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Success of Kidney Transplantations from Deceased Donors with Acute Kidney Injury

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Background: The acceptance of organs from deceased donors with acute kidney injury (AKI) varies considerably, with uncertain outcomes. The current organ shortage has led to increased use of marginal donor organs.


Material/Methods: This retrospective, single-center study included 642 patients who underwent kidney allograft transplantation between 2005 and 2016. The recipients were categorized into 3 groups: AKI-1 (n=214), comprising donors with a peak serum creatinine (SCr) level of 1.1–2.0 mg/dl; AKI-2 (n=89), comprising donors with a peak SCr level >2 mg/dl; and non-AKI (n=339), comprising donors with normal kidney function (SCr <1.1 mg/dl).

Results: The cumulative survival rates for patients and grafts did not significantly differ among the AKI-1, AKI-2, and non-AKI groups at the 1-year (91.6%/79.4%, 92.1%/83.1%, 95.3%/88.5%, respectively) and 5-year assessments (79.4%/67.8%, 86.8%/71.7%, 80.5%/71.1%, respectively). These findings were corroborated by mean SCr values and estimated glomerular filtration rates at the 1-year ($2.08 \pm 1.7/51.16 \pm 23.45$, $2.01 \pm 1.52/56.46 \pm 23.63$, $1.81 \pm 1.13/55.44 \pm 23.26$ mg/dl, respectively) and 5-year assessments ($1.91 \pm 1.28/51.06 \pm 24.65$, $1.74 \pm 0.66/57.44 \pm 31.21$, $1.7 \pm 0.88/58.56 \pm 26.04$ mg/dl, respectively). The incidence of delayed graft function in each group was 29.9%, 44.9%, and 28.6%, respectively.

Conclusions: Kidney transplantation from donors with AKI, although associated with a higher rate of delayed graft function, results in good long-term transplant survival and reliable kidney functionality after 5 years. The inclusion of donors with AKI may widely extend the pool of available organs; however, careful donor selection is necessary.

MeSH Keywords: Acute Kidney Injury • Delayed Graft Function • Graft Survival • Kidney Transplantation

Full-text PDF: <https://www.annalsoftransplantation.com/abstract/index/idArt/912660>

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Background

In Germany, there is still a considerable discrepancy between the number of organs available for transplantation and patients on waiting lists for kidney transplantation. This causes an increase in the patients' waiting periods until transplantation as well as their numerical mortality rates [1–4]. For many patients, early transplantation means a reduction in the mortality risk and an improvement of their quality of life [5–7]. The mean waiting time for a renal transplant, depending on the blood group, ranged between 62 and 90 months for German patients transplanted in 2016 [3]. The severe shortage of organs available for standard transplantation has led to an increase in living-donor kidney transplants on the one hand, and increased acceptance of marginal donor organs on the other. Feasible marginal donor strategies include the use of double-kidney transplants, including organs from elderly donors with an already reduced renal function [8,9], or the transplantation of organs derived from expanded criteria donors (ECDs) [10–12]. In addition, the transplantation of organs from donors with a history of acute kidney injury (AKI) is also possible, and is increasingly utilized [13]. It is still the case that kidneys from donors with AKI are considered suboptimal and refused, since the chance of full recovery of kidney function is difficult to assess and the concerns about successful transplantation have remained until today [14–16]. Thus, the use of organs from donors with AKI has been the subject of persistent controversy. While some studies have reported comparable rates of graft and patient survival after transplantation of kidneys from standard donors and those with AKI [17–21], others have described more unfavorable results [22]. Few studies on the long-term outcome of transplantation of organs from donors with AKI are currently available [14,17,21]. Therefore, the aim of the present retrospective study was to assess kidney graft and patient survival rates and parameters of organ function after AKI-derived transplantation in a large-cohort German study.

Material and Methods

The present study included all patients who received a kidney transplant from a brain-dead organ donor at the Transplantation Center of Bochum, Germany in the period between January 2005 and March 2016. The pre-operative cross-match analysis was negative in all cases. Living-donor and double-kidney transplants were excluded from the study. The analysis comprised patients' files, laboratory values derived from the electronic databank as well as the evaluation of EUROTRANSPLANT donor reports. Based on the donors' renal function, 3 groups were formed and compared: (i) the AKI-1 group, consisting of 214 patients who received a transplant from a donor with AKI combined with a peak serum creatinine (SCr) level of 1.1–2 mg/dL; (ii) the AKI-2 group, 89 patients with transplants from donors with AKI and peak SCr level of >2 mg/dL; and (iii) the Non-AKI

group, 339 patients who received transplants from donors with normal kidney function (SCr <1.1 mg/dL). Data collected from the donors' medical records included age, gender, body mass index (BMI), cause of death, history of hypertension or diabetes, SCr, ECD status, and cardiac arrest. We analyzed the following recipient parameters: patient and graft survival, SCr, estimated glomerular filtration rate (eGFR), the rate of biopsy-proven acute rejection episodes at one year, and the rates of delayed graft function (DGF) and primary non-function (PNF).

