ELSEVIER

Outcomes of Renal Transplantation in Patients With Major Lower Limb Amputation

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ABSTRACT

Introduction. The impact of severe peripheral vascular disease on graft survival in patients undergoing renal transplantation is poorly defined. The aim of our study is to establish outcomes in renal transplant recipients who have severe peripheral vascular disease necessitating major lower limb amputation.

Methods. Data for patients undergoing renal transplantation from January 2001–December 2010 was extracted from a regional transplantation database. Patients undergoing lower limb amputation pre- and post-transplantation were identified and outcome measures including delayed graft function, biopsy-proven acute rejection, serum creatinine level at 1 year, and graft loss and recipient survival at 1 year and long-term were compared with patients who did not undergo amputation. Student t and Pearson's chi-squared tests were used to compare patients with and without amputation and Kaplan-Meier curves were used for survival analysis. A P value $< .05$ is considered statistically significant.

Results. A total of 762 patients underwent renal transplantation. Four (0.5%) patients had an amputation before transplantation and 16 (2.1%) underwent amputation after transplantation. Serum creatinine levels at 1 year were significantly higher in patients who had amputation after transplantation (308.5 $\pm$ 60.8 μmol/l vs 177.6 $\pm$ 6.4 μmol/l; $P = .03$). During longer follow-up (mean: 2053.1 $\pm$ 58.3 days), patients who underwent amputation after transplantation had a higher rate of graft loss ($P < .01$) and higher death rate ($P < .01$).

Conclusion. The requirement for amputation after renal transplantation is associated with poor long-term graft and patient survival and higher serum creatinine levels at 1 year. Patients at increased risk of severe peripheral vascular disease should be identified and measures taken to reduce the long-term risk.

DISEASE of the peripheral vasculature is common in patients with end-stage renal failure (ESRF), with a prevalence of approximately 25% [1]. Risk factors for the development of generalized atherosclerosis in this group of patients include advancing age, hypertension, and diabetes. Furthermore, patients on hemodialysis treatment have additional risk factors for vascular calcification such as hyperphosphatemia and hypercalcemia [2]. In the unique subgroup of patients undergoing renal transplantation, the risk of developing peripheral vascular disease (PVD) may also be increased by immunosuppression therapy which is thought to contribute to or exacerbate hyperglycemia, hypertension, and hyperlipidemia [3].

There are a number of specific concerns when considering transplantation in patients who have severe PVD. These include the presence of calcified iliac vessels which may complicate or preclude a vascular anastomosis at time of surgery [4,5] and a syndrome analogous to steal, whereby the kidney transplant results in redirection of blood flow from an already vulnerable limb that could result in distal ischemia. The latter is a theoretical risk that has been suggested by several authors [6,7], but the direct impact of transplantation on distal blood flow is yet to be ascertained.

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0041-1345/13/$–see front matter
http://dx.doi.org/10.1016/j.transproceed.2013.07.073

Patients with PVD are generally considered high risk for renal transplantation. As such, many patients will undergo preoperative imaging of their iliac vessels to ensure a suitable site for implantation and maximize safety in this patient group. Lately the increasing trend to improve access to renal transplantation in older, more comorbid patients [8] has led to an expansion of this practice.

The aim of our study is to assess outcomes in renal transplant recipients who have severe PVD necessitating major lower limb amputation with regard to graft function and long-term recipient survival. We have also observed the subgroup of patients who have had a lower limb amputation before transplantation with regard to their graft function and long-term survival. By assessing outcomes, we can establish the importance of identifying high-risk patients before transplantation to improve outcomes.

METHODS

Study Population

All patients undergoing deceased and living donor renal transplantation at the Western Infirmary, Glasgow, United Kingdom, between January 2001 and December 2010 were included in the study. Retrospective analysis of a prospectively collected regional transplantation database was performed. Basic patient characteristics and risk factors for PVD were recorded. Patients who underwent major lower limb amputation in the form of above-knee amputation (AKA) or below-knee amputation (BKA) were identified. Timing of amputation in relation to the transplantation was ascertained and outcome measures for patients undergoing amputation pre- and post-transplantation were compared to those who were not amputated. For the group of patients who were amputated post-transplantation, details regarding other revascularization procedures and attempts at limb salvage were recorded.

Outcomes

For all patients who underwent lower limb amputation either before or after transplantation the following outcomes were established: delayed graft function (DGF, defined as the need for dialysis within the first week after transplantation); biopsy-proven acute rejection (BPAR); primary nonfunction (PNF; as defined by failure of the transplanted kidney to function within the first 6 weeks post-transplantation); and creatinine level, graft loss, and patient survival at 1 year. Long-term graft and patient survival rates were also established. These outcomes were compared with patients who did not undergo amputation.

Statistical Analysis

All data were analyzed with statistical software SPSS for Windows, version 16 (SPSS Inc, Chicago, Ill, United States). Descriptive statistics are presented as frequencies for categorical variables, mean (standard error of the mean [SEM]) for continuous variables, and median (interquartile range) for ordinal variables.

Continuous variables with normal distribution were compared using the Student t test. A Mann-Whitney U test was used for variables that were not normally distributed. Categorical variables were assessed using Pearson's chi-squared test. A Kaplan-Meier method was used for comparison of graft loss and time to death in patients who had amputations pre- and post-transplantation. A P value $< .05$ was regarded to be statistically significant. Backward stepwise multiple regression analysis was performed to include all factors, with a P value $< .1$ showing statistical significance on univariate analysis. Results are presented as relative risks (95% confidence intervals).

RESULTS

A total of 762 patients underwent kidney transplantation at the Western Infirmary, Glasgow between January 2001 and December 2010. Patient demographics, characteristics and the incidence of pre- or post-operative amputation for each group are listed in Table 1.

Amputations Pre–Kidney Transplantation

A total of four (0.5%) patients had undergone major lower limb amputation before transplantation. All of these patients suffered from diabetic nephropathy as their underlying etiology of ESRF. Two patients had undergone a left BKA, one patient underwent a right BKA, and one patient underwent a left AKA. In all patients, the kidney was transplanted into the contralateral side to the amputation. All patients were imaged using computed tomography

Table 1. Patient Characteristics

	Whole Population	Amputations Pretransplantation	Amputations Post-transplantation	*P* Value
No. of patients (%)	762	4 (0.5)	16 (2.1)	
Mean age (y ± SEM)	43.3 ± 0.5	46.3 ± 0.72	50 ± 0.62	<.01
Gender (%)				
Male	450 (59)	3 (75)	9 (56.3)	
Female	312 (41)	1 (25)	7 (43.7)	NS
Type of donor (%)				
DBD	536 (70.2)	3 (75)	14 (87.5)	NS
DCD	25 (3.3)	0 (0)	0 (0)	NS
LD	200 (26.2)	1 (25)	2 (12.5)	NS
Dual transplant	1 (0.1)	0 (0)	0 (0)	NS
Mean donor age (y ± SEM)	44.9 ± 0.52	54.3 ± 0.77	55.6 ± 0.56	<0.01
Mean duration of pre-transplant dialysis (y ± SEM)	3.3 ± 0.14	4.0 ± 0.45 (1 pre-dialysis)	4.3 ± 0.24	0.02
No. with diabetic nephropathy (%)	53 (6.9)	4 (100)	6 (37.5)	<0.01
No. with hypertensive nephropathy (%)	33 (4.3)	0 (0)	0 (0)	NS

Abbreviations: DBD, donor after brain death; DCD, donor after cardiac death; LD, living donor.