# **ORIGINAL ARTICLE**

# To close or not to close: fistula ligation and cardiac function in kidney allograft recipients

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#### **KEY WORDS**

#### ABSTRACT

arteriovenous fistula, left ventricular hypertrophy, renal transplantation **INTRODUCTION** Arteriovenous fistulas are a preferred access for hemodialysis. Subsequent hemodynamic changes in systemic circulation may cause heart failure. The general conclusions that can be drawn from the few available studies are that high-flow fistulas causing symptomatic heart failure should be subjected either to reconstruction or ligation. However, it is still unclear whether a well-functioning fistula should be ligated after successful kidney transplantation.

**OBJECTIVES** The aim of our study was to assess the effect of the fistula on heart function in patients after kidney transplantation.

**PATIENTS AND METHODS** The study included 18 patients after kidney transplantation. Five patients underwent fistula ligation for esthetic reasons; 4 fistulas thrombosed shortly after transplantation. A group of 9 patients with a patent fistula was matched for age and sex. Heart function was assessed by physical examination and echocardiography.

**RESULTS** The study group consisted of 6 women and 3 men, aged 32 to 64 years, with 6 forearm and 3 arm fistulas, and with hemoglobin levels ranging from 6.95 to 9.63 mmol/l. The control group consisted of 6 women and 3 men, aged 38 to 66 years, with 5 forearm fistulas and hemoglobin levels ranging from 7.32 to 9.25 mmol/l. Control echocardiography was performed in each patient 3 months after fistula closure and did not reveal any significant differences compared with baseline examination.

**CONCLUSIONS** Fistula ligation performed in a stable kidney allograft recipient does not seem to have a beneficial effect on cardiac function during short-term follow-up. Decision making should be cautious and balanced, because the creation of a new access may be extremely difficult and not always feasible.

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**INTRODUCTION** There have been numerous attempts to improve survival in patients with end-stage renal disease (ESRD) treated with dialysis.<sup>1</sup> Arteriovenous (AV) fistulas are a preferred access for hemodialysis in the treatment of ESRD. Brachial artery flow volume in normal conditions is about 60 to 120 ml/min, whereas effective hemodialysis requires a flow rate of 400 to 600 ml/min. In most fistulas, the average flow rate ranges between 400 and 1800 ml/min. These values may be achieved thanks to an increased cardiac output, from 4 to 8 l/min or even higher. Sometimes such change may be asymptomatic, while at other times it may result in heart failure.

The conclusions that can be drawn from the few available studies are that high-flow fistulas causing

symptomatic heart failure should be subjected either to reconstruction or ligation. There is no consensus as to the definite borderline flow values. Even the relatively low values of the AV fistula flow of 800 ml/min or AV graft of 1200 ml/min were the selection criterion treatment of cardiac failure and steal syndrome resulting from high-flow vascular access.<sup>2</sup> One study clearly showed high predictive power for the occurrence of cardiac failure with high arterial flow (Qa) exceeding 2.0 l/min.<sup>3</sup> Most experts agree that high flow means a flow rate higher than 1600 ml/min.<sup>4</sup> However, the number of studies on vascular access closure among kidney allograft recipients is limited. Mainly the cases of giant fistula ligation have been reported.<sup>5</sup> An aneurysmatic fistula after a successful transplantation can be safely closed.<sup>6</sup>

#### TABLE 1 Patients' characteristics

	Patients (n $=$ 9)	Controls ( $n = 9$ )	Р
age, y	49 ±11	$54 \pm 10$	0.38
sex, female/male	6/3	6/3	_
time after fistula creation, mo	23 ±9	25 ±7	0.58
time after transplantation, mo	$10.1 \pm 9.9$	10.9 ±7.5	0.43
fistula flow, ml/min	717 ±209	$593 \pm 89$	0.12
body mass index, kg/m²	26 ±1.3	25 ±2.3	0.39
serum creatinine, µmol/l	$115.9 \pm 26.6$	118.46 ±17.68	0.77
hemoglobin, mmol/l	7.66 ±0.8	7.79 ±0.62	0.74
systolic blood pressure, mmHg	138 ±8	136 ±5	0.46
diastolic blood pressure, mmHg	82 ±4	78 ±3	0.06
heart rate, beats/min	73 ±5	76 ±6	0.21

Nevertheless, there is still a controversy whether or not to ligate a well-functioning fistula after a successful kidney transplantation, particularly in patients with good and stable graft function. The aim of our study was to assess the effect of the fistula on heart function in patients with ESRD after kidney transplantation.