The criteria for donors were defined based on EUROTRANSPLANT donor reports, which included age, gender, cause of death, BMI, SCr at the time point of admission, SCr maximum value, latest determined SCr value prior to organ removal, eGFR according to the Cockcroft-Gault formula, and presence of diabetes mellitus and hypertension. Further criteria were previous cardiac arrest, smoking status, as well as catecholamine therapy. Group assignments were performed according to ECD and standard criteria donor (SCD). In accordance with the definition of the United Network of Organ Sharing, ECDs were defined as brain-dead organ donors, 60 years of age or older; or organ donors between 50 and 59 years fulfilling at least 2 of the 3 criteria of cerebrovascular cause of death, a last SCr value >1.5 mg/dL, or history of hypertension [11].

Analysis of recipient criteria included the following parameters: age, gender, BMI, duration and type of dialysis, cold ischemia time, duration of surgery, human leucocyte antigen (HLA) mismatch, cytomegalovirus serological status, panel-reactive antibodies, as well as induction and maintenance immunosuppression.

The primary objective of the study was to calculate patient and graft survival at 1, 3, and 5 years. Kidney graft function was assessed using eGFR rates according to the Cockcroft-Gault formula. Rejections were graded according to the Banff classification. Further outcome measures were the rates of DGF and PNF, as well as the duration of hospitalization. DGF was defined as the need for one or more hemodialysis treatments within the first week after transplantation [23]. Patients whose grafts never functioned were defined as having PNF.

Renal transplant failure was defined as patient death with a functioning graft, allograft nephrectomy, or the need for permanent dialysis or re-transplantation.

For statistical analysis, the chi-square test and Fisher's exact test were used to compare categorical variables. Continuous variables were compared between 2 groups using the Mann-Whitney U test, while the Kruskal-Wallis test was used to compare more than 2 groups. Patient and graft survival were calculated using the Kaplan-Meier method based on the log-rank test. All p-values <0.05 were considered statistically significant. Analysis was performed using SPSS version 23 (SPSS Inc, Chicago, IL).

Table 1. Donor characteristics.

	Non-AKI-group (n=339)	AKI-1 group (n=214)	AKI-2 group (n=89)	
Age (years)	55.28±16.08	56.91±15.68	49.31±16.34	p=0.001 ^{2,3}
Gender				
Female	206 (60.8)	82 (38.3)	19 (21.3)	p<0.001
Male	133 (39.2)	132 (61.7)	70 (78.7)	
Cause of death				
cerebrovascular/cardiovascular	275 (81.1)	173 (80.8)	67 (75.3)	NS
trauma	64 (18.9)	41 (19.2)	22 (24.7)	
BMI (kg/m ²)	25.9±4.1	27.8±4.6	29.8±6.9	p<0.001
Preservation solution				
HTK	280 (82.6)	186 (86.9)	78 (87.6)	NS
UW	57 (16.8)	28 (13.1)	7 (7.9)	
Unknown/others	2 (0.6)	0 (0)	4 (4.5)	
Serum creatinine at admission (mg/dL)	0.75±0.18	1.08±0.29	1.42±0.51	p<0.001
Terminal serum creatinine (mg/dL)	0.73±0.19	1.25±0.32	2.8±1.31	p<0.001
Peak serum creatinine (mg/dL)	0.81±0.17	1.39±0.24	3.19±1.52	p<0.001
Urine production during last hour (mL)	178.8±159.3 (n=323)	189.2±117.2 (n=193)	147.9±106.9 (n=81)	p=0.012 ^{1,2}
eGFR at admission (mL/min)	114.8±40.2	90.5±37.1	90.3±40.7	p<0.001 ^{1,3}
Terminal eGFR (mL/min)	120.5±49.2	80.3±39.7	47.2±20.9	p<0.001
Renal replacement therapy	0 (0.0)	1 (0.5)	9 (10.1)	p<0.001 ^{2,3}
Cardiac arrest	42 (12.4)	86 (40.2)	56 (62.9)	p<0.001
Use of catecholamines	292 (86.1)	185 (86.4)	83 (93.3)	NS
History of diabetes	24 (7.1)	37 (17.3)	12 (13.5)	p=0.001 ¹
History of hypertension	125 (36.9)	97 (45.3)	25 (28.1)	p=0.012 ²
Smoking	137 (40.4)	90 (42.1)	36 (40.4)	NS
ECD	167 (49.3)	125 (58.4)	39 (43.8)	p=0.032 ^{1,2}

¹ Significant difference between the Non-AKI group and the AKI-1 group; ² Significant difference between the AKI-1 group and the AKI-2 group; ³ Significant difference between the Non-AKI-group and the AKI-2 group. Values are given as mean ± standard deviation or n (% of group). Only p-values from the Kruskal-Wallis test are given. AKI – acute kidney injury; BMI – body mass index; ECD – expanded criteria donors; eGFR – estimated glomerular filtration rate; HTK – histidine-tryptophan-ketoglutarate; NS – not significant; UW – University of Wisconsin solution.

The study was approved by the local ethics board of the Faculty of Medicine at the Ruhr University of Bochum, Germany (registry number: 17-6106).

Results

In total, 642 kidney transplant recipients were included in this study. Among these, 303 (47.2%) received grafts from donors who suffered from renal functional impairment. The donor SCr was 1.1–2.0 mg/dl in 214 patients (33.3%; AKI-1 group),

>2 mg/dl in 89 patients (13.9%; AKI-2 group), and within normal values in 339 patients (52.8%; Non-AKI group). In addition, among the 642 donor kidneys, 331 (51.6%) had been classified as ECD organs and were mostly transplanted to patients in the AKI-1 group (n=125; 58.4%). The rate of ECD organs was 49.3% (n=167) in the Non-AKI group and 43.8% (n=39) in the AKI-2 group.

