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NEPHROLOGY ROUNDS

High Output Heart Failure Associated With Arteriovenous Fistula in the Setting of Kidney Transplantation

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CASE PRESENTATION

A 21-year-old man with VATER syndrome–related end-stage kidney disease (ESKD) and 2 previous kidney transplantations, hypertension, and frequent urinary tract infections presented to the hospital with 2 weeks of watery diarrhea, nonbloody vomiting, and nausea. A right upper extremity transposed brachiobasilic arteriovenous fistula (AVF) had been placed 4 years prior for hemodialysis due to his failing first kidney transplant, but had not been used in the 3 years since his second kidney transplant. He was admitted and initially treated with 3.7 L of i.v. fluids over 2 days for suspected prerenal acute kidney injury (Table 1) resulting from gastrointestinal losses from infectious gastroenteritis. However, as his diarrhea resolved, he developed marked dyspnea, worsening abdominal swelling, and lower extremity swelling. His troponin I rose to 1.0 ng/ml (reference range, <0.04 ng/ml) and B-type natriuretic peptide (BNP) was 8487 pg/ml (reference range, 10–100 pg/ml).

On examination, he was ill-appearing. He had symmetric lower facial edema. His neck examination revealed the jugular venous pressure to be >15 cm and rose to his earlobe. His cardiac examination reveales a harsh mid-systolic crescendo–decrescendo murmur best heard at the right upper sternal border, a loud P2, and right ventricular heave with no rubs or gallops. His lungs were clear to auscultation bilaterally. His abdomen was soft, mildly distended, but with no tenderness to palpation; there was no hepatomegaly. He had a large aneurysmal brachiobasilic AVF in his right upper extremity (Figure 1). He had 1+ bilateral lower extremity, forearm, and chest edema. He had 2+ pulses on all extremities.

Chest radiographs showed increased cardiomegaly and prominence of the main pulmonary arteries. His echocardiogram demonstrated the following: a small, hyperdynamic left ventricle with severe concentric left ventricular (LV) hypertrophy; LV ejection fraction (LVEF) >65%; estimated pulmonary artery systolic pressure >100 mm Hg; severe right ventricular dilation, hypertrophy, and dysfunction with a right ventricle systolic pressure of 130 mm Hg; severe pulmonary artery dilation and dilated inferior vena cava and coronary sinus; and moderate tricuspid regurgitation and pulmonic regurgitation. This demonstrated a marked change from his last echocardiogram 4 years prior in May 2015, which showed only mild dilation of the left atrium and ventricle, with mild left ventricular hypertrophy, mild dilation of the aortic root, and increased velocity over the aortic and pulmonary valves. With these findings as well as a persistent creatinine elevation of 4.1 to 4.6 mg/dl, it was suspected that his persistent acute kidney injury was now due to cardiorenal syndrome/heart failure.

At this point, the cause of the patient's heart failure and pulmonary hypertension remained uncertain. Workup for other causes of high-output heart failure, including thyroid function studies, complete blood count, and liver function tests, remained normal. To examine the hemodynamics, contribution, and future

Table 1. Laboratory analyses on admission

Laboratory analyses	At admission	Reference range
Sodium	135	135–145 mEq/L
Potassium	5.3	3.6–5.1 mEq/L
Chloride	107	101–111 mEq/L
HCO_3	11	24–36 mEq/L
Anion gap	17	<12 mEq/L
BUN	59	8–20 mEq/L
Creatinine	4.11	0.6–1.2 mEq/L (baseline low 2's)
WBC	5.7	4.5–11 × 10^3 cells/mm^3
Hemoglobin	15.6	13.5–17.5 g/dl
Hematocrit	51	41%–53%
Platelets	183	150,000–400,000/mm^3
Total bilirubin	2.3	0.1–1.0 mg/dl
Direct bilirubin	0.8	0.0–0.3 mg/dl
ALT	32	8–20 U/L
AST	46	8–20 U/L
LDH	335	45–90 U/L
Lactate	2.3	0.7–2.1 mmol/L
Troponin I	0.08	< 0.04 ng/mL
BNP	8487	< 100 ng/L
D-dimer	1.31	< 0.5 ng/ml
Haptoglobin	<8	36–195 mg/dl
UA	100 Protein, negative ketones, negative glucose, negative bilirubin, negative leukocyte esterase or nitrite, moderate blood	Negative
UA Micro	23 UWBC, 4 URBC, trace U bac. <1 hyaline casts or granular casts	Negative

ALT, alanine transaminase; AST, aspartate aminotransferase; bac., bacteria; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; LDH, low-density lipoprotein; U, urine; UA, urinalysis; URBC, urinary red blood cells; UWBC, urinary white blood cells; WBC, white blood cell.

