Acute Graft Pyelonephritis Occurring up to 30 Days After Kidney Transplantation: Epidemiology, Risk Factors, and Survival

L.V. Kroth*, F.F. Barreiro, D. Saitovitch, M.A. Traesel, D.O.L. d'Avila, and C.E. Poli-de-Figueiredo

Programa de Pós-graduação em Medicina e Ciências da Saúde, FAMED/IPB/HSL, Pontifícia Universidade Católica do Rio Grande do Sul (Nefrologia), Porto Alegre, Brazil

ABSTRACT

Acute graft pyelonephritis is a very common infection in renal transplantation. The impact of acute graft pyelonephritis (AGPN) on graft and patient outcome has not yet been established. Eight hundred seventy kidney and kidney-pancreas transplants were retrospectively studied, over last 13 years, to verify occurrence of AGPN in the first 30 days post-transplantation. We found that 112 patients (15.8%) presented post-transplantatiom AGPN up to 30 days after a kidney transplantation. The occurrence was higher in older patients ($P = .005$) and in those with ureteral stents ($P = .06$). *Escherichia coli* was the most frequent microorganism in urine cultures (32%). Ureteral stent (relative risk = 1.7; confidence interval [CI], 1.1–2.5; $P = .018$) was a major risk factor for AGPN as well as older ages (RR = 1.02; CI 1.01–1.04; $P = .001$), length of hospitalization stay (RR = 1.01; CI, 1.01–1.02; $P < .001$), and anti-thymocyte globulin (ATG) induction (RR = 1.6; CI, 1.022–2.561; $P = .04$). Long-term graft and patient survival was significantly lower in patients with pyelonephritis in the first 30 days after transplantation (OR 1.43; 95% CI, 0.95–2.16; $P = .024$ and OR 1.77; 95% CI, 1.12–2.80; $P = .006$, respectively). Acute pyelonephritis in the first 30 days after transplantation is therefore associated with a lower long-term graft and patient survival.

URINARY TRACT INFECTIONS (UTIS) are the most common infection in renal transplant recipients and are an important cause of morbidity and graft failure [1].

Some risk factors are independent predictors of acute pyelonephritis. Pretransplantatiom episodes of pyelonephritis, recurrent asymptomatic bacteriuria, ureteral stent, urinary tract malformations, cytomegalovirus infection, use of mycophenolate, and rejection were identified as risk factors for occurrence of graft pyelonephritis [2–4]. Biopsy-proven rejection in the first month after treatment of graft pyelonephritis suggests acute pyelonephritis as a risk factor for rejection [5].

The impact of acute graft pyelonephritis (AGPN) on graft and patient outcome has not yet been established. Pellé et al reported AGPN as an independent risk factor associated with decrease in creatinine clearance, although with no effect on graft and recipient survival [6]. Fiorante et al in a retrospective study suggested that acute graft pyelonephritis does not impair long-term graft function [2]. Kamath et al and Giral et al, also in retrospective analysis, found lower graft survival in patients with AGPN, however, without statistical significance. On the other hand, Giral demonstrated worse graft outcome in an analysis of pyelonephritis in the first 3 months [3,4].

The present study was aimed to assess the prevalence, characteristics, and risk factors for early AGPN, occurring in the first 30 days post-transplantatiom, and to evaluate the impact of this complication on long-term graft and patient survival.

MATERIALS AND METHODS

We performed a retrospective cohort study of kidneys and pancreas-kidneys transplantatioms at São Lucas Hospital, a tertiary-care university hospital. All transplantatioms from January 1, 2000 to April 30, 2013 were considered to be included into the study, and follow-up until April 30, 2014. Patients whodied in the first 30 days post-transplantatiom or had primary graft failure, defined as permanent absence of graft function starting immediately post-transplantation, were excluded from the study.

*Address correspondence to Leonardo Viliano Kroth, Division of Nephrology, Hospital São Lucas, Av. Ipiranga 6690, 3rd Floor, CEP 90610-000 Porto Alegre, RS, Brazil. E-mail: leonardo.kroth@pucrs.br

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Acute pyelonephritis was diagnosed when a patient had fever or bacteremia and a urine culture showing $>10^5$ colony forming units (CFU)/mL with the presence of urinary symptoms (graft pain, dysuria, or frequency) in the absence of other foci of infection.

We collected information on clinical characteristics, including age, gender, type and number of transplantations, cold ischemic time, delayed graft function (DGF), acute rejection, donor characteristics, mortality, and laboratory data. Patients were divided into two groups according to the presence (AGPN group) or absence (non-AGPN group) of acute pyelonephritis 30 days before the transplantatiom.