The characteristics of all organ donors are shown in Table 1. The donors of the AKI-2 group were significantly younger (mean age, 49.3±16.3 years) than those of the AKI-1 (mean age:

Table 2. Recipient characteristics.

	Non-AKI-group (n=339)	AKI-1 group (n=214)	AKI-2 group (n=89)	
Age (years)	54.6±12.9	56.2±13.0	55.6±11.4	NS
Gender				
Male	204 (60.2)	136 (63.6)	60 (67.4)	NS
Female	135 (39.8)	78 (36.4)	29 (32.6)	
BMI (kg/m ²)	25.7±4.2	25.8±4.7	26.4±3.9	NS
Time spent on dialysis (months)	78.3±45.2 (n=338)	76.3±45.9 (n=213)	84.0±39.5	NS
Type of dialysis				
HD	299 (88.2)	194 (90.7)	79 (88.8)	NS
CAPD	23 (6.8)	10 (4.7)	6 (6.7)	
HD/CAPD	14 (4.1)	9 (4.2)	4 (4.5)	
CMV				
R+/D+	150 (44.2)	90 (42.0)	45 (50.5)	NS
R+/D-	83 (24.5)	58 (27.1)	21 (23.6)	
R-/D+	63 (18.6)	37 (17.3)	15 (16.9)	
R-/D-	43 (12.7)	29 (13.6)	8 (9.0)	
HLA mismatch	2.6±1.7	3.0±1.7	2.9±1.5	p=0.014 ¹
Highest PRA >20%	33 (9.7)	23 (10.8)	10 (11.2)	NS
Cold ischemic time (min)	727.7±271.4	743.1±292.1	714.6±239.6	NS
Operation time (min)	198.4±52.4 (n=328)	200.1±55.5 (n=201)	225.5±73.1 (n=87)	p=0.004 ^{2,3}
Immunosuppressants				
ATG	268 (79.1)	160 (74.8)	65 (73.0)	NS
Tacrolimus	305 (90.0)	178 (83.2)	77 (86.5)	
CsA	25 (7.4)	19 (8.9)	7 (7.9)	

¹ Significant difference between the Non-AKI group and the AKI-1 group; ² Significant difference between the AKI-1 group and the AKI-2 group; ³ Significant difference between the Non-AKI-group and the AKI-2 group. Values are given as mean ± standard deviation or n (% of group). Only p-values from the Kruskal-Wallis test are given. ATG – anti-thymocyte globulin; BMI – body mass index; CAPD – continuous ambulatory peritoneal dialysis; CMV – cytomegalovirus; CsA – cyclosporine A; D – donor; HD – haemodialysis; HLA – human leucocyte antigen; NS – not significant; PRA – panel reactive antibodies; R – recipient.

56.9±15.7 years) and Non-AKI groups (mean age: 55.3±16.1 years; p<0.001). Regarding the gender distribution of the donors, a significantly higher portion of male donor organs was used for transplantation in both AKI groups compared to the Non-AKI group (p<0.001). In addition, donors in the AKI-1 and AKI-2 groups had significantly higher BMI values than those in the Non-AKI group (p<0.001). Consistent with the intergroup differences in donor characteristics, significant differences in kidney function parameters were observed. The eGFR of the organ donors, measured at admission, was significantly lower in the AKI-1 (90.5±37.1 mL/min) and AKI-2 groups (90.3±40.7 mL/min) than in the non-AKI group (114.8±40.2 mL/min). While regular improvement in kidney function was observed in the non-AKI group during the period between admission and organ removal (mean eGFR: 120.5±49.2 mL/min), a significant drop in eGFR values was noted in both AKI groups

during the same period (AKI-1 group: 80.3±39.7 mL/min; AKI-2 group: 47.2±20.9 mL/min). Renal replacement therapy with hemofiltration was required in 9 organ donors (10.1%) in the AKI-2 group, and 1 (0.5%) in the AKI-1 group. The highest measured mean SCr values were 3.2±1.5 mg/dL in the AKI-2, 1.4±0.2 mg/dL in the AKI-1, and 0.8±0.2 mg/dL in the Non-AKI groups. Moreover, previous cardiac arrests requiring cardiopulmonary resuscitation were significantly more frequent in the AKI-1 and AKI-2 groups, with the highest frequency observed in the AKI-2 group. The requirement for catecholamine therapy, however, did not differ between the 3 groups. With respect to previously existing diseases in the donor, arterial hypertension and diabetes mellitus were most frequent in the AKI-1 group. No significant differences were noted between the groups regarding cause of death, the use of perfusion solutions, or the number of smokers.