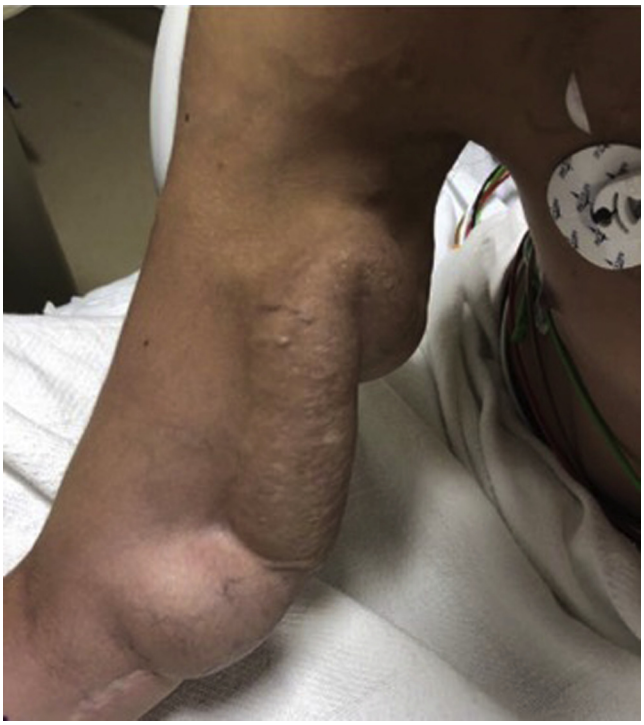

Figure 1. Patient's right upper extremity arteriovenous fistula.

utility of the patient's large AVF, a right heart catheterization was performed, which showed a mean pulmonary arterial pressure of 51, cardiac output of 6.4 L/min, and cardiac index of 4.24 L/min per m^2. The SVR was 13.6 Wood units. When the AVF was manually compressed, the mean pulmonary arterial pressure improved to 36, and the cardiac output and cardiac index decreased to 4.27 L/min and 2.83 L/min/m^2, respectively (Table 2). Given his signs and symptoms of heart failure, right heart catheterization findings of an elevated CI of 4.24 L/min/m^2 with marked reduction following occlusion of the AVF, and echocardiographic findings, we suspected that the AVF was a major factor leading to high-output heart failure (HOHF). The AVF volume was not assessed with ultrasound. Given his diuretic-refractory heart failure, the AVF was ligated. Following the ligation, his renal function began to improve the next day. One month later, he had significant improvement of symptoms and renal function with a creatinine of 1.4 mg/dl, further supporting the patient's diagnosis of AVF-associated HOHF. An echocardiogram 3 months postdischarge showed improved right ventricular function, with mild dilation and hypertrophy of the right ventricle with mildly depressed systolic function, and improved pulmonary artery pressures (estimated at 56/25 mm Hg). There was persistent severe pulmonary artery dilation and dilated coronary sinus, along with mild tricuspid regurgitation and moderate pulmonic regurgitation.

DISCUSSION

In this report, we present a medically complex kidney transplant recipient with new-onset HOHF and pulmonary hypertension who improved after AVF ligation. This report highlights the importance of considering all etiologies of HOHF (Figure 2) in a patient with unexplained edema and dyspnea, and describes the successful treatment of heart failure upon ligation of the AVF. Below, we review the presentation, pathophysiology, and management of this disease process, and discuss an ongoing dilemma faced by clinicians in whether to pursue closure of an AVF in stable kidney transplant recipients.

