Chapter 11

Left Ventricular Assist Device Infections

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Abstract

Left ventricular assist device (LVAD) infections are important causes of morbidity and mortality in patients who receive these mechanical circulatory supports as a bridge to transplantation (BTT) or as destination therapy (DT) (for individuals who are not candidates for cardiac transplant). Infections are more common among persons who received pulsatile flow LVADs as opposed to newer continuous flow (CF) devices. Other risk factors for infection include obesity, renal failure, depression and immunosuppression. An LVAD infection increases the risk of infections in persons who undergo cardiac transplantation. Infections include percutaneous site, driveline, pump pocket and pump/cannula infections; sepsis, bacteremia, mediastinitis and endocarditis. Diagnosis is achieved by monitoring LVAD flow parameters and observing typical clinical and laboratory manifestations of infection. Imaging such as PET-CT or SPECT-CT imaging can be helpful to establish a diagnosis of pump pocket infection. Echocardiography may aid in detecting native valve endocarditis and thrombus associated with the LVAD. The most common pathogens include *Staphylococcus*, *Corynebacterium*, *Enterococcus*, *Pseudomonas* and *Candida* spp. Treatment requires targeted antimicrobials plus surgical debridement of infected tissue and device components. In cases of pump/cannula/LVAD endocarditis, especially if fungal pathogens or *Mycobacterium chimaera* are involved, LVAD removal/reimplantation vs. transplant is necessary, combined with extended antimicrobial therapy.

Keywords: left ventricular assist device, driveline infections, pocket infection, endocarditis

1. Introduction

Surgical management of heart failure has revolutionized the lives of patients with symptomatic end stage heart disease of all causes (reviewed in [1–3]). The first left ventricular assist device (LVAD) was implanted in 1963 by Liotta and Crawford ([4] and references therein),

followed by the implantation of the first artificial heart by Cooley in 1969, as a bridge to transplant. The famous Jarvik 7 artificial heart was implanted in 1984 by De Vries. It was not until 1994 that the FDA first approved the LVAD as a bridge to transplant, and only in 2010, was the HeartMate II LVAD, a continuous flow (CF) device, approved as destination therapy ([4, 5] and references therein). After January 2010, only continuous flow devices i.e. HeartMate II have been implanted. The HeartMate III, Heartware HVAD and the Jarvik 2000 LVADs are currently under study in clinical trials [6–8]. An increasing number of patients are receiving non-surgically deployed LVADs such as the Impella 5.0 (5 L/min flow) as they await a decision regarding cardiac transplantation versus destination therapy with a larger (10 L/min flow) standard device [9]. More and more patients who are not considered candidates for transplantation are receiving destination LVADs and have significant improvement in their NYHA functional class and quality of life despite the numerous potential complications that these patients often face [1, 10, 11]. As devices evolve, becoming ever smaller, more compact and potentially entirely contained within the patient, it is anticipated that many of the complications, particularly infectious complications, will diminish in frequency. However, with the current state-of-the-art, infectious complications including drive line infections, pocket infections, bacteremia and the most dreaded infectious complication, endocarditis and associated mycotic aneurysms, remain important causes of morbidity and mortality in LVAD recipients, both destination therapy (DT) and as a bridge-to-transplant (BTT). In this review, we will not consider complications of devices used in so-called "bridge to decision" therapy such as the Impella 5.0.

The continuous axial flow HeartMate II is now the most common LVAD in use in the US; between 2006 and 2016 a total of 17,008 CF LVADS have been implanted with 81% 1 year survival [12]. LVADs including HeartMate II and other devices have been reviewed in [1, 3, 4, 13–17]. Newer centrifugal flow devices, HeartMate III and HeartWare HVAD that are smaller and reportedly less prone to thrombosis and device failure are in clinical trials in the US [7, 8, 18] but have been utilized successfully in other parts of the world [19].

