American Journal of Transplantation 2004; 4: 2038–2044
Blackwell Munksgaard

doi: 10.1111/j.1600-6143.2004.00608.x

Regression of Left Ventricular Hypertrophy After Arteriovenous Fistula Closure in Renal Transplant Recipients: A Long-Term Follow-Up

Philippe Unger[a,*], Sonia Velez-Roa[a], K. Martin Wissing[b], Anh Dung Hoang[b] and Philippe van de Borne[a]

[a] *Department of Cardiology,*
[b] *Department of Nephrology, Erasme Hospital, Université Libre de Bruxelles, Brussels, Belgium*
* *Corresponding author: Philippe Unger, punger@ulb.ac.be*

The long-term effects of hemodialysis arteriovenous fistula (AVF) closure on left ventricular (LV) morphology are unknown. Using echocardiography, we prospectively studied 17 kidney transplant recipients before, 1, and, 21 months after AVF closure (mean fistula flow 1371 ± 727 mL/min). Eight kidney transplant recipients with a patent AVF, matched for age, time after AVF creation, and time after transplantation, served as controls. LV mass index (LVMI) decreased from 139 ± 44 g/m^2 before AVF closure to 127 ± 45 g/m^2 and 117 ± 40 g/m^2 at 1 and 21 months post-closure, respectively ($p < 0.001$), but remained unchanged in controls. LV hypertrophy prevalence (LVMI > 125 g/m^2) decreased from 65% before, to 41% early, and 18%, late, after surgery ($p = 0.008$), mostly from a decrease in LV end-diastolic diameter. Consequently, the prevalence of LV concentric remodeling (relative wall thickness > 0.45 without hypertrophy) increased from 12% before, to 35% early, and 65% late, after surgery ($p = 0.003$). Diastolic arterial blood pressure increased from 78 ± 15 mmHg before, to 85 ± 13 mmHg early, and 85 ± 10 mmHg late, after surgery ($p < 0.015$).In conclusion, closure of large and/or symptomatic AVF induces long-term regression of LV hypertrophy. However, residual concentric remodeling geometry as well as diastolic blood pressure increase may blunt the expected beneficial cardiac effects of the procedure.

Key words: Left ventricular hypertrophy, arteriovenous Fistula, renal transplantation, echocardiography

Received 11 May 2004, revised and accepted for publication 9 July 2004

Introduction

Left ventricular (LV) hypertrophy is highly prevalent among patients with end-stage renal disease, and is an independent and strong predictor of morbidity and mortality (1–3). It is mainly the result of chronic systemic hypertension, volume overload and anemia. The prevalence of LV hypertrophy remains high in renal transplant patients despite the expected beneficial cardiovascular effects of kidney transplantation (4), and probably contributes to the high cardiac mortality rate observed in this population (5). Persisting patency of the arteriovenous fistula (AVF) may contribute substantially to this hypertrophy after renal transplantation (4). In addition, prospective data have shown that AVF closure reduces LV diameter and mass in the short term (6,7). van Duijnhoven et al. reported regression of LV hypertrophy 3 to 4 months after surgery (7). In our own series, LV mass was reduced as early as 3 to 10 weeks after surgery, despite a small, albeit significant, increase in diastolic and mean arterial blood pressure (BP), and a large increase in total peripheral resistance (6). In the long term, these hemodynamic changes may blunt the early flow-dependent beneficial effects of fistula closure on LV mass and volume (2), and whether LV mass reduction persists late after fistula closure is unknown. Therefore, the aim of our study was to assess prospectively the long-term effects of surgical AVF closure on cardiac morphology.

Patients

The protocol was approved by the Ethics Committee of our institution, and all patients gave informed consent for participation in the study.

Patients referred for surgery

Between October 1999 and December 2002, 27 kidney transplant patients were referred to the cardiology department for cardiac assessment before closure of an AVF and were considered for enrolment. Of these patients, four were excluded for the following reasons: regional wall motion abnormalities on echocardiography (n = 1), congenital heart disease (n = 2) and heart transplantation (n = 1). No patient had valvular heart disease and all were in sinus rhythm. During the follow-up period, one patient died of a non-cardiac cause, one had chronic graft rejection and returned to hemodialysis, and four were lost to follow-up. Thus, the final study group consisted of 17 patients. These patients were candidates for surgical closure of the AV access at the request of the referring nephrologist, for one or more of the following reasons: exertional dyspnea,

