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REDUCTION OF LEFT VENTRICULAR DIAMETER AND MASS AFTER SURGICAL ARTERIOVENOUS FISTULA CLOSURE IN RENAL TRANSPLANT RECIPIENTS[1]

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Background. **Left ventricular hypertrophy and dilatation is a frequent finding in kidney transplant recipients, which may be favored by the persistent patency of arteriovenous fistula. The purpose of the current study was to prospectively investigate whether surgical closure of the fistula allows reduction of abnormalities of left ventricular morphology in stable renal transplant patients. Furthermore, we studied the ability of preoperative echocardiographic and noninvasive hemodynamic measurements, including the effects of a temporary occlusion of the fistula, to predict postoperative left ventricular diameter and mass reduction.**

Methods. **Seventeen kidney transplant recipients referred for surgical arteriovenous fistula closure were prospectively studied. Standard echocardiographic parameters, heart rate, and blood pressure were assessed preoperatively at baseline and during an acute pneumatic fistula occlusion. These measurements were repeated 3 to 10 weeks after surgical closure. Six kidney transplant recipients with patent arteriovenous fistulas referred for routine echocardiographic follow-up served as a control group.**

Results. **Surgical fistula closure decreased left ventricular end-diastolic diameter and mass indexes (29.9±2.4 to 27.4±2.1 mm/m^2, $P<0.001$, and 141±37 to 132±39 g/m^2, $P<0.05$, respectively), whereas no changes were seen in controls after a similar delay. Postoperative left ventricular end-diastolic diameter and mass reductions correlated best with the increases in total peripheral resistance ($r=0.85$, $P<0.0001$) and mean arterial blood pressure ($r=0.64$, $P=0.006$) during pneumatic occlusion, respectively.**

Conclusions. **Surgical closure of arteriovenous fistula reduces left ventricular diameter and mass in kidney transplant recipients. Increases in blood pressure and total peripheral resistance induced by temporary fistula occlusion are the best predictors of these morphological changes.**

Left ventricular (LV) hypertrophy is the most common cardiac alteration in patients with end-stage renal disease and is an independent prognostic factor (*1–3*). In addition, volume overload, characterized by an increased stroke volume and cardiac output and by LV enlargement, is not infrequent in this condition and is associated with subsequent development of heart failure and high mortality rates (*1*, *4–6*). Arteriovenous (AV) fistulas used for hemodialysis often remain patent after kidney transplantation and may contribute to the deleterious effects of LV hypertrophy and dilatation (*7*).

This detrimental role of fistula patency has been supported by various case reports of high output cardiac failure subsiding after surgical closure (*8*, *9*). However, whether surgical closure of AV fistulas reverses cardiac morphological abnormalities remains a matter of debate. A retrospective study suggested little impact of large, high-flow AV fistulas on cardiac mass (*10*), whereas the prospective but uncontrolled study of van Duijnhoven et al. (*11*) showed some regression of LV diameter and mass after surgical closure of these fistulas.

In addition, the contribution of AV fistula to cardiac performance, hypertrophy, and dilatation in an individual patient is often difficult to ascertain. It could be evaluated through the assessment of the hemodynamic effects of an acute, temporary occlusion of the fistula. However, only one report, established in patients with traumatic AV fistulas, showed moderate agreement between preoperative cardiac output during compression and early postoperative cardiac output as determined by ballistocardiography (*12*). Subsequently, and despite the lack of any additional evidence of a predictive value of the changes induced by an acute fistula occlusion, short manual compression has been repeatedly used to determine the hemodynamic burden induced by AV fistulas (*9*, *13–15*).

