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 reveals 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 dilatation 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
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 m². 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/m², respectively (Table 2). Given his signs and symptoms of heart failure, right heart catheterization findings of an elevated CI of 4.24 L/min/m², 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 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   |
| HCO₃⁻                | 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 x 10⁹ cells/mm³ |
|----------------------|--------------|------------------------|
| Hemoglobin           | 15.6         | 13.5–17.5 g/dL         |
| Hematocrit           | 51           | 41%–53%                |
| Platelets            | 183          | 150,000–400,000/mm³   |
| Total bilirubin      | 0.8          | 0.0–0.3 mg/dL          |
| Direct bilirubin     | 0.0          | 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 mg/dL            |
| Haptoglobin          | <8           | 36–195 mg/dL           |
| UA                   | 100 Protein, negative ketones, negative bilirubin, negative leukocyte esterase or nitrile, moderate blood |
| UA Micro             | 23 UWB, 4 URBC, trace U bac. < 1 hyaline casts or granular casts |

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; UWB, urinary white blood cells; WBC, white blood cell.

Figure 1. Patient’s right upper extremity arteriovenous fistula.
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 \text{ 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.\textsuperscript{51} Increased LV mass is linked to higher cardiovascular morbidity and mortality.\textsuperscript{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) \textgreater 2.0 \text{ L/min}.\textsuperscript{2,3} The finding of Qa/CO ratios \textgreater 0.3 has also been suggested as a risk factor for high-output heart failure and decompensation.\textsuperscript{4} Brachiocephalic fistulas can have double the flow of radiocephalic fistulas, given the former’s proximity to the heart.\textsuperscript{5}

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 (\textasciitilde 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 \text{ L/min/m}\textsuperscript{2}.\textsuperscript{5,6} Especially in patients with high-flow AVFs (Qa \textgreater 2.0 \text{ 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.

**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

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**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\textsuperscript{2} | 2.83 L/min per m\textsuperscript{2} |

PAP, pulmonary artery pressure; thermo, thermodilution.
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. 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, 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.

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/m², pre | LVMi, g/m², post | EF (pre) | CI (pre) | CI (post) | Outcome                                                                 |
|-------------------------------|--------------------|--------------|-------------------------------|-----------------------------------|------------------------------------|----------------|----------------|----------|----------|-----------|--------------------------------------------------------------------------|
| De Lima et al., 1999         | 40 ± 12 (N = 39)   | 46           | Persistent functioning AVF    | 53 ± 5                            | 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. |
| PMID: 10844383                |                    |              | Closed AVF                    | 49 ± 5                            | NR                                 | 142 ± 30        | NR             | 70 ± 5   | 3.2 ± 0.6 | NR        | Reduction of LVMi and LVEDD 4–5 mo after AVF closure                    |
| Van Duijnhoven et al., 2001  | 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        | Reversal of LVMI was observed in patients undergoing AVF closure.         |
| PMID: 11158414                |                    |              |                               |                                    |                                    |                 |                |          |          |           | Reduction of LVEDD and LVMi post AVF closure                             |
| Unger et al., 2002            | 40 ± 6 (N = 6)     | 33           | Persistent AVF (controls)     | 29 ± 3.3                          | 29.2 ± 3.6                         | 153 ± 63        | 151 ± 59       | NR       | NR       | NR        | Decreased LVMI and LVEDD in patients compared to persistent AVF patients. (not statistically significant) |
| PMID: 12134102                |                    |              | Closed AVF                    | 29.9 ± 2.2                        | 27.4 ± 2.1                         | 141 ± 37        | 132 ± 39       | NR       | NR       | NR        | Decreased LVEDD and LVMi after AVF closure                               |
| Sheashaa et al., 2004         | 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 patients compared to persistent AVF patients.         |
| PMID: 15308876                |                    |              | Spontaneously thrombosed AVF  | 43.6 ± 6                          | NR                                 | 169.5 ± 61.3    | NR             | 71 ± 10  | 2.44 ± 0.96 | NR        | Decreased LVEDD in patients compared to persistent AVF patients.         |
| Unger et al., 2004            | 49 ± 6 (N = 8)     | 62.5         | Persistent AVF (controls)     | 29.5 ± 3.4 (LVEDD used)           | 29.0 ± 3.2 (post 1 mo); 28.9 ± 2.7 (post 21 mo) | 139.44          | 114 ± 19        | 68 ± 9   | 3.86 ± 0.78 | 3.58 ± 0.87 (post 1 mo)        | Decreased LVMi and LVH prevalence after surgical AVF closure             |
| PMID: 15575907                |                    |              | Closed AVF                    | 29.5 ± 3.4                        | 28.9 ± 2.9 (post 1 mo); 26.2 ± 3.2 (post 21 mo) | 139.44          | 115 ± 18        | 68 ± 9   | 3.86 ± 0.78 | 3.04 ± 0.55 (post 1 mo); 2.97 ± 0.83 (post 21 mo) | Decreased LVMi and LVH prevalence after surgical AVF closure             |
| Cordig et al., 2008           | 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. |
| PMID: 18537919                |                    |              | Closed AVF                    | 48.5 ± 6                          | NR                                 | 112.4 ± 28      | NR             | 66.5 ± 10.1 | NR       | NR        | Reduction of LV mass 1 mo after AVF closure                              |
| Unger et al., 2008            | 54 ± 12 (N = 16)   | 50           | Closure of AVF                | 29.5 ± 3.4 (LVEDDI, mm²)          | 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                              |
| PMID: 18301341                |                    |              |                               |                                    |                                    |                 |                |          |          |           | Reduction of LV mass 1 mo after AVF closure                              |
| Gorgulu et al., 2011          | 39 ± 12 (N = 60)   | 40           | Persistent AVF                | 46 ± 5                            | NR                                 | 129 ± 37        | NR             | 62 ± 5    | NR       | NR        | No significant difference in hemodynamic measurements between open-AVF and closed-AVF cohorts. |
| PMID: 22161285                |                    |              | Closed or spontaneously thrombosed AVF | 46 ± 6                            | NR                                 | 125 ± 42        | NR             | 63 ± 6    | NR       | NR        | No significant difference in hemodynamic measurements between open-AVF and closed-AVF cohorts. |