This review will focus on several aspects of LVAD infections including the rare complication of endocarditis, and will identify gaps in knowledge regarding diagnosis of LVAD infections, treatment and prevention of these infections. Differences in rates of infection in bridge vs. destination therapy will be discussed but the focus of review will be on destination therapy as that is where we see the most infectious complications. The epidemiology and microbiology of LVAD infections will also be addressed including risk factors and the impact of device related complications on post-transplant infectious complications. *Mycobacterium chimaera* LVAD infections will also be discussed.

2. Epidemiology and risk factors for LVAD infections

Several studies have looked at various aspects of LVAD candidates in terms of their risk of developing complications including infections. A significant reduction in infections has already been noted in a randomized trial comparing older pulsatile flow LVADs to current continuous flow (CF) LVADs [5]. The improvement in infection rates was felt to be due to the smaller size of the device and the driveline caliber [20]. An observational study of LVAD type

(pulsatile versus CF) spanning 2000–2009 in a single institution concluded that differences in infectious complications in that cohort were more related to when the device had been implanted, with more recent implantations showing fewer infections [21]. Subsequent innovations (axial to centrifugal flow) have not resulted in a reduction in infectious complications [7, 8] with an actual increase in sepsis with the Heartware HVAD device compared to HeartMate II control [7]. Studies have looked at factors including age [22], gender [23], body habitus including both small patients [24] and obesity [25], trauma [26], duration of LVAD support [27] as well as presence of comorbid conditions such as diabetes [28–30], depression and chronic kidney disease (CKD) [31], alcoholism and immunosuppression [29], and malnutrition ([32, 33] and references therein). In a Japanese multicenter trial looking at 300 patients receiving HeartMate II between April 2013 and December 2016, patients older than 60 had similar overall survival and risk of driveline and pocket infections [22]. An older study found that age and the presence of diabetes were associated with increased risk of LVAD endocarditis [34] with a median age of 59 among patients with endocarditis compared with a median age of 53 in those without ($p = 0.02$). Women receiving LVADs were often sicker (Interagency Registry of Mechanically Assisted Circulatory Support (INTERMACS) cohorts 1 or 2) and had significantly higher bleeding complications, arrhythmias and right heart failure, but not infectious complications [23]. Driveline infections were slightly more common in smaller (body surface area (BSA) < 1.5 m^2) patients (13 vs. 12 patients, $p = 0.003$) but mediastinal infections occurred in 2 patient with BSA > 1.5 m^2 with no cases among smaller patients [24]. Clerkin et al. examined data from a BTT cohort of 3856 patients between 2004 and 2014, and found that patients with a body mass index (BMI) >35 kg/m^2 had a trend towards increased infection risk (hazard ratio 1.59, 95% confidence interval 0.99–1.94, $p = 0.058$) [25]. Diabetes mellitus as a risk factor for infection was studied among 341 individuals who underwent LVAD implantation at Mayo Clinic between 2007 and 2016 [28]. Thirty-eight percent of the LVAD recipients had diabetes, and those patients also had significantly more ischemic cardiomyopathy as a cause for LVAD implantation, more were receiving LVADS as destination therapy and these patients also had higher BMI than those without diabetes. Looking at a composite endpoint of stroke, pump thrombosis and infections, patients with diabetes were 2.1 times more likely to have a poor outcome. There was a 1.73 fold increased risk of all cause mortality among diabetic patients as well. Interestingly, pre-operative hemoglobin A1C (HgbA1c) levels were not related to adverse outcomes, and LVAD recipients experienced lower HgbA1cC levels and lower diabetes medication requirements post-implantation. A large prospective multicenter trial of 86 HeartMate II recipients identified depression and CKD as independent risk factors for infection [31], with adjusted hazard ratios of 2.8 ($p = 0.007$) and 1.7 ($p = 0.023$) respectively. A multicenter trial in France looked at 159 patients who received LVADs between 2007 and 2012 and found that 22.6% of the patients had at least one infectious complication [29]. LVAD infections in this cohort were associated with alcoholism in 33%, diabetes in 11% and other immunosuppression in 11%. Of note, a small case series of 4 HIV patients implanted with LVADs did not show an increased risk in infection and one of the patients was successfully transplanted [35]. The implantation of an LVAD itself seems to result in reduced cell mediated immunity with decreased interleukin-2 (IL-2) and tumor necrosis factor (TNF) production, and increased IL-10 by T-lymphocytes. Greater numbers of suppressive regulatory T-lymphocytes (T_{regs})