Moreover, there are no data correlating the acute hemodynamic changes induced by a temporary occlusion of an AV fistula to the changes in LV morphology after fistula closure. The only prospective evaluation of the effects of surgical closure of AV fistulas in renal transplant recipients did not assess the predictive value of acute compressions of AV fistulas and provided only limited information on which baseline hemodynamic or echocardiographic parameters best predicted the postoperative changes (*11*). Although closure of an AV fistula may benefit the patient, it also jeopardizes a valuable vascular access should kidney function deteriorate and the patient need further hemodialysis. Thus, more information is required to determine which patients, if any, are most likely to benefit from surgical closure. The present prospective study was undertaken (1) to assess the changes in LV morphology and function induced by elective surgical fistula closure in stable renal transplant patients and (2) to determine the value of several preoperative echocardio-

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graphic and noninvasive hemodynamic measurements, at baseline and during acute, temporary AV fistula occlusion, in predicting postoperative changes in LV diameter and hypertrophy.

PATIENTS

The protocol was approved by the Ethics Committee of our institution.

Patients Referred for Surgery

After giving informed consent, 20 consecutive kidney transplant patients referred for surgical closure of an AV fistula were considered for enrollment. Three patients were excluded for the following reasons: regional wall motion abnormalities on echocardiographic examination (n=1), congenital heart disease (n=1), and heart transplantation (n=1). No patient had valvular heart disease and all were in sinus rhythm. Thus, the study group consisted of 17 patients (Table 1) with AV fistulas considered clinically large by the referring nephrologist, who were candidates for surgical closure of the AV access for one or more of the following reasons: exertional dyspnea, palpitations, and/or heart failure (n=13), venous hypertension, with local fatigue, swelling of the extremity, and/or erythrocyanosis (n=4), and cosmetic reason (n=4). All patients had stable kidney graft function. There were nine radiocephalic, five brachiocephalic, one brachiobasilic, one radiobasilic, and one femorosaphenous fistulas.

For safety reasons, medications were not interrupted for this study. During the preoperative examination, 12 subjects used one or more antihypertensive drugs: 6 patients were treated with a calcium entry blocker, 10 with a β-blocking agent, 6 with an angiotensin-converting enzyme inhibitor, and 3 with diuretics. No patient was receiving nitrate therapy. Immunosuppression consisted of cyclosporine (n=10), mycophenolate mofetil (n=8), tacrolimus (n=5), azathioprine (n=5), and prednisolone (n=11). Except for one patient who had the dosage of enalapril reduced from 10 to 5 mg/day, there was no change in medication during the study period.

Controls

Six consecutive kidney transplant recipients with patent AV fistulas referred for routine echocardiographic follow-up served as controls (Table 1). These patients were matched for the time elapsed since renal transplantation and fistula creation to the patients who underwent surgical closure of their AV fistulas (Table 1).

METHODS

Echocardiography, blood pressure measurements, and blood chemistry analysis were performed within 4 weeks (11±9 days, range 1–28) before the surgical closure and 3 to 10 weeks after the procedure (35±13 days, range 21–69). The time elapsed between the two echocardiographic studies was similar in the study group and in the controls (Table 1).

Echocardiography. Echocardiographic studies were performed using Sonos 5500 Ultrasound System (Agilent Technology, Andover MA) with standard imaging transducer. M-mode tracings were recorded on paper (100 cm/sec). Posthoc blind analysis was performed according to the American Society of Echocardiography recommendations and indexed when appropriate (*16*). These measurements included LV end-diastolic and systolic diameters, shortening fraction, left atrial dimensions, interventricular septal, and posterior wall end-diastolic wall thickness (*16*). LV outflow tract diameter was measured using two-dimensional echocardiography. Doppler echocardiography allowed the measurements of stroke volume and cardiac output at the level of the LV outflow tract (*17*). LV ejection fraction was calculated using the Teichholz method (*18*). LV mass was calculated based on the American Society of Echocardiography convention using the Devereux formula (*19*). The changes in LV end-diastolic diameter and mass indexes induced by surgical closure of the fistula were expressed as: $(X_{postsurgery} - X_{baseline})/X_{baseline}$

Total peripheral resistance (TPR; dyne.sec.cm^{-5}) was calculated from cardiac output (CO; L/min) and mean arterial blood pressure (MABP; mmHg) using the following formula: TPR=80×MABP/CO.