Pathophysiology of AVF–Associated HOHF

In HOHF, vascular flow functions like a circuit in which the AVF and the peripheral circulation are arranged in parallel, where the AVF has low pressure and resistance due to the presence of a shunt, causing reduced systemic vascular resistance and increased venous return. In compensatory response to the reduced systemic vascular resistance, heart rate, contractility, and systemic filling, pressures increase, increasing cardiac output. In addition, because blood

Table 2. Right heart catheterization showing mean pulmonary artery pressure, cardiac output, and cardiac index before and after occlusion of arteriovenous fistula (AVF)

	Before occlusion of AVF	After occlusion of AVF
Mean pulmonary arterial pressure	51 (PAP 76/36)	36 (PAP 46/32)
Cardiac output (thermo)	6.4 L/min	4.27 L/min
Cardiac index (thermo)	4.24 L/min/m^2	2.83 L/min per m^2

PAP, pulmonary artery pressure; thermo, thermodilution.

flowing through the AVF bypasses the capillary bed, to maintain peripheral perfusion the increase in cardiac output must at least equal the flow that is diverted through the AVF, which is usually 1 to 2 L/min. The cycle is perpetuated as increased cardiac output increases venous return (Figure 3). The increased venous return increases right atrial, pulmonary artery, and LV end-diastolic volumes, causing LV hypertrophy as a result of the increased workload.[S1] Increased LV mass is linked to higher cardiovascular morbidity and mortality.[1] In addition, reduced systemic vascular resistance in AVF-associated HOHF leads to activation of the sympathetic nervous system and renin–angiotensin–aldosterone system, further inducing pathologic cardiac remodeling.

Epidemiology, Manifestations, and Diagnosis of AVF-Associated High-Output Heart Failure

The incidence of AVF-associated HOHF is poorly defined. Risk factors for AVF-associated HOHF include upper arm AVF, male sex, history of vascular access surgery, and vascular access blood flow (Qa) >2.0 L/min.[2,3] The finding of Qa/CO ratios >0.3 has also been suggested as a risk factor for high-output heart failure and decompensation.[4] Brachiocephalic fistulas can have double the flow of radiocephalic fistulas, given the former's proximity to the heart.[3]

Patients with HOHF present with signs and symptoms of heart failure, such as dyspnea, orthopnea, paroxysmal nocturnal dyspnea, reduced exercise tolerance, peripheral edema, and fatigue. In contrast to low- or normal-output heart failure, manifestations of HOHF may include a wide pulse pressure, warm extremities, and a hyperdynamic precordium, along with a systolic murmur secondary to a high-flow state. Patients with HOHF from AVF will additionally have a history of ESKD and an AVF on 1 of their extremities, usually the upper arm, that is large and aneurysmal. The Nicoladoni–Branham sign is the phenomenon in which temporary occlusion of the high-flow AVF may lead to a modest reduction in heart rate (~7 bpm) via the vagus nerve–mediated baroreceptor reflex.

In patients with an AVF with new or worsening heart failure, right heart catheterization can be used to evaluate cardiac hemodynamics at rest and with occlusion of the AVF to evaluate volume status, pulmonary artery pressures, and cardiac output to guide management. The presence of HOHF is defined as signs and symptoms of systemic or pulmonary venous congestion with an above-normal cardiac index on right heart catheterization, which is variably defined and which has been reported to range from 3.0 to 3.9 L/min/m^2.[5,6] Especially in patients with high-flow AVFs (Qa > 2.0 L/min), occlusion of the AVF leads to a markedly reduced cardiac index. Resolution of symptoms and intracardiac pressures after occlusion/closure is the *sine qua non* of diagnosis.

