By Edgar Lerma

In 2019, a randomized controlled trial to evaluate the effect of arteriovenous fistula (AVF) ligation on cardiac structure and function in stable kidney transplant recipients was published in *Circulation*.

Kidney transplant recipients (>12 months post-transplantation) with stable allograft function were randomized to AVF ligation versus no intervention. The primary outcome was the change in left ventricular (LV) mass [obtained by performing cardiac magnetic resonance imaging (MRI) at baseline and at 6 months], whereas secondary outcomes included changes in LV volumes, left and right atrial areas, LV ejection fraction (LVEF), N-terminal pro-hormone B-type natriuretic peptide (NT-proBNP) levels, cardiac output/index, brachial flows (ipsilateral to AVF), and pulmonary artery (PA) velocity.

Sixty-four of 93 screened patients were randomized to the AVF ligation (n = 33) versus no intervention/control (n = 31) groups. A mean decrease of 22.1 g (95% confidence interval [CI], 15.0–20.1) was observed in LV mass in the AVF ligation group versus an increase of 1.2 g (95% CI, 4.8 to 7.2) in the control group (p < 0.001). In addition, decreases in LV end-diastolic volumes (LVEDVs), LV end-systolic volumes (LVEVs), cardiac output (CO), cardiac index, atrial volumes, and NT-proBNP were also demonstrated in the AVF ligation group (p < 0.01).

The authors of this study concluded that “Elective ligation of patent AVF in adults with stable kidney transplant function resulted in clinically significant reduction of LV myocardial mass.”

In this set of articles, Dr. Aisha Shaikh and Dr. Loay Salman discuss the clinical and practical implications of these findings to everyday practice.

Edgar V. Lerma, MD, FASN, FASDIN, is clinical professor of Medicine in the section of nephrology at the University of Illinois at Chicago College of Medicine, and is affiliated with Associates in Nephrology, SC, in Chicago, IL.

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**Kidney Controversy**

**TO LIGATE OR NOT LIGATE**

By Aisha Shaikh, MD

An arteriovenous fistula (AVF) is the preferred vascular access in hemodialysis patients because of its superior long-term patency and lower risk of infection (1). The impact of AVF on the cardiovascular (CV) system has been an area of interest to the scientific community for decades, from the time soldiers sustained traumatic AVF in the battlefield to the first description of AVF use in dialysis patients in 1966 (2).

The creation of an AVF between an artery and a vein diverts the blood from the high-resistance capillary system to the low-resistance venous system. The diastolic flow of blood causes an immediate decline in peripheral vascular resistance, increases the venous return to the heart, and increases the cardiac output. These hemodynamic changes lead to an increase in left ventricular (LV) filling pressure and can cause LV hypertrophy (LVH) as a result of cardiac remodeling (3). In some patients, the cardiac remodeling can become maladaptive and result in high-output heart failure. In a prospective study, Basile et al. (4) demonstrated that patients with AVF flow rate of ≥2 L/min have a higher risk for the development of high-output heart failure.

LVH is highly prevalent among ESKD patients, and it is associated with increased risk of heart failure and death. Several factors contribute to the development of LVH in ESKD, including hypertension, volume overload, anemia, and the presence of an AVF. A study by Dundon et al. (5) showed a 12.7% increase in LV mass within 6 months of AVF creation.

It is important to note that observational studies have shown that AVF use is associated with better CV outcomes compared with central venous catheter use in ESKD patients (6). It should be noted, however, that the observational data are riddled with selection bias, and the superior patient outcomes associated with AVF use are at least partly due to patient-related factors rather than solely to the type of vascular access (7). In summary, on one hand the AVF can have an adverse impact on the cardiac structure and function in some patients, but on the other hand AVF use is associated with better clinical outcomes in the majority of ESKD patients. Hence, AVF is the vascular access of choice in hemodialysis patients unless a contraindication to AVF creation exists, such as heart failure, severe vascular disease, advanced age, or poor life expectancy.

Kidney transplantation is the preferred treatment for ESKD. CV disease remains the leading cause of death in ESKD patients even after kidney transplantation. Several factors contribute to the higher prevalence of CV disease in kidney transplant recipients, and many of these CV risk factors are acquired before the kidney transplantation. LVH is common in kidney transplant recipients and is associated with increased CV morbidity and mortality. Although LVH improves after kidney transplantation, it does not completely reverse (8). Therefore, the impact of a functioning AVF on cardiac structure and function becomes relevant in kidney transplant recipients with a stable allograft function. Several nonrandomized observational studies have demonstrated that AVF ligation in kidney

**Controversy**

**To Ligate or Not Ligate Arteriovenous Accesses: PRO**

By Aisha Shaikh, MD

Does elective AVF ligation affect cardiovascular remodeling?

<table>
<thead>
<tr>
<th>Primary Outcome</th>
<th>Secondary Outcome</th>
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<tr>
<td><strong>AVF Ligation</strong></td>
<td><strong>No Intervention</strong></td>
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<tr>
<td>22.1 gms (15% CI 0.0 to 29.1)</td>
<td>1.2 gms (95% CI 4.9 to 7.2)</td>
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<tr>
<td>p &lt; 0.001</td>
<td>p = 0.07</td>
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**Conclusions**

Elective ligation of patient AVF in adults with stable kidney transplant function resulted in clinically significant reduction of LV myocardial mass.

