Nephrol Dial Transplant (2001) 16: 368–372

Nephrology Dialysis Transplantation

Original Article

Effect of closure of the arteriovenous fistula on left ventricular dimensions in renal transplant patients

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Abstract

Background. Left ventricular hypertrophy is common in renal transplant patients. One of the factors that might contribute to this phenomenon is the persisting presence of an arteriovenous (AV) fistula. Several reports have described the presence of high-output cardiac failure, which subsided after closure of the AV fistula. However, the long-term effects of elective closure of the AV fistula on left ventricular dimensions in stable renal transplant patients have never been prospectively studied.

Subjects and methods. Twenty patients (15 male, 5 female; mean age 51 ± 12 years) with a well-functioning renal transplant were included. Patients with severe heart failure (NYHA III or IV) were excluded. Before and 3–4 months after closure of the AV fistula, an echocardiogram was performed. Fistula flow was assessed by colour duplex-Doppler sonography.

Results. Mean fistula flow was 1790 ± 648 ml/min. After closure of the fistula, left ventricular end-diastolic diameter (LVEDD) (51.5 ± 5.8 *vs* 49.3 ± 5.4 mm, $P < 0.01$) and left ventricular mass index (LVMi) (135.0 ± 34.1 *vs* 119.8 ± 23.2) decreased. The change in LVMi after fistula closing was significantly related to the LVMi and LVEDD before operation ($r = 0.74$ and $r = 0.60$, $P < 0.01$), but not to fistula flow. Interventricular septal and posterior-wall diastolic thickness did not change. Heart rate decreased (72 ± 10 *vs* 69 ± 9, $P = 0.03$) Blood pressure and creatinine clearance did not change.

Conclusion. Closure of the arteriovenous fistula in stable renal transplant patients results in a decrease in LVMi, due to a reduction in LVEDD. The change in LVMi is significantly related to the LVMi and LVEDD before fistula closing. In patients with a well-functioning allograft and persistent LV dilatation, closure of the AV fistula might be considered.

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Introduction

Left ventricular hypertrophy (LVH) is very common in patients with end-stage renal failure. This is especially important in view of the relationship between LVH and mortality in these patients. The cause of LVH in renal patients is multifactorial and includes factors such as hypertension, anaemia, the uraemic state itself, and the presence of an arteriovenous fistula (AV) [1]. It has been shown that left ventricular dimensions may improve after renal transplantation, although complete regression of LVH is usually not obtained [2–4]. One of the factors that may contribute to the persistence of LVH after renal transplantation is the presence of an AV fistula. The presence of an AV fistula lowers systemic vascular resistance, resulting in an increase in stroke volume and cardiac output in order to maintain blood pressure [5]. In the end, this may lead to left ventricular volume overload and eccentric LVH. Various case reports have described high-output cardiac failure in patients with high-flow fistulae, which subsided after closure of the fistula [6,7]. However, the cardiac effects of closure of AV fistulae in patients without clinical heart failure have until now not been studied systematically. In this study we prospectively assessed the effect of closure of an AV fistula on left ventricular dimensions in stable renal transplant patients.

Subjects and methods

Patients

After giving informed consent, 20 patients with a functioning kidney transplant with stable renal function were included. Seventeen patients had a Cimino fistula, two patients a brachial fistula, and one patient a PTFE graft. Patient characteristics are summarized in Table 1. Patients with heart failure NYHA III or IV were excluded, because in these patients the progression of the cardiac disease might complicate the interpretation of the effect of fistula closing. The aetiology of the renal disease was renal artery stenosis ($n = 1$), nephrosclerosis ($n = 3$), adult polycystic disease

Table 1. Clinical characteristics

Age (years)	51.3 ± 12.0 (25–69)
Sex	15 male; 5 female
Time post-transplantation (months)	46.2 ± 38.8 (8–162)
Time after construction of fistula (months)	104.8 ± 65.8 (36–252)
Body weight (kg)	71.4 ± 12.0 (50.5–96.3)
Body surface area (m^2)	1.86 ± 0.19 (1.43–2.15)

($n=4$), diabetes mellitus ($n=1$), haemolytic–uraemic syndrome ($n=1$), chronic glomerulonephritis of unknown origin ($n=3$), membranoproliferative glomerulonephritis ($n=1$), extracapillary glomerulonephritis ($n=2$), Alport's disease ($n=1$), chronic pyelonephritis ($n=2$), and IgA nephropathy ($n=1$).

Five patients had a history of ischaemic cardiac disease: angina pectoris NYHA II ($n=1$), coronary-artery bypass grafting ($n=3$), and myocardial infarction ($n=3$).