are found in these patients for an average of 6 months post-implantation ([36], also reviewed in [33]). LVAD induced immune deficits appear to resolve in CF devices as compared to older pulsatile devices ([33] and references therein).

2.1. Impact on post-transplant infections

Additional studies have looked at outcomes in transplant patients who developed LVAD infections either as BTT or DT (where the infection was treated in part by removal of the DT device, with subsequent receipt of an organ) [20, 30, 34, 37, 38]. In US studies, pre-transplant LVAD infections appear to influence outcomes in cardiac transplant patients, with more infectious complications in those with prior LVAD infectious complications. Other risk factors in multivariate analysis included age, ICU length of stay and use of an anti-thymocyte agent [38]. A sub-study of the Swiss Transplant Cohort Study found that pre-transplant LVAD infections did not have an impact on post-transplant outcomes with slightly lower rates of infection and slightly higher survival rates among LVAD BTT patients [37]. Enterococcal infections including with VRE and Staphylococcal infections were most common among LVAD associated post transplant infections [30, 34]. The presence of infections with molds such as *Aspergillus* spp. are felt to be a strong relative contraindication for transplantation [6].

3. Microbiology of LVAD infections

The microbiology of LVAD infections has been extensively reviewed [20, 26, 27, 29–31, 33, 34, 37, 39–43]. In the main, LVAD infectious etiology is related to the particular clinical syndrome e.g. driveline infection vs. pocket infection vs. endocarditis. The International Society for Heart and Lung Transplantation classifies infections as "VAD related" or "VAD specific" to refer to bacteremia, endocarditis and mediastinitis versus driveline, pocket and pump/cannula infections [13]. INTERMACS lists non-device related infections, device related infections (internal pump infections; percutaneous site infections and pocket infections (listed together)) and sepsis [12].

3.1. Bacteremia and sepsis

Bacteremia and sepsis are seen most frequently in the peri-operative period and often these infectious disease syndromes are associated with non-VAD infections such as central line associated blood stream infections (CLABSIs), ventilator and hospital associated pneumonia, urinary tract infections, *Clostridium difficile* associate diarrhea and colitis. The microbiology of these peri-operative non-VAD infections has been reviewed in the references above and will not be covered again in this chapter.

LVAD related bacteremias can also occur with associated sepsis, and may be related to device infections (pump pocket, pump/cannula), infective endocarditis and mediastinitis. The organisms detected in bacteremic patients (e.g. Staphylococci, Enterobacteriaceae, *Pseudomonas aeruginosa*, Enterococci, *Candida* spp.) are indicative of at least some of the possible device related organisms causing infection [20, 31, 34, 37, 40, 43, 44].

