeficiency syndrome, and malignancy represent an absolute contraindication for Tx and therefore were not present.

The study was conducted in accordance with the principles of the Declaration of Helsinki, as revised in 2013 and the Declaration of Istanbul. The study was approved by the Institutional Ethics Committee of the Charité (EA1/048/14).

Statistical analyses

The risk of death, overall graft failure, and death-censored graft failure for ADPKD patients and matched controls was analyzed by Cox-proportional hazard models. Conditional logistic regression analysis was applied to compare the likelihood for UTI and urosepsis between ADPKD and matched controls. The association of defined risk factors with survival outcomes (death, death-censored graft failure, overall graft failure) was estimated by Cox-proportional hazard models. The likelihood for UTI or urosepsis during the initial Tx hospitalization was analyzed by a generalized linear model with robust error variances, the assumption of a Poisson distribution for onset of infections and the log link function including the defined risk factors and initial therapy after Tx. The entire observation period was divided into single treatment episodes based on immunosuppressive therapy administered during follow-up. Episodes of UTI or urosepsis were assigned to the treatment episode during which they occurred. The resulting patient-treatment episode data were analyzed by a multilevel mixed-effects Poisson regression model including the time under treatment as exposure to assess the association between UTI or urosepsis with time-depended therapy and defined baseline risk factors. The course of eGFR during follow-up was analyzed by a multilevel mixed-effect linear regression model. A worst-case imputation for missing eGFR values was performed in case of death-censored graft failure by 5 ml/min/1.73m². All defined risk factors were tested in univariable models for each outcome. LASSO (least absolute shrinkage and selection operator) regression was performed to identify a multivariable model for each defined outcome. LASSO is suited for models with high levels of multicollinearity. Relevant variables were included in the model regardless of their significance in univariate association with the outcome by LASSO. Continuously distributed variables were included as continuous in the regression models, the unit for interpretation is given in the tables. Variables resulting in <10 cases in cells in a cross table were not included in the regression analysis to assure reliable estimates. All statistical analyses were performed with SAS v.9.3 (SAS Institute Inc., Cary, NC, USA).

Table 1: Patient characteristics at transplantation.

	ADPKD complete $n = 193$	ADPKD matched-pair $n = 189$	Control matched-pair $n = 189$	P value
Recipient age (years), mean ± SD	55.1 ± 10.2	55.1 ± 10.1	55.2 ± 10.2	.924
Waiting time (months), mean ± SD	47.9 ± 42.1	48.2 ± 42.4	50.1 ± 37.0	.643
Female recipient, *n* (%)	81 (42.0)	80 (42.3)	80 (42.3)	
Recipient HbA1c, mean ± SD	5.4 ± 0.7	5.6 ± 0.8	5.7 ± 0.9	.254
Recipient BMI (kg/m^2), mean ± SD	26.0 ± 3.9	26.0 ± 3.9	26.2 ± 4.9	.661
Recipient CCI score, mean ± SD	3.6 ± 1.3	3.6 ± 1.3	4.0 ± 1.8	.069
Unilateral nephrectomy before Tx, *n* (%)	61 (31.6)	61 (32.3)	12 (6.3)	<.001
Bilateral nephrectomy before Tx, *n* (%)	22 (11.4)	22 (11.6)	9 (4.8)	.015
Underlying cause of chronic kidney disease				
Diabetic nephropathy, *n* (%)			18 (9.5)	
Vascular nephropathy, *n* (%)			19 (10.1)	
Primary glomerulopathy, *n* (%)			70 (37.0)	
Systemic disease, *n* (%)			8 (4.2)	
Hereditary kidney disease, *n* (%)			10 (5.3)	
Obstructive nephropathy/chronic pyelonephritis, *n* (%)			26 (13.8)	
Miscellaneous, *n* (%)			13 (6.9)	
Undetermined, *n* (%)			25 (13.2)	
vPRA %, mean ± SD	6.5 ± 21.5	6.6 ± 21.7	11.3 ± 26.5	.061
Donor age (years), mean ± SD	54.1 ± 13.9	54.2 ± 14.0	53.8 ± 14.8	.787
Donor $eGFR_{cr}$ (ml/min/1.73 m^2), mean ± SD	83.4 ± 24.6	83.6 ± 24.7	84.5 ± 24.7	.723
Living donor, *n* (%)	68 (35.2)	65 (34.4)	65 (34.4)	
Preemptive Tx, *n* (%)	23 (11.9)	22 (11.6)	12 (6.4)	.072
AB0 compatible Tx, *n* (%)	177 (91.7)	174 (92.1)	183 (96.8)	.073
Steroids, *n* (%)	193 (100.0)	189 (100.0)	189 (100.0)	
Basiliximab, *n* (%)	183 (94.8)	179 (94.7)	177 (93.7)	.660
Cyclosporine A, *n* (%)	85 (44.0)	83 (43.9)	83 (43.9)	
Tacrolimus, *n* (%)	104 (53.9)	102 (54.0)	102 (54.0)	
Everolimus, *n* (%)	3 (1.6)	3 (1.6)	2 (1.1)	.653
Belatacept, *n* (%)	1 (0.5)	1 (0.5)	3 (1.6)	.315
Mycophenolate, *n* (%)	179 (92.7)	175 (92.6)	182 (96.3)	.116
Fingolimod, *n* (%)	2 (1.0)	2 (1.1)	1 (0.5)	.562
Sotrastaurin, *n* (%)	12 (6.2)	12 (6.3)	5 (2.7)	.082

Immunosuppression refers to the initial treatment after Tx.
Note: in the control group one patient concomitantly received cyclosporine A and everolimus.
Abbreviations: ADPKD, polycystic kidney disease; BMI, body mass index; CCI, Charlson Comorbidity Index; eGFRcr, creatinine-based estimated glomerular filtration rate; SD, standard deviation; Tx, transplantation; vPRA, virtual panel reactive antibodies (Eurotransplant Reference Laboratory, HLA database version 4).
Chi-square test for categorical variables, Wilcoxon signed-rank-test for continuously distributed variables.

RESULTS

Table 1 shows patient characteristics at the time of transplantation. As expected, more patients in the ADPKD group underwent nephrectomy before Tx as compared to the control group. All other patient characteristics were similar between groups.

The mean observation time of the complete ADPKD cohort ($n = 193$) was 78.9 ± 51.9 months. The mean observation time of the matched-pair cohorts ($n = 189$) was 79.4 ± 52.0 (ADPKD) and 74.4 ± 48.6 months (control), respectively.