(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 | LVM, g/m², pre | LVM, g/m², post | EF (pre) | CI (pre) | CI (post) | Outcome                                                                 |
|---------------------------|--------------------|---------------|-----------|-----------------------------------|------------------------------------|----------------|----------------|----------|---------|----------|-------------------------------------------------------------------------|
| Soleiman et al., 2012     | 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 |
| Glowinski et al., 2012    | 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 LVM and LVDD after AVF closure (not statistically significant) |
| Dundon et al., 2014       | 58.5 ± 6 (N = 18)  | 22            | Closure of AVF | NR                                 | NR                                 | 186 ± 56 (LVM, 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          | 59.9 ± 10.2 (N = 27) | 29            | Persistent AVF (controls) | 171.7 ± 45.5 (LVEDD 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 |
| Papasotiriou et al., 2019 | 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 |

AVF, arteriovenous fistula; CI, cardiac index; CO, cardiac output; EF, ejection fraction; LV, left ventricle; LVEDD, left ventricular end-diastolic diameter; LVM, left ventricular mass index; NR, not reported.

*Left ventricular end-diastolic dimension (mm).

**Prospective intervention.

*Left ventricular end-diastolic diameter index (mm/m²).
There is a need for more randomized controlled trials of AVF management in kidney transplant recipients, resulting from the systematic search strategy detailed in Supplementary Table S3.

**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†  | Unknown (N = 4)    | Unknown       | AVF closure | Serum creatinine | 4.28 ± 1.11 | 2.54 ± 1.24 | Improvement of kidney allograft function in 7 days after AVF closure (reduction of proteinuria, albuminuria, improved urine output) |
| Fraser III et al., 2017† | 56.8 ± 10.3 (N = 36) | 56            | AVF closure | Serum creatinine | 1.8          | 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† | 54.2 ± 13.7 (N = 81) | 48.8 ± 13 (N = 114) | Persistently functioning 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 | 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† | 55 ± 9 (N = 16.068) | 53 ± 10 (N = 779) | Persistently functioning AVF closure | 3-yr Allograft failure (% of cohort) (mean ± SD) | 0 | 9.5 ± 0.5 | Post-transplantation AV ligation is not significantly associated with allograft failure |
| Magnetti et al., 2020† | 60 ± 10 (median ± IQR) (N = 22) | 27 | AVF closure | Kidney allograft RI (median) | 0.71 | 0.66 | Kidney allograft RI improvement of 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.

*Prospective intervention.

**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.

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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 fistulas, resulting from the systematic search strategy detailed in Supplementary Table S3.

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.†
- 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.
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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