3.2. Driveline infections

Driveline infections are most common, and skin flora from patient's skin are the predominant pathogens detected (reviewed in [40]). Often, trauma of the driveline tunnel, due to rough manipulation of the driveline, and lack of skin fixation that reduces tension on the driveline, leads to infections. The microbiology includes *Staphylococcus aureus*, both methicillin susceptible (MSSA) and resistant (MRSA), coagulase negative *Staphylococci* (CNS) (*S. epidermidis*), *Corynebacterium* spp. [21, 26, 27, 33, 34, 45, 46], viridans streptococci [31], *Enterococcus faecalis* [31, 34], *E. faecium* including vancomycin resistant strains "VRE" [30], Gram negative enteric bacilli such as Enterobacteriaceae (*Enterobacter cloacae* and *E. aerogenese* [31] *Escherichia coli*, *Klebsiella* spp. [34], *Proteus mirabilis* [31], *Serratia marcescens* [21]), *Pseudomonas aeruginosa* [20, 26, 31] and *Stenotrophomonas maltophilia* [31]. There have been rare instances of fungal driveline infections with *Candida* spp. such as *C. albicans, glabrata* [20, 31, 34]. There have been recent series of reports of infections with *Mycobacterium chimaera*, related to open chest surgery and cooling units employed for cooling cardioplegia solution [47]. In rare cases, patients developed endocarditis in the setting of recent valvular surgery. To date, one case of a complicated LVAD driveline infection with abdominal wall abscess by *M. chimaera* has been reported [48].

Biofilm formation by many different organisms contributes to persistence of infections due to the poor efficacy of antibiotics against organisms within biofilms, even when drug resistance is not present [33, 40, 43, 49].

3.3. Pocket infections

Pocket infections can occur at the time of implantation, during trauma to the driveline and pocket from driveline manipulation or bleeding into the pocket from coagulopathies [20]. The microbiology of pocket infections is thus very similar to driveline infections, with skin flora such as Staphylococci and Corynebacteria predominating, as well as *Enterobacteriaceae*, Enterococci, *Pseudomonas* and *Candida* spp. [20, 26, 31, 40]. We are in the process of reporting on a patient with a HeartMate II LVAD for DT who cracked his driveline and had extensive hematoma formation in the pump pocket with subsequent persistent infection and bacteremia with *Enterobacter cloacae (*Skalweit, in preparation). Computed tomography images of this patient are shown in **Figure 1**, with hematoma, phlegmon and small air bubbles evident in the pump pocket (a) before debridement. **Figure 1b** is after debridement. **Figure 2a–c** shows the pump pocket wounds after debridement, with placement of a vacuum wound device and after closure of the defect. One case of a pocket infection with *M. chimaera* has been reported in a patient who developed a fluid collection contiguous with the pump pocket [48]. The patient underwent extensive debridement and omental flap coverage of the device. Operative specimens were routinely cultured and he was empirically treated with broad spectrum antibiotics but did not respond to therapy. Subsequent mycobacterial cultures revealed the pathogen and he was maintained on lifelong *M. chimaera* therapy.

3.4. Mediastinitis

As a direct extension of pocket infections or as a result of sternal wound infections, LVAD associated mediastinitis is rarely observed [34, 43, 48]. *S. aureus* (MRSA), CNS, and vancomycin

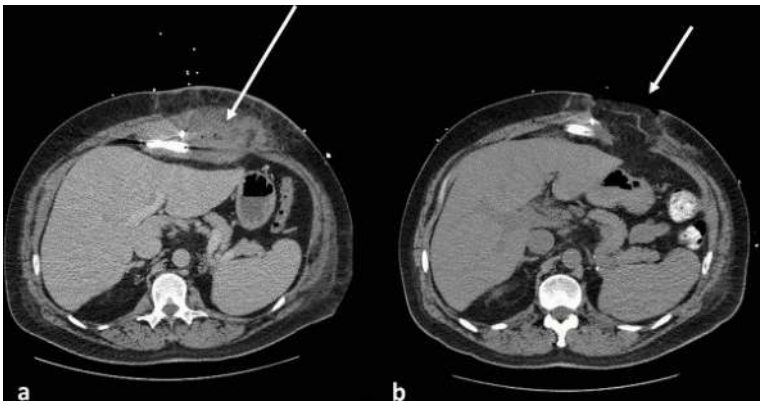

Figure 1. (a and b) Computed tomography (CT) images of pump pocket infection before (a) and after (b) surgical debridement. Solid arrows show the location of a complex hematoma, phlegmon and air bubbles. Operative cultures grew a susceptible *Enterobacter cloacae*.

