ORIGINAL ARTICLE

Cardiac remodeling after reduction of high-flow arteriovenous fistulas in end-stage renal disease

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In patients with end-stage renal disease, excessive blood flow through an arteriovenous fistula (AVF) may lead to volume overload-induced cardiac remodeling and heart failure. It is unclear which patients with hyperfunctional AVF may benefit from AVF reduction or ligation. The indication for the procedure is often based on AVF flow. Because cardiac remodeling is driven by increased venous return, which is equivalent to cardiac output, we hypothesized that an elevated cardiac index (CI) might better identify subjects with reverse remodeling after AVF reduction. Thirty patients (age 52 ± 12 years, 73% male) with AVF flow $\geqslant 1.5\,l\,min^{-1}$ underwent comprehensive echocardiographic evaluations before and after AVF reduction. At baseline, 16 patients had a normal CI ($2.5–3.8\,l\,min^{-1}\,m^{-2}$) and 14 had a high CI ($4.0–6.0\,l\,min^{-1}\,m^{-2}$). A left ventricular end-diastolic diameter decrease after operation was predicted by elevated baseline CI ($P<0.01$), but not elevated AVF flow ($P=0.07$). There was a significant decrease in CI, left ventricular mass, left atrial and right ventricular diameter and pulmonary systolic pressure in the high CI group but not in the normal CI group. After AVF reduction, systemic vascular resistance decreased in the normal CI group, whereas it did not change in the high CI group. In conclusion, reduction of high-flow AVF leads to reverse cardiac remodeling but only in patients with elevated CI. The variability of the response of systemic vascular resistance to AVF flow may explain this observation. Increased CI but not increased AVF flow may better determine candidates for AVF reduction.
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INTRODUCTION

A native arteriovenous fistula (AVF) is recommended for primary hemodialysis vascular access.[1] AVF is simultaneously like both a 'lifeline' and an 'Achilles heel,' because of volume overload of the heart.[2] AVF creation decreases systemic vascular resistance, thus leading to an increased cardiac index via increases in stroke volume, heart rate and left ventricular (LV) ejection fraction.[3] Extremely elevated AVF flow may lead to marked cardiac index elevation, volume overload-induced cardiac remodeling and clinical heart failure.[4,5]

To treat or prevent the development of heart failure, high-flow AVF are commonly closed or reduced. However, there are currently no clear indications to guide this practice. Increases in AVF flow are commonly considered when entertaining AVF modification. Basile et al.[6] have observed that vascular access flow $\geqslant 2\,l\,min^{-1}$ is associated with increased risk of high-output heart failure, and the Vascular Access Society defines high-flow AVF as AVF flow $>1–1.5\,l\,min^{-1}$.[6] Nonetheless, the association of AVF flow and cardiac index is nonlinear, and there is high inter-individual variability

in CI at the same level of AVF flow.[6,7] Until now, no study has evaluated whether the effect of high-flow AVF reduction on heart remodeling is modified by cardiac index (CI). Because cardiac remodeling is driven by increased venous return, which is equivalent to cardiac output, we hypothesized that an elevated cardiac index might better identify subjects with reverse remodeling after AVF reduction than increased AVF flow.

The aim of this study was to identify predictors of cardiac reverse remodeling after AVF reduction and to evaluate the effects of the baseline cardiac index on structural and functional changes in the heart.

METHODS

Population

All consecutive patients with high-flow (defined as AVF flow $\geqslant 1.5\,l\,min^{-1}$) type I aneurysmatic AVF according to the Balaz classification scheme[8] referred to the Institute for Clinical and Experimental Medicine, Prague, Czech Republic for AVF reduction between January 2011 and October 2014 were included in this study. AVF flow and echocardiography were performed before the

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operation and at 3 months and 1 year after the operation. The study complied with the Declaration of Helsinki. Informed consent was obtained from all patients. The study was approved by the local ethics committee.

