

# Arteriovenous Fistula Closure After Renal Transplantation: A Prospective Study With 24-Hour Ambulatory Blood Pressure Monitoring

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We prospectively evaluated the effects of arteriovenous fistula closure on 24-hour ambulatory blood pressure measurements and on left ventricular geometry assessed by echocardiography. Sixteen kidney transplant recipients were studied before and 1 month after surgical fistula closure. The mean of 24-hour diastolic blood pressure increased from  $77 \pm 7$  mmHg to  $82 \pm 8$  mmHg ( $P=0.003$ ) without systolic changes. The diastolic blood pressure increase correlated with the reduction in left ventricular mass ( $P=0.0034$ ). In multivariate analysis, the diastolic blood pressure increase best correlated with preoperative cardiac index ( $P=0.01$ ). After a similar time delay between two studies, blood pressure remained unchanged in 14 kidney transplant controls with a patent fistula not scheduled for closure. Because the increase in diastolic blood pressure after arteriovenous fistula closure occurred regardless of the preoperative level of diastolic pressure, we suggest that blood pressure should be monitored after fistula closure, particularly when preoperative diastolic blood pressure is borderline or elevated.

**Keywords:** Arteriovenous fistula, Renal transplantation, Blood pressure, Blood pressure monitoring, Echocardiography.

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Despite a reduction in left ventricular (LV) mass after closure of large arteriovenous fistulas (AVF) in renal transplant recipients (1–3), LV geometry tends to remain abnormal, with a persisting predominantly concentric morphology (3). This pattern, which likely reflects a shift from predominant volume towards pressure overload (4), might be enhanced by deleterious effects of AVF closure on blood pressure (BP). Both systolic and diastolic BP acutely increase upon compression of AVF (2,5,6). In animals, experimental AVF creation acutely decreases BP (7–9) and increases pulse pressure (8), whereas fistula closure restores BP to normal levels (9). In contrast, data on the chronic BP effects of AVF creation and closure in human are scarce and controversial. Iwashima et al. showed that diastolic BP decreased on day 7 (but not on day 14) after creation of an AVF (10).

Although others did not observe any significant BP change 2 weeks and 3–4 months after surgical AVF closure (1,11), we have previously reported increase in diastolic BP up to 18 months after AVF closure (3). Importantly, previous data were derived from casual BP measurements and not from 24-hr ambulatory blood pressure monitoring (ABPM). The latter better assesses the true BP load, better correlates with target organ lesions, and has superior prognostic significance (12,13). Because hypertension negatively impacts long-term outcomes after renal transplantation (14), the expected clinical benefit of AVF closure may be hindered if BP

increases. We therefore tested the hypothesis that AVF closure influences BP by prospectively analyzing 24-hr ambulatory BP recordings and assessing their relationship to changes in LV morphology.

The protocol was approved by the Ethics Committee of our institution and all patients gave informed consent to participate. Between January 2004 and March 2007, a total of 16 kidney transplanted patients referred for AVF closure were enrolled. The referring nephrologist requested AVF surgical closure (7 radioradial and 9 brachial communicating) for one or more of the following reasons: exertional dyspnea, palpitations, and/or heart failure ( $n=9$ ); venous hypertension with swelling of the extremities and/or erythrocytosis ( $n=7$ ); and/or cosmetic reasons ( $n=1$ ). All patients had stable kidney graft function. At inclusion, 15 patients were using at least one antihypertensive drug (median 2.5 drugs per patient): calcium entry blockers ( $n=5$ ), angiotensin-converting enzyme inhibitors or angiotensin-2 receptor antagonists ( $n=4$ ),  $\beta$ -blocking agents ( $n=14$ ),  $\alpha$ -blocking agents ( $n=4$ ), and/or diuretics ( $n=10$ ). One patient had the dosage of metoprolol increased from 200 mg to 300 mg/day and another had perindopril 2 mg/day added; there was no other change in antihypertensive and immunosuppressive medications during the study period.

Fourteen kidney transplant patients with patent AVF referred for routine echocardiographic follow-up served as controls. Twelve controls were being treated with one or more antihypertensive drugs (median two drugs per patient), without changes during the study period: calcium entry blockers ( $n=6$ ), angiotensin-converting enzyme inhibitors or angiotensin-2 receptor antagonists ( $n=3$ ),  $\beta$ -blocking agents ( $n=8$ ),  $\alpha$ -blocking agents ( $n=3$ ), and/or diuretics ( $n=5$ ). Patients and controls did not differ in terms of age ( $54 \pm 12$  vs.  $52 \pm 13$  y in patients and controls, respectively,  $P=0.69$ ), sex ratio (7 vs. 9 males,  $P=0.30$ ), time elapsed since transplantation ( $44 \pm 61$  months, median 20 vs.  $51 \pm 55$  months, median 24;  $P=0.75$ ), and time since AVF creation

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(73±65 months, median 53 vs. 80±55 months, median 66;  $P=0.75$ ).