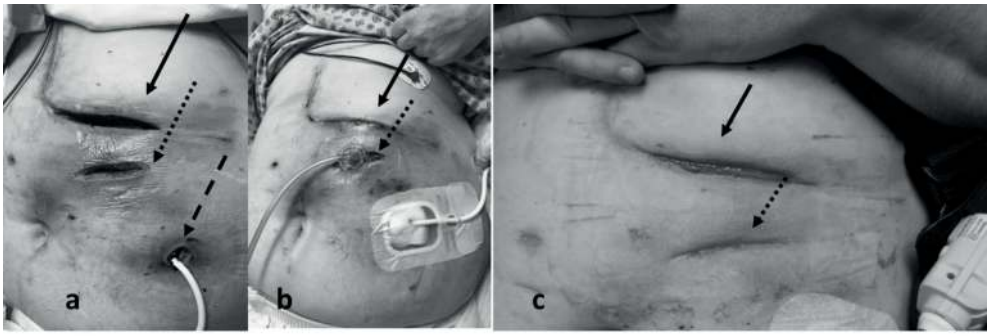

Figure 2. (a–c) Wound care in *Enterobacter cloacae* pump pocket infection, post debridement (a), with wound vacuum device placement (b) and after healing (c). Heavy and dotted arrows indicate the pump pocket wounds, dashed arrow is the driveline.

susceptible *E. faecalis* were the reported pathogens in five patients with LVAD mediastinitis [34]. A single case of fungal mediastinitis presenting with LVAD outflow obstruction caused by growth of *Syncephalastrum racemosum* has been reported [50]. The concern with mediastinal infection is always one of extension to involve the great vessels, the pericardium and bone, requiring potential additional source control and extended antibiotic therapy.

3.5. Infective endocarditis and pump/cannula infections

Endovascular infections can occur on native valves, prosthetic valves as well as in association with the LVAD pump body and cannula and are associated with high mortality [26]. Early case reports with older generation pulsatile flow devices described LVAD valve replacement on a Novacor N100 LVAD [51]; pathology revealed Gram positive cocci. A series of fungal LVAD

infections revealed that 3% met criteria for LVAD endocarditis (cultures of blood and explanted LVADs positive for fungal pathogens) [50]. *Candida albicans*, *C. parapsilosis* and *S. racemosum* were isolated in 3, 1 and 1 case respectively. More recently in the continuous flow era, LVAD associated endocarditis has been defined as "clinical evidence of pump and/or cannula infection along with the presence of vegetations on echocardiography or a vascular phenomenon as defined by modified Duke's criteria" ([26] and reviewed in [42]). *Staphylococcus aureus* (MRSA, MSSA) predominates, as well as CNS (MRSE, MSSE) and *Pseudomonas aeruginosa* (reviewed in [42]). Cases of linezolid resistant *Streptococcus sanguinis* [52] and *Listeria monocytogenes* [53] with associated leukocytoclastic vasculitis have also been reported.

3.6. Cerebrovascular microbleeds/stroke/mycotic aneurysm

Other complications related to LVAD infections can include hemorrhagic stroke and mycotic aneurysm. Patients with heart failure are already at risk of thrombosis, and increased infectious complications and coagulopathy associated with LVADs increases the risk of device thrombosis and stroke (reviewed in [54]). Aggarwal et al. [55] studied the relationship between bacteremia and stroke in LVAD patients in a retrospective chart review study. They studied 80 patients who had undergone LVAD placement in their institution, of whom 30 developed blood stream infections. Among those 30, 13 developed hemorrhagic strokes (43%) compared to 5/ 50 (10%) in LVAD recipients without bacteremia. In their report, the majority of BSI were caused by Staphylococci (CNS, MRSA). Yoshioka et al. found a similar association with hemorrhagic stroke in patients with either bacteremia or pump pocket infection [56, 57]. Organisms isolated among the nine patients in their study with hemorrhagic stroke included methicillin susceptible *S. epidermidis* (MSSE), MSSA, *Corynebacterium* spp., MRSA, CNS, *E. faecalis*, *Bacillus* sp. and *Campylobacter* sp. A rare complication in an LVAD recipient is mycotic aneurysm related to prior recurrent *Klebsiella rhinoscleromatis* bacteremia and subarachnoid hemorrhage [58].

