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Invited Review

Renal Replacement Therapy in Patients with Left Ventricular Assist Device: What do the Cardiologists Need to Know?

Hesham R. Omar, MD

Department of Internal Medicine, Mercy Medical Center, Clinton, Iowa, USA

Corresponding author: hesham.omar@apogeephysicians.com

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Abstract

Renal failure after left ventricular assist device (LVAD) implantation occurs either due to worsening chronic kidney disease which is common in end-stage heart failure, or due to acute kidney injury in the peri-implantation period, and is associated with high morbidity and shortterm mortality. The increased utilization of LVAD in refractory heart failure either as a bridge to transplantation or destination therapy will eventually create a population of patients with LVADs who are dialysis-dependent. There are multiple challenges encountered during dialysis of patients with LVADs including the unfamiliarity of nephrologists with the LVAD technology, difficulty in hemodynamic monitoring with continuous flow devices, risk of access site infection or bleeding and poor arteriovenous fistula maturation and these reasons are the source for the reluctance of outpatient dialysis centers to accept such cases. The nephrologists as well as cardiologists should be familiar with these obstacles to avoid adverse consequences to these high risk patients. Herein, we explore the challenges encountered during dialysis of patients with LVADs.

Keywords

Ventricular assist device; hemodialysis; peritoneal dialysis; heart transplantation; heart failure

Introduction

Left ventricular assist devices (LVADs) have become an integral tool in the treatment of patients with refractory heart failure either as a bridge to transplantation or as destination therapy (DT) in those who are not candidates for heart transplantation (HT) [1, 2] as it decrease morbidity, improve the quality of life [3] and prolong survival [4]. According to the INTERMACS registry, more than 10000 LVADs have been implanted since 2006 in yearly increasing increments with nearly 2500 LVADs implanted in 2013 [5]. This continued rise in LVAD placement will generate a population of patients with LVAD-related complications including the requirement for long term renal replacement therapy (RRT). Acute renal failure after LVAD implantation is mainly related to irreversible kidney injury occurring in the peri-implantation period [6, 7] especially in the setting of chronic kidney disease which is common in up to 45% of patients with ambulatory heart failure [8] and 64% of patients hospitalized with decompensated heart failure [9]. LVAD recipients who require RRT post implantation have unfavorable outcomes due to the high morbidity and short-term mortality [7, 10] especially in those not bridged to HT. The mortality of LVAD patients who develop postoperative acute kidney injury has been estimated at approximately 57% to 93% in prior studies [11- 16].

The International Society for Heart and Lung Transplantation (ISHLT) guidelines for mechanical circulatory support have thus recommended that the requirement for permanent RRT is a contraindication for LVAD implantation as a DT [17] but is not a contraindication in those receiving LVAD as a bridge to HT. The technical problems faced by nephrologists and dialysis centers managing patients with LVADs requiring RRT include: unfeasibility of hemodynamic monitoring in patients without a pulse, risk of drive line infection through dialysis catheters, and anticoagulant management and risk of bleeding. This has resulted in the reluctance of outpatient dialysis centers to accept patients with LVADs and therefore they may remain hospitalized leading to prolonged hospital stay which is detrimental to the patients' quality of life [18]. This warrants a close collaboration between the cardiologist and nephrologist to ensure a smooth transition of patients with LVADs requiring RRT from inpatient to outpatient dialysis. Herein, we aim to review the various obstacles facing the nephrologists and dialysis centers treating patients with LVADs requiring RRT.