After Tx, altogether 29 endogenous kidneys were removed in the ADPKD group; both kidneys in five patients, the first kidney in nine patients and the second kidney in 10 patients. In the control cohort, 16 endogenous kidneys were removed after Tx, both kidneys in three patients and the first kidney in 10 patients ($P = .161$).

Posttransplant immunological data including calcineurin-inhibitor trough levels, frequencies and types of rejection, drugs used for the treatment of rejection, and white blood cell (WBC) counts according to groups are shown in Table 2. There were no differences between both groups except for the number of pre- and posttransplant WBC counts, which were significantly lower in ADPKD patients as compared to the control group.

UTI and liver cyst infection episodes

Episodes of UTI/urosepsis requiring hospitalization are summarized in Table 3a. The total number of UTI episodes during the entire observation period was 126 vs. 79 (ADPKD vs. non-ADPKD), the total number of urosepsis episodes was 50 vs. 36. Altogether, 41 vs. 27 patients suffered from recurrent UTI/urosepsis episodes. During the initial hospital stay at the time of Tx, the number of patients who experienced UTI/urosepsis was not different between both cohorts. By contrast, the number of patients with UTI during the entire observation period was higher in the ADPKD cohort compared to the control cohort. Also, the number of UTI episodes per patient

Table 2: Immunological parameters after transplantation.

	ADPKD complete $n = 193$	ADPKD matched-pair $n = 189$	Controlmatched-pair $n = 189$	*P* value
Cyclosporin A trough level				
Month 1–3, median (IQR)	177 (162–195)	177 (162–195)	176 (155–196)	.562
Month 4–12, median (IQR)	110 (96–123)	110 (95–122)	112 (102–124)	.224
Month >12, median (IQR)	92 (84–102)	91 (84–103)	93 (84–103)	.733
Tacrolimus trough level				
Month 1–3, median (IQR)	9.95 (9.10–11.00)	10.00 (9.10–11.00)	9.83 (8.55–11.10)	.277
Month 4–12, median (IQR)	7.35 (6.50–8.25)	7.32 (6.50–8.26)	7.15 (6.35–8.35)	.719
Month >12, median (IQR)	6.00 (5.30–6.81)	6.00 (5.30–6.82)	6.00 (5.49–6.70)	.832
Number of patients with rejection, *n* (%)	43 (22.3)	41 (21.7)	41 (21.7)	
TCMR, *n* (%)	38 (19.7)	36 (19.1)	33 (17.5)	.690
ABMR, *n* (%)	5 (2.6)	5 (2.7)	5 (2.7)	
Mixed TCMR/ABMR, *n* (%)	1 (0.5)	1 (0.5)	5 (2.7)	.100
Number of rejection episodes, mean ± SD	0.25 ± 0.51	0.24 ± 0.51	0.29 ± 0.55	.699
TCMR, mean ± SD	0.20 ± 0.40	0.19 ± 0.39	0.17 ± 0.38	.691
ABMR, mean ± SD	0.03 ± 0.16	0.03 ± 0.16	0.03 ± 0.16	
Mixed TCMR/ABMR, mean ± SD	0.01 ± 0.07	0.01 ± 0.07	0.03 ± 0.17	.101
Rejection treatment				
Steroid pulse, *n*	49	47	55	.354
Thymoglobulin, *n*	2	2	4	.410
Bortezomib, *n*	1	1	4	.177
Plasmapheresis/IVIG, *n*	6	6	9	.491
Rituximab, *n*	0	0	1	.317
WBC count ($\times 10^9$/l)				
Pretransplant, median (IQR)	8.00 (6.26–9.97)	7.97 (6.22–9.96)	9.46 (7.73–11.77)	<.001
Day 1–14, median (IQR)	8.55 (6.82–10.25)	8.41 (6.81–10.18)	9.61 (7.89–11.19)	<.001
Day 15–month 3, median (IQR)	7.78 (6.43–9.48)	7.74 (6.40–9.48)	8.57 (6.75–10.11)	.011
Month 4–12, median (IQR)	6.23 (5.09–7.65)	6.21 (5.09–7.56)	7.17 (5.82–8.80)	<.001

Abbreviations: ABMR, antibody mediated rejection; ADPKD, polycystic kidney disease; IQR, interquartile range; IVIG, intravenous immunoglobulins; SD, standard deviation; TCMR, T cell mediated rejection.
Chi-square test for categorical variables; Mann–Whitney *U*-test for continuously distributed variables.

Table 3a: UTI and urosepsis: matched-pair comparison between ADPKD patients and control group.

	ADPKD ($n = 161$)	Control ($n = 161$)	OR[a]	95%CI	*P* value
Patients with UTI or urosepsis during initial hospitalization, *n* (%)	14 (8.8)	12 (8.2)	1.09	0.49; 2.43	.841
Entire observation period					
Patients with UTI, *n* (%)	63 (39.1)	43 (26.7)	1.81	1.09; 3.02	.022
UTI episodes per patient, mean ± SD	0.8 ± 1.4	0.5 ± 1.1	1.68	1.27; 2.24	<.001
Patients with urosepsis, *n* (%)	34 (21.1)	28 (17.4)	1.26	0.68; 2.33	.456
Urosepsis episodes per patient, mean ± SD	0.3 ± 0.8	0.2 ± 0.5	1.49	0.96; 2.29	.074
Patients with UTI or urosepsis, *n* (%)	71 (44.1)	55 (34.2)	1.65	0.99; 2.74	.055
UTI and urosepsis episodes per patient, mean ± SD	1.1 ± 1.9	0.7 ± 1.4	1.63	1.28; 2.01	<.001

Patients were censored from the time at which both native kidneys had been removed. In 22 ADPKD patients and in 9 control patients both native kidneys had been removed before Tx resulting in 161 matched pairs (in three pairs both native kidneys had been removed before Tx in both, the ADPKD patient and the control patient).
[a]Odds ratio for ADPKD patients versus control patients estimated by a conditional logistic regression model adjusted for unilateral nephrectomy before Tx.
Abbreviations: ADPKD, polycystic kidney disease; CI, confidence interval; OR, odds ratio; SD, standard deviation; Tx, transplantation; UTI, urinary tract infection.

was higher in the ADPKD group. The number of patients with urosepsis and the number of urosepsis episodes per patient were slightly higher in the ADPKD group, but differences were not statistically significant. Table 3b shows a comparison of the risk of UTI and urosepsis between ADPKD patients and subgroups of the control group. Compared to ADPKD patients the risk of UTI and urosepsis was lower in patients with primary glomerulopathy, but higher in patients with obstructive nephropathy/chronic pyelonephritis.

