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Functional Status of Hemodialysis Arteriovenous Fistula in Kidney Transplant Recipients as a Predictor of Allograft Function and Survival

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ABSTRACT

There is no accepted policy for preserving or ligating arteriovenous fistula (AVF) after successful kidney transplantation. The aim of this study was to compare kidney graft function and survival between patients with a functional AVF at 1 year after-transplantation with those having a nonfunctional AVF. This historical cohort study included 311 kidney transplant recipients between January 2000 and December 2008 with a functional AVF at the time of transplantation. Patients were divided into 2 groups according to functional status of AVF at 1 year after transplantation. Graft function was assessed at 1 year by serum creatinine and estimated glomerular filtration rate (eGFR) using the 4-variable Modification of Diet in Renal Disease formula. Kaplan-Meier and Cox proportional hazards analyses were used to assess the relationship between the functional status of the AVF and graft survival. The 311 recipients had a mean age of 47 ± 11 years (range, 14 to 70) with 188 (60.5%) males. Patients with functional AVF at 1 year (n = 239) showed higher serum creatinine and lower eGFR values than those with nonfunctional AVF (n = 72): namely 110 ± 38 μmol/L and 69 ± 21 mL/min/1.73 m^2 versus 99 ± 30 μmol/L and 74 ± 19 mL/min/1.73 m^2, respectively ($P < .05$). Persistence of a functional AVF at 1 year after transplantation was associated with a greater incidence of eGFR <60 mL/min/1.73 m^2 compared with nonfunctional AVF: 36.8% versus 23.6% (odds ratio, 1.885; 95% confidence interval [CI], 1.031–3.450; $P = .038$). The 5-year allograft survival rates were 60% among patients with a functional AVF versus 75% among those with a nonfunctional AVF ($P = .045$). The adjusted analyses revealed the persistence of a functional AVF to be associated with an increased risk for future allograft loss (hazard ratio, 1.336; 95% CI, 1.018–1.755; $P = .037$). In conclusion, the persistence of a functional AVF was associated with a lower eGFR at 1 year after-transplantation and an increased risk for future allograft loss.

THE ARTERIOVENOUS fistula (AVF) for hemodialysis remains functional after kidney transplantation in many patients. There is no accepted policy to preserve or close the AVF after successful transplantation.[1] Recent Kidney Disease: Improving Global Outcomes guidelines on kidney graft recipients have not addressed this problem.[2] A few studies on AVF after kidney transplantation have focused on cardiac morphology and function. A regression of left ventricular hypertrophy after surgical AVF closure was demonstrated, in the short term[3] as well as the long term.[4] However, residual concentric remodeling hypertrophy as well as increased diastolic pressure may blunt the expected beneficial cardiac effects.[4,5] The effects of a functional AVF on kidney allograft function are unclear. The aim of the present historical cohort analysis was to evaluate the natural history of AVF among renal allograft recipients

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This study was supported in part by Grant No. J3-9183-0312 of the Ministry of Education, Science and Technology of the Republic of Slovenia.

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0041-1345/10/$–see front matter
doi:10.1016/j.transproceed.2010.09.057

comparing kidney function and survival between patients with versus without (spontaneous or surgical closure) a functional AVF at 1 year after transplantation.

PATIENTS AND METHODS

We transplanted 402 consecutive recipients with deceased-donor kidney grafts between January 1, 2000, and December 31, 2008. Because the aim of the study was to investigate the influence of the functional status of the AVF on graft function and survival, we only considered patients with a functional AVF at the time of transplantation. We did not evaluated recipients with early graft loss, nonfunctioning kidneys, technical failures, or patient deaths during the first year. The final study cohort included 311 recipients who were on hemodialysis treatment with functional AVFs at the time of transplantation. The follow-up ranged from 1 to 9 years. Donor and recipient variables were collected from the prospectively maintained institutional database. Patients were divided into 2 groups according to the functional status of the AVF at 1 year after transplantation: a functional versus a nonfunctional AVF. The functional status of AVF was recorded during regular check-ups after transplantation. Kidney graft function was assessed at 1 year after-transplant by estimated glomerular filtration rate (eGFR) using the 4-variable Modification of Diet in Renal Disease equation.[6]