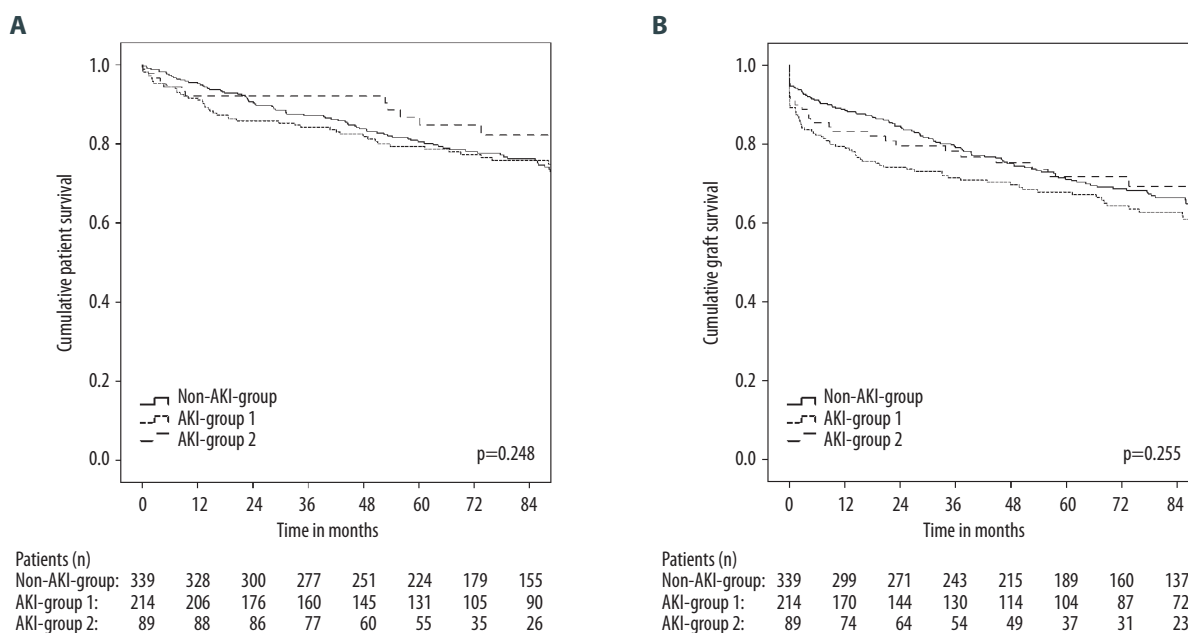


Figure 1. Kaplan-Meier curves for patient (A) and graft (B) survival. There was no significant difference in patient survival (log-rank test, $p=0.248$) and graft survival (log-rank test, $p=0.255$) between the AKI- groups and the non-AKI group. Graft loss includes death with a functioning graft. The number of patients at risk at each time point is shown in the lower portion of each figure. AKI – acute kidney injury.

The characteristics of all organ recipients are shown in Table 2. Most characteristics did not differ significantly between the 3 groups, with the exception of HLA mismatch and the duration of surgery. Regarding HLA mismatch, recipients in the Non-AKI group had significantly better matching rates. Similarly, our analysis showed a significantly longer duration of surgery in the AKI-1 and AKI-2 groups ($p=0.004$).

All patients received antibody induction therapy in combination with calcineurin inhibitors, mycophenolate mofetil, and tapered steroids. In most patients (76.8%), antithymocyte globulin (1.5 mg/kg per day, 1–5 times) was administered for induction therapy. In other cases, basiliximab (20 mg, twice) was used. Tacrolimus was typically started on posttransplant day 1, except when an organ from an AKI-donor was used. In such cases, tacrolimus therapy initiation was delayed by 3–5 days depending on renal function. Dosages were adjusted to achieve whole blood trough concentrations of 8–12 ng/ml for the first 2 months and 5–8 ng/ml thereafter. Mycophenolate mofetil was given orally from postoperative day 1 in a dose of 2 g/day. The steroid regimen consisted of 500 mg prednisolone intraoperatively and 250 mg prednisolone on posttransplant day 1. Thereafter, steroids were steadily tapered from 20 mg on day 2 to 5 mg by day 60.

The mean follow-up duration was 55.82 ± 34.97 months. Patient survival at 1 year was 95.3%, 91.6%, and 92.1% in the Non-AKI,

AKI-1, and AKI-2 groups, respectively. Patient survival at 5 years was 80.5%, 79.4%, and 86.8%. Log-rank testing showed no statistically significant differences ($p=0.248$) in survival at 1 and 5 years (Figure 1A). The 1-year survival rates of the kidney allografts were 88.5%, 79.4% and 83.1% in the Non-AKI, AKI-1, and AKI-2 groups, respectively, while the 5-year graft survival was 71.1%, 67.8% and 71.7%, respectively (log-rank test $p=0.255$). No significant difference was observed at either time point (Figure 1B).

The results of kidney transplantations performed in the 3 groups are shown in Table 3. DGF was significantly more frequent in the AKI-2 group (44.9%) than in the Non-AKI (28.6%) and AKI-1 groups (29.9%; $p=0.011$). PNF was similarly frequent in the AKI-1 and AKI-2 groups (10.3% and 10.1%, respectively) but was less frequent in the Non-AKI group (5.6%). No statistically significant differences were noted between the 3 groups ($p=0.09$). The cumulative biopsy-proven acute rejection rates (including borderline Banff changes) at 1 year were 26.3%, 29.4% and 25.8% in the Non-AKI, AKI-1, and AKI-2 groups, respectively. There was no difference between the groups.

The period of hospitalization was comparable in the 3 groups. The mean SCr value at discharge from inpatient treatment was 2.3 ± 1.7 mg/dL and 2.3 ± 1.2 mg/dL in the AKI-1 and AKI-2 groups, respectively, poorer than the values in the Non-AKI group (2.1 ± 1.6 mg/dL). A statistically significant difference was

Table 3. Results.

