Transplant International

LETTER TO THE EDITOR

Closure of high-volume arteriovenous fistulas improves kidney allograft function in patients with right heart failure

doi:10.1111/j.1432-2277.2009.00968.x

Potential kidney transplant recipients (KTRs) are screened intensively for the prevalence of coronary artery disease and left ventricular hypertrophy [1], but less attention is given to the prevalence of right heart failure (RHF) or pulmonary hypertension (PH) in patients with end-stage renal disease (ESRD). As PH with consecutive chronic RHF is associated with tricuspid regurgitation [2], inferior cavous vein congestion and subsequent iliac congestion [2,3], accompanied by deleterious effects on kidney allograft perfusion may arise from reduced venous efflux [3].

Arteriovenous fistulas (AVFs) have been shown to contribute to cardiac abnormalities in KTRs [4,5], but their impact on RHF, right ventricular dilatation or kidney allograft function has thus far not been evaluated. To emphasize the importance of RHF in ESRD patients and to demonstrate the impact of iliac congestion on the kidney allograft, we retrospectively analysed four patients who presented with an echocardiographic finding of a dilated right ventricle after kidney transplantation.

Patients and methods

All four patients included in this study were identified in our transplant center in 2008 (8% of all deceased donor kidney transplantations) and did not differ in their usual transplant conditions. None of these patients complained about reduced physical condition or pulmonary distress. They were on hemodialysis prior to kidney transplantation (6 ± 2.2 years) and were among the 23% of KTRs in our center that had at least one dialysis treatment within the first week post-transplant (delayed graft function, DGF). All four patients were biopsied showing acute tubular necrosis and absence of rejection. These KTRs received triple immunosuppression regimen consisting of methylprednisolone, mycophenolate mofetil and one of the calcineurin inhibitors.

Duplex ultrasound measurements and echocardiographic studies were performed according to current guidelines [6,7]. Right heart catheterization (RHC) was performed after 30 min of rest. After measuring the cardiac index (CI), the AVF was compressed with a blood pressure cuff until fistula flow was barely audible with a stethoscope. Mean pulmonary artery pressure (MPAP), CI and pulmonary capillary wedge pressure (PCWP) were re-evaluated under compression of the AVF. PH was diagnosed, wherever the MPAP was equal or >25 mmHg [8]. As RHC confirmed RHF resulting from high-flow AVF in the KTRs, closure of AVF was performed about 17 ± 3 days post-transplant in our center to improve kidney allograft function.

Results

Duplex ultrasound detected high-flow AVF (>2.5 l/min fistula flow) as well as a pathologic biphasic flow pattern in the kidney allograft vein of all four KTRs. This was indicative for tricuspid regurgitation and iliac congestion (Fig. 1a). After AVF closure, normal linear flow patterns in the allograft and iliac vein were detected in these patients (Fig. 1b).

Echocardiographic investigation revealed a moderately to severely dilated right ventricle with a flattened septum, paradoxical septal movements and severe tricuspid regurgitation associated with elevated pulmonary artery pressure (PAP) (Table 1, Fig. 1c). The measured ejection fraction was above 65% prior to and after AVF closure, demonstrating that left ventricular function was not impaired in any of the patients. RHC demonstrated a significant elevated MPAP and CI but normal PCWP, which confirmed the echocardiographic findings. After AVF obliteration, PAP and MPAP decreased significantly ($P < 0.05$, paired t-test, Table 1) and CI decreased about 25% to 3.2 ± 0.8 l/min/m^2 ($P = 0.055$). Subsequently, right ventricle dilatation resolved (Fig. 1d).

Impressively, urine output significantly improved within 24 h after AVF closure from 630 ± 120 ml/day to 2360 ± 830 ml/day ($P < 0.01$, paired t-test). This was associated with significant improvement of kidney allograft function in the patients (Table 1). Interestingly, the improvement of allograft function after AVF closure in the KTRs was associated with a significant reduction of total proteinuria, albuminuria and alpha$_1$-microglobulinuria by 55%, 60% and 70% respectively within 24 h after intervention (Table 1).