Echocardiography and BP measurements were performed at baseline 22±6 days before (median 9 days, range 1–80 days), and 35±10 days (median 32 days, range 21–49 days) after AVF closure. Controls were also studied twice. The time delay between the two studies was similar for patients and controls (56±25 days, median 48 and 64±72 days, median 44, respectively;  $P=0.70$ ).

Twenty-four hour ABPM was recorded at 20-min intervals by oscillometry (Spacelab 90207, SpaceLabs MEDICAL GmbH, Kaarst, Germany) on the opposite arm to the AVF. A minimum of 80% valid readings was required for data acceptance. The following parameters were analyzed: average of 24-hr systolic and diastolic BP measurements, of daytime (between 8:00 a.m. and 10:00 p.m.) and nighttime (between 12:00 a.m. and 6:00 a.m.) readings, and heart rate. Pulse pressure was defined as the average of the difference between systolic and diastolic BP for each 24-hr measurement.

Echocardiographic studies were performed using a Philips Sonos 5500 system. Analysis was performed according to the American Society of Echocardiography recommendations and indexed when appropriate (15). Doppler echocardiography allowed the measurement of stroke volume and cardiac output (CO) (16). Total peripheral resistance (TPR; dyne/sec/cm<sup>5</sup>) was calculated from CO (L/min) and simultaneous mean arterial BP (MABP; mmHg) using the following formula:  $TPR=80 \times MABP/CO$ . LV ejection fraction was calculated using the Teichholz method (17). LV mass was calculated using the Devereux formula (18) and indexed to body surface area (LVMI).

Fistula flow was assessed using an ultrasound color-flow scanner with a linear-array transducer. It was expressed

as the flow in the brachial artery approximately 2 cm above the elbow proximal to the fistula (1).

Data are reported as mean±standard deviation. Student's *t* test for unpaired data was used to compare patients with controls and a paired *t* test was used to compare visit 1 to visit 2 in patients and in the control subjects. Correlations between variables were assessed by the Pearson coefficient. Differences in the proportions of patients were assessed by Fisher's exact test. A multiple regression analysis was used to assess which of the preoperative independent hemodynamic parameters accounted for the postoperative increase in diastolic BP. A *P* value <0.05 was considered significant.

AVF flow was similar in patients and controls (1.52±0.48, range 0.53–2.4 L/min vs. 1.67±0.65, range 0.53–2.7 L/min, respectively;  $P=0.48$ ). Renal function and plasma hematocrit remained unchanged after AVF closure.

Ambulatory diastolic BP increased after AVF closure, whereas 24-hr systolic BP remained unaltered, resulting in a decrease in pulse pressure (Table 1). The percentage of non-dippers (decrease in nocturnal BP <10%) remained unchanged (69% before to 56% after AVF closure for both systolic and diastolic BP, respectively;  $P=0.72$ ).

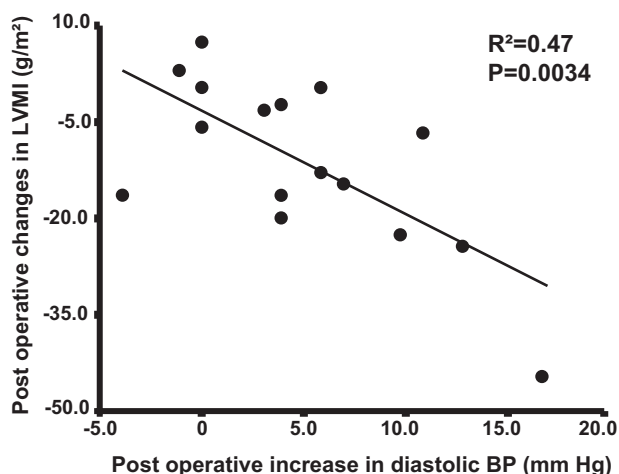
LV mass was reduced after AVF closure (Table 1). The increase in diastolic BP correlated with the decrease in LVMI (Fig. 1). Baseline 24-hr ABPM and echocardiographic parameters in the controls did not differ from those observed preoperatively in the study group and did not change during the follow-up (Table 1). Both preoperative cardiac index and fistula flow were correlated with the increase in diastolic BP (Table 2). However, only cardiac index was an independent predictor of an increase in diastolic BP in the multivariate analysis. The level of preoperative diastolic BP did not predict the changes in diastolic BP.