palpitations and/or heart failure (n = 10), venous hypertension with swelling of the extremities and/or erythrocyanosis (n = 6), and/or cosmetic reasons (n = 5). All patients had a stable kidney graft function. Among the patients, 12 had participated in a prior study on the acute effects of AVF closure (6). There were seven radiocephalic, five radioradial, three brachial communicating, one radiobasilic and one femorosaphenous fistula. At the time of the pre-operative examination, nine patients were using one or more anti-hypertensive drugs: three patients were being treated with a calcium entry blocker, eight with a β-blocking agent, six with an angiotensin-converting enzyme inhibitor or an angiotensin 2 receptor antagonist and three with diuretics. No patient was receiving nitrate therapy. Immunosuppression consisted of cyclosporin (n = 9), mycophenolate mofetyl (n = 8), tacrolimus (n = 6), azathioprin (n = 7) and prednisolone (n = 11). During the study period, the decision to change medication was left to the referring nephrologist. At the end of the study, 10 patients had had no changes in anti-hypertensive drugs, two patients had been prescribed β-blocking agents, two had stopped taking an angiotensin-converting enzyme inhibitor (replaced in one patient by moxonidine), one patient had had the dosage of enalapril reduced from 10 to 5 mg/day, and two patients had been prescribed furosemide. The mean number of anti-hypertensive medications per patient was 1.2 ± 1.4 at entry, and 1.4 ± 1.3 at the end of the study (p = 0.33).

Controls

Twelve kidney transplant patients with patent AVF who were referred for routine echocardiographic follow-up served as controls. These controls were matched for age, sex ratio, body mass index and time elapsed since renal transplantation and fistula creation to the patients who underwent surgical AVF closure. Among them, four were lost to the follow-up. The clinical characteristics of the remaining eight are shown in Table 1. Controls tended to have a smaller AVF flow, but the difference did not reach statistical significance.

At the time of the first echocardiography, five controls were being treated with one or more anti-hypertensive drugs: three patients with a calcium entry blocker, three with a β-blocking agent, one with an angiotensin-converting enzyme inhibitor, and three with diuretics. At the time of the second examination, four patients had had no change in anti-hypertensive therapy; one had had a calcium antagonist replaced by a β-blocking agent plus moxonidine; one had been prescribed an angiotensin-converting enzyme inhibitor plus furosemide; one had been prescribed an angiotensin-converting enzyme plus a calcium antagonist; and one had received a calcium antagonist plus an increase in metoprolol dosage (from 200 to 300 mg daily). The mean number of anti-hypertensive medications was 1.4 ± 1.4 at entry, and 1.6 ± 1.9 at the end of the follow-up (p = 0.52).

Methods

Echocardiography, BP measurements and blood chemistry analysis were performed within 4 weeks (11 ± 9 days, range 1–28) prior to the surgical closure (baseline), early after the procedure (35 ± 13 days, range 21–69), and late after surgery (21 ± 10 months, range 12–36). The duration of follow-up was similar in the study group and in the controls (Table 1).

Echocardiography

Echocardiographic studies were performed using a Philips Sonos 5500 ultrasound system with standard imaging transducer. M-mode tracings were recorded on paper (100 cm/sec). Post-hoc blind analysis was performed according to the American Society of Echocardiography (ASE) recommendations and indexed when appropriate (8). These measurements included LV end-diastolic and systolic diameters, shortening fraction, left atrial dimensions, and interventricular septal and posterior wall end-diastolic wall thickness (8). LV outflow tract diameter was measured using two-dimensional echocardiography. Doppler echocardiography allowed the measurement of stroke volume and cardiac output (CO) at the level of the LV outflow tract (9). Total peripheral resistance (TPR; dyne/sec/cm^5) was calculated from CO

Table 1: Clinical characteristics

	Patients (n = 17)	Controls (n = 8)	p
Age (years)	48 ± 11	49 ± 6	0.79
Male/female	7/10	3/5	0.41
Body surface area (m^2)	1.74 ± 0.21	1.72 ± 0.19	0.80
Body mass index (kg/m^2)	24.4 ± 3.5	24.3 ± 6.2	0.94
Time after transplantation (mo)	30 ± 16	33 ± 27	0.75
Median	30	25	
Time after fistula creation (mo)	87 ± 64	90 ± 81	0.92
Median	69	61	
Fistula flow (mL/min)	1371 ± 727	886 ± 558	0.13
Range	140–2523	154–1593	
Median	1410	936	
Duration of follow-up (mo)	21 ± 10	24 ± 14	0.52
Median	16	21	

Data are mean ± SD.

