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Ureteral Complications: Analysis of Risk Factors in 1000 Renal Transplants

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PUBLICATIONS on ureteral complications in renal transplantation usually only discuss technical factors. Very few investigators have assessed the role of other risk factors in the development of this problem. Some researchers have pointed out the role of rejection in the development of ureteral stenosis. However, they neither characterize the lesions nor propose any etiologic pathogenic mechanism,[1–3] or believe that the ureteral lesions are a consequence of ischemia from rejection of the renal vessels.[4,5] Even recent studies from renowned investigators ignore the role of rejection in the development of ureteral complications.[6–8]

PATIENTS AND METHODS

We analyzed 1000 consecutive renal transplants performed at our institution from July 1980 to February 2001, regarding the occurrence of ureteral complications. A database was constructed from the records of all donors and recipients. We evaluated parameters of the donor (age, cause of death, weight, ventilation time, harvesting technique, perfusion solution, cold ischemia time), the recipient (age, time on dialysis, associated pathology, weight, etiology of renal failure, HLA mismatches, ureteral implantation technique, ureteral length, duration of surgery), and the transplant course (immunosuppression, delayed graft function [DGF], acute rejection [AR] episodes, cyclosporine [CyA] dose at 1 year). The occurrence of ureteral complications was correlated with the development of chronic graft dysfunction (CGD) and with graft survival. The ureteral fragments retrieved during revision surgeries were studied for the presence of lesions suggestive of rejection. A multiple logistic regression analysis was used to assess the adjusted effect of all donor, recipient, and transplant parameters on ureteral complications. Univariate analysis was evaluated with the Fisher Exact Test. The Kaplan-Meier method was employed to estimate graft survival and the log-rank test to compare survival rates between the two groups (with or without ureteral complications). For all tests a P value $<.05$ was considered significant (two-tailed).

RESULTS

Fifty-six patients (5.6%) developed ureteral complications, including 31 stenoses and 25 fistulae. One patient with a fistula died. The patient, a 60-year-old man with coronary disease, presented with a fistula on the fourth day and underwent ureteric reimplantation, but he developed cardiorespiratory failure that was complicated by sepsis. The kidney graft was removed on the 23rd day, but he died the next day. All other ureteral complications were successfully treated; no other patient or graft was lost as a direct consequence of a ureteral complication. Twenty-four of 25 fistulae presented in the first month after transplant, whereas for the 31 stenoses the average time for presentation was 20.5 months, ranging from 10 days to 11 years.

None of the donor factors were significantly associated with the occurrence of ureteral complications. Without reaching statistical significance, some factors were theoretically even more favorable among the cases that developed complications. The global cold ischemia time for the 1000 transplants was 20.7 hours, versus 19.6 and 19.9 hours in cases that developed stenoses and fistulae, respectively. Similarly, no recipient factor was significantly associated with the development of ureteral complications. The low number of ureteroureterostomies performed does not allow any conclusion to be drawn from the relatively high number of complications observed with this technique (Table 1). In the absence of a measurement, the probable ureteral length was calculated from the site of placement of the arterial vascular anastomosis, assuming that the ureteral segment was long when the graft was anastomosed on the aorta, medium when anastomosed on the common iliac, and short when on the external or internal iliac vessels. Only 977 cases of bladder implantation were considered, the *psoic* bladder case being excluded. The analysis did not reveal statistically significant association between ureteral length and the development of ureteral complications (Table 2).

The development of ureteral complications was significantly associated with the occurrence of CGD ($P = .019$). Furthermore, the association with DGF was close to statistical significance ($P = .054$), an association that was statistically significant when the stenoses were considered separately ($P = .000$) (Table 2).

Actuarial graft survivals at 1, 3, 5, 10, and 15 years were 96%, 86%, 72%, 62%, and 40%, respectively, for the group with ureteral complications, and 91%, 85%, 78%, 63%, and 54%, respectively, for the group without, a difference that was not statistically significant.

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Table 1. Correlation Between Technical Factors and Development of Ureteral Complications

Implantation Technique (n = 1000)	Ureteral Complications: Fistulae	Stenoses	Fistulae + Stenoses/Total
LG + external stent (594)	17	19	6.0%
LG + "JJ" stent (248)	5	5	4.0%
LG without stent (28)	–	1	3.6%
Politano–Leadbetter (88)	1	3	4.5%
Barry–Hatch (17)	–	1	5.9%
Ureteroureterostomy (17)	2	2	23.5%
Other (8)	–	–	–
Ureteral Length* (n = 977)			
Long (7)	1	–	14.2%
Medium (828)	25	16	4.9%
Short (142)	3	7	7.0%

LG, Lich-Gregoir.
*Presumed after the arterial anastomoses placement.

For comparisons between fistulae and stenoses, we studied the same donor, recipient, and transplant parameters. The small number of cases limited the analysis, but we found that many more stenoses than fistulae presented with a history of DGF, a difference that was statistically significant ($P = .000$). Similarly, more stenoses than fistulae were associated with a history of AR episodes, a difference that was not statistically significant ($P = .098$) (Table 3). Only six ureteral fragments from surgical revision of complications were available for histological study: three from stenosis cases and three from fistula cases. While the three fistula cases showed only nonspecific inflammatory infiltrates, all fragments from the stenotic ureters presented lesions suggestive of AR, including epithelial permeation and interstitial infiltration by T lymphocytes and arterial endothelialitis with intimal fibrosis.

DISCUSSION

The incidence of ureteral complications, which varies between 3% and 20%, has not changed substantially over the last decades. Reports on surgical complications of kidney transplantation only seldom address the hypothetical etiological role of immunological factors in the study of risk factors. The correlation that we observed between ureteral complications and evolution to CGD may signify that some ureteral complications result from rejection phenomena. These same episodes occurring at the kidney level may favor the development of CGD. Conversely, the resemblance between the kidney lesions secondary to ureteral obstruction and the lesions of CGD suggest another hypothesis. Recent studies of CGD and obstructive nephropathy in rat models demonstrate that both conditions are correlated with macrophage infiltration, cytokine liberation, tubular atrophy, and interstitial fibrosis.[9–12] This finding raises the question whether ureteral stenoses, even incipient ones, contribute to chronic graft rejection processes.[8]

Table 2. Correlation Between Ureteral Complications and Risk Factors

Factors	Ureteral Complications (n = 56)	*P* Value	Odds Ratio	Confidence Interval 95%
Chronic dysfunction (n = 918)				
Yes	8.6%	.019	1.960	1.107–3.470
No	4.7%			
DGF (n = 971)				
Yes	9.1%	.054	1.845	0.982–3.468
No	5.1%			
	Stenoses (n = 31)			
DGF (n = 971)				
Yes	7.8%	.000	3.549	1.686–7.472
No	2.3%			

DGF, delayed graft function.

Table 3. Comparison Between Fistulae and Stenoses

Factors	Ureteral Complications (n = 56): Fistulae	Stenoses	*P* Value
DGF			
Yes	8%	38.7%	.000
No	92%	61.3%	
Acute Rejection			
Yes	20.8%	41.9%	.098
No	79.2%	58.1%	

DGF, delayed graft function.

CONCLUSION

We identified a statistically significant relationship between ureteral complications and DGF and CGD. Graft survival in the patients with ureteral complications was the same as in patients without these complications. The early appearance of fistula suggests a technical or ischemic origin, whereas the late development of stenosis may be due to rejection episodes, according to our histopathological findings.

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