Continuous variables were expressed as mean ± SD or as median (interquartile range). The differences between patient groups were compared using unpaired Student *t* test or Mann-Whitney *U* test for normally and nonnormally distributed data, respectively. Categoric variables were compared using the chi-square test. Kaplan-Meier and Cox proportional-hazards analyses were used to assess the relationship between AVF function and graft survival. All statistical analyses were performed using the SPSS statistical software (version 16.0; SPSS, Chicago, IL, USA). Two sided *P* values of <.05 were considered to be statistically significant.

RESULTS

Table 1 shows the baseline characteristics of the study population according to the functional status of the AVF at 1 year after transplantation. Among 311 recipients, whose mean age was 47 ± 11 years (range, 14–70), 188 (60.5%) were male. At 1 year after transplantation, 239 recipients (76.8%) had a functional AVF. Among all AVF, 284 (91.3%) were located in the forearm, 24 (7.7%) in the upper arm, and 3 (0.9%) in the thigh. Age, gender, and fistula location showed no significant influence on AVF patency at 1 year after transplantation. Among 72 recipients with a nonfunctional AVF, 70 recipients had spontaneous closure, and only 2 needed surgical closure. Both groups were similar regarding recipient gender and age, donor age, positive versus negative panel-reactive antibodies, delayed graft function, and acute rejection episodes.

Table 1. Baseline Characteristics of the Study Population 1 Year After Kidney Transplantation According to Functional Status of Arteriovenous Fistula

Characteristic	Arteriovenous Fistula at 1 Year		*P* Value
	Functional (n = 239)	Nonfunctional (n = 72)	
Recipient age (y)	47.9 ± 11.1	45.4 ± 11.6	.09
Recipient gender (M/F)	147/92	41/31	.48
Donor age (y)	39.3 ± 14.1	37.3 ± 14.1	.71
PRA (%)	5.35 ± 12.58	5.47 ± 10.2	.94
HLA mismatch	2.62 ± 1.16	2.97 ± 0.97	.02
Delayed graft function	64	16	.44
Acute rejection	16	8	.22

Data are total number, percentage, mean ± SD, or median (interquartile range).

Table 2. Kidney Graft Function and Survival According to Functional Status of Arteriovenous Fistula 1 Year After Transplantation

Variable	Arteriovenous Fistula at 1 Year		*P* Value
	Functional (n = 239)	Nonfunctional (n = 72)	
Serum creatinine (μmol/L)	110 ± 38	99 ± 30	.046
eGFR (mL/min/1.73 m^2)	69 ± 21	74 ± 19	.047
eGFR <60 mL/min/1.73 m^2 (%)	36.8	23.6	.038
5-year graft survival rate (%)	60.0	75.0	.045

Data are mean ± SD or percentage.

Patients with functional AVF displayed a higher serum creatinine and a lower eGFR than those with nonfunctional AVF (Table 2). Persistence of a functional AVF at 1 year after-transplantation was associated with a greater incidence of eGFR <60 mL/min/1.73 m^2 compared with nonfunctional AVF: 36.8% versus 23.6% (odds ratio, 1.885; 95% confidence interval [CI], 1.031–3.450; $P = .04$). The 5-year graft survival rates were 60% among patients with functional AVF and 75% with nonfunctional AVF ($P = .045$; Table 2).

The average duration of follow-up was 5.8 years for the entire cohort. Altogether, 24 patients lost their grafts: 20 (6.4%) with a functional AVF and 4 (1.2%) patients with a nonfunctional AVF ($P = .38$). The adjusted hazard ratio for graft loss among patients with functional AVF compared with patients with nonfunctional AVF is presented in Table 3 Patients with a functional AVF at 1 year after-transplant showed a significantly greater risk for future graft loss ($P = .037$).

