Systemic Effects of Hemodialysis Access

Anil K. Agarwal

Patients with advanced chronic kidney disease are at a high risk of cardiovascular events. Patients with end-stage renal disease have a particularly high morbidity and mortality, in part attributed to the complications and dysfunction related to vascular access in this population. Creation of an arteriovenous access for HD is considered standard of care for most patients and has distinct advantages including less likelihood of infections, less need for intervention, and positive impact on survival as compared with usage of a catheter. However, creation of an arteriovenous shunt incites a series of events that significantly impacts cardiovascular and neurohormonal health in both positive and negative ways. This article will review the short- and long-term effects of dialysis access on cardiovascular, neurohormonal, and pulmonary systems as well as a brief review of their effect on survival on HD. Presence of other comorbidities in a patient with dialysis access can amplify these effects, and these considerations are of paramount importance in individualizing the approach to not only the choice of vascular access but also the modality of kidney replacement therapy.

Key Words: Systemic effects of dialysis access, High-flow fistula, Vascular access, Pulmonary hypertension

INTRODUCTION

Patients with ESRD suffer from failure of a vital organ with diverse roles in maintenance of "milieu interieur," often with concomitant suboptimal function of other vital organs, in the backdrop of multiple comorbidities including diabetes mellitus, hypertension, heart failure, and infections. Kidneys regulate cardiovascular hemodynamics through regulation of blood volume and BP as well as mineral metabolism. Ineffective regulation of these essential functions leads to cardiovascular consequences including left ventricular (LV) hypertrophy, volume overload, and endothelial dysfunction. Consequently, the patient with kidney dysfunction is considered to be at the highest level of cardiovascular risk. AVF for HD remains a singular important advance that made chronic HD feasible.[1] However, creation of AV access for HD imparts another degree of complexity to this already complex physiology.

Aside from making obvious alterations in the vascular anatomy, the AV accesses cause changes in cardiovascular hemodynamics, including the systemic and pulmonary circulations that have been recognized for over half a century, starting soon after the placement of the first AVF.[2,3] These alterations result in adaptations and maladaptations of cardiac structure, function, and pulmonary circulation that impact normal function, quality of life, and survival of patients on HD. Use of AV grafts and catheters has been noted to be associated with higher levels of circulating pro-inflammatory cytokines. Vascular access can lead to other systemic complications including ischemia (steal), thromboembolic phenomenon, infections, and psychological complications. Dialysis catheters can cause central vein stenosis (CVS) in addition to a high incidence of infections. This review will focus primarily on hemodynamic alterations associated with AV accesses and their downstream effects because most studies have examined AVF or mixed AV accesses. AV grafts are likely to cause similar hemodynamic consequences as AVF. However, AV grafts are associated with a higher level of inflammation than AVF. Systemic effects of central venous catheters (CVCs) will be briefly mentioned, primarily related to infectious and mechanical effects not related to physiologic changes, because of their adverse impact on survival and quality of life of patients on HD.

Cardiovascular and Neurohormonal Effects

Creation of AVF has immediate and late effects on systemic circulation.[2–6] The procedure is followed by an increase in cardiac contractility and decrease in peripheral resistance, which result in increased cardiac output (CO). There is also an increase in blood volume and LV end-diastolic volume along with restrictive physiology in diastole. At the same time, vascular endothelium undergoes structural and functional changes responding to the shear stress and increase in blood flow. There is production of nitric oxide and vasorelaxation. The diameters of the artery and the vein increase as a result of increased flow through this newly created low-resistance parallel circuit.

Short-term effects of AVF creation have been studied extensively. An echocardiographic study of 16 patients with chronic kidney failure assessed echocardiographic changes before and 3, 7, and 14 days after creation of AVF [4] Concentrations of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) were also checked on day 1, 3, 6, 10, and 14. The study showed that within 10 days to 2 weeks after creation of AVF, CO increased by 15%, fractional shortening increased by 8%, and LV end-diastolic diameter increased 4%. There was shortening of the deceleration time of the early diastolic filling wave (−12%) and the ratio of the peak velocity of early diastolic to atrial filling (E-A ratio) increased (+18%). The difference in duration of LV inflow and pulmonary venous flow at atrial contraction, a marker of LV end-diastolic pressure, significantly shortened by day 14 after the operation (−37%). The authors concluded that the creation of an AV fistula induced LV diastolic dysfunction and a restrictive filling pattern. There was an increase in ANP and

From the Section of Nephrology at University Hospital East, The Ohio State University Wexner Medical Center, Columbus, OH.

Financial Disclosure: The author declares that he has no relevant financial interests.

Address correspondence to Anil K. Agarwal, MD, FACP, FASN, FNKF, Section of Nephrology at University Hospital East, The Ohio State University Wexner Medical Center, Columbus, OH 43210 E-mail: Anil.agarwal@osumc.edu

1548-5595/$36.00
http://dx.doi.org/10.1053/j.ackd.2015.07.003

BNP levels with maximal increase after 10 days (ANP, +48%; BNP, +68%; Fig. 1). The increase in CO was associated with elevation of ANP levels but not BNP levels. The increase in E-A ratio correlated only with BNP level elevation.