In eight ADPKD patients (two females/six males) altogether 19 liver cyst infections occurred, eight of which with a septic course. One patient experienced eight episodes of liver cyst

Table 3b: UTI and urosepsis during the entire observation period: comparison between ADPKD patients and control subgroups.

	ADPKD[a] (n = 161)	Diabetic nephropathy (n = 16)	Vascular nephropathy (n = 18)	Primary glomerulopathy (n = 59)	Systemic disease[b] (n = 8)	Hereditary kidney disease[b] (n = 7)	Obstructive nephropathy/chronic pyelonephritis (n = 20)	Miscellaneous[b] (n = 12)	Undetermined (n = 21)
Patients with UTI, n (%), P	63 (39.1)	6 (37.5), .938	4 (22.2), .234	9 (15.3), .002	1 (12.5)	1 (14.3)	10 (50.0), 0.318	4 (33.3)	6 (28.6), 0.382
UTI episodes per patient, mean ± SD, P	0.8 ± 1.4	0.9 ± 1.7, 0.636	0.5 ± 1.1, 0.253	0.3 ± 0.7, 0.001	0.1 ± 0.4	0.1 ± 0.4	1.1 ± 1.6, 0.076	0.3 ± 0.5	0.6 ± 1.1, 0.041
Patients with urosepsis, n (%), P	34 (21.1)	4 (25.0), 0.748	5 (27.8), 0.358	7 (11.9), 0.166	2 (25.0)	2 (28.6)	4 (20.0), 0.872	1 (8.3)	3 (14.3), 0.434
Urosepsis episodes per patient, mean ± SD, P	0.3 ± 0.8	0.5 ± 1.0, 0.366	0.4 ± 0.6, 0.687	0.1 ± 0.3, 0.028	0.3 ± 0.5	0.3 ± 0.5	0.3 ± 0.7, 0.596	0.1 ± 0.3	0.2 ± 0.5, 0.097
Patients with UTI or urosepsis, n (%), P	71 (44.1)	8 (50.0), 0.654	7 (38.9), 0.830	13 (22.0), 0.006	3 (37.5)	2 (28.6)	10 (50.0), 0.543	4 (33.3)	6 (28.6), 0.178
UTI and urosepsis episodes per patient, mean ± SD, P	1.1 ± 1.9	1.5 ± 2.0, 0.349	0.8 ± 1.3, 0.548	0.4 ± 1.0, 0.001	0.5 ± 0.8	0.4 ± 0.8	1.4 ± 2.1, 0.032	0.4 ± 0.7	0.8 ± 1.3, 0.002

Patients were censored from the time at which both native kidneys had been removed. In 22 ADPKD patients and in 9 control patients both native kidneys had been removed before Tx resulting in 161 matched pairs (in three pairs both native kidneys had been removed before Tx in both, the ADPKD patient and the control patient).

[a]Reference group.

[b]Infection rates and number of infections were not compared to ADPKD patients because of limited group size.

P value for ADPKD patients versus control subgroups estimated by a conditional logistic regression model adjusted for unilateral nephrectomy before Tx.

Abbreviations: ADPKD, polycystic kidney disease; SD, standard deviation; Tx, transplantation; UTI, urinary tract infection.

infection necessitating inpatient treatment, six of which with a septic course. The patient finally died with a functioning graft because of a septic liver cyst infection. Another patient also died because of severe liver cyst infection, but was not included in the statistics, because she died a few weeks after her kidney failed.

Patient survival, graft survival and graft function

Figure 1a shows that the risk of death/death with functioning graft in ADPKD patients was comparable to matched controls. Altogether, 24/189 patients of the ADPKD cohort died, 7/24 because of infectious events, 7/24 because of malignancy, and 8/24 because of cardiovascular events. In 2/24 patients, the cause of death remained unknown. In the control cohort, 25/189 patients died, 4/25 because of infectious events, 5/25 because of malignancy, and 8/25 because of cardiovascular events. In 8/25 cases the cause of death was unknown.

The overall risk of graft failure was lower in ADPKD patients as compared to their matched controls (Fig. 1b). This difference was mainly caused by a reduced risk of death-censored graft failure (Fig. 1c). As expected, the frequency of graft loss due to recurrence of the underlying disease was lower in the ADPKD group (0 vs. 5) and cardiorenal syndrome (1 vs. 6) was also less frequent. Graft loss due to rejection (9 vs. 12) and calcineurin-inhibitor nephrotoxicity (2 vs. 1) were comparable.

Concerning the eGFR course during follow-up estimated by $eGFR_{cr}$ according to the CKD-EPI formula [9] with imputation for graft loss, we observed no significant differences between both groups (Fig. 1d).

Risk factor analysis

Nearly one half of all ADPKD patients (82/193, 42.5%) experienced at least one major change of maintenance immunosuppression during the observation period, for example from a calcineurin-inhibitor containing to a calcineurin-inhibitor-free regimen. In 27/193 (14.0%) patients, maintenance immunosuppression was changed more than once. Therefore, maintenance immunosuppression was excluded from the analysis of risk factors for patient survival, graft survival, and graft function. Concerning UTIs and urosepsis, however, immunosuppression at diagnosis was included.

Risk factors for UTI and urosepsis during the initial hospitalization for Tx are shown in Table 4. Immunosuppression refers to the initial treatment after Tx. Steroids were not included because at this early stage all patients received steroids. Univariable analysis indicates that tacrolimus and rejection increased the risk of UTI/urosepsis, while cyclosporine decreased it. Multivariable analysis confirmed the effect of tacrolimus and rejection.

Table 5 shows the risk factors for UTI and urosepsis during the entire observation period. Maintenance immunosuppression at the time of diagnosis was included by comparing the number of episodes of UTI/urosepsis on a specific substance with the total exposure time of all ADPKD patients on this substance. According to the univariable analysis recipient age, comorbidity, donor age, donor $eGFR_{cr}$, and rejection episodes as well as the use of steroids and tacrolimus influenced the risk of UTI/urosepsis. Multivariable analysis shows that only increasing recipient age and steroid medication increased the risk.