The AV fistula was occluded at the end of the echocardiographic study by inflating a sphygmomanometer cuff to a 50-mmHg suprasystolic pressure for 30 sec. This pressure was shown in preliminary experiments to offset any increase in systolic blood pressure induced by the occlusion of the AV shunt. We also verified that the application of this pressure on the contralateral arm (sham occlusion) did not induce any hemodynamic changes. Cardiac output was determined within 1 minute before pneumatic occlusion and during the last 10 sec of the AV fistula closure. Fistula flow was not directly measured but was estimated through the decrease in cardiac output during compression. Indeed, previous observations have shown that this decrease correlates with fistula flow, (*20*) and this parameter has been used as a substitute for direct fistula flow measurement (*21*). All measurements were performed in triplicate and averaged.

Blood Pressure and Heart Rate. Casual blood pressure was measured on the contralateral arm to the AV fistula using a standard sphygmomanometer. Blood pressure and heart rate were measured in the supine position after a 30-minute rest. Changes in blood pressure during the 30-sec occlusion of the fistula were monitored continuously on the middle finger of the nonfistula arm with the Finapres (TNO, The Netherlands) (*22*). Changes in MABP were calculated as the difference between the last 10 sec of the AV fistula closure and the 20-sec period that preceded the occlusion (Fig. 1). The percentage change in each parameter (X), namely heart rate, blood pressure, stroke volume, cardiac output, and TPR, during the acute occlusion was calculated as follows: $(X_{compression} - X_{baseline})/X_{baseline}$

Statistical Analysis. For statistical analysis (Statview, SAS), Student's two-tailed t test for paired and unpaired data was used to compare the mean of the data obtained before and after surgical closure and to compare the controls with the group that underwent fistula occlusion, respectively. Data are reported as mean ± SD. Comparisons of means of data obtained at baseline, during temporary occlusion, and after surgical closure were analyzed by a paired t test with a Bonferroni correction for multiple comparisons. Correlations between variables were assessed by the Pearson coefficient. Forward stepwise regression analysis was performed to determine which parameter best predicted LV mass and diameter regression after fistula occlusion. P values <0.05 were considered significant.

TABLE 1. Clinical characteristics

	Patients (n=17)	Controls (n=6)
Age (yr)	46±13	40±6
Gender	8 male, 9 female	4 male, 2 female
Body surface area (m^2)	1.76±0.14	1.89±0.26
Time after transplantation (mo)	37±28 (range 10–116)	38±13 (range 17–51)
Time after fistula creation (mo)	108±58 (range 39–248)	98±51 (range 45–180)
Time between the two studies (days)	46±17 (range 21–89)	52±27 (range 21–90)

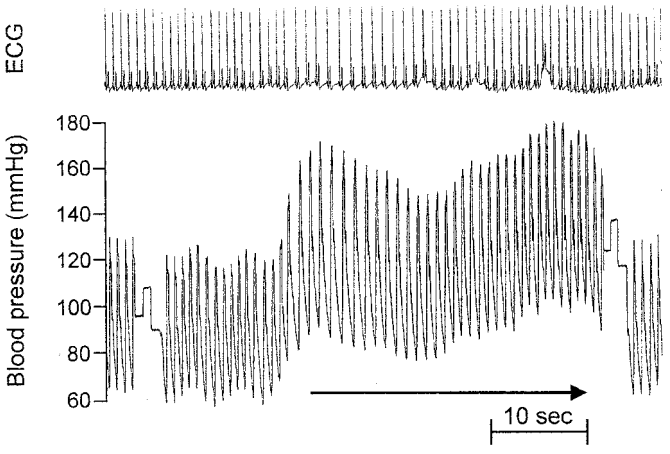

FIGURE 1. Rise in blood pressure and electrocardiogram showing a reduction in heart rate during temporary AV fistula occlusion (arrow). Blood pressure during occlusion was calculated from the mean of the last 10 sec of the occlusion.