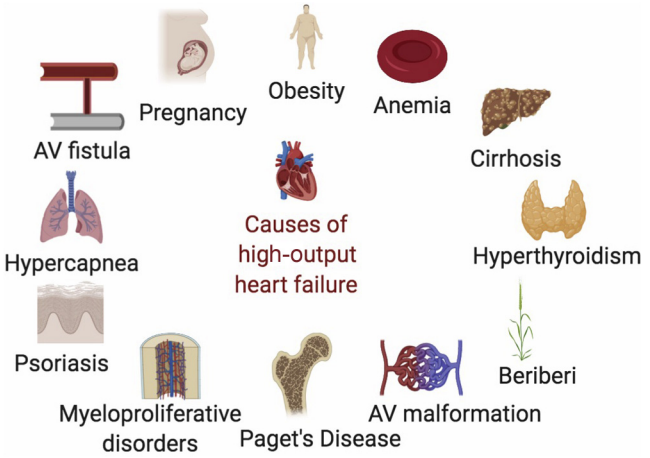

Figure 2. Differential for high-output heart failure. The differential for high-output heart failure includes etiologies that increase metabolic demand necessitating increased blood circulation, such as myeloproliferative disorders, hyperthyroidism, hypercapnia secondary to lung disease, anemia, and pregnancy; and etiologies that decrease systemic vascular resistance due to a bypass in the arteriolar and capillary bed, or due to widespread inflammation, necessitating increased blood circulation for peripheral perfusion, such as obesity, sepsis, liver disease, arteriovenous fistulas, arteriovenous malformations, Paget disease of bone, psoriasis, and thiamine deficiency.

Treatment of AVF-Associated HOHF

There are 2 major approaches to treating AVF-associated HOHF refractory to diuretics: ligation and flow restriction (Figure 4). Arteriovenous fistula ligation, or closure, entails completely stopping the flow, often with excision of the AVF. Because the AVF is sacrificed by definition, the AVF will no longer be available for use if dialysis is needed in the future. On the other hand, flow restriction banding involves the creation of a surgical stenosis within the AV access site to reduce the radius of the AVF. Alternative flow restriction options include minimally invasive limited ligation endoluminal-assisted revision, which uses a balloon to achieve the precise amount of narrowing, or revision using distal inflow, which involves ligating

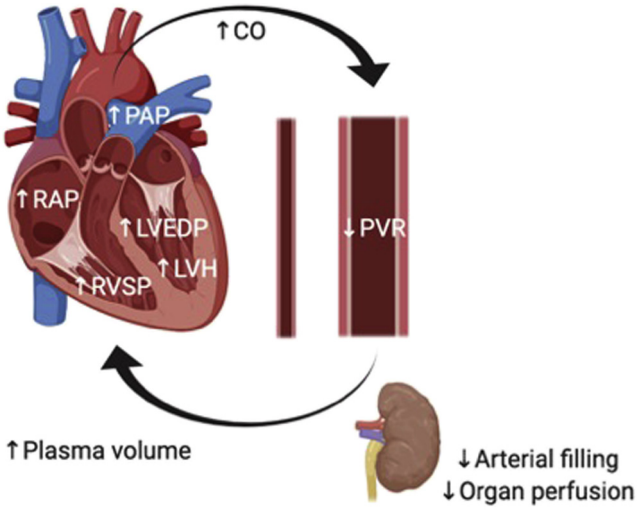

Figure 3. Pathophysiology of arteriovenous fistula–related high output heart failure. CO, cardiac output; LVEDP, left ventricular end diastolic pressure; LVH, left ventricular hypertrophy; PAP, pulmonary artery pressure; PVR, peripheral vascular resistance; RAP, right atrial pressure; RVSP, right ventricular systolic pressure.

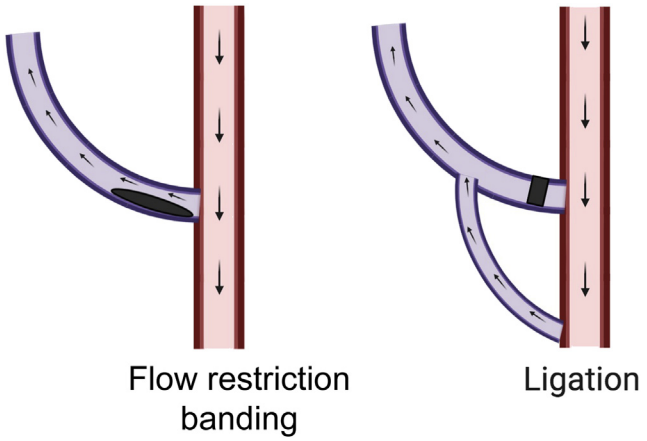

Figure 4. Two surgical approaches to arteriovenous fistula–related high-output heart failure: (left) flow restriction banding and (right) ligation.

the fistula and then reattaching it more distally with jump grafts. In a systematic search (Supplementary Figure S1) of case reports (Supplementary Table S1) and case series (Supplementary Table S2) of AVF-associated HOHF in kidney transplant patients, we found that ligation was the most commonly practiced solution (among 29 case patients, 20 underwent ligation, 5 underwent banding, 1 underwent another surgical treatment, and 3 did not undergo intervention).