(L/min) and mean arterial blood pressure (MABP; mmHg) using the following formula:

$$TPR = 80 \times \frac{MABP}{CO}.$$

LV ejection fraction was calculated using the Teichholz method (10). LV mass was calculated based on the ASE convention using the Devereux formula (11) and was indexed to body surface area (LVMI). LV hypertrophy was defined as a LVMI $\geq$ 125 g/m^2 in both men and women (12). Relative wall thickness (RWT) was calculated as follows: (ventricular septal thickness + posterior wall thickness)/LV internal diastolic diameter. Patients were divided into four mutually exclusive groups: normal LV geometry (normal LVMI and RWT $<$ 0.45); concentric hypertrophy (increased LVMI and RWT $\geq$ 0.45); eccentric hypertrophy (increased LVMI and RWT $<$ 0.45); and concentric remodeling (normal LVMI and RWT $\geq$ 0.45).

LV diastolic filling was examined using pulsed-wave Doppler echocardiography, with the sample volume at the tips of the mitral valve in the apical four-chamber view and recorded at the end-expiratory phase during quite breathing. Peak velocity of early diastolic filling (E) and peak velocity of atrial filling (A) were recorded, and the E-A ratio was calculated (13).

Fistula flow was estimated through the decrease in CO produced by compression of the AVF. Indeed, previous observations have shown that this decrease correlates with fistula flow (14), and this parameter has been used as a substitute for direct fistula flow measurement (6,15,16). The AVF was occluded at the end of the initial echocardiographic study by inflating a sphygmomanometer cuff to a 50 mmHg suprasystolic pressure for 30 s (6). CO was determined within 1 min before pneumatic occlusion and during the last 10 s of the AVF closure.

All measurements were performed in triplicate and averaged.

Blood pressure and heart rate

Casual BP was measured on the contralateral arm to the AVF using a standard sphygmomanometer. BP and heart rate were averaged from two measurements performed by the same investigator at 10-min intervals in the supine position, following a 30-min rest.

The early and late changes in LVMI, RWT and in BP produced by surgical closure of the fistula were expressed as: $(X_{earlypost-surgery} - X_{baseline})/X_{baseline}$, and $(X_{latepost-surgery} - X_{baseline})/X_{baseline}$, respectively.

Statistical Analysis

Data are reported as mean $\pm$ SD. For statistical analysis (Statview, SAS, Cary, NC), Student's t test for unpaired data and Fisher exact test were used to compare patients with controls, and a paired t test was used to compare visit 1 to visit 2 in the control subjects. A p value $<$ 0.05 was considered significant. Comparisons of means of data obtained at baseline, early and late after AVF closure were performed by an ANOVA for repeated measurements. Significance of contrasts was estimated using Bonferroni comparisons. For this analysis, p values $<$ 0.0167 were considered significant. Comparisons of proportions between baseline, early and late post-operative visits were performed by a 2 $\times$ 2 McNemar χ^2 test or exact binomial test, followed by a Bonferroni correction. Correlations between variables were assessed by the Pearson coefficient.

Results

Baseline clinical characteristics of patients and controls are presented in Table 1.

In the patients, plasma hematocrit, plasma creatinine, creatinine clearance and blood urea nitrogen remained unchanged after AVF closure as compared to baseline (Table 2). Patient weight increased during the follow-up period, from 66 $\pm$ 14 kg to 68 $\pm$ 16 kg (p = 0.023). Changes in echocardiographic parameters are shown in Table 3. LV end-diastolic diameter and LVMI decreased early after surgery, and these reductions were even more striking late after the operation. We did not find a correlation between pre-operative fistula flow, and the changes in LVMI at the end of the follow-up. The correlation coefficient was $-$0.34 and the p value was 0.18. We analyzed LVMI regression in the nine patients with a flow rate $\leq$ the median (fistula flow 833 $\pm$ 458 mL vs. 886 $\pm$ 558 mL in controls, p = 0.84). LVMI decreased in these nine patients from 141 $\pm$ 49 to 130 $\pm$ 52 and 118 $\pm$ 49 mg/m^2 at baseline, at 1 month (p = 0.08 vs. baseline), and at 21 months (p = 0.008 vs. baseline), respectively.