RESULTS

As compared with baseline, plasma hematocrit did not change after the surgical closure of the AV fistula (39.4±4.4 versus 39.0±4.1%; P=NS). Creatinine clearance remained unchanged (54.3±13.1 versus 56.0±13.5 ml/min; P=NS). There was a slight postoperative decrease in plasma creatinine (1.55±0.41 versus 1.48±0.38 mg/dl; P=0.04), whereas blood urea nitrogen remained unchanged (29.6±12.6 versus 27.6±10.8 mg/dl; P=NS).

Changes in Echocardiographic Parameters After Fistula Closure

The changes in echocardiographic parameters are shown in Table 2. Surgical closure decreased LV end-diastolic diameter and mass indexes and reduced left atrial diameter (P<0.05). The postoperative decrease in LV mass was the result of a decrease in LV end-diastolic diameter rather than a decrease in wall thickness. Indeed, interventricular septum thickness was unchanged, and a slight but significant increase in posterior wall thickness was observed.

Baseline echocardiographic parameters did not significantly differ between patients and controls, and parameters remained unchanged between the two studies in the controls. However, the AV fistulas tended to be smaller in controls as compared with the patients, as suggested by the smaller decrease in cardiac output on compression (0.9±0.4 L/min in controls and 1.51±0.7 L/min in patients; P=0.09).

Correlation Between Changes in Hemodynamic Parameters Induced by Temporary Occlusion and by Surgical Closure

Hemodynamic data at baseline, during acute pneumatic occlusion (Fig. 1), and 1 month after surgical closure are listed in Table 3.

Heart rate decreased during acute compression of the fistula (P<0.001) but returned to baseline values after surgery. As compared with baseline, MABP increased during compression (P<0.001) and, to a lesser degree, after the surgical procedure (P<0.05). Temporary AV occlusion led to a slight decrease in stroke volume and stroke volume index, which was more pronounced after surgery (P<0.001). Cardiac output and index were markedly reduced both during the acute occlusion and after surgery (P<0.001). Cardiac output decreased by less than 1 L/min in only two patients during the compression of the fistula. These two patients had exertional dyspnea as the main complaint. The reduction in cardiac output, cardiac index, and stroke volume observed after surgery correlated only moderately with the acute response. The net effect of the closure of the AV fistula on cardiac output (and to a lesser degree on blood pressure) resulted in a large increase in TPR that was still present after surgery (P<0.01), but the correlation between acute and postsurgical increase in TPR was not significant.

Predictive Factors of LV Diameter and Mass Regression

The parameters associated with a regression in LV end-diastolic diameter and mass indexes in univariate analysis are shown in Table 4. The changes in heart rate, MABP, cardiac index, and TPR (Fig. 2, upper panel) induced by acute fistula occlusion were significantly associated with a decrease in LV end-diastolic diameter index (P<0.05), whereas the acute increases in MABP (Fig. 2, lower panel) and TPR were associated with LV mass index regression (P<0.05).

TABLE 2. Echocardiographic parameters before and after surgical fistula closure

	Patients			Controls		
	Baseline	After surgery	P (baseline vs. after surgery)	Study 1	Study 2	P (study 1 vs. study 2)
LVEDDI (mm/m^2)	29.9±2.4	27.4±2.1	0.0001	29±3.3	29.2±3.6	NS
LVESDI (mm/m^2)	17.9±2.6	16.5±2.3	0.003	19.4±2.8	18.6±3.7	NS
IVS (mm)	12.4±2.7	13±2.9	NS	13.4±3.9	12.9±3.1	NS
PW (mm)	11±1.7	11.7±1.9	0.005	11.2±1.7	11.4±1.8	NS
LVMI (g/m^2)	141±37	132±39	0.023	153±63	151±59	NS
LAD (mm)	45.3±5.2	43.0±4.9	0.014	46.4±6.2	46.8±5.8	NS
RVEDD (mm)	30.2±4.5	29.6±4.3	NS	28.9±4.5	27.8±4.5	NS
FS (%)	0.40±0.08	0.40±0.08	NS	0.33±0.04	0.36±0.07	NS
EF (%)	0.70±0.10	0.69±0.10	NS	0.61±6	0.65±0.10	NS

Abbreviations used in tables: LVEDDI, left ventricular end-diastolic diameter index; LVESDI, left ventricular end-systolic diameter index; IVS, interventricular septum; PW, posterior wall; LVMI, left ventricular mass index; LAD, left atrial diameter; RVEDD, right ventricular end-diastolic diameter; FS, left ventricular fractional shortening; EF, left ventricular ejection fraction.