AVF reduction

A reinforced aneurysmorrhaphy with external polytetrafluoroethylene mesh tube was used to reduce the high-flow AVF. This technique was developed by our group in 2008[9] and has been validated[10] and internationally adopted for aneurysmal AVF salvage.[11] A detailed video of this procedure can be found online (http://aneurysmorrhaphy.eu—How to use section). In brief, the aneurysmal fistula was mobilized, and general heparinization (5000–10 000 IU) was performed. The supplying artery and non-dilated vein above the aneurysm were clamped, and the aneurysmal sac was resected to an appropriate diameter. The vein wall was sewn with a continuous running suture. The repaired vein was scaffolded with an external mesh polytetrafluoroethylene prosthesis (ProVena; BBraun Medical, Melsungen, Germany), and arteriovenous re-anastomosis was performed. The distal anastomosis of an upper-arm AVF was relocated to forearm arteries, whereas a reduction of the distal anastomosis was performed in the case of a forearm AVF. Heparin was neutralized by protamine sulfate, and the wound was closed with drainage. All patients used 100 mg of acetylsalicylic acid after the operation. The AVF after aneurysmorrhaphy was usually used for dialysis after 4 weeks.

AVF flow measurement

AVF flow was measured in the brachial artery using an Aplio500 ultrasound system (Toshiba, Tokyo, Japan) as previously described.[2] AVF flow was calculated by multiplying the brachial artery cross-sectional area by the time-averaged mean velocity. The examinations were conducted by one angiology specialist with expertise in ultrasound examination.

Echocardiographic examination and hemodynamics

Echocardiographic examination was performed 24–48 h after dialysis to obtain similar and representative body fluid status. The examination was conducted by one medical doctor (VP) with expertise in echocardiography, and a Vivid7 ultrasound system (General Electric Healthcare, Wauwatosa, WI, USA) was used. The velocity–time integral in the LV outflow tract and the LV outflow tract diameter were used to calculate stroke volume and cardiac output. The cardiac index was calculated by dividing the cardiac output by the body surface area. A cardiac index $\geqslant 3.9 \, l \, min^{-1} m^{-2}$ was considered the cutoff for an elevated cardiac index.[12] The LV mass was calculated by using the cube formula, as previously recommended.[13] The right ventricular systolic pressure was estimated from the tricuspid regurgitation velocity (available in 58% of patients), and the right atrial pressure estimate was based on the inferior vena cava diameter and collapsibility. The LV ejection fraction was used as a parameter of LV function, and the tricuspid annular plane systolic excursion was used as a parameter of right ventricular systolic function. The mean blood pressure (MBP) was calculated by using the equation MBP = $1/3 \times SBP + 2/3 \times DBP$, where SBP is the systolic blood pressure and DBP is the diastolic blood pressure. The total vascular resistance (TVR) was calculated as TVR = 80 (MBP/CO). The systemic vascular resistance (SVR, vascular resistance omitting AVF) was calculated as SVR = 80 (MBP/(CO-AVF flow)).

Statistical analysis

Continuous data with normal distributions are presented as the mean ± s.d. and non-normally distributed variables are presented as the median (interquartile range—IQR). Categorical data are shown as frequencies and percentages. To account for the correlation of measures on the same patient, a random-effect mixed-linear model[14] was used to assess the ability of baseline CI and AVF flow to predict LV diameter change after aneurysmorrhaphy. To increase the statistical power, and because we were interested in comparing the changes after operation between groups rather than determining the time point when these changes occurred, data examined at 3 months and 1 year after the operation were analyzed as a single time point (the after-operation time point). Patients were dichotomized on the basis of baseline CI ($<3.9 \, l \, min^{-1} m^{-2}$—normal CI group, $\geqslant 3.9 \, l \, min - 1 \, m^{-2}$—high CI group) and median AVF flow (<3.2, $\geqslant 3.2 \, l \, min^{-1}$). The null hypothesis tested was

that the change in end-diastolic diameter after operation is independent of the baseline CI or AVF group. Differences between normal and high CI groups at baseline were compared using the t-test, Mann–Whitney U-test, χ^2 or Fisher exact test, as appropriate. The random-effect mixed-linear model was also used to analyze sequential data by the baseline cardiac index group. Gamma regression was used for right-skewed data. Calculations were performed with SPSS version 21 (IBM SPSS Statistics; IBM Corporation, Armonk, New York, NY, USA) and JMP10 (SAS Institute, Cary, NC, USA). A two-sided P value <0.05 was considered to be statistically significant.