3.7. Drug resistance

Prior treatment with antibiotics and extended therapy with narrow spectrum antibiotics did not appear to increase risk for LVAD infections with multidrug resistant organisms (MDRO) [59]; MDRO infections were related to indication (DTT > BT), obesity and driveline technique ("velour exposed" versus buried). However, a recent case series reported that high level daptomycin resistance in *Corynebacterium striatum* LVAD infections was selected for by using daptomycin as treatment [60].

4. Diagnosis of LVAD infections

LVAD infections can manifest in many ways from indolent infections in patients that are minimally symptomatic to septic patients requiring intensive care. Most sources [13, 27, 39, 40, 43, 61, 62] agree on general investigations that should occur in order to diagnose an LVAD related or device specific infection. If LVAD infection is suspected, driveline and three sets

of blood bacterial cultures before antibiotics are administered should be obtained, in addition to routine laboratories: complete blood count (CBC); complete chemistries including LDH; coagulation studies (fibrinogen, platelets, D-Dimer, Factor VIII, INR, PTT); erythrocyte sedimentation rate, C-reactive protein). Procalcitonin is elevated in the initial postoperative period and does not appear to be a useful marker of infectious complications [63]. Imaging of the driveline and pump pocket using ultrasound has been suggested by some groups to assess for fluid in the pump pocket or tracking along the driveline. Computed tomography (CT) scanning is of limited utility due to the reflective properties of the pump body. However positron emission tomography (PET-CT) [64]; or gallium single photon emission computed tomography (SPECT-CT) [64–66], reviewed in [40]) have been used to diagnose infection of LVAD components as well as to assess for metastatic sites of infection often found with prolonged bacteremia with pathogens such as *S. aureus* and *P. aeruginosa* (reviewed in [40, 67, 68]). Erba et al. [69] showed that ^{99m}Tc-hexamethypropylene amine oxime labeled autologous white blood cell (^{99m}Tc-HMPAO-WBC) SPECT-CT had 94% sensitivity at detecting cardiac implantable electronic device infections, with 95% negative predictive value in patients with other sources of infection. Inflammation from driveline trauma may result in a positive PET-CT image, even in the absence of infection. Transesophageal echocardiography is utilized in the setting of positive blood cultures to look for vegetations on native valves or on device components [26, 44, 62]. However, it has been previously acknowledged that echocardiography may be of limited use in evaluating for vegetations, due to reflections off of the device's reflective metal surfaces [50]. The role of echocardiography [70] and the application of newer techniques such as real time three dimensional (3D) echo has been reviewed [71] and discusses utility in evaluating native valves and presence of thrombus.

LVAD parameters such as flow rates may also be an indication of infectious complications [61]. Elevations of B-type natriuretic peptide (BNP) were also found to be a marker of serious adverse events in LVAD patients, including severe infections such as sepsis, mediastinitis and pump pocket infections [72]. Thrombosis, alteration in coagulation parameters, stroke, acute renal failure may also be early indicators of infection as well as more routine signs such as fever, leukocytosis and localizing signs and symptoms.

Additional microbiologic techniques such as fluorescent *in situ* hybridization (FISH) and polymerase chain reaction (PCR) have been used to identify additional pathogens in biofilm obtained from explanted LVADs and may provide supplemental information on which to base antimicrobial selection [73].