**PATIENTS AND METHODS** Eighteen patients after kidney transplantation were recruited. The following inclusion criteria were used: stable clinical state, serum creatinine level <177 µmol/l, hemoglobin level >5.6 mmol/l, without diabetes, without a history of cardiovascular events within the last 12 months, without a history or symptoms of heart failure. All patients were normotensive or with well-controlled hypertension. A study group consisted of patients with occluded vascular access. Five patients underwent fistula ligation for esthetic reasons; 4 fistulas thrombosed shortly after transplantation. The control group of 9 patients with a patent fistula was matched according to age and sex. Heart function was assessed by physical examination (shortness of breath, fatigue, and reduced exercise tolerance) and echocardiography (left ventricular [LV] hypertrophy, LV dilation, systolic and diastolic dysfunction, LV ejection fraction, LV mass was indexed to body surface using the Devereux formula<sup>7</sup>). Fistula flow was assessed using the Siemens Acuson X300 ultrasound system with a linear transducer. Blood pressure was measured on the contralateral arm to the AV fistula, using a standard sphygmomanometer. Data are reported as means ± standard deviation. For statistical analysis (Statistica 9.0, Statsoft, Tulsa, Oklahoma, United States), the *t* test for unpaired data was used to compare patients with controls and the t test for paired data was used to compare the visits before and after surgery. Statistical significance was set at P < 0.05.

**RESULTS** The study group consisted of 6 women and 3 men, aged 32 to 64 years, with 6 forearm and 3 arm fistulas, and hemoglobin levels ranging from 6.95 to 9.63 mmol/l. The control group consisted of 6 women and 3 men, aged 38 to 66 years, with 5 forearm fistulas, and hemoglobin levels ranging from 7.32 to 9.25 mmol/l. Characteristics of the patients are presented in TABLE 1. Laboratory tests were performed at first visit. No differences between the groups were observed during the visit. Control echocardiography was performed in each patient 3 months after fistula ligation (TABLE 2). The only differences were noticed in the LV diastolic diameter and LV mass index (LVMI), but the differences were not statistically significant (P = 0.17 and P = 0.08, respectively). A postoperative decrease in the LVMI was caused by the change in the LV diameter rather than in the interventricular septum and posterior wall thickness, and it was not significantly different from the baseline values.

**DISCUSSION** There is no consensus as to whether to preserve or ligate the AV fistula after a successful kidney transplantation. Complications of fistulas, and grafts in particular, are not rare. Steal syndrome and edema, inflammation, cosmetic defects, and the risk of heart failure are the most common reasons for AV fistula closure. Several studies have shown a decrease in the LV volume after the surgery. However, the studies involved mainly patients with symptomatic fistulas and LV hypertrophy. Moreover, it has been shown that LV hypertrophy may improve after kidney transplantation.<sup>8</sup> Of note, anemia, which is a common finding in patients with chronic kidney disease of native kidneys or of a graft, may also worsen heart failure.9 Patients were referred for fistula closure because of exertional dyspnea and heart failure.<sup>10</sup> It is generally acknowledged that hyperkinetic fistulas, with a flow exceeding 2000 ml/min, should be closed. Most studies conducted in the selected population of patients with symptomatic AV fistulas showed regression of LV hypertrophy.<sup>11</sup> On the other hand, it is agreed that the procedures of flow reduction should be considered in all patients with high-flow fistulas.<sup>4,12</sup>

The question is how to deal with relatively healthy kidney recipients, with no cardiac symptoms and a normal-flow fistula. To our best knowledge, this issue has not been investigated so far. We evaluated the effect of fistula flow below

TABLE 2	Comparison of	echocardiogra	phic and Do	oppler parameters
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Patients			Controls					
	B1	S1	P (B1 vs. S1)	B2	P (B1 vs. B2)	S2	P (B2 vs. S2)	P (S1 vs. S2)
LVDD, mm	$46.4 \pm 3.8$	$45.3 \pm 3.6$	0.17	45.2 ±3.1	0.2	$46.3 \pm 4.1$	0.3	0.026
IVS, mm	11.0 ±0,9	11.0 ±0.8	1	10.5 ±1.2	0.18	11.1 ±0.9	0.07	0.8
PWT, mm	11.3 ±0,8	11.1 ±0.6	0.16	$11.4 \pm 1.0$	0.54	$11.3 \pm 0.9$	0.59	0.2
LVMI, g/m <sup>2</sup>	$118.5 \pm 26.3$	113.1 ±21.6	0.09	116 ±22.5	0.76	$115.6 \pm 18.5$	0.9	0.16
LVEF, %	62.3 ±4	60 ±3	0.78	61.2 ±3	0.84	63.4 ±4	0.26	0.46

B1 – baseline 1: initial echocardiography in the study group; S1 – study 1: control echocardiography 3 months post arteriovenous closure in the study group; B2 – baseline 2: initial echocardiography in the control group; S2 – study 2: control echocardiography 3 months post inclusion

Abbreviations: LVEF – left ventricular ejection fraction, IVS – interventricular septum, LVDD – left ventricular diastolic diameter, LVMI – left ventricular mass index, PWT – posterior wall thickness

1000 ml/min on the sufficient circulatory system. Forearm fistulas rarely require closure because of heart failure or hand ischemia. Previous studies did not provide unambiguous recommendations concerning fistula ligation "on patients' demand". Cosmetic reasons appeared as a minor indication in some publications.<sup>13</sup> A pulsatile and dilated vein may not be esthetic. However, it should be kept in mind that such condition causes at least partial functional disability for everyday life and difficulties in returning to work.