Additionally, we compared the risk for UTI/urosepsis between ADPKD patients after removal of the first native kidney ($n = 74$) and ADPKD patients in whom both native kidneys were

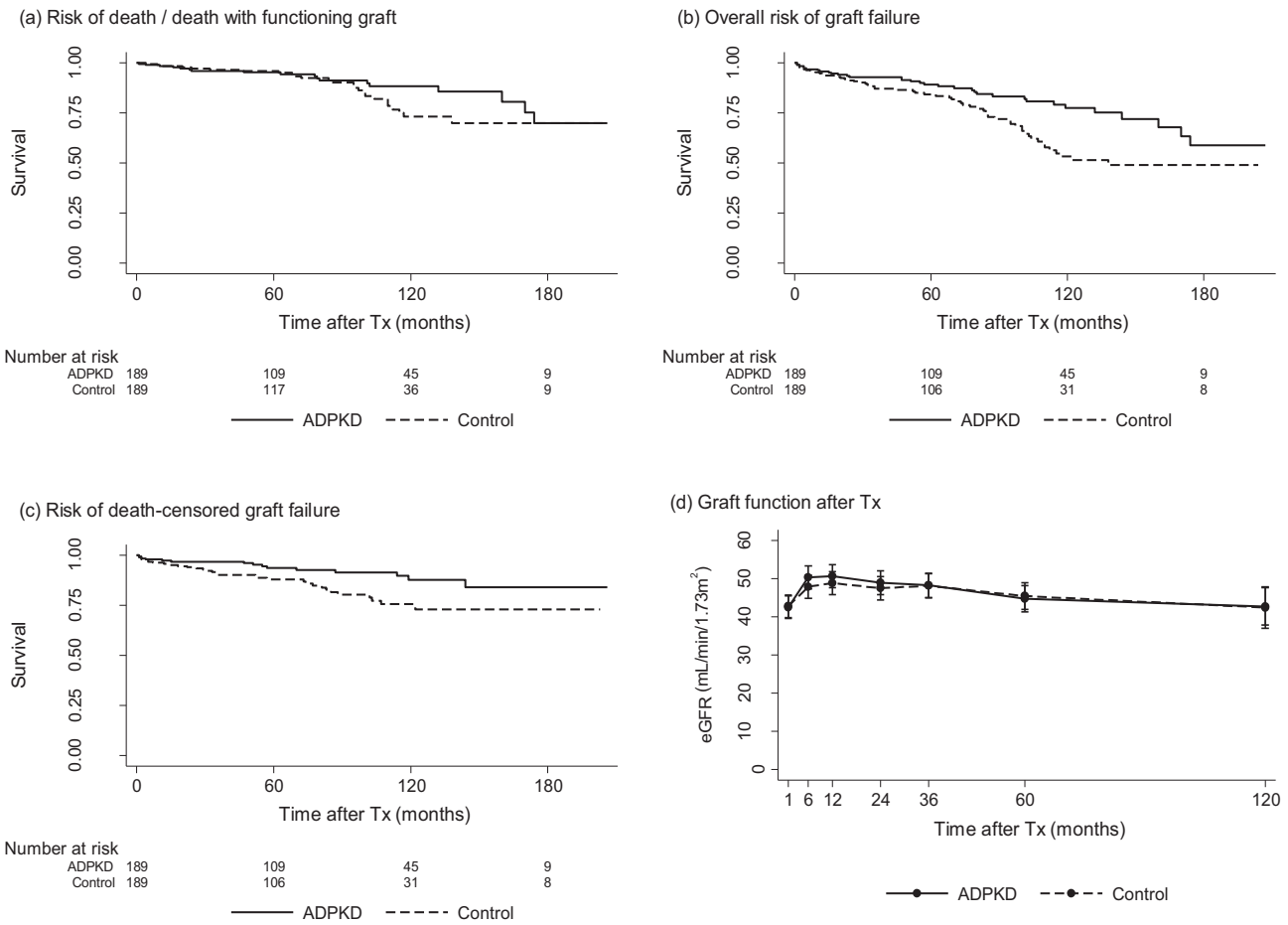


Figure 1: Matched-pair comparison between ADPKD patients and matched control group. (**a**) Risk of death/death with functioning graft (HR 0.92; 95%CI 0.52; 1.61; $P = .791$). (**b**) Overall risk of graft failure (HR 0.67; 95%CI 0.45; 0.99; $P = .047$). (**c**) Risk of death-censored graft failure (HR 0.47; 95%CI 0.24; 0.87; $P = .014$). (**d**) Graft function shown as $eGFR_{cr}$ (mean; 95%CI) (beta 0.26; 95%CI −2.82; 3.34; $P = .868$); number of ADPKD patients and control patients, at baseline: 189/189, 6 months: 182/184, 12 months: 174/179, 24 months: 164/163, 36 months: 147/148, 60 months: 113/109 and 120 months: 53/63. Abbreviations: ADPKD, polycystic kidney disease; CI, confidence interval; HR, hazard ratio; Tx, transplantation.

in situ ($n = 110$). The incidence rate of combined UTI/urosepsis episodes (related to time under risk) was reduced after removal of the first native kidney, although not significantly (RR 0.60; 95%CI 0.33; 1.08; $P = .088$). In comparison, the incidence rate of combined UTI/urosepsis episodes was significantly lower after nephrectomy of the second native kidney ($n = 37$) compared to patients in whom at least one native kidney was *in situ* ($n = 171$) (RR 0.45; 95%CI 0.23; 0.88; $P = .020$).

Risk factors for death/death with functioning graft are shown in Table 6. Univariable analysis indicates that recipient age, waiting time, comorbidity, donor age, and donor $eGFR_{cr}$ had a significant influence on both outcomes. Multivariable analysis shows that only waiting time and comorbidity significantly influenced the risk of death/death with functioning graft.

Table 7 shows risk factors for death-censored graft failure. Univariable analysis indicates that recipient age, comorbidity, donor age, rejection, and UTI/urosepsis had a significant influence on the risk of death-censored graft failure. Multivariable analysis shows that only donor age and rejection significantly influenced the risk. UTI/urosepsis is not included in the multivariable model, because its association with death-censored graft failure is explained by rejection as shown in the combined model of both variables [hazard ratio (HR) 9.10; $P < .001$ for rejection and HR 2.78; $P = .185$ for UTI/urosepsis].