RESULTS

In total, 32 patients with high-flow AVF without clinical signs of heart failure underwent AVF reduction between January 2011 and October 2014 in our institution. Two patients were excluded from analyses, owing to valvular heart surgery during the follow-up (one aortic valve replacement, one mitral valve replacement). Data from thirty patients (mean age 52 ± 12 years, 73% male) with high-flow AVF and a mean AVF flow of 3.3 ± 1.1 l min^{-1} (range 1.5–5 l min^{-1}) were analyzed. None of the patients included in the analyses had a significant valvular disease. As assessed by the corrected Akaike information criterion weight, linear regression (Figure 1) provided a better fit of the association between AVF flow and cardiac index (Akaike information criterion weight = 0.65, $R^2 = 0.13$) than did quadratic regression (Akaike information criterion weight = 0.35, $R^2 = 0.17$). At baseline, the LV end-diastolic diameter was associated with cardiac output (Pearson $r = 0.45$, $P = 0.03$) but not with AVF flow (Pearson $r = 0.13$, $P = 0.51$).

Predictors of reverse remodeling

The cardiac index discriminated patients with end-diastolic diameter (EDD) decrease after operation (interaction between CI group and time $P < 0.01$), and increased CI was associated with EDD decrease after aneurysmorrhaphy ($P = 0.01$) (Figure 2a). However, AVF flow was not able to discriminate patients with EDD decrease after operation (interaction between AVF flow and time $P = 0.94$), and AVF flow over the median ($3.2 \, l \, min^{-1}$) was not associated with an EDD decrease ($P = 0.07$) (Figure 2b). When EDD was adjusted for
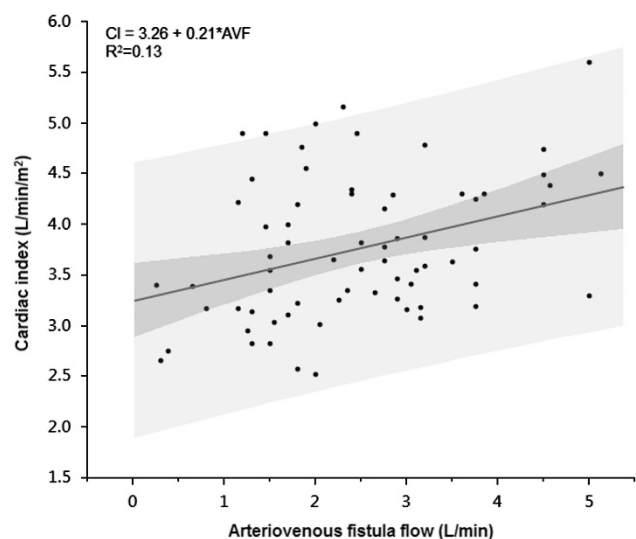

Figure 1 Association between arteriovenous fistula flow and cardiac index. Dark shaded area represents 95% CI of fit; light shaded area represents 95% CI of prediction. Data before and after operation are shown together. A full colour version of this figure is available online at the *Hypertension Research* website.
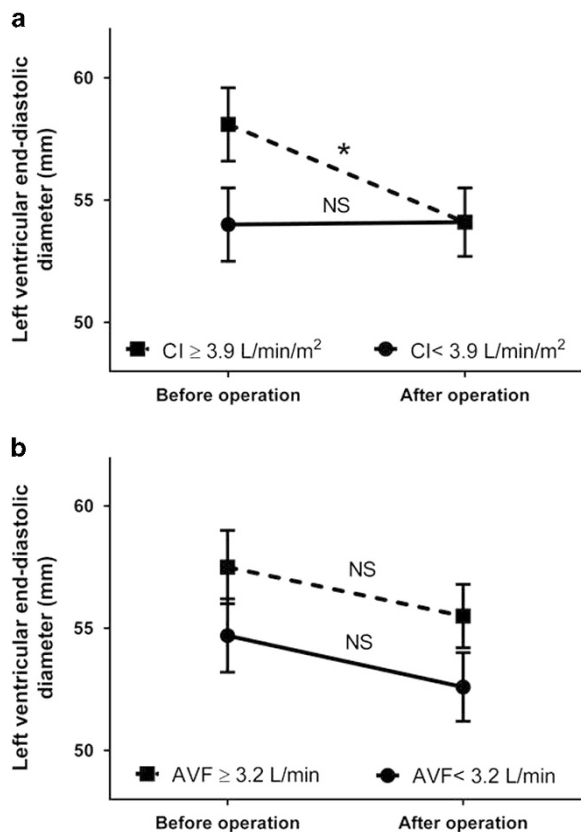
a