Hemodialysis access challenges and concerns regarding arteriovenous fistula maturation

Hemodialysis access is a main challenge for patients with LVADs requiring RRT. These patients typically do not already have arteriovenous (AV) fistula or graft because they are not dialysis dependent pre-implant and RRT is usually started post LVAD placement. In the general dialysis population, AV fistula is known to be the optimal hemodialysis access as it is associated with prolonged survival, lower risk of infection, lesser hospitalization rates and reduced cost [19]. Nonetheless, there are concerns for poor AV fistula maturation in patients with LVAD due to lack of vascular reactivity as a result of the nonpulsatile blood flow [20]. This was demonstrated by Amir and colleagues who showed that

nonpulsatile blood flow is associated with decreased flow-mediated vasodilation [21]. It is recommended to maintain the mean arterial pressure in the range of 70 to 80 mmHg and not to exceed 90 mmHg in LVAD patients, as high afterload my compromise unloading of the left ventricle [22]. Also, the patient's low blood pressure after LVAD implantation may be a risk of access thrombosis.

Thrombosis of AV fistula due to low blood pressure may happen even in the absence of anatomical lesions [23]. Sasson and colleagues reported that spontaneous AV fistula maturation has not occurred in any of the patients with LVAD at their institution but suggested the option of assisted AV fistula maturation [24]. They have reported two cases demonstrating the assisted maturation of AV fistula for long term fistula patency (cumulative patency 329 days and 511 days in the two presented patients) [24]. However, there are no formal studies examining the AV fistula in LVAD patients [25]. Because of these concerns with AV fistula, Patel and colleagues have recommended the use of AV graft as the preferred long term hemodialysis access [25].

Dialysis access-related infection

The risk of access-related blood stream and drive line infection is another challenge in patients with LVAD requiring RRT. Patients with LVAD are already at risk for infection that may be introduced through the lead electrode in the skin [20]. LVAD driveline exit site infection and subsequent bacteremia can spread to the LVAD itself and is a common cause of morbidity and mortality [26]. Topkara and colleagues showed that patients with LVAD requiring postoperative hemodialysis had a higher rate of sepsis and shorter post-LVAD survival [15].

Argenziano and colleagues demonstrated that the occurrence of endocarditis in patients post LVAD implantation portended a poor prognosis [27]. In the general dialysis population, infectious complications are the second major cause of death only after cardiovascular disease [28, 29]. Because infection is found to be a leading cause of death in the peri-implant period, it has warranted a change in status to "urgent" for patients with LAVD awaiting HT [30].

Dialysis access is an important source of infection in patients with LVAD requiring RRT. Several studies investigated the relationship between dialysis access type and subsequent infection risk [28, 29, 31-34]. The incidence of bacteremia was highest with temporary dialysis catheters and the second highest was tunneled cuffed dialysis catheters compared with AV grafts and AV fistulas [31, 32]. The risk of bacteremia was significantly reduced in the peritoneal dialysis population [31]. Moreover, peritoneal dialysis catheter-related peritonitis seldom leads to bacteremia [35]. The LVAD driveline is placed in the retroperitoneal space and the peritoneum is not entered. It was therefore suggested that peritoneal dialysis may pose a lower risk of systemic infection compared with hemodialysis in patients with LVAD and may theoretically reduce their morbidity and mortality [36].

Hemodialysis versus peritoneal dialysis

There is lack of comparative trials to identify superiority of hemodialysis versus peritoneal dialysis in patients with LVAD requiring RRT. However, experts have

suggested a probable favorable outcome for peritoneal dialysis for several reasons [35, 36]. Most importantly is the lower risk of infectious complications: a main cause of morbidity and mortality in patients with LVAD. Peritoneal dialysis catheters can be placed with conscious sedation and local anesthetic allowing dialysis to be started immediately [35]. It also allows the patient to perform dialysis at home –and thus decrease hospitalization costs- unlike patients on hemodialysis who usually end up having dialysis in the hospital because many dialysis centers do not accept LVAD cases owing to their unstable hemodynamics and the perceived difficulty in measuring the blood pressure.