The post-operative decrease in LVMI resulted from a decrease in LV end-diastolic diameter rather than a decrease in wall thickness. Indeed, no significant changes in interventricular and posterior wall thickness were found (Table 3). At baseline, both concentric and eccentric hypertrophy patterns were predominant, whereas at the late follow-up visit, the concentric remodeling pattern was the most prevalent, with the disappearance of the eccentric hypertrophy pattern (Figure 1). The prevalence of LV hypertrophy decreased from 65% at baseline to 41% early post-operatively (p = NS vs. baseline) and 18% late post-operatively (p = 0.008 vs. baseline, NS vs. early post-operatively). The prevalence of the concentric remodeling pattern increased from 12% at baseline to 35% early post-operatively (p = NS vs. baseline) and 65% late post-operatively (p = 0.003 vs. baseline, NS vs. early post-operative). Only three patients had a normal LV pattern at the end of the follow-up. There was a slight correlation between early changes in diastolic BP and the early increase in RWT (R = +0.51; p = 0.036), but no correlation was found between the late changes in diastolic BP and the late increase in RWT (R = $-$0.23; p = 0.37). Neither early nor late changes in LVMI correlated with changes in diastolic BP.

Left atrial diameter was reduced early after AVF closure and remained lower late after surgery, whereas right ventricular diameter was not significantly altered by surgery. The peak velocity of the E wave was decreased both early and late after surgery, whereas A wave velocity was unchanged, resulting in a sustained decrease in the E–A ratio (Table 3). There was a slight but significant increase in diastolic BP both early and late after surgery (Table 4). Total peripheral resistance also increased both early and late after surgery,

Table 2: Laboratory parameters at baseline, early and late after arteriovenous fistula (AVF) closure

	Baseline	Early post-AVF closure	Late post-AVF closure	p value (ANOVA)
Hematocrit (%)	37.5 ± 3.1	38.4 ± 4.1	38.3 ± 3.7	0.51
Plasma creatinine (mg/dL)	1.44 ± 0.44	1.41 ± 0.39	1.47 ± 0.46	0.67
Creatinine clearance (mL/min)	58 ± 17	57 ± 14	58 ± 20	0.99
Blood urea nitrogen (mg/dL)	28 ± 13	27 ± 11	27 ± 9	0.78

Data are mean ± SD.

Table 3: Comparison of echocardiographic and Doppler parameters at baseline, early, and late after arteriovenous fistula (AVF) closure, in patients and in controls

Variables	Patients			Controls			
	Baseline	Early post-AVF closure	Late post-AVF closure	Study 1	p (study 1 vs. baseline)	Study 2	p (study 1 vs. study 2)
LVDDI (mm/m^2)	29.5 ± 3.4	26.9 ± 2.9*	26.2 ± 3.2*	29.0 ± 3.2	0.74	28.9 ± 2.7	0.81
LVESDI (mm/m^2)	18.1 ± 3.2	16.6 ± 3.4*	16.0 ± 3.5*	17.9 ± 2.7	0.90	17.4 ± 2.7	0.41
IVS (mm)	12.4 ± 3.0	12.8 ± 3.1	12.2 ± 2.1	10.8 ± 0.8	0.15	11.0 ± 1.1	0.54
PW (mm)	11.2 ± 1.7	11.6 ± 1.7	11.4 ± 1.7	10.4 ± 1.1	0.24	10.5 ± 1.4	0.89
RWT (%)	46.9 ± 10.6	52.7 ± 10.2*	51.7 ± 7.6*	43.2 ± 4.9	0.35	43.7 ± 5.6	0.76
Median	44.1	50.1	49.7	41.5		43.5	
LVMI (g/m^2)	139 ± 44	127 ± 45*	117 ± 40*†	114 ± 19	0.14	115 ± 18	0.85
Median	135	110	107	115		123	
LAD (mm)	45.2 ± 6.0	42.0 ± 5.7*	42.2 ± 5.8*	41.9 ± 3.0	0.17	42.9 ± 3.0	0.57
RVEDD (mm)	30.1 ± 4.6	30.2 ± 4.1	27.8 ± 5.7	27.1 ± 4.1	0.13	27.3 ± 3.2	0.56
FS (%)	38.7 ± 6.9	38.4 ± 8.5	39.2 ± 7.6	38.2 ± 6.3	0.86	39.9 ± 6.6	0.34
EF (%)	68 ± 9	68 ± 11	69 ± 10	68 ± 8	0.91	70 ± 8	0.36
E (cm/s)	80 ± 20	56 ± 13*	60 ± 18*	90 ± 24	0.31	84 ± 22	0.41
A (cm/s)	80 ± 21	75 ± 15	76 ± 17	96 ± 24	0.09	90 ± 19	0.40
E/A	1.08 ± 0.46	0.77 ± 0.20*	0.81 ± 0.21*	0.94 ± 0.18	0.40	0.95 ± 0.23	0.89

Data are mean ± SD; *$p < 0.0167$ vs. baseline; †$p < 0.0167$ vs. early post-operative.
LVEDDI: Indexed LV end-diastolic diameter; LVESDI: Indexed LV end-systolic diameter; IVS: interventricular septum; PW: posterior wall thickness; RWT: relative wall thickness; LVMI: indexed LV mass; LAD: left atrial dimension; RVEDD: right ventricular end-diastolic diameter; FS: LV fractional shortening; EF: LV ejection fraction; E: early transmitral velocity; A: late transmitral velocity.