b

Figure 2 The influence of baseline cardiac index (**a**) and arteriovenous flow (**b**) on left ventricular end-diastolic diameter change after aneurysmorrhaphy. CI, cardiac index; AVF, arteriovenous fistula flow; *$P < 0.05$ from baseline; NS, not significant. Estimated marginal mean +s.e.m. are shown.

body size (height or body surface area), the results did not change. Age ($P = 0.78$), sex ($P = 0.49$), baseline hemoglobin ($P = 0.11$) and systolic blood pressure ($P = 0.57$) did not predict EDD decrease after operation. On the basis of a univariate search for predictors of reverse remodeling, CI was the only predictor of LV diameter decrease after aneurysmorrhaphy. Thus, changes in other parameters of cardiac structure and function were analyzed by baseline CI category.

High CI and normal CI groups

There were 16 patients (54%) in the normal CI group (nCI) with CI < $3.9\, l\,min^{-1}\,m^{-2}$ (range 2.5–$3.8\, l\,min^{-1}\,m^{-2}$) and 14 patients in the high CI group (hCI) (46%) with an increased cardiac index (range 4.0–$6.0\, l\,min^{-1}\,m^{-2}$). Whereas the mean AVF flow did not differ between groups (3.1 ± 1.4 *vs.* $3.4 \pm 0.8\, l\,min^{-1}$, $P = 0.34$ for nCI *vs.* hCI groups), there were significant differences in cardiac index, systemic vascular resistance, hemoglobin level and LV diameter between groups (Table 1).

The effect of aneurysmorrhaphy

After aneurysmorrhaphy, the nCI and hCI groups had similar reductions in AVF flow (-1.22 (-1.81 to -0.64) *vs.* -1.55 (-2.18 to -0.92) $l\,min^{-1}$, $P = 0.45$) (Figure 3a). In contrast, the cardiac index decreased significantly only in hCI (-1.01 (-1.43 to -0.58) $l\,min^{-1}\,m^{-2}$, $P < 0.001$) and not in the nCI group (-0.01 (-0.40 to 0.38) $l\,min^{-1}\,m^{-2}$, $P = 0.97$) (Figure 3b). The total vascular resistance did not change in the nCI and increased in the hCI group

(Figure 3c), whereas the systemic vascular resistance decreased in the nCI group and did not change in the hCI group (Figure 3d).

In the hCI group, there were significant decreases in LV end-diastolic diameter, mass, left atrial and right ventricular diameters, and estimated pulmonary systolic blood pressure (Table 2). In contrast, none of these parameters changed in the nCI group. There was a small decrease in the LV ejection fraction in both groups, but no patients developed new systolic dysfunction (EF < 55%). There was a small decrease in the parameters of right ventricular systolic function (tricuspid annular plane systolic excursion, Sm) in the hCI group, but after correction for right ventricular diameter change, this difference was not significant.

DISCUSSION

In the present study in patients with high-flow arteriovenous fistulas, we demonstrated that the effect of AVF reduction on heart remodeling is dependent on cardiac index before operation but does not depend on increased AVF flow. AVF flow reduction decreased LV end-diastolic diameter and mass, left atrial and right ventricular diameter and pulmonary pressure in the high CI group but not in the normal CI group. The variability of the response of systemic vascular resistance to AVF flow reduction may explain these observations.