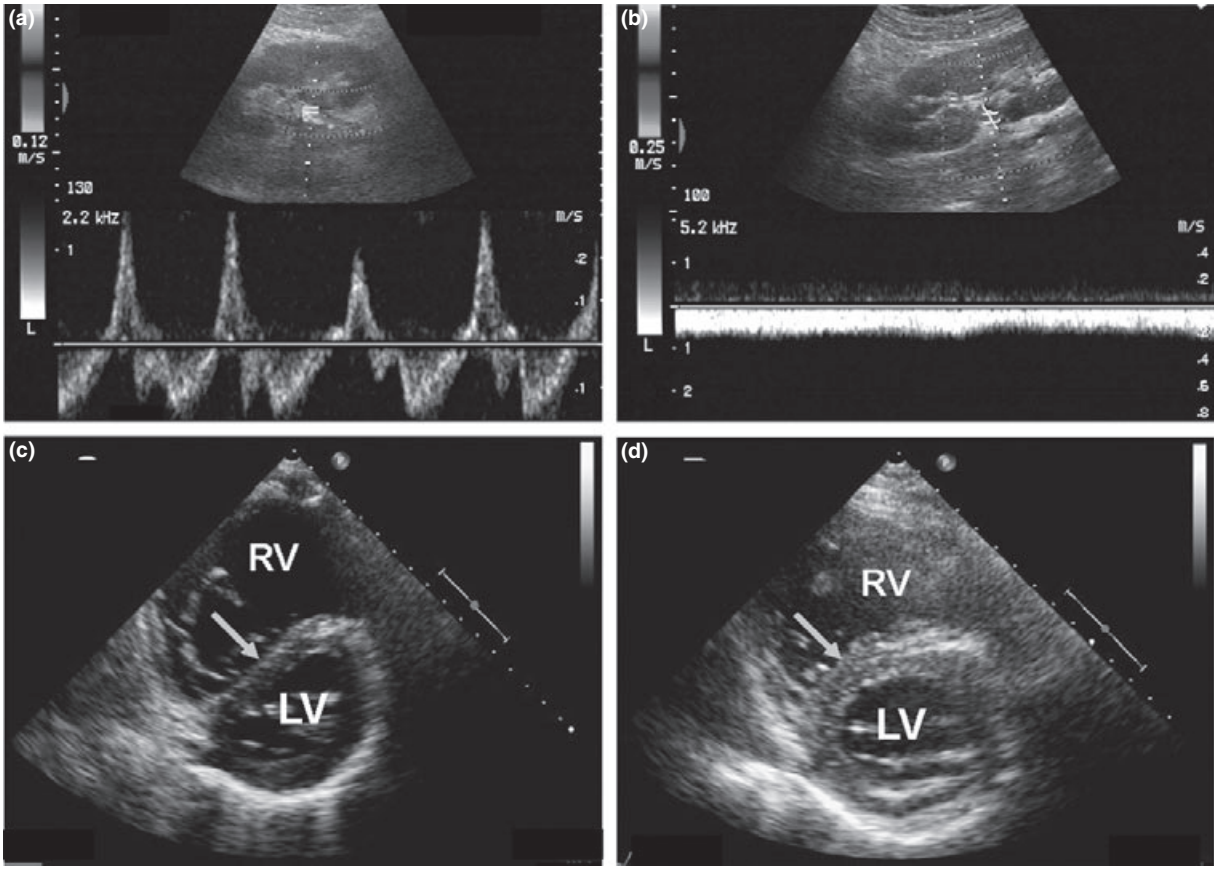

Figure 1 Duplex ultrasound of kidney allograft vein (a, b) and echocardiography (c, d) prior to (a, c) and after arteriovenous fistula (AVF) closure (b, d). The arrow indicates the septum. RV, Right ventricle; LV, Left ventricle.