TABLE 3. Hemodynamic parameters at baseline, during acute pneumatic occlusion, and after surgical closure

	Baseline	Temporary occlusion	Acute changes (temporary occlusion minus baseline)	After surgery	Postsurgical changes (after surgery minus baseline)	Correlation between acute and postsurgical changes
HR (bpm)	72±9	64±10[a]	−8±5	71±6	−1±10	r=0.10 P=NS
MABP (mmHg)	96.5±16.3	107.0±16.9[a]	10.5±8.2	103.3±13.6[b]	6.7±11.0	r=0.27 P=NS
CO (L/min)	7.10±1.32	5.59±1.08[a]	−1.51±0.66	5.63±1.17[a]	−1.47±1.10	r=0.57 Slope=0.95 P=0.018
CI (L/min.m^2)	4.03±0.66	3.17±0.54[a]	−0.85±0.36	3.20±0.62[a]	−0.82±0.62	r=0.56 Slope=0.98 P=0.02
SV (ml)	99±20	88±18[a]	−11±8	79±14[a]	−20±13	r=0.55 Slope=0.94 P=0.023
SVI (ml/m^2)	56±10	50±9[a]	−6±4	45±8[a]	−11±7	r=0.51 Slope=0.89 P=0.04
TPR (dyn.sec.cm^{-5})	1127±301	1601±476[a]	474±275	1532±383[a]	405±243	r=0.30 P=NS

Abbreviations used in tables: HR, heart rate; CO, cardiac output; CI, cardiac index; SVI, stroke volume (index).
[a] $P<0.001$ vs. baseline.
[b] $P<0.05$ vs. baseline.

TABLE 4. Predictors of postoperative left ventricular end-diastolic diameter and mass indexes regression (univariate analysis)

Parameter	Chronic changes[a] in LVEDDI (%)			Chronic changes[a] in LVMI (%)		
	r	Slope[c]	P	r	Slope[c]	P
Baseline LVEDDI (mm/m^2)	0.47	−1.2	0.06	0.12		0.64
Baseline LVMI (g/m^2)	0.20		0.44	0.04		0.89
Baseline SVI (ml/m^2)	0.19		0.46	0.14		0.60
Baseline HR (bpm)	0.13		0.62	0.006		0.98
Baseline MABP (mmHg)	0.24		0.36	0.05		0.86
Baseline CI (L/min.m^2)	0.15		0.57	0.11		0.68
Baseline TPR (dynes.s.cm^{-5})	0.18		0.48	0.12		0.66
Acute SVI changes[b] (%)	0.39		0.12	0.01		0.97
Acute MABP changes[b] (%)	0.69	−0.46	0.002	0.64	−0.64	0.006
Acute HR changes[b] (%)	0.55	0.45	0.02	0.39		0.12
Acute CI changes[b] (%)	0.73	0.54	0.0008	0.32		0.22
Acute TPR changes[b] (%)	0.85	−0.23	<0.0001	0.58	−0.23	0.01

[a] Chronic changes denotes changes induced by surgical closure of the fistula.
[b] Acute changes denotes changes induced by acute fistula compression.
[c] The slope is presented for correlations with $P<0.10$.

Using forward stepwise regression analysis, the acute increase in TPR during the pneumatic fistula occlusion emerged as the only independent predictor of the changes in LV end-diastolic diameter index induced by surgery (r=0.85, $P<0.0001$). Using the same analysis, MABP changes during acute occlusion were the only independent predictor of LV mass index regression (r=0.64, P=0.006).

DISCUSSION

We determined the value of several preoperative echocardiographic and noninvasive hemodynamic parameters in predicting the reduction in LV diameter and hypertrophy after surgical AV shunt closure in renal transplant recipients. The most striking finding of our study is that acute changes in TPR and MABP induced by temporary AV fistula compression are the best predictors of postoperative improvements.