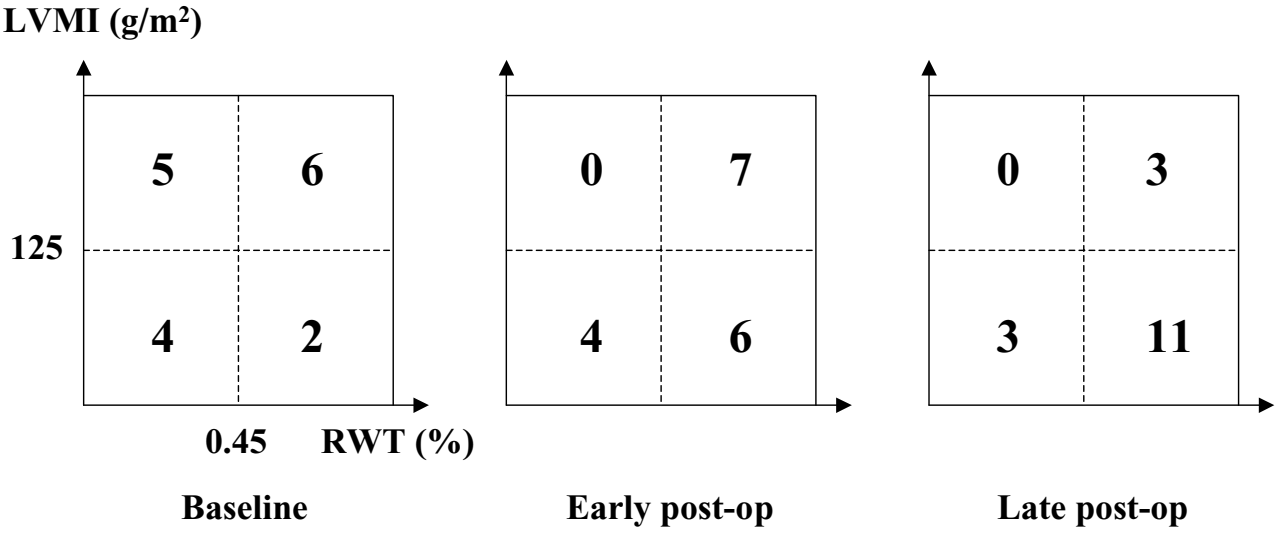

Figure 1: LV morphology at baseline (left), and at the times of the early (middle) and late post-operative visit (right). Patients are divided into four groups according to LV mass index (LVMI) and relative wall thickness (RWT): normal LV geometry (lower left case); concentric remodeling (lower right case); eccentric hypertrophy (upper left case); and concentric hypertrophy (upper right case). At baseline, both concentric and eccentric hypertrophy patterns are predominant, whereas at the late follow-up visit, the concentric remodeling pattern is the most prevalent.

Table 4: Hemodynamic parameters at baseline, early and late post-arteriovenous fistula (AVF) closure

Variables	Baseline	Early post-AVF closure	Late post-AVF closure	p value (ANOVA)	Controls (study 1)	p (vs. baseline)
HR (bpm)	73 ± 10	70 ± 7	68 ± 8	0.17	74 ± 7	0.82
MABP (mmHg)	96 ± 16	101 ± 13	103 ± 11	0.049	98 ± 9	0.75
SBP (mmHg)	131 ± 19	134 ± 16	138 ± 14	0.30	134 ± 17	0.73
DBP (mmHg)	78 ± 15	85 ± 13*	85 ± 10*	0.015	79 ± 6	0.78
CI (L/min·m^2)	3.86 ± 0.78	3.04 ± 0.66*	2.97 ± 0.83*	<0.0001	3.58 ± 0.87	0.43
SVI (mL/m^2)	53 ± 11	43 ± 8*	43 ± 9*	<0.0001	49 ± 10	0.31
TPR (d/·s/cm^{-5})	1190 ± 304	1627 ± 443*	1710 ± 456*	<0.0001	1330 ± 296	0.30

Data are mean ± SD; *$p < 0.0167$ vs. baseline.
HR: heart rate; MABP: mean arterial blood pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure; CI: cardiac index; SVI: stroke volume index; TPR: total peripheral resistance.

mainly as a result of reduced stroke volume and cardiac index.