Management of AVF in Stable Transplant Recipients

Prevention of HOHF through ligation of an AVF that is not being used by a stable kidney transplant recipient remains a topic of controversy. Current guidelines on AVF do not address whether AVFs should be ligated after kidney transplantation, when they are no longer in use. This issue is especially important, given that cardiovascular disease is the leading cause of mortality in kidney transplant patients.

In a systematic search of studies of cardiac function with respect to AVF closure in kidney transplant recipients (Supplementary Figure S2), we found that 9 of 13 studies demonstrated either an improved cardiac function after AVF closure or worsened cardiac function in patients with open (vs. closed) AVFs. Four studies found no significant difference in cardiac function with AVF closure (Table 3). In the only randomized controlled trial to date, AVF ligation in kidney transplant recipients resulted in decreased LV mass, LV end-diastolic volume, LV end-systolic volume, cardiac output, cardiac index, atrial volume, and NT-proBNP, whereas LV ejection fraction remained unchanged.[7] A pooled meta-analysis, albeit of nonrandomized studies, demonstrated that kidney transplant recipients with an occluded AVF had lower LV mass index, and LV end-diastolic diameter compared to those with patent AVFs,[8] demonstrating that AVF closure may improve cardiac morphology. However, no studies to date have demonstrated a reduction in CV-related mortality in patients whose AVF was ligated.

Some have raised the concern that AVF closure may lead to graft dysfunction. However, in our systematic review, we have found the majority of studies suggesting otherwise. In a systematic search of studies on allograft function with respect to AVF closure in kidney transplant recipients (Supplementary Table S3), we found that 3 of 6 studies demonstrated kidney allograft function improvement with AVF closure; 2 studies found that AVF closure allowed patients to maintain normal kidney function and was not significantly associated with allograft failure; and 1 study found acceleration of glomerular filtration rate decline after AVF closure (Table 4). In 1 retrospective study, patients who underwent AVF closure experienced a significant acceleration in estimated glomerular filtration rate decline over the 12 months after closure, at −0.159 ml/min per month after AVF closure compared to 0.038 mL/min per month before AVF closure. Nevertheless, a pooled meta-analysis showed that AVF closure was associated with improved serum creatinine levels.[8]

It remains to be studied whether patients can be risk stratified using factors such as AVF blood flow rate or site of AVF. It may be argued that preservation of the AVF (or, if treatment is pursued, a flow reduction procedure instead of complete occlusion) could be considered in young patients who have a greater chance of returning to hemodialysis during

Table 3. Case series, cohort studies, and randomized trials concerning left ventricular end-diastolic diameter, left ventricular mass index, and ejection fraction in kidney transplant recipients who did and did not undergo closure of their arteriovenous fistulas, resulting from the systematic search strategy detailed in Supplementary Table S3