In Table 8, the risk factors for overall graft failure are summarized. Univariable analysis indicates that recipient age, waiting time, comorbidity, donor age, donor $eGFR_{cr}$, donor type, rejection, and UTI/urosepsis all had a significant influence on the overall risk of graft failure. Supporting the results of our previous analyses on death with functioning graft (Table 6) and death-censored graft survival (Table 7), multivariable analysis confirmed that waiting time, comorbidity, donor age, and rejection all significantly contribute to the overall risk of graft failure. The effect of UTI/urosepsis on overall graft failure is explained by rejection as the joint analysis of rejection and UTI/urosepsis shows (HR 2.27; $P = .016$ for rejection and HR 2.34; $P = .116$ for UTI/urosepsis).

Factors influencing the $eGFR_{cr}$ course over time are shown in Table 9. Univariable analysis indicates that recipient age, comorbidity, donor age, donor $eGFR_{cr}$, donor type, preemptive Tx, and rejection had a significant influence on the $eGFR_{cr}$ course. Multivariable analysis shows that increasing donor age and rejection had a negative impact on the $eGFR_{cr}$ course while living donor status had a positive impact.

Table 4: Risk factors for UTI and urosepsis during the initial Tx hospitalization in ADPKD patients.

UTI or urosepsis during initial Tx hospitalization	Yes $n = 14$	No $n = 157$	Univariable			Multivariable[b]		
			RR[a]	95%CI	*P* value	RR[a]	95%CI	*P* value
Recipient age at Tx, mean ± SD (per 5 years)	58.2 ± 8.8	54.9 ± 10.7	1.18	0.92; 1.51	.198	1.10	0.71; 1.69	.679
Waiting time, mean ± SD (per 12 months)	47.7 ± 37.3	43.4 ± 38.2	1.09	0.96; 1.23	.180			
Female recipient, *n* (%) (yes vs no)	6 (42.9)	69 (44.0)	0.87	0.32; 2.35	.781			
Recipient diabetes mellitus, *n* (%) (yes vs no)	3 (21.4)	20 (12.9)	1.77	0.54; 5.84	.346			
Recipient BMI, mean ± SD (per 1 kg/m^2)	27.4 ± 3.3	25.9 ± 4.0	1.04	0.92; 1.17	.501			
Recipient CCI score, mean ± SD (per 1 point)	3.9 ± 1.0	3.5 ± 1.3	1.35	0.94; 1.93	.104	1.13	0.59; 2.19	.707
Unilateral nephrectomy before Tx, *n* (%) (yes vs no)	4 (28.6)	57 (36.3)	0.70	0.21; 2.34	.564			
Donor age, mean ± SD (per 5 years)	59.0 ± 11.2	54.8 ± 13.7	1.00	0.84; 1.20	.966			
Donor $eGFR_{cr}$, mean ± SD (per 5 ml/min/1.73 m^2)	80.0 ± 27.8	83.9 ± 24.0	1.01	0.92; 1.12	.781			
Living donor, *n* (%) (yes vs no)	3 (21.4)	60 (38.2)	[c]					
Preemptive Tx, *n* (%) (yes vs no)	2 (14.3)	21 (13.4)	0.92	0.20; 4.27	.912			
AB0 compatible Tx, *n* (%) (yes vs no)	12 (85.7)	143 (91.1)	0.70	0.14; 3.34	.650			
Basiliximab, *n* (%) (yes vs no)	13 (92.9)	148 (94.3)	0.92	0.11: 7.72	.940			
Cyclosporine A, *n* (%) (yes vs no)	3 (21.4)	69 (44.0)	0.23	0.06; 0.81	.023			
Tacrolimus, *n* (%) (yes vs no)	11 (78.6)	84 (53.5)	4.83	1.35; 17.28	.015	6.44	1.66; 25.10	.007
Mycophenolate, *n* (%) (yes vs no)	12 (85.7)	147 (93.6)	0.34	0.08; 1.34	.121			
Rejection episode, *n* (%) (yes vs no)	8 (57.1)	32 (20.4)	3.20	1.18; 8.71	.023	5.24	1.68; 16.30	.004

Immunosuppression refers to the initial treatment after transplantation. Patients were censored from the time at which both native kidneys had been removed. In 22 patients both native kidneys had been removed before transplantation. Steroids were not included because at this early stage after Tx all patients received steroids. Immunosuppression applied in <10 cases was excluded from the analysis to assure reliable risk estimates: belatacept, bortezomib, everolimus, fingolimod, plasmapheresis/intravenous immunoglobulins, rituximab, sotrastaurin, thymoglobulin.

[a]Relative risk estimated by a generalized linear model by Poisson regression with robust error variance.

[b]Multivariable model was identified by LASSO regression.

[c]Parameter was not analyzed because of small population of cells in cross table.

Abbreviations: ADPKD, polycystic kidney disease; BMI, body mass index; CCI, Charlson Comorbidity Index; CI, confidence interval; eGFRcr, creatinine-based estimated glomerular filtration rate; SD, standard deviation; Tx, transplantation.

DISCUSSION

In this single-center case-control study we compared the occurrence, frequency, and severity of UTIs and liver cyst infections in hospitalized ADPKD patients transplanted between 2000 and 2017 with a matched control group. In addition, we analyzed patient survival, graft survival, and graft function as well as risk factors for the corresponding endpoints.

More ADPKD patients experienced more episodes of UTI necessitating hospitalization during the entire observation period compared to controls. Increasing recipient age and the use of steroids increased the risk of UTI/urosepsis. During the initial hospitalization at transplantation no such difference was evident probably reflecting the routine use of antibiotic prophylaxis [16]. Notably, DJ stents were routinely removed at 3–6 weeks after Tx and nephrolithiasis did not play an important role, as it was detected in only two patients of each group. We deliberately decided to assess episodes of UTI and urosepsis requiring hospitalization because in our experience despite intense follow-up a considerable part of uncomplicated UTI episodes is treated by local nephrologists or general practitioners and may therefore escape our notice. In accordance with our results, Stiasny *et al.* [17] and Jänigen *et al.* [18] also observed an increased incidence of UTI in ADPKD patients, while Hadimeri *et al.* [19] and Jacquet *et al.* [20] did not. Detailed analyses on the necessity of inpatient treatment, the severity and frequency of infections as well as the underlying risk factors are not reported.