Fifteen patients used one or more vasoactive drugs: angiotensin-converting enzyme inhibitors ($n=3$), beta-receptor antagonists ($n=8$), calcium antagonists ($n=10$), diuretics ($n=2$), angiotensin-receptor antagonists ($n=1$), and alpha-receptor antagonists ($n=4$). No change in the prescription of vasoactive medication occurred throughout the study period. All patients used one or more immunosuppressive drugs: cyclosporin ($n=10$), prednisolone ($n=13$), azathioprine ($n=7$), and tacrolimus ($n=8$).

Methods

The first measurements were performed within 2 months before the closure of the fistula. The second echocardiogram was performed within 4–5 months after fistula closure. Each patient was used as his/her own control.

Echocardiography

Left ventricular dimensions were assessed by echocardiography. Two-dimensional echocardiography was performed using a Hewlett Packard 2500 or 5500 ultrasound system with standard imaging transducers. The following parameters were assessed: left atrial diameter (LAD), left ventricular end-diastolic diameter (LVEDD), posterior wall end-diastolic thickness (PW-EDWT), interventricular septal end-diastolic wall thickness (IVS-EDWT), left ventricular ejection fraction (LVEF), and left ventricular volume index. Left ventricular mass (LVM) was calculated according to the formula of Devereux and Reichek: $LVM = 1.04\ ((LVEDD + IVST + PWT)^3 - (LVEDD)^3) - 13.6$. LVM was also indexed for body surface area (BSA) (LVMi). Left ventricular volume index was calculated according to the Teichholz formula: $(7.0/(2.4 + LVEDD)) * LVEDD^3) : BSA$.

Fistula flow

Fistula flow was assessed using an ultrasound colour-flow scanner with a linear-array transducer operating at 5 MHz in Doppler mode and 7.5 MHz in imaging mode. Fistula flow was expressed as the flow in the brachial artery 2 cm above the elbow (in the fistula arm) proximal to the fistula, assessed at the same height. This method was used as measurement of flow over the fistula itself can be unreliable because of the possible presence of irregularities.

Volume status

Volume status was assessed by echography of the inferior vena cava. In healthy controls and haemodialysis patients, this method was found to correlate very well with right atrial pressure and blood volume [8].

Blood pressure and heart rate

Blood pressure was measured using standard sphygmomanometry. Blood pressure and heart rate were measured in supine position after a 15-min rest.

Statistical analysis

Changes in haemodynamic parameters before and after fistula closing were analysed by the Mann–Whitney U test. Correlations between various variables were assessed by Pearson's r. A P value <0.05 was considered significant.

Results

Change in cardiac parameters

Mean fistula flow was 1790 ± 648 (range 1015–3540) ml/min. After fistula closing, LAD, PW-EDWT, IVS-EDWT, and LVEF did not change significantly, as summarized in Table 2. In contrast, LVEDD, LVM, and LVMi decreased (Figure 1). Before fistula closure, the prevalence of LVH (LVMi >100 g/m^2 in females and >131 g/m^2 in males [9]) was 60% in the study population, and 33% after fistula closure.

The change in LVMi after fistula closure was significantly related both to LVMi and LVEDD before operation ($r=0.74$, $P<0.001$, and $r=0.60$, $P<0.01$). The relationship between fistula flow and the change in LVMi was not significant ($r=-0.35$, $P=0.17$). The change in LVMi was also not related to haemoglobin level ($r=-0.04$), the duration of the fistula ($r=-0.05$), or the time after transplantation ($r=0.12$).

Five patients had clinically symptomatic cardiac disease. In these patients the reduction in LVMi was 14.8 ± 15.0 g/m^2 compared to 15.4 ± 25.8 in patients without clinically symptomatic cardiac disease ($P=$ NS). Two of the patients with clinically symptomatic cardiac disease had regional dyskinesia on the echocardiogram, which was not influenced by fistula closure.

Four patients were classified as anaemic in our study (haemoglobin <8.0 mmol/l in males and <7.4 mmol in females). Left ventricular mass index was somewhat higher in these patients (143 ± 7.3 *vs* 133 ± 37.9 g/m^2, $P=$ NS); however, the change in LVMi was not clearly different (−16.5 ± 17.7 *vs* −14.9 ± 24.9 g/m^2).