Reference	Age, yr, mean ± SD	Sex, % female	Treatment	LV end-diastolic diameter, mm, pre	LV end diastolic diameter, mm, post	LVMI, g/m^2, pre	LVMI, g/m^2, post	EF (pre)	CI (pre)	CI (post)	Outcome
De Lima *et al.*, 1999[S2] PMID: 10844383	40 ± 12 (N = 39)	46	Persistent functioning AVF	53 ± 5[a]	NR	156 ± 38	NR	72 ± 5	3.2 ± 0.6	NR	LVEDD was significantly increased in persistent AVF patients compared to closed-AVF patients No difference of LVMI, EF, and CI between the 2 groups
	33 ± 12 (N = 22)	50	Closed AVF	49 ± 5[a]	NR	142 ± 30	NR	70 ± 5	3.2 ± 0.6	NR	
Van Duijnhoven *et al.*, 2001[S3,b] PMID: 11158414	51 ± 12 (N = 20)	25	Closure of AVF	51.5 ± 5.8	46.2 ± 6.6	135 ± 34.1	119.8 ± 23.2	NR	NR	NR	Reduction of LVMI and LVEDD 4–5 mo after AVF closure
Unger *et al.*, 2002[S4,b] PMID: 12134102	40 ± 6 (N = 6)	33	Persistent AVF (controls)	29 ± 3.3[c]	29.2 ± 3.6	153 ± 63	151 ± 59	61 ± 6; 65 ± 10	NR	NR	Decreased LVEDDI and LVMI post AVF closure
	46 ± 13 (N = 17)	53	Closed AVF	29.9 ± 2.2[c]	27.4 ± 2.1	141 ± 37	132 ± 39	70 ± 10; 69 ± 10	4.03 ± 0.66	3.20 ± 0.62	
Sheashaa *et al.*, 2004[S5,b] PMID: 15308876	25.6 ± 7 (N = 34)	20.6	Persistent AVF	46.6 ± 6	NR	176.3 ± 41.4	NR	70.8 ± 7	3.41 ± 1.23	NR	Decreased LVEDD in closed AVF patients compared to persistent AVF patients (not statistically significant)
	28.6 ± 8.5 (N = 17)	23.5	Spontaneously thrombosed AVF	43.6 ± 6	NR	169.5 ± 61.3	NR	71 ± 10.8	2.44 ± 0.96	NR	
Unger *et al.*, 2004[S6,b] PMID: 15575907	49 ± 6 (N = 8)	62.5	Persistent AVF (controls)	29.5 ± 3.4[c] (LVEDDI used)	29.0 ± 3.2[c] (post 1 mo); 28.9 ± 2.7[c] (post 21 mo)	139.44	114 ± 19 (post 1 mo); 115 ± 18 (post 21 mo)	68 ± 9	3.86 ± 0.78	3.58 ± 0.87 (post 1 mo)	Decreased LVMI and LVH prevalence after surgical AVF closure
	48 ± 11 (N = 17)	30	Closure of AVF	29.5 ± 3.4[c]	26.9 ± 2.9[c] (post 1 mo); 26.2 ± 3.2[c] (post 21 mo)	139.44	127 ± 45 (post 1 mo); 117 ± 40 (post 21 mo)	68 ± 9	3.86 ± 0.78	3.04 ± 0.55 (post 1 mo); 2.97 ± 0.83 (post 21 mo)	
Cridlig *et al.*, 2008[S7] PMID: 18537919	49.5 ± 8.1 (N = 38)	34.2	Persistent AVF	52.1 ± 7.1	NR	135.1 ± 30.3	NR	62.4 ± 8.6	NR	NR	LVMI significantly higher in patients with functioning AVF; increased risk of LVH 4 times that of closed-AVF group
	49.07 ± 10.4 (N = 38)	34.2	Closed AVF	48.5 ± 6	NR	112.4 ± 28	NR	66.5 ± 10.1	NR	NR	
Unger *et al.*, 2008[S8,a] PMID: 18301341	54 ± 12 (N = 16)	50	Closure of AVF	29.5 ± 3.4[c] (LVEDDI,[c] mm/m^2)	27.5 ± 2.5	148 ± 44	137 ± 40	NR	3.53 ± 0.83	2.62 ± 0.68	Reduction of LV mass 1 mo after AVF closure
Gorgulu *et al.*, 2011[S9] PMID: 22161285	39 ± 12 (N = 60)	40	Persistent AVF	46 ± 5[c]	NR	129 ± 37	NR	62 ± 5	NR	NR	No significant difference in hemodynamic measurements between open-AVF and closed-AVF cohorts
	37 ± 11 (N = 49)	42.9	Closed or spontaneously thrombosed AVF	46 ± 6	NR	125 ± 42	NR	63 ± 6	NR	NR	

(Continued on following page)

Table 3. (Continued) Case series, cohort studies, and randomized trials concerning left ventricular end-diastolic diameter, left ventricular mass index, and ejection fraction in kidney transplant recipients who did and did not undergo closure of their arteriovenous fistulas, resulting from the systematic search strategy detailed in Supplementary Table S3