Acute and chronic hemodynamic changes at 24 hour and 8 weeks after placement of a radiocephalic AVF were studied in 17 subjects at 24 hours with a Swan-Ganz catheter.[5] At baseline, all patients had normal right atrial pressure; pulmonary artery wedge pressure, stroke volume index (SVI), high normal heart rate (HR), and systemic vascular resistance index (SVRI). The PAP, MAP, cardiac index (CI), and pulmonary vascular resistance index (PVRI) were high at baseline. At 24 hours after the AV fistula creation, there was an insignificant rise in HR, CI, PAP, and PVRI, and a fall in SVRI and MAP with no change in right atrial pressure, pulmonary artery wedge pressure, and SVI. A rising trend of HR and CI with a fall in SVRI was observed in 10 of 17 patients. At the sixth week, the 8 patients studied showed a significant increase in the systolic pressure and MAP and PVRI. Also, there was a rise in SVI in all patients and CI in 6 patients, with insignificant change in the cardiac filling pressure. None of the patients developed congestive heart failure due to AVF. Increase (although insignificant) in CI after AVF despite a decrease in preload after AVF was not well explained by these findings. The authors concluded that the creation of an AVF for HD does not lead to a significant change in the cardiac hemodynamic parameters and is not an appreciable factor leading to circulatory congestion or pulmonary edema in these patients.

CLINICAL SUMMARY

- Arteriovenous access for hemodialysis is preferred over catheter access due to the less likelihood of infections and interventions and a positive impact on survival as compared to using a catheter.
- Access creation leads to changes in heart rate, blood pressure, blood volume, cardiac output, pulmonary and systemic resistance, changes in natriuretic peptides as well as structural changes in vascular endothelium and left ventricular mass.
- Access flow to cardiac output ratio >0.3 may predict heart failure.
- Potential short and long term effects of AV access should be carefully considered in individualizing the approach to the choice of vascular access and the modality of renal replacement therapy, especially in patients with preexisting cardiovascular morbidity.

Timing of various changes was also studied in another prospective echocardiographic and neurohormonal study of 12 predialysis patients before and 1 and 3 months after creation of a primary AV access.[6] After creation of access, the weight, BP, or hemoglobin level did not change, but CI increased and SVR decreased. LV mass corrected to height significantly increased from 63.8 ± 5.5 to 68.9 ± 4.9 g/m^2 at 1 month and 72.5 ± 8.9 g/m^2 at 3 months (Fig. 2). The increase in mass was mostly due to an increase in interventricular septal thickness. LV end-diastolic diameter and posterior wall thickness did not change. The incidence of LV hypertrophy (LVH) increased from 67% at baseline to 83% and 90% at 1 and 3 months, respectively. Left atrial area increased, and early diastolic transmitral flow increased. Inferior vena cava diameter increased at 1 month and did not change at 3 months. A remarkable increase in ANP was seen 2 weeks after creation of AVF associated with increased contractility, CO, and decrease in peripheral resistance. There was decreased renin activity with no change in aldosterone levels. Plasma angiotensin II, angiotensin-converting enzyme, and endothelin levels did not change. The authors concluded that creation of AV access is independently associated with further progression of already existing LVH.

AVF can affect cardiac load by increasing preload and decreasing afterload. In 10 patients with AVF, a 60-second compression and reconstruction of aortic pressure waves from finger pressure recordings showed a small increase in LV oxygen demand, but a larger decline in cardiac oxygen supply.[7] During fistula compression, systolic, diastolic, and mean arterial pressures increased, and HR decreased significantly. Although stroke volume decreased slightly, there was a significant decrease in CO and increase in SVR.

It is well recognized that arterial stiffness, as measured by carotid-femoral pulse wave velocity, is increased in dialysis patients and causes increased central BP and myocardial hypoperfusion. In a small study of 43 patients, 30 of the 43 patients with successful AVF showed decreased total peripheral resistance, increased SV and CO with decreased systolic and diastolic BP 2 weeks after placement of AV fistula.[8] This study demonstrated potential benefits of AVF creation in HD patients although overall benefits of AV access have to be considered in an individual patient.

Heart Failure

Presence of AVF, especially when associated with high access flow, has been observed to be associated with heart failure, which is generally attributed to an increase in CO.[9] However, relatively uncommon occurrence of heart failure with such AVF suggests presence of intrinsic heart disease in those who develop heart failure. It is also likely that many cases of heart failure due to AVF are missed and attributed to other risk factors. Upper arm AV access is more likely to have higher access flow and result in heart failure as compared with an access in forearm although there is no difference between AVF and AV graft (Fig. 3).[10]

There are many AV access–associated risk factors for occurrence of heart failure. It is well known that a high-flow AVF can cause significant adverse changes in CO, BP, and HR. An access flow (Qa) over 2 L per minute is a risk factor for occurrence of heart failure.[10] Another risk factor is the occurrence of a high degree of cardiopulmonary recirculation. One study showed a strong positive correlation between Qa, CO, and CI and a negative correlation with SVR (Fig. 4).[11] There was an average Qa:CO ratio of 14% to 20% in stable long-term HD patients, but a ratio higher than 0.3 was associated with high output heart failure.