5. Outcomes in LVAD infections

Clinical outcomes for LVAD implantation have been extensively reviewed (see for example [10, 61, 74, 75]) including for infection. It is estimated that 15% of LVAD recipients die due to infectious complications, with the majority of deaths occurring within the first 30 days of receipt [76]. More than half of the data available for review is for patients receiving CF devices for BTT indications. Overall rates of infection for CF devices in trials and registries with more

than 100 patients were follows: local site infections 20–49%; driveline infections 12–22%; pocket infections 2–5%; sepsis 3–36%; other types of infections 26–35% [10]. It is estimated from the INTERMACS registry data [12] that there are 8 infectious complications per 100 patient-months in CF LVAD recipients. The European Registry for Patients with Mechanical Circulatory Support (EUROMACS), a European registry of LVAD recipients includes data from 52 hospitals from 2681 patients with 2947 implants since 2014 [77]. Overall serious infection rates were 6.18 per 100 patient months within the first 3 months of implantation. Three year survival was only 44% in patients with CF devices, and 20% of the deaths were attributable to infections. In a retrospective study of 88 CF LVAD implantations (22% DT) between 2006 and 2014 at the Toronto General Hospital, 129 readmissions occurred, of which 17% were related to infections [78]. Despite this readmission rate (63% with at least one readmission), outcomes were excellent with only 6 deaths. Other analysis of the INTERMACS registry revealed that 19% of LVAD recipients developed a percutaneous site infection within 12 months of receiving a CF LVAD [79]. Ten percent of patients with these infections died, with sepsis being the most common cause of death (26%) [79]. In general, DT is associated with greater infection risk, and recurrence of infection, especially driveline infections. The majority of these infections are driveline infections and outcomes are generally good (reviewed in [80, 81]). Fortunately with infection control techniques, rates of driveline infections appear to be decreasing [82]. Pocket infections are less common but can confer greater risks of morbidity including hemorrhagic stroke [56, 57]. In a large prospective study of infections after cardiac operations, Perrault et al. found that LVAD and transplant patients experienced 5.8 times higher rates of mediastinal infections (95% CI 2.36–14.33) with five times higher readmission and mortality rates [83]. Nearly all cases of LVAD endocarditis will require explanation and replacement of the device as well as prolonged antimicrobial therapy, and the risks associated with these [42]. Outcomes are improving overall however. Among 156 patients who survived more than 4 years in one center, the mean survival was 7 years with ~1 readmission per year [84]. In terms of overall quality of life, 92% of these patients were NYHA Class I or II. The most common reason for readmission was infection (10%).

6. Treatment and prevention of LVAD infections

Management of LVAD infections is related to the specific LVAD infectious clinical syndrome [13, 26, 27, 30, 31, 42, 43]. Typically, combined medical-surgical treatment is needed, with infectious disease consultation to determine the best selection of empiric and microbiologically driven antimicrobials. Site infections and driveline infections are typically managed with local wound care and a combination of intravenous then oral antibiotics if possible as dictated by the organism isolated from the infected site. Percutaneous site infections have even been treated with topical agents such as crystal violet [85]. Sometimes the tunnel must be excised, and a new tunnel created with the application of a vacuum wound device to close the defect. Certain infections have been prevented by reducing exposed driveline material (velour) by keeping it entirely in the subcutaneous tunnel [82]. Preventing trauma to the driveline by use of anchoring devices [86], and use of sterile technique when changing the driveline dressing are key in preventing driveline infections. Standardized strategies for driveline dressings, and

in overall LVAD infection control within hospitals are also helpful in preventing infections [86–88]. Pocket infections must typically be managed with surgical debridement in the operating room with techniques such as omental wrapping of the pump housing to cover exposed metal and to close surgical defects [89, 90]. In rare instances, extrapolating from the orthopedic surgery literature, antibiotic impregnated beads have been placed in the pocket (reviewed in [91, 92]) although this has not been studied in a rigorous manner. Arguably, tissue levels of parenteral antibiotics are sufficient to treat residual infection once source control has been achieved. Placement of an additional foreign body in the pocket may not be advised, especially since the antibiotic concentrations from the beads will eventually wane, requiring subsequent bead exchange or removal. Repeated exposure to sub-inhibitory concentrations of antibiotic can lead to selection of antibiotic resistant organisms. Indolent pathogens such as *M. chimaera* or in the case of fungal infections may necessitate exchange of the pump and other components that are involved. LVAD endocarditis requires explanation and extended antimicrobial therapy, potentially with lifelong suppression if re-implanted or if cardiac transplantation occurs [42, 48, 50].