Sustained daily ultrafilteration with peritoneal dialysis offers more hemodynamic stability [36]. Peritoneal dialysis is known to be 25% less costly than hemodialysis [37]. Peritoneal dialysis also preserves residual renal functions compared to hemodialysis and therefore there is a higher chance of renal recovery [38] in those with viable renal parenchyma [35]. On the other hand, peritoneal dialysis may impede nutritional recovery in patients with LVAD who are usually malnourished [39]. In addition, some patients may have LVAD placed in the preperitoneal space which may pose challenges to safely conducting peritoneal dialysis [39]. Precise volume removal is also difficult with peritoneal dialysis compared to hemodialysis. Peritoneal dialysis may cause worsening of diabetes mellitus control due to the continuous glucose absorption from glucose-containing peritoneal dialysis solutions [40].

Concerns with hemodialysis in patients with LVAD include the fixed speed settings of continuous flow pumps. Most LVADs will not automatically adjust speed to cope with volume shifts and reduced preload which is a common hallmark during hemodialysis [36]. The temporary decrease of speed in some pumps in settings of reduced preload may also be insufficient to prevent hazards of volume shifts [36]. So far, the ideal dialysis technique in patients with LVAD is still debatable. Randomized controlled trials are mandatory to compare the outcome of peritoneal dialysis and hemodialysis in subjects with LVAD requiring RRT.

Intradialytic blood pressure monitoring in patients with LVAD

Hypotension is estimated to occur in 15 to 30% of the general hemodialysis population [41] and can reach up to 50% in high risk patients and those with LVADs [39, 42] and therefore blood pressure monitoring is crucial. Continuous-flow LVADs offer several advantages over the older version pulsatile devices, such as smaller size, better durability and long-term outcomes [43, 44]. Unfortunately, the resultant continuous unloading of the left ventricle during the whole cardiac cycle causes diminished or absent pulse pressure [45]. Therefore the standard method of auscultation of the blood pressure is usually unfeasible unless a pulse pressure is present from residual ventricular function [25]. A significantly lower systolic, diastolic and mean arterial blood pressure is obtained with automated blood pressure devices compared with intra-arterial blood pressure recording and its success rate in continuous-flow -LVAD patients is only approximately 50% [46].

Doppler ultrasonography has proven excellent success rates (~95%) with high validity and reliability and is considered the gold standard in measuring blood pressure in subjects with continuous-flow LVADs [39, 46, 47]. However, there is some controversy regarding whether the initial audible sound with Doppler ultrasonography represent the systolic blood pressure or the mean arterial pressure [46-48]. Studies showed that in patients with high pulse pressure, the initial audible sound with the Doppler technique is closer to the systolic blood pressure [47], while in cases with low pulse pressure, the initial Doppler sound is closer to the mean arterial pressure. Lanier and colleagues demonstrated a 90% success rate in measuring systolic blood pressure and mean arterial pressure using an automated Terumo Elemano blood pressure monitor (Somerset, NJ) which uses a double-cuff oscillometric slow deflation technology designed to improve sensitivity of blood pressure readings [47]. One should attempt validation of blood pressure devices against arterial line and/or Doppler recordings prior to its utilization in patients with continuous-flow LVAD [47].

Other concerns in patients with LVAD on chronic hemodialysis

Patients with post LVAD acute kidney injury requiring RRT will need a hemodialysis catheter insertion. A concern in this instance is the risk of bleeding since anticoagulant therapy is crucial in all patients with LVADs to avoid thrombotic complications. Most of these patients are on various combinations of heparin, warfarin, aspirin and dipyridamole to decrease the risk of pump thrombosis and ischemic stroke [22, 49]. The operator should therefore be prepared to place the hemodialysis catheter in a patient with therapeutic level anticoagulation and to ensure adequate hemostasis of the chest tunnel in case of tunneled catheter placement [50].

Anticoagulation also represents a risk for blood loss from an AV fistula during cannulation and this is compounded by uremic platelet dysfunction in chronic kidney disease. Dialysis catheter insertion should preferably be performed in a procedure room rather than bedside for better sterilization. Femoral access in obese patients who are at increased risk of infection should be avoided [50]. It is advised that the nephrologist does not adjust or reverse anticoagulant medications without consulting with the cardiac team [50]. A tunneled dialysis catheter is preferred over non-tunneled ones because of lower risk of infection. It is also advised that before starting any procedure to make sure that the batteries will cover the expected procedure duration, to have charged spare batteries available and to preferably have a technician specialized in LVAD management on standby till completion of the procedure [50]. There are also concerns that the placement of an AV fistula or AV graft may worsen heart failure (high cardiac output failure) in this subset of patients [50].