Reduction in LV End-Diastolic Diameter and Mass Indexes

The reduction in LV mass after AV fistula closure was a result of the reduction in LV end-diastolic diameter. The validity of LV mass calculation with M-mode echocardiography in the presence of rapid variations of LV diameter has been well documented (*23*). LV hypertrophy in end-stage renal disease is the result of combined effects of chronic flow and pressure overload and of nonhemodynamic factors associated with uremia. The flow overload and the associated LV dilatation are tightly related to the hyperkinetic circulation caused by anemia, plasma volume overload, and the presence

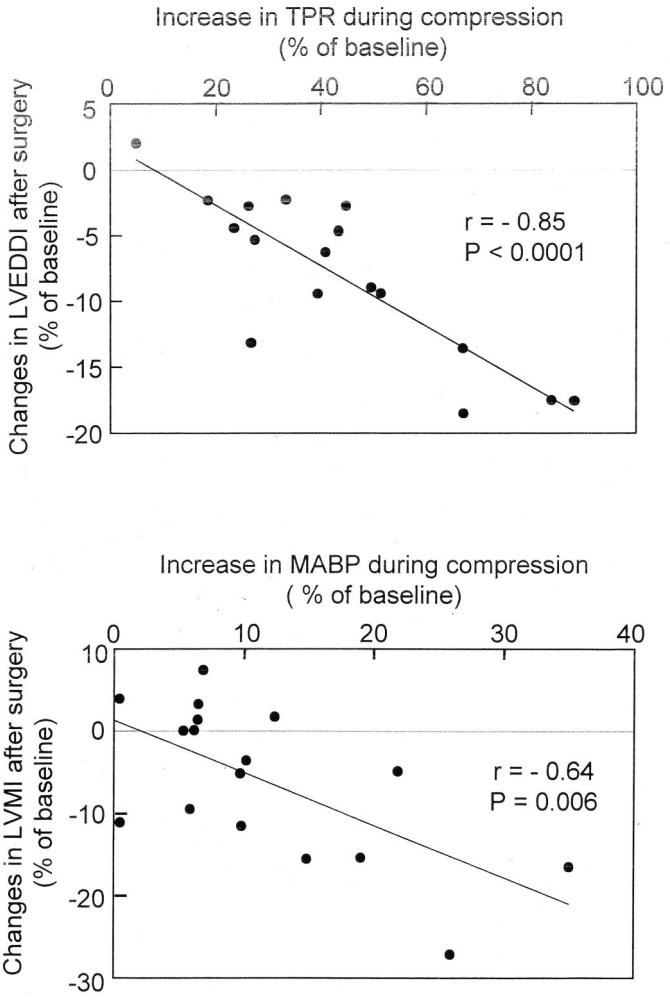

FIGURE 2. (Top) Correlation between the acute increase in TPR and the postoperative decrease in left ventricular end-diastolic diameter index (LVEDDI). (Bottom) Correlation between the acute increase in MABP and the postoperative decrease in left ventricular mass index (LVMI).

of an AV access (*1*, *4*, *6*). Correction of the uremic state by renal transplantation has been associated with reduced LV dimensions and mass, although the latter is usually only partial (*7*, *24*).