Reference	Age, yr, mean ± SD	Sex, % female	Treatment	LV end-diastolic diameter, mm, pre	LV end diastolic diameter, mm, post	LVMI, g/m^2, pre	LVMI, g/m^2, post	EF (pre)	CI (pre)	CI (post)	Outcome
Soleiman *et al.*, 2012[S10] PMID: 22555484	49.1 ± 11.8 (N = 23)	31	Persistent AVF	47.4 ± 4.6	NR	NR	NR	54.3 ± 2.3	NR	NR	Spontaneous AVF closure did not offer significant cardiac beneficial effect
	39.2 ± 12.4 (N = 17)	29.4	Spontaneously thrombosed AVF	48.5 ± 4.7	NR	NR	NR	54.1 ± 2	NR	NR	
Glowinski *et al.*, 2012[S11,b] PMID: 22743626	54 ± 10 (N = 9)	67	Persistent AVF (controls)	45.3 ± 3.6	46.3 ± 4.1	116 ± 22.5	115.6 ± 18.5	NR	NR	NR	Decrease in LVMI and LVDD after AVF closure (not statistically significant)
	49 ± 11 (N = 9)	67	Closure or spontaneous thrombosis of AVF	46.4 ± 3.8	45.3 ± 3.6	118.5 ± 26.3	113.1 ± 21.6	NR	NR	NR	
Dundon *et al.*, 2014[S12,b] PMID: 24931318	58.5 ± 6 (N = 18)	22	Closure of AVF	NR	NR	166 ± 56 (LVMM, g)	149 ± 51	73 ± 8	CO: 9.6 ± 2.9	CO: 8.1 ± 2.3	Decreased LV mass and CO 6 mo after AVF ligation
Rao *et al.*, 2019[S13,b] PMID: 31045455	59.9 ± 10.2 (N = 27)	29	Persistent AVF (controls)	171.7 ± 45.5 (LVED volume, ml)	164.6 ± 51.1	76.1 ± 18.7	77.1 ± 17.9	69.3 ± 6.7	3.4 ± 0.6	3.4 ± 0.7	Significant decrease in LV end-diastolic and systolic volume, CI, and LV mass 9 mo after AVF ligation
	60.2 ± 11.9 (N = 27)	33	Closure of AVF	161.5 ± 52.3	133.3 ± 43.9	80.5 ± 18.7	68.7 ± 17.2	67.7 ± 9.9	3.3 ± 0.6	2.5 ± 0.4	
Papasotiriou *et al.*, 2019[S14] PMID: 31180298	55.8 ± 11.8 (N = 52)	30.8	Persistent AVF	50.6 ± 5.4	NR	NR	NR	62.5 ± 5.1	NR	NR	Larger LVEDD at 2 and 5 yr post transplantation in patients with persistent AVF
	55.3 ± 11.3 (N = 47)	44.7	No functioning AVF	48.6 ± 4.4	NR	NR	NR	62.1 ± 5.6	NR	NR	

AVF, arteriovenous fistula; CI, cardiac index; CO, cardiac output; EF, ejection fraction; LV, left ventricle; LVEDD, left ventricular end-diastolic diameter; LVMI, left ventricular mass index; NR, not reported.
[a]Left ventricular end diastolic dimension (mm).
[b]Prospective intervention.
[c]Left ventricular end-diastolic diameter index (mm/m^2).

Table 4. Case series and cohort studies concerning kidney allograft function in kidney transplant recipients who did and did not undergo closure of their arteriovenous fistulas, resulting from the systematic search strategy detailed in Supplementary Table S3

Reference	Age, yr, mean ± SD	Sex, % female	Treatment	Measure	Before treatment	After treatment	Outcome
Meier *et al.*, 2010[S15] PMID: 19761552	Unknown age (N = 4)	Unknown	AVF closure	Serum creatinine Urine output (ml/24 h) Proteinuria (g/ g Cr)	4.28 ± 1.11 630 ± 120 0.9 ± 0.2	2.54 ± 1.24 2360 ± 830 0.4 ± 0.2	Improvement of kidney allograft fxn 7 days after AVF closure (reduction of proteinuria, albuminuria, improved urine output)
Fraser III *et al.*, 2017[S16,a] PMID: 29886220	56.8 ± 10.3 (N = 36)	56	AVF closure	Serum creatinine	1.6	NR	Majority have maintained near-normal renal function after 1.9 ± 2.2 yr (mean ± SD) All had improvement of symptoms
Weekers *et al.*, 2017[S17] PMID: 27798197	54.2 ± 13.7 (N=81) 488 ± 13 (N = 114)	34.6 35.1	Persistently functioning AVF AVF closure or spontaneous thrombosis	eGFR rate of decline over time (ml/min per mo) (mean ± SD)	−0.164 ± 0.037 0.038 ± 0.062	NR −0.159	Acceleration of GFR decline of closed AVF cohort over 12 mo (−0.159 ml/min per mo from before AVF closure)
Hicks *et al.*, 2019[S18] PMID: 30853386	55 ± 9 (N = 16,066) 53 ± 10 (N = 779)	36.6 40.4	Persistently functioning AVF Closed AVF	3-yr Allograft failure (% of cohort) (mean ± SD)	0 0	9.5 ± 0.5 4.9 ± 1.3	Post-transplantation AV ligation is not significantly associated with allograft failure
Magnetti *et al.*, 2020[S19,a] PMID: 32524867	60 ± 10 (median ± IQR) (N = 22)	27	AVF closure	Kidney allograft RI (median)	0.71	0.66	Kidney allograft RI improvement at 6 mo post ligation of AVF 90% of Cohort had persistently improved RI values at 6 mo