Echocardiographic parameters did not change in the controls during the follow-up, nor did baseline parameters in the controls differ from those observed pre-operatively in the study group (Table 3). Heart rate, BP, cardiac index, stroke volume index and TPR did not differ from those observed pre-operatively in the study group ($p > 0.30$ for all these parameters).

Discussion

Previous studies have shown that LV hypertrophy is significantly reduced in the early weeks or months after AVF closure in renal transplant patients (6,7). However, an increase in blood pressure BP and in peripheral resistance could hamper these beneficial effects, and the long-term effects of AVF closure on cardiac morphology have not yet been investigated. Using a prospective design and non-invasive methods, our results document for the first time that the regression in LV hypertrophy seen early after AVF closure is even more pronounced after 21 months of follow-up. It is of interest that the observed reduction in LV mass was larger than that which was observed in a large study on anti-hypertensive therapy in patients with LV hypertrophy (17). LV hypertrophy in end-stage renal disease is the result of the combined effects of chronic flow and pressure overload and of non-hemodynamic factors associated with uremia. The flow overload and the associated LV dilatation are related to the hyperkinetic circulation caused by anemia, plasma volume overload and the presence of an AV access (1,18,19). Renal transplantation reduces LV dimensions and mass through correction of the uremic state (4). In order to differentiate the effects of renal transplantation on LV morphology from the effects of AVF closure, we also studied a group of kidney transplant recipients with patent AVFs. This group was closely matched to the study group of patients referred for AVF closure in terms of post-transplantation and post-fistula creation periods, and had a similar delay between the two echocardiographic studies. No reduction in LV diameter or mass was found in these controls. Thus, the observed regression in LV hypertrophy cannot be ascribed to a long-term effect of kidney transplantation. AVF tended to be smaller in controls as compared with the patients; it is, however, unlikely that patency of smaller fistula would have prevented a spontaneous regression of LV hypertrophy after kidney transplantation. One might expect the opposite, if any, effect to occur, i.e. lesser LV hypertrophy regression in patients with larger AVF. Moreover, in our population, estimated pre-operative fistula flow did not predict the decrease in LVMI, as previously shown early after surgery (6), and a reduction in LVMI was found even when comparing patients with similar fistula flow rate to the controls (i.e. those with a flow $\leq$ the median).

We have previously shown that regression in LV mass index 1 month after surgery is best predicted by the magnitude of the acute increase in mean arterial BP caused by AVF compression (6). In the present study, we performed the same analysis in a subset of 13 patients. We observed that this acute rise in BP predicted LV mass reduction even better in the long term, as the correlation coefficient between these parameters increased from 0.67 early after surgery to 0.83 late after surgery.

LV hypertrophy, as documented by echocardiography, is an independent risk factor for cardiovascular events in renal transplant patients, even when controlling for BP and other risk factors (1–3). LV hypertrophy regression during anti-hypertensive therapy has been associated with a 59% reduction in the risk of subsequent cardiovascular events when compared with persistence, or new development, of LV hypertrophy (20). One might therefore speculate that patients who undergo AVF closure will experience fewer cardiovascular events than those with a patent AVF. However, whether such dramatic reduction in the cardiovascular risk can be extrapolated to renal-transplanted patients remains to be determined, considering the multi-factorial and markedly increased cardiovascular risk of this population. In the present study, AVF closure did not restore a normal LV geometry, rather it resulted in a change to a predominantly concentric remodeling pattern. This result is in line with the previous observation made in hypertensive patients that relative wall thickness, a measure of LV concentricity, is independently and inversely related to stroke volume (21). We also found sustained changes in

the LV filling pattern. Indeed, fistula closure induced decreases in E wave velocity and E–A ratio. These changes in LV filling pattern, together with the decrease in left atrial dimensions, indicate an improvement in LV filling, from a pseudo-normalized toward an impaired relaxation pattern (22). Indeed, deterioration from normal toward impaired relaxation, despite exhibiting a similar Doppler flow morphology, would have been associated with an increase rather than a decrease in left atrial dimensions (22).