Discussion

The results of our study show that KTRs with RHF, consecutive tricuspid regurgitation [2] and iliac congestion are at risk for the development of delayed and marginal graft function. We hypothesized, that reduction of venous efflux of the kidney allograft resulting from PH [2,3] represents the underlying mechanism for DGF in our patients. This is supported by our finding that successful treatment of PH significantly improved allograft function in KTRs within 24 h after intervention. This improvement of allograft function was associated with a decrease of 'congestion albuminuria', and a reduction of alpha$_1$-microglobulinuria reflecting the recovery of renal tubular function after AVF closure.

Even if the natural course of DGF is favorable in most KTRs, the immediate response to intervention (24 h) and absence of other adverse factors such as volume depletion or rejection further strengthens our hypothesis. Several investigations revealed that high renal venous pressure is associated with higher creatinine levels or kidney injury in patients with decompensated heart failure [3,9]. These studies indicate that our observed effect of PH on renal function is not only restricted to transplanted kidneys, as similar effects might play a role in native kidneys as well [3,9].

The incidence of PH varies between 10% and 40% of KTRs and is related to patient survival [10,11]. Thus treatment of PH and RHF in ESRD patients seems to be essential to reduce the risk of DGF and poor long-term outcome after kidney transplantation [3]. High volume AVF have been proven to elevate left ventricular end-diastolic diameter (LVEDD), cardiac index and right atrial area [12,13] as observed in our study. Thus, increasing right ventricular cardiac output [14] and LVEDD produced by high-volume AVF can contribute to an elevated PAP. This pathological mechanism is supported by recent studies demonstrating that AVF flow is the most significant variable correlating with PH in ESRD patients [11] and AVF closure may reverse elevated LVEDD [5,15].

To optimize post-transplant outcomes, we recommend routine echocardiographic and duplex ultrasound investi-

Table 1. Echocardiography, right heart catheterization and laboratory results

Parameters	Prior to intervention	After intervention	*P*-value
Echocardiographic parameters	7 days prior to AVF closure	7 days after AVF closure	
Left ventricular diameter			
LVEDD (mm)	48.0 ± 3.8	46.4 ± 3.7	NS
LVESD (mm)	30.6 ± 2.0	27.3 ± 1.6	NS
Ejection fraction (%)	64 ± 4	68 ± 7	NS
LAD (mm)	47 ± 4.9	44 ± 3.6	NS
RVD (mm)	43 ± 5.8	33 ± 6.1	0.013
PAP (mmHg)	38 ± 8	28 ± 9	0.008
Right heart catheterization parameters	Within one session 5 days prior to AVF-closure		
MPAP [mmHg]	32 ± 8	22 ± 7*	0.022
CI [l min/m^2]	4.7 ± 1.8	3.2 ± 1.1*	NS
PCWP [mmHg]	17 ± 2	16 ± 2*	NS
Laboratory parameters	24 h prior to AVF closure	24 h after AVF closure	
Plasma creatinine (μmol/l)	378 ± 98	225 ± 110	0.031
Creatinine clearance (ml/min)	12 ± 2.5	29 ± 14	0.022
Urine output (ml/24 h)	630 ± 120	2360 ± 830	0.007
Proteinuria (g/g creatinine)	0.9 ± 0.2	0.4 ± 0.2	0.021
Albumin (mg/g creatinine)	376 ± 101	153 ± 62	0.041
α_1-Microglobulin (mg/g creatinine)	349 ± 281	102 ± 34	0.038
Weight (kg)	76 ± 21	77 ± 22	NS

LVD, left ventricular diameter; LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end systolic diameter; LAD, left atrial diameter; RVD, right ventricular diameter; PAP, pulmonary artery pressure; MPAP, mean pulmonary artery pressure; CI, cardiac index; PCWP, pulmonary capillary wedge pressure; NS, not significant. Shown are means ± SD; *after AVF compression.

gations prior to kidney transplantation with a focus on right ventricular dilatation and iliac congestion to detect hemodynamic-relevant high-flow AVF. To clarify the impact of PH on allograft survival, larger studies are needed to address this problem.

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