Two patients had brachial fistulae and one had a PTFE graft. Mean shunt flow in these patients (2072 ± 513 and 1085 ml/min respectively) was not different compared to patients with radiocephalic

Table 2. Parameters before and after fistula closing

	Before	After	*P*
LAD (mm)	47.1±5.2 (40–58)	46.2±6.6 (38–61)	NS
LVEDD (mm)	51.5±5.8 (42–64)	49.3±5.4 (40–59)	<0.01
PW-EDWT (mm)	10.5±1.3 (8–14)	10.2±1.2 (8–13)	NS
IVS-EDWT (mm)	10.6±2.0 (7–16)	10.4±1.5 (8–13)	NS
LVM (g)	252.0±70.2 (120–409)	222.4±47.9 (131–333)	<0.01
LVMi (g/m^2)	135.0±34.1 (84–232)	119.8±23.2 (89–167)	<0.01
Left ventricular volume index (ml/m^2)	69.4±16.2 (38.1–97.0)	62.9±15.5 (34.0–93.6)	<0.01
Vena cava diameter (mm)	15.1±4.2 (9–27)	14.8±4.7 (9–25)	NS
Systolic blood pressure (mmHg)	135.2±17.2 (105–170)	135.8±17.8 (120–180)	NS
Diastolic blood pressure (mmHg)	78.8±6.8 (70–95)	81.2±10.4 (60–110)	NS
Heart rate	72.4±9.9 (58–97)	69.2±8.5 (56–89)	0.03
Haemoglobin (mmol/l)	8.5±1.1 (6.3–10.4)	8.7±1.0 (5.8–10.4)	NS
Serum creatinine (μmol/l)	144.9±43.5 (97–270)	150.2±56.6 (82–264)	NS
Creatinine clearance (ml/min)	51.5±12.4 (33–80)	53.6±18.4 (28–98)	NS

LAD, left atrial diameter (LAD); LVEDD, left ventricular end-diastolic diameter; PW-EDWT, posterior wall end-diastolic thickness; IVS-EDWT, interventricular septal end-diastolic wall thickness; LVEF, left ventricular ejection fraction; LVM, left ventricular mass; LVMi, left ventricular mass index.

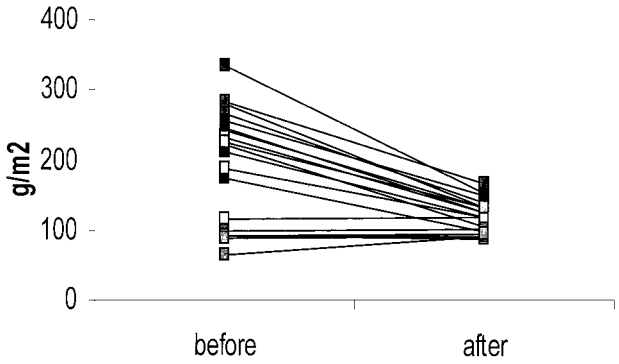

Fig. 1. Change in LVMi after fistula closure.

fistula (1821±690 ml/min). Also if these patients were excluded, the change in LVMi after fistula closure remained significant (−15.2±23.2 g/m^2, $P<0.01$). Because the time after transplantation may also influence the change in LVMi, the reduction in LVMi was analysed separately in patients who had been transplanted more than 18 months previously ($n=16$). Also in this subgroup, the reduction in LVMi was significant (135.9±37.0 *vs* 123.2±23.4 g/m^2).

Other parameters

Systolic and diastolic blood pressure did not differ before and after fistula closing. However, heart rate decreased significantly ($P=0.03$). Volume status, as assessed by the diameter index of the inferior vena cava, did not differ before and after fistula closing (Table 2). Also, haemoglobin and renal function did not change (Table 2).

Discussion

In this study we showed that left ventricular mass decreased significantly in renal transplant patients after closure of an AV fistula. Although various case reports described the effects of fistula closing in patients with high-output cardiac failure, this is the first study in which cardiac dimensions were studied prospectively after routine closure of the fistula. The follow-up echocardiogram was performed 3–4 months after closure of the fistula, because at this time possible effects on left ventricular dimensions may be expected [10].