Although several previous studies[7,15,16] have assessed the effects of AVF closure on the heart, this study is the first to address the effect of AVF reduction on heart remodeling. The advantages of aneurysmorrhaphy compared with ligation are the preservation of vascular access and an excellent long-term patency with minimal periprocedural complications.[10] In previously published studies, AVF closure has been shown to decrease left ventricular diameter and mass.[7,15,16] However, results of the present study show that the effect of AVF reduction on heart remodeling is not present in all patients and is dependent on cardiac index before operation but does not depend on increased AVF flow. This conclusion is supported by a previous observation of patients after kidney transplant undergoing AVF closure,[16] in which the magnitude of LV mass reduction was independent of AVF flow but correlated with baseline LV diameter and mass. In our study, left ventricular diameter at baseline was associated with cardiac output but not AVF flow, thus suggesting that LV dilatation is driven by increased cardiac output but not high-flow AVF.

In previous studies, the association between AVF flow and cardiac index/output has been found to be nonlinear.[6,7] In the present study, the association was linear but with high CI variability at the same level of AVF flow. This finding may be explained by a variable degree of systemic vasoconstriction/vasodilatation as a response to AVF creation. At baseline, despite similar AVF flow, patients in the hCI group had lower total vascular resistance and a higher cardiac index. Aneurysmorrhaphy in patients in the nCI group caused a decrease in SVR as a response to the AVF resistance increase, and thus, total vascular resistance and cardiac output did not change. In the hCI group, systemic vascular resistance did not change after aneurysmorrhaphy. Instead, the increase in total vascular resistance in these patients was coupled to decreasing cardiac output. The importance of the systemic vascular response found in our study is in line with results from a study by Unger et al.,[17] in which the decrease in LV mass and diameter after AVF closure was predicted by the acute increase in total vascular resistance and MBP during pneumatic compression of AVF. In another study,[18] the post-AVF closure 24 h diastolic blood pressure change (which is related to SVR) has been found to be negatively associated with LV mass change. This finding suggests that LV remodeling after AVF closure is present

Table 1 Descriptive statistics by cardiac index at baseline

Variable	Normal cardiac index (n = 16)	High cardiac index (n = 14)	P
Age, years	50.9 ± 9.1	53.0 ± 13.5	0.63
Gender (female), n (%)	4 (25)	4 (29)	0.83
Height, cm	173.5 ± 7.1	173.7 ± 6.5	0.94
Weight, kg	78.3 ± 15.6	80.6 ± 20.6	0.73
Systolic BP, mm Hg	134.4 ± 21.6	151.3 ± 20.1	**0.04**
Diastolic BP, mm Hg	77.6 ± 8.2	84.4 ± 13.5	0.11
Mean BP, mm Hg	96.5 ± 10.0	106.7 ± 13.9	**0.03**
Heart rate, bpm	67.6 ± 9.2	76.5 ± 9.0	**0.01**
Hemoglobin, g l^{-1}	118.4 ± 20.7	103.9 ± 15.3	**0.04**
AVF flow, l min^{-1}	3.1 ± 1.4	3.4 ± 0.8	0.34
Cardiac output, l min^{-1}	6.7 ± 1.8	9.7 ± 1.4	**<0.001**
Cardiac index, l $min^{-1} m^{-2}$	3.4 ± 0.7	4.8 ± 0.5	**<0.001**
TVR, dyn s cm^{-5} m^2	1187 ± 323	902 ± 229	**0.04**
SVR, dyn s cm^{-5} m^2	2183 ± 584	1551 ± 785	**0.04**
LV end-diastolic diameter, mm	54.1 ± 5.8	58.4 ± 5.6	**0.049**
LV mass, g	215.2 ± 87.2	263.5 ± 62.6	0.09
LV mass index, g m^{-2}	109.6 ± 45.7	135.2 ± 25.3	0.07
Relative wall thickness	0.37 ± 0.04	0.36 ± 0.04	0.64
LV hypertrophy, n (%)	7 (47)	9 (64)	0.34
LV remodeling, n (%)			0.41
Concentric remodeling	1 (7)	0 (0)	
Excentric hypertrophy	6 (40)	9 (64)	
Concentric hypertrophy	1 (7)	0 (0)	
LV ejection fraction, %	60.8 ± 5.2	61.6 ± 6.0	0.69
E/Em	13.4 ± 3.4	10.9 ± 8.5	0.39
Left atrial diameter, mm	42.1 ± 7.4	44.0 ± 5.9	0.45
RV diameter, mm	36.4 ± 4.1	40.0 ± 5.4	0.09
TAPSE, mm	22.1 ± 5.6	27.3 ± 5.8	0.06
Tricuspid Sm, m s^{-1}	12.8 ± 3.1	15.7 ± 3.6	0.05
RV dysfunction, n (%)	2 (13)	1 (8)	0.67
Pulmonary systolic BP, mm Hg	41.8 ± 14.3	39.8 ± 19.4	0.81
Inferior vena cava diameter, mm	16.4 ± 7.0	17.8 ± 5.0	0.56
Medication			
ACEi/ARB, n (%)	5 (31)	7 (50)	0.46
Beta-blockers, n (%)	13 (81)	10 (71)	0.68
Calcium channel blockers, n (%)	8 (50)	10 (71)	0.28
Diuretics, n (%)	10 (63)	10 (71)	0.71
Others, n (%)	3 (19)	6 (43)	0.24
Comorbidities			
Hypertension, n (%)	12 (75)	14 (100)	0.10
Diabetes, n (%)	1 (6)	1 (7)	1.0
Stroke, n (%)	0 (0)	1 (7)	0.47
Coronary heart disease, n (%)	3 (19)	2 (14)	1.0
AVF type			0.85
Radiocephalic, n (%)	7 (44)	5 (36)	
Brachiocephalic, n (%)	8 (50)	8 (57)	
Other, n (%)	1 (6)	1 (7)	