The relief of the volume overload induced by the procedure improved, but failed to normalize, LV geometry. This could reflect inadequate BP control, as suggested by the correlation between early RWT changes and the increase in diastolic BP. However, this BP increase was only mild. In addition, late changes in RWT did not correlate with the BP increase. These morphological changes might also represent some sequel to the chronic flow overload or represent a transient pattern toward normalization. Several studies have provided evidence of increased cardiovascular morbidity and mortality in hypertensive patients with a concentric LV geometry, even in the absence of LV hypertrophy (12,23). In addition, not only changes in LV mass but also changes in the pattern of LV geometry during therapy may have additional prognostic significance, with the risk being substantially higher for those with concentric geometry (24).

Compression of an AVF increases both systolic and diastolic BP acutely (6,15), but whether this elevation persists in the long term has not been consistently studied. We previously found an increase in mean arterial BP 1 month after AVF closure (6), but this observation was not noted by others 3 to 4 months after surgery (7). An important finding of the present study is that AVF closure might increase diastolic BP even late after surgery, although this was a secondary end-point of our study. These results mirror the early (within 14 days) drops in mean and diastolic arterial BP after creation of an AVF in animal and in human studies (25,26), although this finding has not been unequivocal (27). Interestingly, in the present study, LV mass decreased despite the elevation in BP and peripheral vascular resistance, showing the net beneficial cardiac effect of stopping the flow overload by AV fistula closure. The majority of our patients remained on the same anti-hypertensive regimen, making it unlikely that the minor therapeutic modifications made in the remaining seven patients could have accounted for the large observed reduction in LV mass, especially as similar changes were made in controls. BP measurements were obtained in carefully standardized supine resting conditions. Further prospective studies are, however, needed to confirm this observation using 24-h ambulatory monitoring pressure recordings. In the meantime, the clinician should be aware that BP elevation may occur following AVF closure.

Prospective studies have demonstrated that LV remodeling takes place in response to sustained lowering of BP, weight reduction or valve replacement for aortic valve disease (20,28,29). Our data demonstrate that another therapeutic intervention, namely closure of large AVFs in renal transplant recipients, is associated with long-term regression of LV hypertrophy, which may have important prognostic significance. However, the expected clinical benefit induced by regression of LV hypertrophy must be balanced against the lack of complete normalization of LV geometry and the possibility of a deleterious effect on BP control. In addition, the results of the present study were obtained in a selected population that included a majority of symptomatic AVFs. Whether similar results would be observed in renal transplant recipients with asymptomatic or in minimally symptomatic patent AVFs remains to be determined.

Acknowledgments

This study was supported by the Foundation for Cardiac Surgery, Belgium (PU, PVDB), the Belgian National Fund for Scientific Research (PVDB), and the Erasme Foundation (SV). We thank Prof. M. Dramaix for her expert statistical assistance.

References

1. Harnett JD, Kent GM, Barre PE, Taylor R, Parfrey PS. Risk factors for the development of left ventricular hypertrophy in a prospective followed cohort of dialysis patients. J Am Soc Nephrol 1994; 4: 1486–1490.
2. Rigatto C, Foley R, Jeffery J, Negrijn C, Tribula C, Parfrey P. Electrocardiographic left ventricular hypertrophy in renal transplant recipients: prognostic value and impact of blood pressure and anemia. J Am Soc Nephrol 2003; 14: 462–468.
3. Meeus F, Kourilsky O, Guerin AP, Gaudry C, Marchais SJ, London GM. Pathophysiology of cardiovascular disease in hemodialysis patients. Kidney Int 2000;76:S140–S147.
4. Parfrey PS, Harnett JD, Foley RN et al. Impact of renal transplantation on uremic cardiomyopathy. Transplantation 1995; 60: 908–914.
5. McGregor E, Stewart G, Rodger RS, Jardine AG. Early echocardiographic changes and survival following renal transplantation. Nephrol Dial Transplant 2000; 15: 93–98.
6. Unger P, Wissing KM, de Pauw L, Neubauer J, van de Borne P. Reduction of left ventricular diameter and mass after surgical arteriovenous fistula closure in renal transplant recipients. Transplantation 2002; 74: 73–79.
7. van Duijnhoven EC, Cheriex EC, Tordoir JH, Kooman JP, van Hooff JP. Effect of closure of the arteriovenous fistula on left ventricular dimensions in renal transplant patients. Nephrol Dial Transplant 2001; 16: 368–372.
8. Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation of M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978; 58: 1072–1083.
9. Zoghbi WA, Quinones MA. Determination of cardiac output by Doppler echocardiography: a critical appraisal. Herz 1986; 11: 258–268.
10. Teichholz LE, Kreulen T, Herman MV, Gorlin R. Problems in echocardiographic volume determinations: echocardiographic-angiographic correlations in the presence or absence of asynergy. Am J Cardiol 1976; 37: 7–11.