	Non-AKI group (n=339)	AKI-1 group (n=214)	AKI-2 group (n=89)	
Length of hospital stay (days)	33.4±39.1 (n=328)	31.0±27.8 (n=202)	30.6±15.7 (n=86)	NS
Serum creatinine at discharge (mg/dL)	2.1±1.6 (n=323)	2.3±1.7 (n=198)	2.3±1.2 (n=83)	p=0.04 ³
Primary function	223 (65.8)	128 (59.8)	40 (44.9)	p=0.001 ^{2,3}
DGF	97 (28.6)	64 (29.9)	40 (44.9)	p=0.011 ^{2,3}
PNF	19 (5.6)	22 (10.3)	9 (10.1)	NS
1-year rejection	89 (26.3)	63 (29.4)	23 (25.8)	NS
Rejection grade (Banff)				
Borderline	53 (59.5)	33 (52.4)	12 (52.2)	NS
IA	15 (16.9)	10 (15.9)	3 (13.0)	
IB	5 (5.6)	4 (6.3)	2 (8.7)	
IIA	15 (16.9)	14 (22.2)	6 (26.1)	
IIB	1 (1.1)	2 (3.2)	0	
Serum creatinine after 1 year (mg/dL)	1.81±1.13 (n=290)	2.08±1.7 (n=168)	2.01±1.52 (n=80)	NS
eGFR after 1 year (mL/min)	55.44±23.26 (n=288)	51.16±23.45 (n=167)	56.46±23.63 (n=77)	NS
Serum creatinine after 3 years (mg/dL)	1.65±0.77 (n=219)	2.18±2.1 (n=129)	2.3±2.23 (n=62)	p=0.001 ^{1,3}
eGFR after 3 years (mL/min)	59.31±25.31 (n=218)	50.99±23.94 (n=129)	52.28±27.17 (n=62)	p=0.006 ^{1,3}
Serum creatinine after 5 years (mg/dL)	1.7±0.88 (n=164)	1.91±1.28 (n=96)	1.74±0.66 (n=36)	NS
eGFR after 5 years (mL/min)	58.56±26.04 (n=164)	51.06±24.65 (n=96)	57.44±31.21 (n=36)	p=0.049 ¹

¹ Significant difference between the Non-AKI group and the AKI-1 group; ² Significant difference between the AKI-1 group and the AKI-2 group; ³ Significant difference between the Non-AKI-group and the AKI-2 group. Values are given as mean ± standard deviation or n (% of group). Only p-values from the Kruskal-Wallis test are given. AKI – acute kidney injury; DGF – delayed graft function; eGFR – estimated glomerular filtration rate; NS – not significant; PNF – primary non-function.

only noted between the AKI-2 and Non-AKI groups (p=0.04). The mean SCr values at 1, 3, and 5 years were 2.1±1.7, 2.2±2.1, and 1.9±1.3 mg/dL, respectively, in the AKI-1 group; 2.0±1.5, 2.3±2.2, and 1.7±0.7 mg/dL, respectively, in the AKI-2 groups; and 1.8±1.1, 1.7±0.8, and 1.7±0.9 mg/dL, respectively, in the Non-AKI group. Only the 3-year SCr value in the Non-AKI group was significantly different from that in the AKI groups (p<0.001).

Figure 2 shows the eGFR rates in all 3 groups at 1, 3, and 5 years. The Non-AKI group showed a significantly higher mean eGFR than the 2 AKI groups after 3 years (59.3±25.3 mL/min vs. 51±23.9 mL/min and 52.3±27.2 mL/min, respectively), whereas after 5 years, the only significant difference was between the Non-AKI and AKI-1 groups (58.6±26 mL/min vs. 51.1±24.7 mL/min).

Discussion

Kidney transplantation is a life-saving treatment for many patients suffering from end-stage kidney failure. Many patients, however, receive transplantations unacceptably late due to the long waiting time for appropriate donor organs. In Germany in particular, this limitation has increasingly resulted in the acceptance and transplantation of organs from marginal donors, donors whose age is no longer limited by any maximal limit or those with accompanying diseases or a reduced kidney function. This delimitation of selection stringency, however, has made decision making in transplant medicine more challenging. Patients must be transplanted in a timely manner, but the acceptance of organs from marginal donor may compromise successful transplantation. The present study, in which successful renal transplantation was confirmed in 642

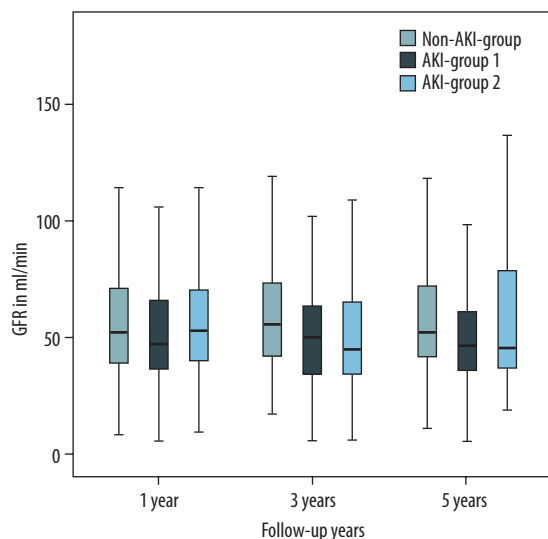


Figure 2. Estimated glomerular filtration rate (GFR in ml/min) 1, 3, and 5 years posttransplant.

patients with almost half the patients (47.2%) having received an organ from donors with reduced kidney function, may provide a solution to this conflict. Importantly, the study revealed promising long-term results, comparable to those for organs meeting standard criteria.