Abbreviations: ACEi/ARB, angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker; AVF, arteriovenous fistula; BP, blood pressure; LV, left ventricular; RV, right ventricular; RV Sm, peak systolic tricuspid annular velocity; SVR, systemic vascular resistance; TAPSE, tricuspid annular plane systolic excursion; TVR, total vascular resistance.
Bold P-values are significant at the $P<0.05$.

only if the increase in total vascular resistance by AVF closure/ reduction is not offset by the decrease in SVR.

The inability to increase systemic vascular resistance as a response to high-flow AVF and to decrease systemic vascular resistance as a response to increased AVF resistance after AVF closure/reduction suggests a vasomotor dysfunction in patients in the hCI group. One of the mechanisms affecting vasomotor function is anemia, which decreases systemic vascular resistance[19] and may cause high-output heart failure.[20] In the present study, though hemoglobin levels increased in patients in the hCI group, the hemoglobin increase did not significantly increase systemic vascular resistance, and adjustment for hemoglobin did not attenuate the decrease in LV diameter in this
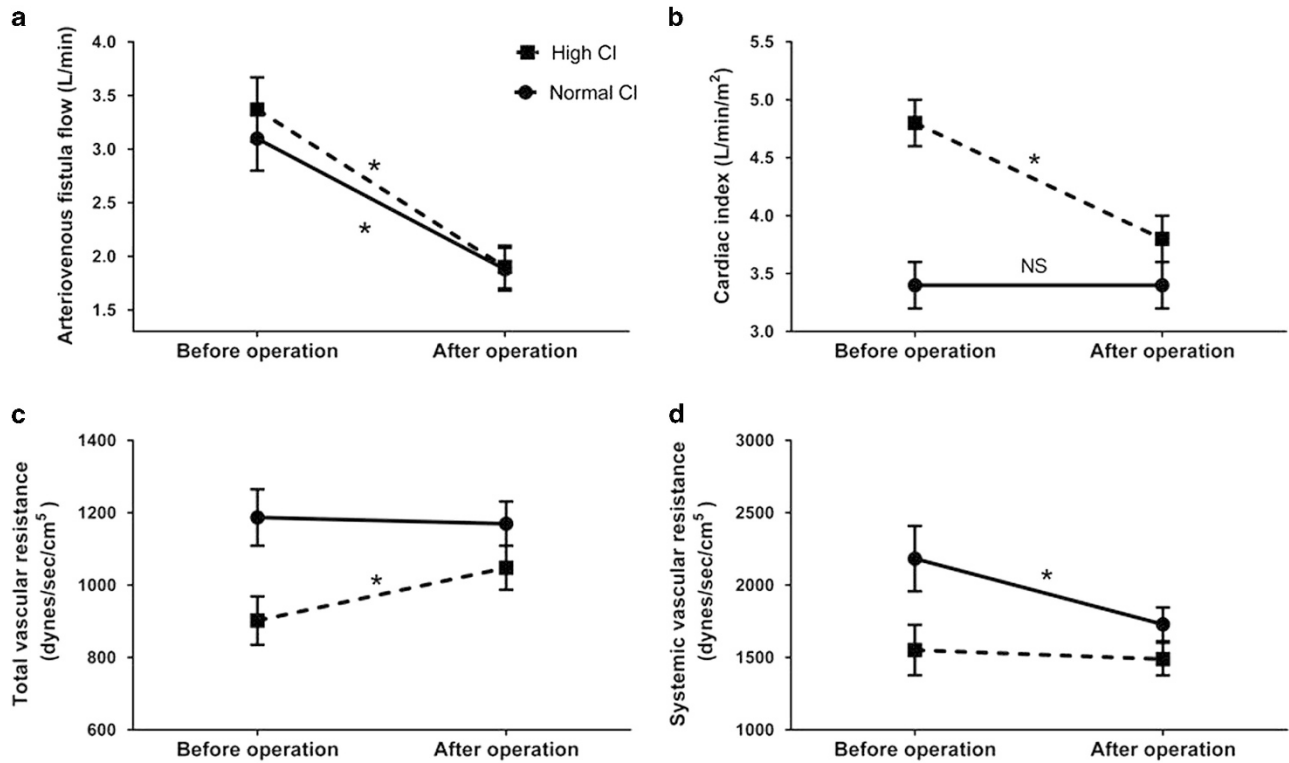
Figure 3 The effect of aneurysmorrhaphy on arteriovenous fistula flow (**a**), cardiac index (**b**), total vascular resistance (**c**) and systemic vascular resistance (**d**) by cardiac index (CI) on baseline. Significant changes from baseline ($P<0.05$) are marked by * Estimated marginal mean +s.e.m. are shown.