Sulikowski *et al.* described that nephrectomy before Tx may decrease the number of posttransplant UTIs [21]. Therefore, we included unilateral nephrectomy as independent variable in the risk factor analysis and censored patients from the time at which both native kidneys had been removed, i.e. the suggested "risk factor" was no longer present. We found that unilateral and bilateral nephrectomy of the native kidneys reduce the risk of UTI/urosepsis. To our knowledge, this is the first report confirming the generalized assumption that nephrectomy of the native kidneys may in fact reduce the risk of infection.

There is a considerable amount of literature concerning the timing and technique of native nephrectomy in ADPKD patients [22–26]. In our view, the timing and technique of native nephrectomy in these patients remains an individual decision in which the specific indication for nephrectomy and the availability of a potential donor play a central role. At our center, we do not perform simultaneous native nephrectomy and kidney transplantation.

Table 5: Risk factors for episodes of UTI and urosepsis during the entire observation period in ADPKD patients.

	Univariable			Multivariable[b]		
UTI and/or urosepsis during the entire observation period	RR[a]	95%CI	*P* value	RR[a]	95%CI	*P* value
Recipient age at Tx (per 5 years)	1.06	1.03; 1.10	.001	1.05	1.02; 1.08	.003
Waiting time (per 12 months)	1.00	0.99; 1.01	.396			
Female recipient (yes vs no)	1.42	0.68; 2.97	.356			
Recipient diabetes mellitus (yes vs no)	0.58	0.20; 1.70	.322			
Recipient BMI (per 1 kg/m^2)	1.00	0.91; 1.10	.923			
Recipient CCI score (per 1 point)	1.52	1.15; 2.02	.003			
Unilateral nephrectomy before Tx (yes vs no)	0.57	0.26; 1.24	.157	0.64	0.32; 1.29	.209
Donor age (per 5 years)	1.03	1.01; 1.06	.011			
Donor eGFR$_{cr}$ (per 5 ml/min/1.73 m^2)	0.98	0.97; 1.00	.040			
Living donor (yes vs no)	0.48	0.22; 1.06	.071			
Preemptive Tx (yes vs no)	0.80	0.26; 2.45	.703			
AB0compatible Tx (yes vs no)	1.47	0.34; 6.41	.605			
Steroids (yes vs no)	3.06	2.12; 4.43	<.001	3.04	2.11; 4.38	<.001
Cyclosporine A (yes vs no)	1.87	0.70; 4.94	.221			
Tacrolimus (yes vs no)	0.57	0.32; 0.98	.039			
Everolimus (yes vs no)	0.79	0.39; 1.60	.513			
Belatacept (yes vs no)	0.47	0.17; 1.27	.135	0.61	0.24; 1.56	.306
Mycophenolate (yes vs no)	1.67	0.76; 3.67	.204			
Rejection episode (yes vs no)	2.58	1.11; 5.95	.027	2.01	0.98; 4.12	.056

Patients were censored from the time at which both native kidneys had been removed. In 22 patients both native kidneys had been removed before Tx. In 15 patients the second kidney was removed after Tx. Maintenance immunosuppression changed during the observation period. Immunosuppression at diagnosis is shown. Immunosuppression with <10 years of total exposure time (entire observation period of all patients) was excluded to assure reliable estimates: basiliximab, fingolimod, sotrastaurin.

[a]Relative risk estimated by a multilevel mixed-effects Poisson regression model.

[b]Multivariable model was identified by LASSO regression.

Abbreviations: ADPKD, polycystic kidney disease; BMI, body mass index; CCI, Charlson Comorbidity Index; CI, confidence interval; eGFRcr, creatinine-based estimated glomerular filtration rate; Tx, transplantation.

Table 6: Risk factors for death/death with functioning graft in ADPKD patients.

			Univariable			Multivariable[b]		
Death/death with functioning graft	Yes *n* = 25	No *n* = 168	HR[a]	95%CI	*P* value	HR[a]	95%CI	*P* value
Recipient age at Tx, mean ± SD (per 5 years)	60.6 ± 12.1	54.3 ± 9.7	1.50	1.20; 1.88	<.001			
Waiting time, mean ± SD (per 12 months)	69.8 ± 44.9	44.7 ± 40.9	1.14	1.05; 1.24	.003	1.12	1.02; 1.23	.017
Female recipient, *n* (%) (yes vs no)	11 (44.0)	70 (41.7)	1.05	0.47; 2.32	.907			
Recipient diabetes mellitus, *n* (%) (yes vs no)	6 (25.0)	22 (13.2)	1.40	0.55; 3.56	.481			
Recipient BMI, mean ± SD (per 1 kg/m^2)	25.1 ± 3.9	26.1 ± 3.9	0.96	0.86; 1.08	.504			
Recipient CCI score, mean ± SD (per 1 point)	4.5 ± 1.5	3.5 ± 1.2	1.81	1.36; 2.41	<.001	1.74	1.31; 2.31	<.001
Unilateral nephrectomy before Tx, *n* (%) (yes vs no)	9 (36.0)	52 (31.0)	1.07	0.47; 2.44	.865			
Bilateral nephrectomy before Tx, *n* (%) (yes vs no)	4 (16.0)	18 (10.7)	1.36	0.47; 3.99	.570			
Donor age, mean ± SD (per 5 years)	58.2 ± 13.9	53.5 ± 13.9	1.16	1.01; 1.35	.042			
Donor eGFR$_{cr}$, mean ± SD (per 5 ml/min/1.73 m^2)	73.4 ± 29.0	84.9 ± 23.6	0.93	0.87; 0.99	.040			
Living donor, *n* (%) (yes vs no)	4 (16.0)	64 (38.1)	0.35	0.12; 1.02	.054			
Preemptive Tx, *n* (%) (yes vs no)	1 (4.0)	22 (13.1)	[c]					
AB0 compatible Tx, *n* (%) (yes vs no)	25 (100.0)	152 (90.5)	[c]					
Rejection episode, *n* (%) (yes vs no)	5 (20.0)	38 (22.6)	0.98	0.36; 2.64	.970			
Patients with UTI or urosepsis, *n* (%) (yes vs no)	15 (60.0)	71 (42.3)	2.01	0.90; 4.52	.090			

[a]Hazard ratio estimated by Cox-proportional hazard model.

[b]Multivariable model was identified by LASSO regression.

[c]Parameter was not analyzed because of small population of cells in cross table.