The major indication for fistula ligation in all the above papers was the possible harmful effect of the shunt on the cardiovascular system. On the other hand, an inevitable need for the future reuse of the fistula should be taken into account. The ideal patient for the procedure should have a minimal risk for graft loss, and long-term benefits from the ligation should be obvious. However, it is difficult to meet these requirements. Moreover, it is still unknown whether fistula closure will reduce cardiac morbidity and mortality. To assess the possible risk of this procedure, we might refer to the European Society of Cardiology 2009 guidelines.14 However, no data are provided on the rationale for fistula ligation in kidney transplant recipients. On the contrary, complications linked with vascular access are the source of significant morbidity in patients on maintenance dialyses, accounting for 15% of hospital admissions. They occur most commonly in patients with vascular catheters and synthetic prostheses.<sup>15</sup> This is an argument for leaving a native fistula intact after kidney transplantation. In addition, we cannot extrapolate data from the studies conducted in the United States, because due to the dialysis prescription (shorter time, higher ultrafiltration, high-flux dialysis), many patients have either proximal fistulas or grafts that allow to achieve much higher flow rates than in native distal fistulas, which are typical for the European countries.

A longer follow-up is scheduled to evaluate the long-term effect of persistent normal-flow AV fistulas on cardiac function. Larger groups are needed to assess the association between AV fistulas and cardiovascular events. We are fully aware of the limitations of our study, namely, a relatively small number of patients. However, we would like to stress that we studied subjects with normal-flow fistulas who underwent AV fistula closure.

Two studies on the fistula reuse showed that the reconstruction of the AV fistula is possible in some cases.<sup>16,17</sup> Forearm fistulas are prone to thrombosis in a posttransplant period. Nearly 50% of the fistulas stopped functioning after kidney transplantation and required reconstruction so that hemodialysis could be restarted.<sup>16</sup> The need for fistula repair or the creation of a new fistula becomes a challenge, particularly if there is an absolute contraindication for a high-flow graft. A real challenge is when heart failure develops together with chronic allograft nephropathy. Then, despite the possible significant contribution of the AV fistula to the worsening of heart function, a decision may be made to avoid the closure of an important vascular access as long as possible. Timing of the procedure is also questionable. It may happen that high cardiac output maintains the ejection fraction, and surgical closure of a fistula in a patient with New York Heart Association class IV heart failure will result in a sudden death within the next few hours.<sup>18</sup>

In conclusion, fistula ligation performed in a stable kidney allograft recipient does not seem to have a beneficial effect on cardiac structure and function in patients without a previous history of heart failure. Decision making should be cautious and balanced, because the creation of a new access may be extremely difficult and not always feasible.

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# **ARTYKUŁ ORYGINALNY**

# Zamknąć albo nie zamknąć – podwiązanie przetoki a czynność serca u biorców przeszczepu nerki

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#### SŁOWA KLUCZOWE STRESZCZENIE

przetoka tętniczo-żylna, przerost lewej komory, transplantacja nerek **WPROWADZENIE** Przetoka tętniczo-żylna jest preferowanym dostępem do hemodializ. Wywołane przez nią zmiany w układzie krążenia mogą prowadzić do niewydolności serca. Na podstawie nielicznych badań wyciągnięto ogólne wnioski, że przetoka o dużym przepływie, powodująca objawową niewydolność serca powinna być poddana rekonstrukcji lub zamknięciu. Jednakże nadal nie jest jasne czy prawidłowa przetoka po udanym przeszczepie nerki powinna zostać poddana zamknięciu.

**CELE** Celem badań była ocena wpływu przetoki na czynność serca u pacjentów po przeszczepie nerki. **PACJENCI I METODY** Do badania włączono 18 pacjentów po przeszczepie nerki. Pięciu pacjentów przebyło operację zamknięcia przetoki z powodów estetycznych, 4 przetoki zakrzepły wkrótce po przeszczepie. Grupa 9 pacjentów z drożną przetoką została dobrana pod względem wieku i płci. Czynność serca oceniono badaniem przedmiotowym oraz echokardiograficznym.

WYNIKI Grupę badaną stanowiło 6 kobiet i 3 mężczyzn, w wieku 32–64 lat, z 6 przetokami na przedramieniu i 3 na ramieniu, z poziomem hemoglobiny w zakresie 6.95–9.63 mmol/l. Grupę kontrolą stanowiło 6 kobiet i 3 mężczyzn, w wieku 38–66 lat, z 5 przetokami na przedramieniu, z poziomem hemoglobiny w zakresie 7.32–9.25 mmol/l. Kontrolne badanie echokardiograficzne zostało wykonane u wszystkich pacjentów 3 miesiące po zamknięciu przetoki i nie wykazało istotnych różnic w stosunku do badania wyjściowego.

WNIOSKI Podwiązanie przetoki, przeprowadzone u stabilnego biorcy nerki nie wykazuje korzystnego wpływu na czynność serca w krótkiej obserwacji. Podjęcie decyzji o zamknięciu przetoki powinno być ostrożne i wyważone, ponieważ wytworzenie nowego dostępu naczyniowego może być bardzo trudne i nie zawsze możliwe.

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