AVF, arteriovenous fistula; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; IQR, interquartile range; NR, not reported; RI, resistive index.
[a]Prospective intervention.

their lifetime. Patients may have a variety of motivations for considering AVF closure, including esthetic reasons and concerns about cardiac health. In the absence of guidelines, the decision of whether to close an AVF after transplantation should involve a conversation between the clinician and patient. Advantages and disadvantages of closure of the AVF must be considered, including advantages such as the avoidance of HOHF, reduction of LV mass, potential reduction of cardiovascular risk, minimization of rupture risk, and cosmetic benefits; and the disadvantages of closure, including loss of an access site, post-ligation hypertension, perioperative complications, and cost.[9]

Table 5. Teaching points

In contrast to low- or normal-output heart failure, manifestations of HOHF may include a wide pulse pressure, warm extremities, and a hyperdynamic precordium along with a systolic murmur secondary to a high-flow state
The Nicoladoni–Branham sign is the phenomenon in which temporary occlusion of the high-flow AVF may lead to a modest reduction in heart rate (~7 bpm) via the vagus nerve–mediated baroreceptor reflex
Right heart catheterization can be used to evaluate cardiac hemodynamics at rest and with occlusion of the arteriovenous fistula to evaluate volume status, pulmonary artery pressures, and cardiac output to guide management
Risk factors for AVF-associated HOHF include upper arm AVF, male sex, history of vascular access surgery, and vascular access blood flow (Qa) >2.0 L/min[3,4]
There are 2 major approaches to treat AVF-related HOHF refractory to diuretics: ligation and flow restriction
Prevention of HOHF by ligation of an AVF that is not being used by a stable kidney transplant recipient remains a topic of controversy
There is a need for more randomized controlled trials of AVF management in kidney transplant recipients

AVF, arteriovenous fistula; HOHF, high output heart failure.

CONCLUSION

In our patient, successful surgical closure of his AVF resulted in marked improvement of his dyspnea, edema, and pulmonary hypertension. Teaching points for this case are summarized in Table 5. Based on our systematic review of this underrecognized diagnosis, there is a need for better clinical characterization of AVF-associated HOHF and more randomized controlled trials of AVFs in kidney transplant recipients, including systematic assessment of their subsequent quality of life and exercise tolerance. This will pave the way for development of guidelines for the diagnosis and management of AVF-associated HOHF, which are currently lacking.

DISCLOSURE

All the authors declared no competing interests.

ACKNOWLEDGMENTS

The authors obtained written consent from the patient. Figures 2, 3, and 4 were created with BioRender.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Case reports of kidney transplant recipients who developed arteriovenous fistula-related high output heart failure, resulting from the systematic search strategy detailed in Supplementary Table S3.

Table S2. Case series and cohort studies of kidney transplant recipients who developed arteriovenous

fistula-related high output heart failure, resulting from the systematic search strategy detailed in Supplementary Table S3.

Table S3. Search strategy on MEDLINE.

Figure S1. Selection and adjudication of studies of high output heart failure from dialysis-related arteriovenous fistula using the search strategy detailed in Supplementary Table S3.

Figure S2. Selection and adjudication of studies of cardiac function and kidney function in kidney transplant recipients who either did or did not undergo closure of the arteriovenous fistula using the search strategy detailed in Supplementary Table S3.

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