Thus, in the present study, the main findings were: (i) the cumulative survival rates of patients and kidney grafts did not differ significantly among the groups at both the 1-year and 5-year assessments; (ii) no significant differences in survival rates were noted among the 3 groups in any of the assessments; (iii) further important parameters, such as mean SCr, mean eGFR, acute rejection episodes, and incidence of DGF, were also considered very promising.

It should be emphasized that in many transplant centers the acceptance of donor kidneys with impaired function remains highly restricted. For the 642 kidney-transplanted patients in our center a maximal SCr value of >2 mg/dl was measured for 89 organ donors. In this group (AKI group 2), organ donors were younger, mostly male, and showed higher BMI. A constellation of factors that has also been associated with more promising kidney transplantation results in other studies [24–26]. It appears very likely that these factors actually contributed to organ acceptance, particularly in the case of young donors. For example, after traumatic death, recovery of kidney function can be expected, particularly in cases of short ischemia periods. In our own center, we have been reluctant to accept organs from elderly donors (>65 years of age) with already impaired renal function and possible co-morbidities, such as diabetes mellitus, arterial hypertension, or proteinuria.

Moreover, patients who received a functionally impaired renal transplant had significantly lower HLA matching rates. This may be because the patients may have received an organ that was ranked lower in the allocation list, as it had not been accepted at other transplantation centers, and this lower ranking could have been associated with an unfavorable HLA matching. These organs, having been rejected by other centers, were then accepted under the label of “rescue offer” or “center offer” with lower HLA matching stringency compared to those received via standard allocation. Notably, this was mostly observed when minimizing the ischemic time was a necessity and a donor kidney had to be accepted after AKI. Thus, it was not surprising that the ischemic period was shortest in the AKI-2 group (714.6 ± 239.6 min), although the difference among groups was not significant. Each kidney transplant from a donor with AKI or other associated functional impairments had explicitly been discussed with the recipient before surgery. Notably, none of the patients refused transplantation, given the opportunity to terminate chronic dialysis treatment as soon as possible. However, this seems to reflect a lack of perspective after years of dialysis.

Kidneys derived from donors with AKI have also been successfully transplanted by other groups [13,17–21,27–29]. In this regard, some authors applied the risk, injury, failure, loss of function, end-stage renal disease classification [30] or Acute Kidney Injury Network criteria [31] to subdivide individual groups of donors with AKI. We decided not to use these criteria in the present study because laboratory results of many organ donors ($n=106$) were only available for one date; therefore, the course of the kidney’s functional recovery could not be predicted. In a study by Jacobi et al. [32], 63 patients with AKI who could serve as kidney transplant donors were found among a total cohort of 382 brain-dead organ donors. The data were evaluated based on SCD (standard criteria donor) and ECD groups, with or without AKI. No significant difference in transplant survival was noted for either group between AKI and Non-AKI donors (SCD 91.8 vs. 91.3%; ECD 84.5 vs. 78.6%). In a further study involving 114 recipients of organs from donors with AKI (including 42 who had received organs from donors with severe AKI), comparable rates of patient and graft survival were seen at 1, 5, and 10 years [17]. In that study, the mean recipient and donor age was 37 years and the rate of ECD-type kidneys was 12.9%; thus, these results cannot be compared with those obtained in Germany. Interestingly, according to a retrospective analysis of the United Kingdom Transplant Registry published by Boffa et al. [15], among 11219 kidney transplantations investigated, 1869 organs were from donors with AKI. Transplant survival after 1 year was only 2% higher than that of organs from donors with AKI (91% vs. 89%). This slightly reduced transplant survival, however, may be negligible considering the otherwise prolonged time the patient would spend on the waiting list, with an annual death rate of 8.2%.

Moreover, DGF rates increased with the AKI stage of the donor (from 28% to 55%) and PNF rates were significantly higher for donor kidneys with severe AKI, such as Acute Kidney Injury Network (AKIN) stage ≥ 3 (9% vs. 4%).

In the present study, the rate of DGF was highest in the AKI-2 group, indicating a larger proportion of subjects with acute tubular necrosis than in the AKI-1 group. In contrast, the mean donor serum creatinine concentration of 1.25 mg/dl at discharge in the AKI-1 group indicates a higher proportion of prerenal AKI in this group. The higher DGF rate in the AKI-2 group was consistent with that reported in previous studies, which also showed an increased DGF rate after transplantation of kidney grafts derived from donors with AKI. Hall et al. reported a DGF rate similar to the one in our Non-AKI group (28%), whereas the DGF rate proportionally increased from 34% to 57% with the severity of AKI [16]. Another study described DGF rates of 66% or 74% in patients who had received SCD or ECD kidneys from donors with AKI, respectively, as compared to a DGF rate of 27% in the Non-AKI group [20]. It is well known that the occurrence of DGF can be associated with an increased rate of acute organ rejection, a lower overall kidney function, as well as a lower rate of transplant survival [33–37]. Such diminished kidney function and survival rates, however, were not detected in the present investigation. On the contrary, both graft survival rates and kidney function in our study were similarly high in patients with and without DGF. Other research groups have reported similar results, whereby the occurrence of DGF after kidney transplantation impaired neither kidney survival nor kidney function [14,17,20,21,28,38]. For example, Farney et al. showed that DGF in an AKI group had no measurable negative impact on transplant survival. In comparison, a significantly lower transplant survival was observed in a Non-AKI group [19]. Despite the higher rates of DGF in the AKI groups, we did not see an increased risk of rejection episodes within the first-year posttransplant.