The present study supports the hypothesis of a deleterious role of persisting large AV fistulas in kidney transplant recipients. Indeed, our prospective assessment of LV diameter and mass demonstrated an early and significant decrease after elective surgical closure, whereas no changes were observed in a control group of kidney transplant recipients with patent AV fistula. Compared with the study group, these controls were studied after a similar posttransplantation period and with a similar delay between the two echocardiographic studies. Therefore, the observed improvement is not the consequence of a spontaneous regression of LV hypertrophy after kidney transplantation (*7*). AV fistulas tended to be smaller in controls as compared with the patients, but it is unlikely that patency of smaller fistulas would have induced a spontaneous slower regression of LV hypertrophy after kidney transplantation, as compared with large fistulas. One might expect the opposite, if any, effect to occur, i.e., a slower LV hypertrophy regression in patients with large fistulas. In addition, other factors that might interfere with cardiac structure such as hematocrit and renal function did not significantly change during the study period. Moreover, blood pressure did not decrease—and even slightly increased—after surgical closure. It is therefore most likely that the observed decrease in LV diameter and hypertrophy was induced by the reduction of the chronic volume overload induced by the AV shunt. Although the optimal delay to evaluate LV hypertrophy regression after closure of a fistula remains to be determined, it is interesting to note that these beneficial effects, namely the reduction in LV diameter and hypertrophy as well as the reduction in left atrial dimension, occurred early after the closure of the AV fistula, thereby suggesting that the loading effect of increased peripheral resistance and blood pressure induced by the closure of the fistula is rapidly offset by the reduction in volume overload. These results mirror the effects observed after the creation of an AV fistula, which induces a decrease in TPR coupled with an increase in cardiac output, stroke volume, and LV end-diastolic diameter (*25*).

Comparison of Acute and Chronic Changes

Continuous recordings of blood pressure allowed us to rule out incomplete occlusion of the AV shunt as a result of the acute blood pressure increase elicited by the compression. The acute bradycardic response induced by shunt compression, known as the Branham sign, has the potential to preclude any direct hemodynamic comparison with the chronic changes induced by surgical closure. However, in an early report, Nickerson et al. (*12*) showed agreement between cardiac output during acute manual compression of a traumatic AV fistula and cardiac output after surgical closure. This report was based on ballistocardiography-derived measurements, a method that has many limitations (*26*), raising concerns about the validity of these conclusions. Nonetheless, and despite the lack of additional evidence of a correlation between the hemodynamics during an acute fistula occlusion and that observed after surgical closure, the chronic effects of fistulas have been derived in many subsequent reports from an assessment performed during short manual compression. Based on Doppler-echocardiography, a well-validated technique, the results of the present study are in accordance with those of Nickerson et al. (*12*), confirming that the acute changes in cardiac output and stroke volume correlate (albeit moderately) with postoperative changes. It has been shown that plasma atrial natriuretic peptide increases while plasma renin activity is suppressed after creation of an AV access, thereby inducing a direct relaxation of blood vessels (*25*). Conversely, opposite hormonal effects may participate in the long-term adaptation to fistula occlusion, namely in the increase in TPR. One might speculate on whether these hormonal changes may be less effective during the sudden cardiovascular changes induced by the temporary AV shunt closure, thereby explaining the lack of correlation between the increase in TPR during acute and chronic occlusion.

Predictive Factors of LV Diameter and Hypertrophy Regression

We prospectively tested the ability of several echocardiographic and noninvasive hemodynamic parameters, all of

which are easy to obtain in clinical practice, to predict the regression in LV end-diastolic dimension and hypertrophy after surgical fistula closure. In a recent study, van Duijnhoven et al. (*11*) found a correlation between preoperative LV mass and end-diastolic diameter and the reduction in LV mass as determined 4 to 5 months after surgical closure of the AV fistula. The hemodynamic effects of a temporary closure of the AV shunt were, however, not assessed in this study (*11*). We did not find this correlation in our patients. Although the reason for the discrepancy between our two studies is unclear, our results likely reflect the fact that the chronic load imposed by the fistula is not the only determinant of LV dimension and mass. Indeed, hypertension, anemia, hypoalbuminemia, and ischemic heart disease may also affect LV geometry and act as confounding factors (*6*). Our results, therefore, suggest that the presence of abnormalities in LV morphology alone is probably insufficient to guarantee that a patient will benefit from fistula closure.