Optimal peri-implant antibiotic prophylaxis has not been established in a rigorous trial. However, "best evidence" was provided in a review by Acharya et al. [93] and consists of antibiotic coverage for Staphylococci, Enterococci, *Pseudomonas* and *Candida* spp. They concluded that use of an extended spectrum beta-lactam plus vancomycin in areas where rates of methicillin resistant *S. aureus* are high, a fluoroquinolone, fluconazole and mupirocin ointment (nasal application) in the "peri/post-operative" period (~3 days) was recommended. Prophylactic antibiotics are not recommended to prevent driveline infection after the immediate post-operative period [94].

7. Future directions

The development of biventricular or LVAD devices with transcutaneous energy sources ("TETs") will eliminate driveline infections [95]. However, this remains the "holy grail" for developers of mechanical circulatory support devices [96, 97]. Magnetically levitated pumps help reduce the rates of reoperation (and attendant complications like infection) [7]. Changes in size and materials involved in these devices can also reduce risk of thrombosis and enable easier explanation and reimplantation should complications arise [98]. Minimally invasive procedures such as off-pump implantation and alternative implant sites may also lead to reduced infection risk [99].

8. Conclusions

Left ventricular assist device (LVAD) infections are important causes of morbidity and mortality in patients who receive these mechanical circulatory supports as a bridge to transplantation (BTT) or as destination therapy (DT) (for individuals who are not candidates for cardiac transplant). Infections are more common among persons who received pulsatile flow LVADs as opposed to newer continuous flow (CF) devices. Other risk factors for infection include obesity, renal failure, depression and immunosuppression although HIV positive LVAD recipients have not had increased rates of infection in the limited number of recipients to

date. An LVAD infection increases the risk of infections in persons who undergo cardiac transplantation. Infections include percutaneous site, driveline, pump pocket and pump/cannula infections; sepsis, bacteremia, mediastinitis and endocarditis. Diagnosis is achieved by monitoring LVAD flow parameters and observing typical clinical and laboratory manifestations of infection (fever, local induration, erythema, abdominal pain, high flow LAVD parameters, leukocytosis, elevated inflammatory markers such as ESR, CRP; markers of coagulopathy). Elevated BNP may herald severe infection such as sepsis and pump pocket infection. PCR and FISH microbiologic techniques increase diagnostic yield of specific pathogens in biofilm on drivelines and other device components. Imaging such as PET-CT or SPECT-CT imaging can be helpful to establish a diagnosis of pump pocket infection. Echocardiography may aid in detecting native valve endocarditis and thrombus associated with the LVAD. The most common pathogens include *Staphylococcus*, *Corynebacterium*, *Enterococcus*, *Pseudomonas* and *Candida* spp. Treatment requires targeted antimicrobials plus surgical debridement of infected tissue and device components. In cases of pump/cannula/LVAD endocarditis, especially if fungal pathogens or *Mycobacterium chimaera* are involved, LVAD removal/re-implantation vs. transplant is necessary, combined with extended antimicrobial therapy. The "holy grail" of future mechanical circulatory support is a fully implantable device that relies on transcutaneous energy supplies. Devices of the future would be less prone to infectious complications potentially but would not entirely eliminate infectious complications. Smaller devices with magnetically levitated pumps, minimally invasive techniques and uniform infection control practices are the state-of the art in preventing infectious complications of LVADs today.

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Conflict of interest

Dr. Skalweit is an employee of the Department of Veterans Affairs. The opinions expressed here are her own and not those of her employer. Dr. Skalweit has no conflicts to declare.

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