Unanswered questions regarding the decision of LVAD placement in patients with non-dialysis dependent renal insufficiency and dialysis dependent patients

Renal insufficiency is a comorbidity associated with early mortality in patients with end-stage heart failure on the waitlist for HT [51], and this include subjects with non-dialysis dependent renal insufficiency and dialysis dependent patients.

In patients with end-stage heart failure who are candidates for heart transplant, dialysis dependence is considered an indication for combined heart–kidney transplantation due to the improved five-year post-transplant survival in HKT recipients compared with isolated HT recipients for both dialysis dependent patients (73% vs. 51%, $p < 0.001$) and non-dialysis dependent patients (80% vs. 69%, $p < 0.001$) [52]. The guidelines are too strict for end-stage heart failure patients with renal failure who are not candidates for HT. Because non-dialysis dependent renal insufficiency and hemodialysis at the time of LVAD implant are strong predictor for adverse outcomes [10], the ISHLT recommends that the need for permanent RRT is a contraindication for LVAD implantation as a DT (class III, level of evidence C) [17] but it is not a contraindication for those who will receive LVAD as a bridge to HT.

An important question is whether patients with non-dialysis dependent renal insufficiency or those who are dialysis dependent would benefit from LVAD as DT? Although this is considered a class III indication for LVAD placement, there are few reports of patients with non-dialysis dependent renal insufficiency who required dialysis in the peri-implantation period and could be weaned off RRT [53] and other patients who received LVAD as DT and became dialysis dependent post-implant and then had uneventful chronic dialysis [54]. LVAD placement may be the only hope for this subset of patients who are not transplant candidates and need LVAD as DT.

Previous studies have demonstrated improvement in renal function following LVAD implantation [55], but again this is difficult to predict [56]. Data by Levin and colleagues showed a favorable outcome in dialysis dependent patients receiving an LVAD as a bridge to transplantation [57]. They studied the outcomes of 35 patients on hemodialysis and 68 not on hemodialysis who received long term LVADs and found no significant difference in 1-year survival (73.3% 84.6% in dialysis and non-dialysis dependent patients, respectively, P=0.183) [57]. These encouraging results should promote further studies to determine the value of LVAD as DT in patients with dialysis dependent end-stage heart failure or non-dialysis dependent renal insufficiency who are otherwise good candidates for DT.

Another unanswered question is whether a patient with non-dialysis dependent renal insufficiency, should receive HT (followed by a staged kidney transplant in those without renal recovery) as opposed to HKT. It is possible that some patients may experience improvement in renal function with HT alone. Also whether patients with LVAD who remain dialysis dependent after implant would benefit more from renal transplantation alone? Till now, LVAD patients have not been considered for non-cardiac transplantation because the risk of driveline infection in an immunocompromised patient is a major concern [53].

In conclusion, the yearly incremental increase in LVAD implantation caused a subsequent rise in the number of patients with LVAD who developed renal failure, some of which are dialysis dependent. The dialysis of these patients is challenging due to multiple factors including the reluctance of outpatient dialysis centers to accept these patient, unfamiliarity of nephrologists with LVADs, difficulty in hemodynamic monitoring during dialysis, risk of access site infection and bleeding since all patients are on anticoagulants. The best mode for dialysis

for these patients (continuous venovenous hemodialysis vs. intermittent hemodialysis vs. peritoneal dialysis) needs further studies. Cardiologists and nephrologists involved in the care of patients with LVAD should be familiar with the physiologic and technologic aspects of these devices as well as obstacles expected during dialysis to avoid adverse consequences to these high risk patients.

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