11. Devereux RB, Alonso DR, Lutas EM et al. Echocardiographic assessment of left ventricular hypertrophy; comparison to necropsy findings. Am J Cardiol 1986; 57: 450–458.
12. Verdechia P, Schillaci G, Borgioni C et al. Adverse prognostic significance of concentric remodelling of the left ventricle in hypertensive patients with normal left ventricular mass. J Am Coll Cardiol 1995; 25: 871–878.
13. Rakowski H, Appleton C, Chan KL et al. Canadian consensus recommendations for the measurement and reporting of diastolic dysfunction by echocardiography. J Am Soc Echocardiogr 1996; 9: 736–760.
14. Frank CW, Wang H-H, Lammerant J, Miller R, Wégria R. An experimental study of the immediate hemodynamic adjustments to acute arteriovenous fistulae of various sizes. J Clin Invest 1955; 34: 722–731.
15. Bos WJW, Zietse R, Wesseling KH, Westerhof N. Effects of arteriovenous fistulas on cardiac oxygen supply and demand. Kidney Int 1999; 55: 2049–2053.
16. Velez-Roa S, Neubauer J, Wissing M et al. Acute arterio-venous fistula occlusion decreases sympathetic activity and improves baroreflex control in kidney transplanted patients. Nephrol Dial Transplant 2004; 19: 1–7.
17. Aurigemma GP, Devereux RB, Wachtell K et al. Left ventricular mass regression in the LIFE study: effect of previous antihypertensive treatment. Am J Hypertens 2003; 16: 180–186.
18. Foley RN, Parfrey PS, Harnett DJ, Kent GM, Murray DC, Barre PE. The impact of anemia on cardiomyopathy, morbidity and mortality in end-stage renal disease. Am J Kidney Dis 1996; 28: 53–61.
19. Foley RN, Parfrey PS, Harnett JD et al. Clinical and echocardiographic disease in patients starting end-stage renal disease therapy. Kidney Int 1995; 47: 186–192.
20. Verdecchia P, Angeli F, Borgioni C et al. Changes in cardiovascular risk by reduction of left ventricular mass in hypertension: a meta-analysis. Am J Hypertens 2003; 16: 895–899.
21. Bella JN, Wachtell K, Palmieri V et al. Relation of left ventricular geometry and function to systemic hemodynamics in hypertension: the LIFE Study. J Hypertens 2001; 19: 127–134.
22. Oh JK, Appleton CP, Hatle LK, Nishimura RA, Seward JB, Tajik AJ. The noninvasive assessment of left ventricular diastolic function with two-dimensional an Doppler echocardiography. J Am Soc Echocardiogr 1997; 10: 246–270.
23. Verdechia P, Schillaci G, Borgioni C et al. Prognostic value of left ventricular mass and geometry in systemic hypertension with left ventricular hypertrophy. Am J Cardiol 1996; 78: 197–202.
24. Muiesan ML, Salvetti M, Monteduro C et al. Left Ventricular concentric geometry during treatment adversely affects cardiovascular prognosis in hypertensive patients. Hypertension 2004; 43: 731–738.
25. Abassi ZA, Brodsky S, Karram T, Dobkin I, Winaver J, Hoffman A. Temporal changes in natriuretic and antinatriuretic systems after closure of a large arteriovenous fistula. Cardiovasc Res 2001; 51: 567–576.
26. Iwashima Y, Horio T, Takami Y et al. Effects of the creation of arteriovenous fistula for hemodialysis on cardiac function and natriuretic peptide levels in CRF. Am J Kidney Dis 2002; 40: 974–982.
27. Ori Y, Korzets A, Katz M, Perek Y, Zahavi I, Gafter U. Haemodialysis arteriovenous access. A prospective haemodynamic evaluation. Nephrol Dial Transplant 1996; 11: 94–97.
28. Schillaci G, Pasqualini L, Vaudo G et al. Effect of body weight changes on 24-hour blood pressure and left ventricular mass in hypertension: a 4-year follow-up. Am J Hypertens 2003; 16: 634–639.
29. Ikonomidis I, Tsoukas A, Parthenakis F et al. Four year follow up of aortic valve replacement for isolated aortic stenosis: a link between reduction in pressure overload, regression of left ventricular hypertrophy, and diastolic function. Heart 2001; 86: 309–316.