Abbreviations: ADPKD, polycystic kidney disease; BMI, body mass index; CCI, Charlson Comorbidity Index; CI, confidence interval; eGFRcr, creatinine-based estimated glomerular filtration rate; HR, hazard ratio; SD, standard deviation; Tx, transplantation; UTI, urinary tract infection.

Table 7: Risk factors for death-censored graft failure in ADPKD patients.

	Yes	No	Univariable			Multivariable[b]		
Death-censored graft failure	n = 17	n = 176	HR[a]	95%CI	P value	HR[a]	95%CI	P value
Recipient age at Tx, mean ± SD (per 5 years)	61.6 ± 9.5	54.5 ± 10.1	1.66	1.22; 2.26	.001			
Waiting time, mean ± SD (per 12 months)	46.5 ± 32.7	48.1 ± 43.0	1.00	0.86; 1.17	.975			
Female recipient, n (%) (yes vs no)	9 (52.9)	72 (40.9)	1.39	0.50; 3.85	.522			
Recipient diabetes mellitus, n (%) (yes vs no)	1 (5.9)	27 (15.5)	[c]					
Recipient BMI, mean ± SD (per 1 kg/m^2)	26.5 ± 3.5	25.9 ± 3.9	1.08	0.95; 1.23	.242			
CCI score, mean ± SD (per 1 point)	4.2 ± 1.3	3.5 ± 1.3	1.67	1.14; 2.43	.008			
Unilateral nephrectomy before Tx, n (%) (yes vs no)	4 (23.5)	57 (32.4)	[c]					
Bilateral nephrectomy before Tx, n (%) (yes vs no)	1 (5.9)	21 (11.9)	[c]					
Donor age, mean ± SD (per 5 years)	65.2 ± 10.3	53.0 ± 13.8	1.44	1.17; 1.76	<.001	1.34	1.12; 1.61	.002
Donor $eGFR_{cr}$, mean ± SD (per 5 ml/min/1.73 m^2)	73.1 ± 23.4	84.4 ± 24.5	0.93	0.85; 1.01	.073			
Living donor, n (%) (yes vs no)	3 (17.7)	65 (36.9)	[c]					
Preemptive Tx, n (%) (yes vs no)	0 (0.0)	23 (13.1)	[c]					
AB0 compatible Tx, n (%) (yes vs no)	15 (88.2)	162 (92.1)	0.22	0.05; 1.06	.059			
Rejection episode, n (%) (yes vs no)	12 (70.6)	31 (17.6)	10.34	3.25; 32.90	<.001	8.47	2.63; 27.31	<.001
Patients with UTI or urosepsis, n (%) (yes vs no)	11 (64.7)	75 (42.6)	3.60	1.14; 11.40	.029			

[a]Hazard ratio estimated by Cox-proportional hazard model.
[b]Multivariable model was identified by LASSO regression.
[c]Parameter was not analyzed because of small population of cells in cross table.
Abbreviations: ADPKD, polycystic kidney disease; BMI, body mass index; CCI, Charlson Comorbidity Index; CI, confidence interval; eGFRcr, creatinine-based estimated glomerular filtration rate; HR, hazard ratio; SD, standard deviation; Tx, transplantation; UTI, urinary tract infection.

Notably, 8/193 patients experienced liver cyst infection, and two of these patients even died of severe liver cyst infection, one patient with functioning graft and another patient soon after graft failure. Altogether, seven patients in the ADPKD cohort died with functioning graft because of infectious events compared to four patients of the control group. These data underline that ADPKD is a systemic disease and that infections of both kidney and liver cysts constitute serious complications after Tx.

Schellekens *et al.* recently described lower peripheral WBC counts in ADPKD patients as compared to non-ADPKD patients before and after transplantation [27]. Our results agree with these data. Whether or not lower WBC counts represent an additional risk factor for infection, which is independent of the underlying kidney disease and pathogenetically relevant is an interesting question that should be addressed in future prospective studies.

Patient survival in ADPKD patients was similar compared to non-ADPKD patients. In this regard, our results are consistent with most of the existing literature [17–20, 28–30]. Graft survival in ADPKD patients was superior compared to controls. Some previous studies also found improved graft survival in ADPKD patients [20, 27, 28] while others described comparable graft survival [17–19, 29, 30]. We therefore analyzed graft survival in depth and found that especially death-censored graft survival was superior in ADPKD patients. The missing risk of recurrence of the underlying kidney disease and a reduced risk of cardiorenal syndrome may partially explain this phenomenon. Major risk factors for death with functioning graft were waiting time and comorbidity; major risk factors for death-censored graft failure were donor age and rejection. UTI/urosepsis seemed to be a significant risk factor for death-censored graft failure in the univariable analysis, but not in the multivariable analysis. This can be explained by the fact that rejection episodes were usually treated with steroids, and steroid treatment increased the risk of UTI/urosepsis.

Most of the existing studies date back more than one [20, 28] or even two [17, 19, 29, 30] decades. Since that time the (peri)transplant procedure including immunosuppression has markedly changed. We deliberately included patients transplanted from 2000 onwards to assure that most patients received current standard immunosuppression including anti-IL-2R-induction together with steroids, calcineurin inhibitors, and mycophenolate. In a more recent study, Bhutani *et al.* compared PKD patients with non-PKD patients transplanted between 1994 and 2014 [31]. They also found that the risk of death-censored graft failure was lower in PKD patients.

Some of the previously mentioned studies used a matched-pair design [17, 19, 29] using three matching variables while others compared ADPKD patients with non-ADPKD patients without matching [20, 28, 30, 31]. Several studies excluded diabetics [17, 19, 28–30]. We decided not to exclude diabetics to generate a complete real-world picture.

Our study has several limitations, chief among them the fact that it represents a retrospective single-center study. Although we adjusted for a number of variables, residual confounding due to parameters, which may not have been completely accounted for in our statistical analysis cannot be excluded. We tried to outweigh these limitations by detailed and thorough data recording, by applying a matched-pair design, and by using complex statistical analyses.

Table 8: Risk factors for overall graft failure in ADPKD patients.