We found that postoperative reductions in LV diameter and hypertrophy are best predicted by the dynamic increase in TPR and blood pressure observed during an acute occlusion of the fistula. This acute increase directly relates to the proportion of the vascular bed that is dependent on the fistula. It is, therefore, not surprising that the acute increase in TPR and MABP best reflects the relative load imposed by the AV shunt and thus best correlates with the postoperative regression in LV dimension and hypertrophy. In the present study, an increase in TPR of more than a third of baseline value predicted a ≥5% reduction in LV end-diastolic diameter index with a sensitivity of 80%, a specificity of 71%, a positive predictive value of 80%, and a negative predictive value of 71%. Similarly, an increase in MABP during compression of more than 10% of baseline predicted a ≥5% reduction in LV end-diastolic diameter index with a sensitivity of 70%, a specificity of 86%, a positive predictive value of 88%, and a negative predictive value of 67%.

Our study also shows that brief periods of fistula occlusion can be safely performed. Indeed, and perhaps because no patients studied had small fistulas, we did not observe any access thrombosis after pneumatic compression.

Clinical Implications

This study confirms that noninvasive estimation of the hemodynamic burden imposed by a fistula is feasible. By allowing postoperative morphological changes to be predicted, the assessment of an acute occlusion of AV fistula may help to select patients with a well-functioning kidney transplant and signs or symptoms suggestive of heart failure for surgical fistula closure. Whether the effects of surgical closure on LV diameter and mass can be translated in terms of clinical benefit and prevention of long-term complications cannot be ascertained from these data. However, the prevalence of LV hypertrophy is high in renal transplant patients (*7*, *24*, *27*), and recent data suggest that, as in the general population (*28*), it contributes to the high cardiac mortality rate in the transplant population (*27*). Our data suggest that surgical closure of persistent AV fistula after renal transplantation is safe and has the potential to rapidly correct abnormalities of LV geometry in a significant proportion of patients. In addition, the majority of our patients presented symptomatic improvement, in terms of exertional dyspnea and palpitations (data not shown). Prospective and randomized studies should therefore investigate whether elective fistula closure in selected patients is able to reduce the high incidence of cardiac morbidity and mortality after renal transplantation.

For obvious reasons, our study population did not include patients currently on hemodialysis. Since there is no reason to believe that the flow through functioning AV fistulas markedly differs in dialysis patients as compared with transplant recipients, noninvasive assessment including an acute temporary fistula occlusion could be easily performed in dialyzed patients with heart failure to evaluate the hemodynamic burden imposed by the shunt and, therefore, to establish the diagnosis of unrecognized high-output cardiac failure due to excessive shunting. Indeed, this diagnosis can be easily overlooked, because anemia, hypertension, and fluid overload may obscure the clinical picture.

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SUCCESSFUL MANAGEMENT OF AN ABO-MISMATCHED LUNG ALLOGRAFT USING ANTIGEN-SPECIFIC IMMUNOADSORPTION, COMPLEMENT INHIBITION, AND IMMUNOMODULATORY THERAPY[1]

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Background. **Successful management of an ABO-mismatched lung allograft recipient has not previously been described.**

Methods. **Because of a clerical error, a 67-year-old blood type B patient with idiopathic pulmonary fibrosis received a left single-lung allograft from a blood type A donor. Cyclophosphamide was added to immunosuppression with anti-thymocyte globulin induction, cyclosporine, mycophenolate mofetil, and prednisone. When increasing anti-A antibody titers were detected, antigen-specific immunoadsorption, anti-CD20 monoclonal antibody, and recombinant soluble complement receptor type 1 (TP10) were administered.**

Results. **Rising anti-A antibody titers were reduced acutely by immunoadsorption, and remained low during long-term follow-up. Humoral injury to the graft was not detected. Acute cellular rejection and multiple complications were successfully managed. Three years after transplantation the patient is clinically well on stable maintenance immunosuppression and prophylactic photochemotherapy.**

Conclusions. **Modulation of anti-A antibody, preserved graft function, and a favorable patient outcome can be achieved for an ABO-mismatched lung allograft.**

Transplantation is generally avoided in the context of ABO blood group mismatch because of the risk of hyperacute rejection or accelerated humoral injury (vascular rejection) (*1*, *2*). However, the ABO barrier is systematically broached for highly selected populations of patients in whom low isoagglutinin titers are present or can be achieved by perioperative depletion of antibodies using plasmapheresis or specific

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