Table 2 Changes after aneurysmorrhaphy by baseline cardiac index

	Normal cardiac index		High cardiac index	
	Δ	P	Δ	P
AVF flow, l min^{-1}	−1.22 (−1.81 to −0.64)	<**0.001**	−1.55 (−2.18 to −0.92)	<**0.001**
CI, l min^{-1}m^{-2}	−0.01 (−0.40 to 0.38)	0.97	−1.01 (−1.43 to −0.58)	<**0.001**
TVR, dyn s cm^{-5} m^2	−17 (−168 to 134)	0.83	145 (8–282)	**0.04**
SVR, dyn s cm^{-5} m^2	−454 (−880 to −27)	**0.04**	−61 (−399 to 276)	0.72
Systolic BP, mm Hg	0.9 (−6.6 to 8.3)	0.82	−14.8 (−23.5 to −6.1)	**0.001**
Diastolic BP, mm Hg	−1.8 (−7.1 to 3.6)	0.51	−7.7 (−13.8 to −1.6)	**0.01**
Mean BP, mm Hg	−1.0 (−6.6 to 4.5)	0.71	−9.9 (−16.2 to −3.4)	**0.003**
Heart rate, bpm	−1.5 (−6.7 to 3.8)	0.58	−3.5 (−9.0 to 2.0)	0.21
Hemoglobin, g l^{-1}	−2.0 (−9.3 to 5.4)	0.60	10.8 (3.0 to 18.6)	**0.01**
LV end-diastolic diameter, mm	−0.5 (−2.5 to 1.4)	0.57	−4.5 (−6.6 to −2.3)	<**0.001**
LV mass index, g m^{-2}	−7.7 (−17.8 to 2.4)	0.13	−20.4 (−33.0 to −7.9)	**0.002**
Relative wall thickness	−0.01 (−0.03 to 0.02)	0.50	0.02 (−0.01 to 0.04)	0.28
LV ejection fraction, %	−2.5 (−4.7 to −0.3)	**0.03**	−2.9 (−5.2 to −0.5)	**0.02**
E/A	−0.14 (−0.37 to 0.10)	0.25	−0.26 (−0.50 to −0.02)	**0.04**
Left atrium diameter, mm	−0.3 (−1.8 to 1.3)	0.71	−2.5 (−4.1 to −0.8)	**0.004**
Right ventricle diameter, mm	1.5 (−0.9 to 3.9)	0.21	−4.5 (−7.4 to −1.5)	**0.004**
TAPSE, mm	0.5 (−2.5 to 3.4)	0.76	−5.1 (−8.6 to −1.6)	**0.005**
TAPSEc, mm	1.3 (−2.0 to 4.5)	0.44	−3.5 (−7.3 to 0.2)	0.07
RV Sm, m s^{-1}	0.5 (−1.0 to 1.9)	0.53	−2.5 (−4.5 to −0.6)	**0.01**
RV Smc, m s^{-1}	0.2 (−1.1 to 1.5)	0.80	−0.5 (−2.1 to 1.2)	0.58
RV/LV diameter ratio	0.03 (−0.02 to 0.08)	0.22	−0.03 (−0.08 to 0.03)	0.34
Inferior vena cava diameter, mm	−3.3 (−6.5 to −0.1)	0.04	−3.0 (−6.7 to 0.6)	0.10
Pulmonary systolic BP, mm Hg	0.05 (−8.1 to 8.2)	0.99	−7.7 (−14.9 to −0.5)	**0.038**