In this set of articles, Dr. Aisha Shaikh and Dr. Loay Salman discuss the clinical and practical implications of these findings to everyday practice.
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transplant recipients leads to a decrease in LV mass, but until recently no randomized controlled study had been conducted to show the impact of AVF ligation on LV mass in kidney transplant recipients (9, 10). In 2019, Rao et al. (11) conducted a randomized controlled trial in which kidney transplant recipients with stable kidney allograft function were randomized to AVF ligation or no AVF ligation 1 year after kidney transplantation. The baseline characteristics were well matched in the two groups. All patients underwent cardiac magnetic resonance imaging (MRI) at baseline and at 6 months to assess the change in LV mass. AVF flow rates were not reported in this study, and both groups had the same proportion of forearm and upper arm AVF. The follow-up cardiac MRI showed that the AVF ligation group (n = 27) had a 15% reduction in LV mass, whereas no significant change in LV mass was observed in the control group (n = 27). The study provides clear evidence that regression in LV mass index occurs after AVF ligation in kidney transplant recipients, but the question that remains unanswered is whether the decrease in LV mass index translates into better CV and overall outcomes. Currently, no guidelines exist to determine the fate of the AVF after kidney transplantation. The advantage of having a functional AVF after kidney transplantation is that it can be used for future dialysis if the kidney allograft fails. AVFs have a high primary failure rate, and a functional AVF is a precious commodity. Therefore, abandoning a functional AVF is not a straightforward decision.

The long-term kidney allograft outcomes have improved, and the decision to ligate an AVF after kidney transplantation should be based on several patient-related and AVF-related factors. The goal should not be to merely preserve an AVF at all costs. Several factors must be taken into account when making the decision regarding the fate of the AVF after kidney transplantation, such as the likelihood of kidney allograft failure, AVF flow rate and its impact on cardiac structure and function, local effects of the AVF (e.g., aneurysms), and patient preference (cosmetic, functional) (12). Clinicians must also be familiar with AVF flow reduction procedures that may help preserve a functional AVF while potentially addressing the complications resulting from the high flow AVF (12).

The approach to AVF ligation after kidney transplantation must be patient-centered, and a one-size-fits-all approach must be avoided. The recent study by Rao et al. (11) offers a clear insight into the impact of AVF ligation on cardiac structure. We look forward to future studies to learn whether these structural cardiac changes translate into better outcomes. Until then we must continue to individualize the decision regarding AVF ligation in kidney transplant patients.

Aloha Shaikh, MD, is affiliated with the James J. Peters Veterans Affairs Medical Center in New York City.

References

Controversy
To Ligate or not Ligate Arteriovenous Accesses: CON

By Loay Salman

Kidney transplantation remains the best treatment option for patients with end stage kidney disease (ESKD). However, a dilemma faces healthcare providers when they care for ESKD patients: whether to ligate the patient’s arteriovenous (AV) access after kidney transplantation or leave it patent and maintain it. There is still considerable disagreement among providers on the best course of action when dealing with an AV access after kidney transplantation (1). In this article, I will discuss the disadvantages of ligating an AV access after kidney transplantation.

The 1-year and 5-year kidney graft survival rates range between 87% and 95% and 65% and 83%, respectively, based on a donor’s status (2). Therefore, significant numbers of kidney transplant recipients will end up receiving dialysis again in the future. And this means that these patients will need AV access when reinitiating dialysis. Creating a new AV access, if the original access was ligated, carries its own challenges and risks. They include not only the risk of the procedure itself, the lead time to maturation, the primary failure rate, the failure rate of related procedures, and the need for tunneled hemodialysis catheters (TDC) but also the difficulty of finding a suitable artery and vein that meet the criteria for AV access creation (3). Two-thirds of patients with a failed kidney transplant start hemodialysis with a TDC (4). Using a TDC by itself adds significant morbidity and mortality to patients with an already higher morbidity and mortality risk than their peers (5).

There is no proven benefit to patient mortality of an access ligation after kidney transplantation. Hicks et al. (6) used the United States Renal Data System to look at 16,845 patients with AV access who received kidney transplants between January 2011 and December 2013. Access ligation occurred in 4.6% of these patients. There was no statistically significant difference between the two groups in all-cause mortality and post-transplantation allograft failure. This study highlighted that the current practice pattern in the United States is to ligate problematic AV accesses only, hence the low rate of access ligation. At the same time, Marquesa et al. (7) evaluated six hemodialysis patients and four transplant patients with high AVF blood flow (>1.5 L/min per 1.73 m²) 73% coupled with symptoms of heart failure. The patients underwent an AVF flow reduction procedure. The flow reduction rate was approximatively 58.4%. The results showed that 80% of patients had an improvement in heart failure symptoms. Improvement in systolic pulmonary artery pressure was also noted. However, there is an increased risk of recurrence of high blood flow after flow reduction procedures. Vass et al. (8) have shown that AV access high flow (>2 L/min) recurred in 52% of patients during the observation period (1 year) among patients who underwent flow reduction procedures.

It is also important to mention that studies have shown some conflicting results of the effect of AV access ligation on cardiac parameters. Rao et al. (9) conducted a randomized controlled trial among kidney transplant recipients (>12 months after transplantation with stable kidney graft function) comparing AVF ligation with no ligation. They randomized 64 patients and used cardiac magnetic resonance imaging at baseline and at 6 months after ligation. AVF ligation resulted in a significant reduction in LV mass in 52% of patients during the observation period (1 year) among patients who underwent flow reduction procedures. It is also important to mention that studies have shown some conflicting results of the effect of AV access ligation on cardiac parameters. Rao et al. (9) conducted a randomized controlled trial among kidney transplant recipients (>12 months after transplantation with stable kidney graft function) comparing AVF ligation with no ligation. They randomized 64 patients and used cardiac magnetic resonance imaging at baseline and at 6 months after ligation. AVF ligation resulted in a significant reduction in LV mass in 52% of patients during the observation period (1 year) among patients who underwent flow reduction procedures.