DISCUSSION

The results of the present study demonstrated that mainly spontaneous closure of the AVF after kidney transplanta-

Table 3. Hazard Ratio for Graft Loss in Patients with a Functioning Arteriovenous Fistula at 1 Year After-Transplantation in the Adjusted Model*

Outcome	Hazard Ratio	95% Confidence Interval	*P* Value
Graft loss	1.336	1.018–1.755	.037

*Covariates: donor and recipient age, transplants from expanded criteria donor kidneys, delayed graft function, and acute rejection in the first year.

tion was associated with better graft function at 1 year after-transplantation with a decreased risk for future graft loss. The majority of previously published studies on AVF after kidney transplantation have focused on cardiac function and morphology. They studied cardiac function before and after surgical closure of high-blood-flow AVF suggesting a significant contribution of patent AVF on residual cardiac hypertrophy.[3,7] Moreover, the presence of a patent AVF was a risk factor for cardiovascular events.[9]

It is important to know that premature cardiovascular disease is a major cause of graft loss and the leading cause of death among renal transplant recipients.[10–12] Among patients with end-stage kidney disease, left ventricular hypertrophy and dilation are frequent.[13] Left ventricular hypertrophy is a major predictor of death and congestive heart failure. Hypertension, anemia, ischemia, and plasma volume expansion appear to be the main stimuli for ventricular remodeling.[14,15] Patent AVF causes additional changes in hemodynamics. It increases cardiac output by reducing peripheral resistance and increases cardiac contractility, stroke volume, and heart rate.[16] Chronic volume overload induces structural and functional cardiac changes, including ventricular remodeling.[3,4] Renal transplantation corrects uremia, anemia, and volume status, but the prevalence of ventricular hypertrophy remains high.[4,5]

Unger et al demonstrated reduction in left ventricular diameter and mass after surgical AVF closure upon short-term[3] and long-term follow-up.[4] However, in a recent prospective study with 24-hour ambulatory blood pressure monitoring, the same authors demonstrated increased diastolic blood pressure after AVF closure, regardless of the preoperative diastolic pressure.[5] In a case-controlled study Cridlig et al demonstrated that a functioning AVF has a significant impact on cardiac mass, cardiac index, and left ventricular dimensions among stable asymptomatic kidney graft recipients.[8]

The present study demonstrated an additional argument in favor of AVF closure after successful kidney transplantation: better kidney graft function at 1 year and better 5-year graft survival. However, it is not clear whether closure of AVF (which was spontaneous in the vast majority of our patients) is the cause or the consequence of better kidney graft function.

Although AVF closure after kidney transplantation may be beneficial for both cardiac and renal function, it is important to stress that AVF can still be useful in some situations. It can be used as a vascular access for chronic plasma exchange or immunoadsorption to treat recurrent focal segmental glomerular sclerosis or during plasma exchange to treat antibody-mediated rejection. Sometimes it can be used for intravenous therapy to avoid central venous catheter placement when peripheral veins are exhausted or the use of large veins is mandatory. In addition, the lifespan of a kidney graft is limited, and permanent vascular access may again be necessary. These are some of the reasons for our reluctance to systematically close the AVF after transplantation, as also illustrated by the results of our study demonstrating that only a minority of our patients underwent a surgical closure. However, if spontaneous closure occurs, we believe that salvage of AVF is not indicated, except for patients with advanced stages of chronic kidney disease. The results of our study and the association of an functional AVF with kidney graft function support this approach. Surgical closure (sometimes with extirpation) is indicated in the presence of an AVF-related clinical problem: high flow, aneurysm, thrombophlebitis, cosmetic effect. Preoperative ultrasonography mapping to assess other possibilities for native AVF construction in the future may provide help in the sometimes complex decision regarding AVF closure.

This possible approach for systematic surgical AVF closure in kidney graft recipients warrants further study. Our work has provided an argument for the possible beneficial effects on kidney graft function of spontaneous AVF closure. Regarding surgical closure, we approach each patient individually, in general we ligate or extirpate an AVF only when there is a clinical problem.

In conclusion, the persistence of a functional AVF was associated with a lower eGFR at 1-year after transplantation and an increased risk for future allograft loss. Prospective studies should investigate whether elective fistula closure in selected patients is associated with kidney graft function and survival.

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