As shown in the present study, PNF was more frequent in the AKI-1 and AKI-2 groups (approximately 10%) than in the non-AKI group (5.6%); however, this difference was not significant. The rate of PNF varies in the literature; for example, it ranged between 2.1% and 2.4% in the study by Farney et al. [19], and 1.5% and 10% in the study by Jacobi et al. [32]. In both reports, however, no correlation was found between PNF and the nature of AKI in the donor. The study by Boffa et al., on the other hand, reported that AKI, particularly AKIN stage 3 or higher, affected the occurrence of PNF [15].

Generally, potential recipients of kidneys from donors with AKI should be informed that permanent kidney non-function or early graft rejection might occur. In the present study, the provision of this information did not prompt any patient to

refuse the transplantation. Besides this necessity to provide additional information, based on our results and those of a number of other research groups, we can confirm that the transplantation of grafts derived from donors with AKI can result in positive long-term results, significantly enlarging the available kidney donor pool.

Nevertheless, the acceptance of organs from donors with AKI remains a controversial issue. This point is substantiated by existing studies describing lower rates of kidney function and survival after transplantation of organs from donors with AKI [15,22] despite the very limited quantitative disadvantage with respect to kidney function and survival of organs from donors with AKI reported by Boffa et al. [15]. Interestingly, Kolonko et al. described an impaired long-term functionality of kidneys from donors with AKI and an increased risk of transplant loss in an AKI group. Thus, the authors suggest restricting the use of organs from donors with AKI, particularly in the case of young recipients [22].

In the context of the present study, we continually tried to strictly follow our own center's strategies concerning the acceptance of organs derived from donors with AKI. These strategies aim to achieve early functional onset of the transplanted organs. Moreover, with these strategies we try to restrict the use of organs to those with short ischemic periods (<12 hours), avoid warm ischemic periods by applying permanent ice-cooling systems during anastomosis, use T-cell-depleting antibodies to induce immunosuppression, and avoid calcineurin inhibitors during the early postoperative course. Nevertheless, this study had some limitations, as is typical of a retrospective, monocentric study. The etiology of kidney failure in the respective organ donors was multifactorial and has not been further evaluated. Moreover, we cannot fully exclude selection bias, since in many cases, the kidneys of donors with AKI had only been accepted when the donors presented no further risks and ischemic periods had been short. Finally, the AKI-2 group was slightly younger than the AKI-1 and the non-AKI groups. These limitations, however, must be considered in light of the described benefits, and future investigations must further clarify this debate based on additional data.

Conclusions

Results of the present study suggest that donor kidneys from individuals with a history of AKI, although associated with a higher rate of DGF, result in long-term transplant acceptance and reliable kidney function after 5 years. Thus, the inclusion of donors with AKI may widely extend the pool of available donor organs; however, careful donor selection is necessary.

References:

1. Meier-Kriesche HU, Ojo AO, Port FK et al: Survival improvement among patients with end-stage renal disease. *J Am Soc Nephrol*, 2001; 6: 1293–96
2. Oniscu GC, Brown H, Forsythe JLR: Impact of cadaveric renal transplantation on survival in patients listed for transplantation. *J Am Soc Nephrol*, 2005; 6: 1859–65
3. Eurotransplant International Foundation. Annual Report 2016 [cited 2018 Apr 20]. Available from: <https://www.eurotransplant.org/cms/mediaobject.php?file=Eurotransplant+JV+PDF.pdf>
4. Wolfe RA, Ashby VB, Milford EL et al: Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med*, 1999; 23: 1725–30
5. Czyżewski L, Sańko-Resmer J, Wyzgał J, Kurowski A: Assessment of health-related quality of life of patients after kidney transplantation in comparison with hemodialysis and peritoneal dialysis. *Ann Transplant*, 2014; 19: 576–85
6. Overbeck I, Bartels M, Decker O et al: Changes in quality of life after renal transplantation. *Transplant Proc*, 2005; 3: 1618–21
7. Tomasz W, Piotr S: A trial of objective comparison of quality of life between chronic renal failure patients treated with hemodialysis and renal transplantation. *Ann Transplant*, 2003; 2: 47–53
8. Rigotti P, Capovilla G, Di Bella C et al: A single-center experience with 200 dual kidney transplantations. *Clin Transplant*, 2014; 28: 1433–40
9. Paolis P de, Colonnelli R, Favaro A et al: Expanded criteria donor kidney transplantation. *Transplant Proc*, 2016; 2: 329–32
10. Yang SS, Yang J, Ahn C et al: The need for new donor stratification to predict graft survival in deceased donor kidney transplantation. *Yonsei Med J*, 2017; 3: 626–30
11. Rosengard BR, Feng S, Alfrey EJ et al: Report of the Crystal City Meeting to maximize the use of organs recovered from the cadaver donor. *Am J Transplant*, 2002; 8: 701–11
12. Ferreira E, Costa J, Romãozinho C et al: Long-term outcomes of kidney transplantation from expanded-criteria deceased donors. *Transplant Proc*, 2017; 4: 770–76
13. Klein R, Galante NZ, Sandes-Freitas TV de et al: Transplantation with kidneys retrieved from deceased donors with acute renal failure. *Transplantation*, 2013; 4: 611–16
14. Kayler LK, Garzon P, Magliocca J et al: Outcomes and utilization of kidneys from deceased donors with acute kidney injury. *Am J Transplant*, 2009; 2: 367–73
15. Boffa C, van de Leemkolk F, Curnow E et al: Transplantation of kidneys from donors with acute kidney injury. *Am J Transplant*, 2017; 2: 411–19
16. Hall IE, Schroppel B, Doshi MD et al: Associations of deceased donor kidney injury with kidney discard and function after transplantation. *Am J Transplant*, 2015; 6: 1623–31
17. Ali T, Dimassi W, Elgamal H et al: Outcomes of kidneys utilized from deceased donors with severe acute kidney injury. *QJM*, 2015; 10: 803–11
18. Benck U, Schnuelle P, Krüger B et al: Excellent graft and patient survival after renal transplantation from donors after brain death with acute kidney injury. *Int Urol Nephrol*, 2015; 12: 2039–46
19. Farney AC, Rogers J, Orlando G et al: Evolving experience using kidneys from deceased donors with terminal acute kidney injury. *J Am Coll Surg*, 2013; 4: 645–55; discussion 655–56
20. Heilman RL, Smith ML, Kurian SM et al: Transplanting kidneys from deceased donors with severe acute kidney injury. *Am J Transplant*, 2015; 8: 2143–51
21. Lee MH, Jeong E-G, Chang JY et al: Clinical outcome of kidney transplantation from deceased donors with acute kidney injury by Acute Kidney Injury Network criteria. *J Crit Care*, 2014; 3: 432–37
22. Kolonko A, Chudek J, Pawlik A et al: Acute kidney injury before organ procurement is associated with worse long-term kidney graft outcome. *Transplant Proc*, 2011; 8: 2871–74
23. Mallon DH, Summers DM, Bradley JA, Pettigrew GJ: Defining delayed graft function after renal transplantation. *Transplantation*, 2013; 10: 885–89
24. Giral M, Nguyen JM, Karam G et al: Impact of graft mass on the clinical outcome of kidney transplants. *J Am Soc Nephrol*, 2005; 1: 261–68
25. Rao PS, Schaebel DE, Guidinger MK et al: A comprehensive risk quantification score for deceased donor kidneys. *Transplantation*, 2009; 2: 231–36
26. Taherimahmoudi M, Mehra S, Nikoobakht M et al: Does donor nephron mass have any impact on graft survival? *Transplant Proc*, 2007; 4: 914–16
27. Yu CC, Ho HC, Yu TM et al: Kidneys from standard-criteria donors with different severities of terminal acute kidney injury. *Transplant Proc*, 2014; 10: 3335–38
28. Jung CW, Park KT, Kim SY et al: Clinical outcomes in kidney transplantation patients from deceased donors with acute kidney injury. *Transplant Proc*, 2013; 8: 2941–45
29. Matos AC, Requião-Moura LR, Clarizia G et al: Expanding the pool of kidney donors. *Einstein (Sao Paulo)*, 2015; 2: 319–25
30. Bellomo R, Ronco C, Kellum JA et al: Acute renal failure – definition, outcome measures, animal models, fluid therapy and information technology needs. *Crit Care*, 2004; 4: R204–12
31. Mehta RL, Kellum JA, Shah SV et al: Acute kidney injury network. *Crit Care*, 2007; 2: R31
32. Jacobi J, Rebhan D, Heller K et al: Donor acute kidney injury and short-term graft outcome in renal transplantation. *Clin Transplant*, 2014; 10: 1131–41
33. Johnston O, O'Kelly P, Spencer S et al: Reduced graft function (with or without dialysis) vs. immediate graft function – a comparison of long-term renal allograft survival. *Nephrol Dial Transplant*, 2006; 8: 2270–74
34. Butala NM, Reese PP, Doshi MD, Parikh CR: Is delayed graft function causally associated with long-term outcomes after kidney transplantation? Instrumental variable analysis. *Transplantation*, 2013; 8: 1008–14
35. Siddiqi N, McBride MA, Hariharan S: Similar risk profiles for post-transplant renal dysfunction and long-term graft failure. *Kidney Int*, 2004; 5: 1906–13
36. Yarlagadda SG, Coca SG, Formica RN et al: Association between delayed graft function and allograft and patient survival. *Nephrol Dial Transplant*, 2009; 3: 1039–47
37. Tapiawala SN, Tinckam KJ, Cardella CJ et al: Delayed graft function and the risk for death with a functioning graft. *J Am Soc Nephrol*, 2010; 1: 153–61
38. Rodrigo E, Miñambres E, Piñera C et al: Using RIFLE criteria to evaluate acute kidney injury in brain-deceased kidney donors. *Nephrol Dial Transplant*, 2010; 5: 1531–37