Abbreviations: Δ, change from baseline; AVF, arteriovenous fistula; BP, blood pressure; CI, cardiac index; E/A, mitral inflow early (E) to late (A) filling velocities; LV, left ventricular; RV, right ventricular; RV Sm, peak systolic tricuspid annular velocity; RV Smc, RV Sm corrected for RV diameter; SVR, systemic vascular resistance; TAPSE, tricuspid annular plane systolic excursion; TAPSEc, TAPSE corrected for RV diameter; TVR, total vascular resistance.
Bold *P*-values are significant at the $P<0.05$.

group (Supplementary Table S1). Another mechanism that may explain abnormal vascular reactivity is autonomic dysfunction, which is common in patients with end-stage renal disease.[21] However, autonomic dysfunction was not evaluated in this study. Furthermore, we did not find any significant differences in baseline antihypertensive medications, thus suggesting that vasodilatative therapy is not responsible for this phenomenon.

There is an ongoing debate regarding whether AVF is beneficial or harmful in patients with end-stage renal disease.[22] In a retrospective study of dialyzed patients, no increased risk of death associated with high levels of AVF flow has been observed.[23] Thus, in most patients, AVF reduction/closure is not required; but clearly, among patients who develop adverse remodeling or heart failure, intervention may be required. On the basis of previous case reports, it seems reasonable to intervene in subjects with high-output heart failure, in which symptoms usually disappear after operation.[24] However, in more advanced stages of heart failure, patients may not benefit from the procedure.[23,25] The current results indicate that among patients without symptoms of heart failure, subjects with elevated cardiac index and left ventricular eccentric hypertrophy might be most likely to respond favorably to AVF reduction. In contrast, patients with high-flow AVF, normal cardiac index, no LV dilation and without symptoms of heart failure may not require surgical AVF reduction but instead would need close follow-up. Other causes of high cardiac index such as anemia, liver disease and hypervolemia should be excluded before intervention. Furthermore, other risk factors increasing morbidity and mortality in this population should be addressed.[26,27]

Our study should be interpreted within the context of its strengths and limitations. Though the sample size of the present study is relatively low, it is the first study to assess the influence of AVF reduction on the heart. Non-invasive hemodynamic data inherently have greater variability than invasive measurements. Echocardiographic assessments were performed after a short interval, and chronic effects of AVF reduction were not assessed. Because we did not measure symptoms of heart failure and functional capacity during the study period, we are unable to compare the effect of AVF reduction on those parameters. We also did not measure cardiac biomarkers, which may provide deeper insight into cardiac changes.

In conclusion, this study shows that in patients with end-stage renal disease, high-flow arteriovenous fistula reduction causes reverse cardiac remodeling only in patients with elevated cardiac output and thus high venous return. This finding suggests that an increased cardiac index, but not increased arteriovenous flow, may be the optimal parameter to assess when considering aneurysmorrhaphy or other AVF reduction techniques in a patient with a high-flow arteriovenous fistula.

CONFLICT OF INTEREST

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