**TABLE 1.** Patient characteristics

Variables	Patients			Controls			
	Baseline	After AVF closure	<i>P</i> value (post AVF closure vs. baseline)	Visit 1	<i>P</i> value (visit 1 vs. baseline)	Visit 2	<i>P</i> value (visit 1 vs. visit 2)
24-hr SBP (mm Hg)	132±15	132±15	0.90	130±10	0.62	129±8	0.81
24-hr DBP (mm Hg)	77±7	82±8	0.003	77±8	0.92	77±7	0.95
Daytime SBP (mm Hg)	134±13	132±16	0.64	133±10	0.88	131±8	0.27
Daytime DBP (mm Hg)	78±7	83±10	0.008	79±8	0.71	79±7	0.72
Nighttime SBP (mm Hg)	128±20	125±17	0.41	122±11	0.37	126±11	0.12
Nighttime DBP (mm Hg)	73±7	75±9	0.44	70±8	0.26	73±9	0.14
24-hr pulse pressure (mm Hg)	55±15	51±11	0.041	53±10	0.58	53±9	0.67
24-hr heart rate (bpm)	67±10	65±11	0.38	68±9	0.77	70±8	0.16
LVEDDI (mm/m <sup>2</sup> )	29.5±3.4	27.5±2.5	<0.001	28.5±2.8	0.36	28.4±2.6	0.67
LVMI (g/m <sup>2</sup> )	148±44	137±40	0.003	133±40	0.30	134±39	0.54
LV ejection fraction (%)	64±8	67±8	0.16	71±7	0.07	70±7	0.91
Cardiac index (L/min/m <sup>2</sup> )	3.53±0.83	2.62±0.68	<0.001	3.52±0.49	0.96	3.60±0.66	0.56
SVI (ml/m <sup>2</sup> )	54±12	41±9	<0.001	52±11	0.61	52±10	0.95
TPR (dyn.sec.cm <sup>5</sup> )	1210±300	1755±397	<0.001	1178±224	0.75	1157±255	0.80

Data are means±SD.

SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEDDI, indexed LV end-diastolic diameter; LVMI, indexed LV mass; SVI, stroke volume index; TPR, total peripheral resistance.



**FIGURE 1.** Correlation between the changes in diastolic BP (expressed as postoperative minus preoperative 24-hour ambulatory diastolic BP) and the decrease in indexed LV mass (LVMI, expressed as postoperative minus preoperative LVMI).

**TABLE 2.** Preoperative predictors of increase in diastolic BP after AVF closure

Parameters	R <sup>2</sup>	Slope	Univariate P value	Multivariate P value
Cardiac index	0.446	0.0045	0.0047	0.01
Fistula flow	0.2597	0.0059	0.0438	0.09
Diastolic BP	0.019	-0.11	0.61	
Systolic BP	0.025	-0.06	0.56	
Left ventricular mass index	0.10	0.04	0.24	

This prospective and controlled study shows that AVF closure induces a sustained increase in ambulatory diastolic BP; this rise is negatively related to LV mass reduction and positively related to preoperative markers of volume overload. Taken together, these findings suggest that large AVFs induce a chronic reduction in diastolic BP that does not offset the deleterious effects of volume overload on LV mass in kidney transplanted patients.

Because renal transplantation itself may alter both the 24-hr BP profile and LV morphology (14,19,20), we also studied a control group matched to the study group in terms of posttransplantation and postfistula creation periods and with patent AVF. Neither BP nor LV morphology changed in controls. In addition, antihypertensive drugs, immunosuppressive therapy, renal function and hematocrit levels remained unchanged during the study period.

That this effect on diastolic BP, observed one month after surgery will persist later during follow-up remains speculative, but is supported by previous casual BP measurements performed 18 months after AVF closure (3).

Only patients with clinical indication of closure were studied. Because the balance between the relative risks and benefits of systematically closing large AVFs after renal transplantation remains unknown (21), it is currently not our practice to close asymptomatic AVF. Regression of LV hyper-

trophy may improve cardiovascular prognosis, but the persistence of a LV concentric geometry (3) could have the opposite effect, particularly if it is secondary to increased BP (22,23). The observed correlation between the magnitude of LV mass reduction and the diastolic BP increase (Fig. 1), and the lack of change in systolic BP, which when measured by ABPM better predicts LV hypertrophy than diastolic BP (14,24), suggest that this persistent concentricity does not result from increased BP after AVF closure. However, the 5 mmHg diastolic BP increase observed in the present study may deleteriously affect the cardiovascular risk profile (25). Whether the decreased pulse pressure is related to changes in arterial compliance (which might have a favorable effect on the subsequent rate of cardiovascular morbid events [26]) or to the complex effects of the correction of the fistula-related hemodynamic changes remains to be elucidated. Nevertheless, because aggressive control of BP in renal transplant recipients favorably affects both long-term graft function and patient survival (27), and because the increase in diastolic BP may occur whatever the level of preoperative diastolic BP, we suggest BP monitoring after closure of AVF in renal transplant patients with evidence of volume overload, particularly if preoperative BP is borderline or elevated.

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