Statistical analysis was performed with IBM SPSS Statistics for Mac, version 22. Kolmogorov-Smirnov test was used to evaluate if variables had a normal distribution. Normally continuous variables were expressed as mean ± standard deviation. Nonparametric distributed variables were presented as median and interquartile range (25th–75th percentile). Fisher exact test was used for comparison of categorical data, *t* test for normal continuous variables, and Mann-Whitney *U* test for nonparametric variables. Univariate analysis was introduced in a multivariate model based on forward stepwise logistic regression to identify independent risk factors for the development of AGPN. Analysis of variance (ANOVA) multivariate analysis for repeated measures was used to verify differences between renal functions in different times. Kaplan-Meier analyses were performed to obtain descriptive curves and univariate log-rank statistics. Associations are given as odds ratios (ORs) with a confidence interval of 95% (95% CI). A 2-sided value of $P < .05$ was considered statistically significant. This study was approved by the University Ethics Committee.

RESULTS

A total of 807 transplantations, including 755 kidney and 52 kidney-pancreas transplantations were performed at our hospital. Seventy-five patients (9.3%) were excluded due to primary graft failure and death within the first month post-transplantation and 24 patients were lost during the follow-up period. The 708 patients who remained were included in the analysis.

The prevalence of 30 days AGPN in transplantation was 15.8% (112 cases), with a 15.4% prevalence rate in women. Most patients, in this study, were male, white, transplanted from deceased donors, and with no differences between the patients who had or did not have pyelonephritis. The average ischemia time was 17.7 ± 10.4 and 18.0 ± 9.7 hours in the graft pyelonephritis group and the non-pyelonephritis group, respectively ($P = .748$). No differences also occurred as Class I Panel-Reactive Antibodies (PRA), Thymoglobulin induction and occurrence of delay graft function (Table 1).

The mean age in the graft pyelonephritis group was significantly higher compared with the nonpyelonephritis group, 45.9 ± 15.9 and 41.1 ± 16.7 years, respectively ($P = .005$). The use of ureteral stent was higher in the pyelonephritis group (66.1% vs 56.4%), however, without reaching a significant statistical difference ($P = .06$).

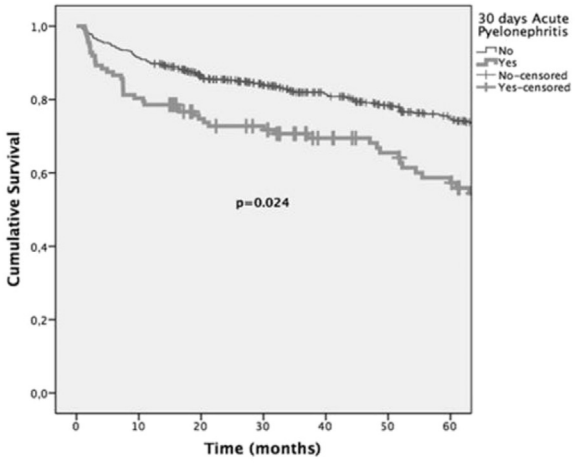
The patients with pyelonephritis had a longer hospitalization period (34.5 ± 29.4 days) compared with patients without pyelonephritis in the first 30 days after transplantation (20.9 ± 17.0 days; $P < .001$). *Escherichia coli* was the most frequent microorganism in urine cultures (32%), followed by *Enterococcus faecalis*, *Klebisella pneumoniae*, and *Enterobacter* species with 19%, 15%, and 15%, respectively.

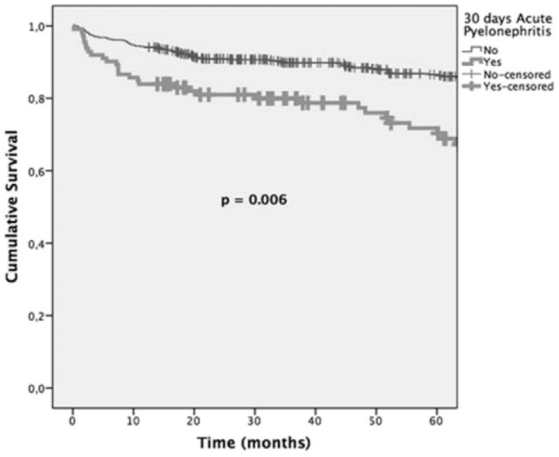
A Cox model analysis was performed in patients who presented 30-day post-transplantation AGPN to determine whether some factors related to transplantation could have an impact on AGPN development. Ureteral stent (relative risk [RR] = 1.7; CI, 1.1–2.5; $P = .018$) was a major risk factor for AGPN as well as older ages (RR = 1.02; CI, 1.01–1.04; $P = .001$), length of hospitalization stay (RR = 1.01; CI, 1.01–1.02; $P < .001$), and anti-thymocyte globulin (ATG) induction (RR = 1.6; CI, 1.01–1.02; $P = .04$).