			Univariable			Multivariable[b]		
Overall graft failure	Yes $n = 42$	No $n = 151$	HR[a]	95%CI	*P* value	HR[a]	95%CI	*P* value
Recipient age at Tx, mean ± SD (per 5 years)	61.0 ± 11.0	53.5 ± 9.4	1.56	1.30; 1.87	<.001			
Waiting time, mean ± SD (per 12 months)	60.4 ± 41.6	44.5 ± 41.8	1.10	1.02; 1.18	.017	1.14	1.02; 1.27	.025
Female recipient, *n* (%) (yes vs no)	20 (47.6)	61 (40.4)	1.17	0.63; 2.18	.625			
Recipient diabetes mellitus, *n* (%) (yes vs no)	7 (17.1)	21 (14.0)	0.90	0.40; 2.07	.812			
Recipient BMI, mean ± SD (per 1 kg/m^2)	25.6 ± 3.8	26.0 ± 4.0	1.01	0.93; 1.10	.857			
Recipient CCI score, mean ± SD (per 1 point)	4.4 ± 1.4	3.4 ± 1.2	1.76	1.40; 2.21	<.001	1.41	1.08; 1.85	.013
Unilateral nephrectomy before Tx, *n* (%) (yes vs no)	13 (31.0)	48 (31.8)	0.94	0.48; 1.83	.858			
Bilateral nephrectomy before Tx, *n* (%) (yes vs no)	5 (11.9)	17 (11.3)	1.00	0.39; 2.56	.999			
Donor age, mean ± SD (per 5 years)	61.1 ± 12.9	52.2 ± 13.6	1.26	1.12; 1.42	<.001	1.18	1.03; 1.35	.014
Donor $eGFR_{cr}$, mean ± SD (per 5 ml/min/1.73 m^2)	73.3 ± 26.6	86.3 ± 23.3	0.93	0.88; 0.98	.006	0.99	0.92; 1.05	.658
Living donor, *n* (%) (yes vs no)	7 (16.7)	61 (40.4)	0.34	0.14; 0.80	.014	0.98	0.33; 2.94	.976
Preemptive Tx, *n* (%) (yes vs no)	1 (2.4)	22 (14.6)	[c]					
AB0 compatible Tx, *n* (%) (yes vs no)	40 (95.2)	137 (90.7)	0.70	0.16; 2.96	0626			
Rejection episode, *n* (%) (yes vs no)	17 (40.5)	26 (17.2)	2.59	1.36; 4.92	.004	2.20	1.10; 4.40	.026
Patients with UTI or urosepsis, *n* (%) (yes vs no)	26 (61.9)	60 (39.7)	2.47	1.28; 4.75	.007			

[a]Hazard ratio estimated by Cox-proportional hazard model.
[b]Multivariable model was identified by LASSO regression.
[c]Parameter was not analyzed because of small population of cells in cross table.
Abbreviations: ADPKD, polycystic kidney disease; BMI, body mass index; CCI, Charlson Comorbidity Index; CI, confidence interval; eGFRcr, creatinine-based estimated glomerular filtration rate; HR, hazard ratio; SD, standard deviation; Tx, transplantation; UTI, urinary tract infection.

Table 9: Factors influencing the $eGFR_{cr}$ course in ADPKD patients.

	Univariable			Multivariable[b]		
$eGFR_{cr}$ course	beta[a]	95%CI	*P* value	beta[a]	95%CI	*P* value
Recipient age at Tx (per 5 years)	−3.58	−4.77; −2.39	<.001	0.13	−1.59; 1.85	.879
Waiting time (per 1 year)	−0.39	−1.14; 0.37	.313			
Female recipient (yes vs no)	−1.93	−7.29; 3.42	.479			
Recipient diabetes mellitus (yes vs no)	0.80	−6.72; 8.32	.835			
Recipient BMI (per 1 point)	−0.26	−0.94; 0.41	.446			
Recipient CCI score (per 1 point)	−4.92	−6.86; −2.98	<.001	−1.47	−3.94; 1.00	0.245
Unilateral nephrectomy before Tx (yes vs no)	3.99	−1.66; 9.64	.166			
Bilateral nephrectomy before Tx (yes vs no)	4.40	−3.86; 12.66	.296			
Donor age (per 5 years)	−3.36	−4.18; −2.54	<.001	−2.69	−3.54; −1.84	<.001
Donor $eGFR_{cr}$ (per 5 ml/min/1.73 m^2)	1.25	0.74; 1.76	<.001	0.44	−0.02; 0.90	.063
Living donor (yes vs no)	11.81	6.52; 17.10	<.001	7.38	1.98; 12.78	.007
Preemptive Tx (yes vs no)	9.51	1.38; 17.65	.022	0.35	−6.96; 7.65	.926
AB0 compatible Tx (yes vs no)	−0.50	−10.21; 9.20	.919			
Rejection episode (yes vs no)	−13.42	−19.46; −7.37	<.001	−13.07	−17.98; −8.16	<.001
Patients with UTI or urosepsis (yes vs no)	−0.72	−2.57; 1.13	.444			

[a]$eGFR_{cr}$ in follow-up was analyzed by a multilevel mixed-effects linear regression model.
[b]Multivariable model was identified by LASSO regression.
Abbreviations: ADPKD, polycystic kidney disease; BMI, body mass index; CCI, Charlson Comorbidity Index; CI, confidence interval; eGFRcr, creatinine-based estimated glomerular filtration rate; Tx, transplantation; UTI, urinary tract infection.

In conclusion, our results indicate that ADPKD patients are at increased risk for UTI and liver cyst infection including sepsis requiring inpatient treatment after kidney transplantation compared to non-ADPKD patients. Nevertheless, patient survival seems to be similar and graft survival, especially death-censored graft survival even superior. Recipient age and steroid treatment were associated with an increased risk for UTI/urosepsis, while nephrectomy of native kidneys seems to reduce it. Individually

tailored, steroid-free immunosuppression and nephrectomy of one or both native kidneys may help to reduce the risk of recurrent and severe infections in these patients.

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AUTHORS' CONTRIBUTIONS

J.W., J.K., L.d'A., and F.B. were responsible for conception and design of the work. J.W., P.G., D.S., M.N., N.L., L.d'A., and F.B. were responsible for data acquisition. J.K. and P.G. were responsible for data analysis. J.W., J.K., P.G., L.L., K.B., J.H., N.L., L.d'A., and F.B. were responsible for interpretation of data. J.W., J.K., P.G., L.L., K.B., J.H., F.H., B.Z., R.P., F.F., N.L., K.-U.E., L.d'A., and F.B. were involved in drafting and critically revising the manuscript. All authors reviewed and approved the final manuscript. J.W. and J.K. are co-first authors. L.d'A. and F.B. are co-senior authors.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

CONFLICT OF INTEREST STATEMENT

None declared.

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