The prevalence of LVH in uraemic patients is very high and bears a strong relationship to cardiovascular morbidity and mortality. In prospective studies, two groups found a reduction in LV mass after renal transplantation, whereas one did not. In the present study the prevalence of LVH was 60%. In general, two main types of LVH can be distinguished: concentric and eccentric hypertrophy. Concentric hypertrophy is primarily characterized by an increase in left ventricular wall thickness, and eccentric hypertrophy by an increase in left ventricular volume. Concentric hypertrophy in uraemic patients is primarily caused by pressure overload and possibly also by myocardial fibrosis, due to the uraemic state. On the other hand, eccentric hypertrophy in uraemic patients has been primarily attributed to volume overload or the presence of a high-output state, due to anaemia or the presence of an AV shunt [1,5]. In the present study, the decrease in left ventricular mass after closure of the fistula was solely due to a decrease in left ventricular diameter, whereas left ventricular wall thickness did not change. Therefore the effects of the AV fistula on cardiac structure are at least partially reversible. Closure of the AV fistula results only in a decrease in eccentric

LVH without an effect on concentric hypertrophy, which is understandable from a pathophysiological point of view. Nevertheless, in 33% of the patients with evidence of LVH before fistula closing, LV mass normalized. The reduction in left ventricular diameter is most probably explained by the reversal of the hyperdynamic state, induced by the AV fistula.

The results of the present study are in agreement with the findings of Ori *et al.*, who assessed the short-term effects of the creation of an AV fistula on cardiac structure and function. As early as 2 weeks after operation an increase in left ventricular diameter was observed, in combination with an increase in cardiac output and a decrease in systemic vascular resistance [11]. Our results are in some disagreement with the findings of Hüting *et al.* and Pereiro *et al.* [3,4]. These authors studied prospectively the influence of renal transplantation on LV mass and function. In the study of Hüting *et al.*, with a mean follow-up time of 41 months after renal transplantation, an increase in left atrial and end-diastolic diameters was found after renal transplantation, whereas LV muscle mass remained stable and LV function improved. Besides a decrease in left atrial diameter in patients with an occluded AV fistula, no difference of fistula patency on the change in cardiac structure or function was found [3]. In the study of Pereiro *et al.* with a mean follow up time of 10 months after renal transplantation, LV mass and LV end-diastolic diameter decreased. Also in this study, no differences regarding LV mass and volume changes were found between patients with or without a patent AV fistula [4]. However, these studies were not exclusively designed to study the effect of AV fistula closure on cardiac structure and function. In these studies, other factors such as normalization of anaemia/haematocrit [4] and blood-pressure control may have confounded the haemodynamic effects of fistula closing. In the present study, no change in haematocrit, blood pressure, or use of antihypertensive medication occurred.

The relationship between the magnitude of the fistula flow and the change in cardiac parameters after fistula closure was not significant (also not after correction for BSA). However, the change in LV mass after fistula closing was highly dependent upon LV mass and LV end-diastolic diameter before the operation. The absence of a relationship between fistula flow and the change in cardiac parameters after closing may seem somewhat confusing. It should, however, be stated that in all patients, fistula flow was higher than 1 l/min. The relatively high fistula flow in the included patients may be explained by the fact that they nearly all had well-developed fistulae for a longer period of time.

Fistula closing did not result in a change in LV ejection fraction. Nevertheless, in most patients, LV function was fairly normal. However, also in the four patients with a significantly impaired LV systolic function, defined by a LV ejection fraction below 40%, LV ejection fraction did not increase after closure of the fistula. In the literature, the effect of fistula closing on LV systolic function is controversial. However, as patients with symptomatic heart failure were excluded, no recommendations regarding the effect of fistula closure on LV function in patients with impaired systolic function can be drawn from the present study.

Despite its prospective design, the main limitation to the study is the absence of a control group. Therefore, the results should be interpreted with some caution. One could actually hypothesize that some changes in LV dimensions could also be due to the effect of the renal transplantation itself. However, we think that this is very unlikely for the following reasons. First, although some patients were transplanted fairly recently, the great majority of the patients were studied for some years after they received their transplant (mean 46 months; range from 8 to 162 months). Also, when only patients who had received their kidney transplant more than 18 months ago were analysed, the change in LV dimensions remained significant. Moreover, as stated previously, no changes in other factors that could influence cardiac structure, such as volume status, serum haemoglobin, or blood pressure levels, occurred within the study period.

In conclusion, closure of the AV fistula after renal transplantation results in a decrease in left ventricular mass, due to a reduction in left ventricular diameter. The change in LV mass is significantly related to the LV mass and LVEDD before fistula closing.

These results are of importance in view of the high prevalence of LVH in renal transplant patients. Whether these effects lead to clinical benefit in view of long-term complications cannot be concluded from the present study. However, it should be remembered that the outcome of dialysis patients with LV dilatation was significantly worse than patients with a normal echocardiogram [9]. Therefore, in patients with well-functioning allografts and persistent LV dilatation, closure of the AV fistula might be considered.

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Received for publication: 2.5.00
Accepted in revised form: 10.8.00