Table 1. Clinical Characteristics of Patients With 30 Days Post-transplantation AGPN and Non-AGPN Group

Characteristics	Total (n = 708)	AGPN Group (n = 112)	Non-AGPN Group (n = 596)	*P*
Age, mean y ± SD	41.85 ± 16.6	46.1 ± 15.7	41.0 ± 17.0	.002
Race, white n (%)	623 (88%)	95 (84.8%)	528 (88.6%)	.268
Gender, female n (%)	325 (45.9%)	50 (44.6%)	275 (46.1%)	.836
Deceased donor, n (%)	561 (79.2%)	91 (81.3%)	470 (78.9%)	.614
Cold ischemia, median h (IQR)	19 (12.9–24.8)	20 (13.8–23.9)	19 (12.8–25.0)	.639
PRA class I, median (IQR)	0 (0–1)	0 (0–2)	0 (0–1)	.587
ATG use, n (%)	288 (40.7%)	41 (36.6%)	247 (41.4%)	.348
ECD, n (%)	114 (16.1%)	14 (12.5%)	100 (16.8%)	.001
Pre-Tx HD time, median mo (IQR)	25 (11–51)	27 (12–55)	25 (11–50.8)	.512
Ureteral stent, n (%)	410 (57.9%)	74 (66.1%)	336 (56.4%)	.061
DGF, n (%)	299 (42.2%)	54 (48.2%)	245 (41.1%)	.176
Length of stay, median d (IQR)	17 (11–27)	27 (17–43)	16 (11–24)	<.001
Pre-Tx diagnosis, n (%)				
Unknown	135 (19.1%)	11 (9.8%)	124 (20.8%)	.006
Diabetes	134 (18.9%)	32 (28.6%)	102 (17.1%)	.008
Glomerulonephritis	134 (18.9%)	20 (17.9%)	114 (19.1%)	.895
Malformations	84 (11.9%)	14 (12.5%)	70 (11.7%)	.873
APKD	54 (7.6%)	10 (8.9%)	44 (7.4%)	.562
Others	301 (42.5%)	45 (40.2%)	256 (43%)	.731

Abbreviations: IQR, interquartile range; ATG, anti-thymocyte globulin induction; ECD, expanded criteria donor; Pre-Tx, pretransplantation; HD, hemodialysis; DGF, delayed graft function; APKD, autosomic polycystic kidney disease; IQR, interquartile range.





	All Patients		30 days Acute Graft Pyelonephritis		30 days Non-Acute Graft Pyelonephritis	
Time (months)	Graft Survival (%)	Patients at Risk	Graft Survival (%)	Patients at Risk	Graft Survival (%)	Patients at Risk
12	88.1	623	89.3	101	89.9	535
24	84.4	516	78.6	89	85.3	444
36	80.2	429	74.7	77	81.9	367
60	72.2	314	69.5	53	75	272

	All Patients		30 days Acute Graft Pyelonephritis		30 days Non-Acute Graft Pyelonephritis	
Time (months)	Patient Survival (%)	Patients at Risk	Patient Survival (%)	Patients at Risk	Patient Survival (%)	Patients at Risk
12	92.4	624	89.3	101	94.1	560
24	89.1	517	81.0	80	90.9	471
36	87.9	430	80.0	68	89.9	398
60	85.4	315	70.3	50	86.6	310

Fig 1. Kaplan-Meier analysis of graft (**A**) and patient (**B**) survival according to AGPN and non-AGPN groups.

Allograft serum creatinine level in months 1, 3, 6, 12, and 60 was worse in the AGPN group, however, no significant relevance was found when compared with the non-AGPN group.

Long-term graft and patient survival was significantly lower in patients with pyelonephritis in the first 30 days after transplantation (OR, 1.43; 95% CI, 0.95–2.16; $P = .024$ and OR, 1.77; 95% CI, 1.12–2.80; $P = .006$, respectively; Fig 1).

Pretransplantation diabetes was found in 28.6% of patients in the AGPN group compared with 17.1% in the non-AGPN group ($P = .008$).

DISCUSSION

Early AGPN, occurring within the first 30 days after transplantation, is a common complication in kidney transplantation. The prevalence of 15.8% in this study is consistent with the prevalence of 16.5% of pyelonephritis occurring at any time of transplantation found in the study bu Kamath et al [3] and 10% and 13% found by Fiorante and Giral, respectively [2,4].

AGPN occurred more frequently in older recipients with a pretransplantation diagnosis of diabetes mellitus. Length of hospital stay was significantly correlated with the occurrence of AGPN, but it may be associated with the risk of developing and or as a consequence of infection on its own.

Like other studies urinary tract malformations and ureteral stent were associated with AGPN [3,4]. In this population we found ureteral stent as the main risk factor.

In patients who have not lost the graft, renal function was worse in the AGPN group, however, no significant difference was found, as in the study by Fiorante et al [2].

The main finding of this study was to demonstrate significantly worse survival of the graft and patient, not found in other studies. Only one retrospective cohort study showed only graft survival in cases of AGPN at the first 3 months after transplantation.

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