

# Does left ventricular assist device increases risks for infections?

## Abstract

Left Ventricular Assist Device (LVAD) is used for the treatment of stage D heart failure as an alternative to heart transplantation. In recent years, LVAD use as destination therapy has significantly increased. One-year survival post-LVAD implantation is now comparable to heart transplantation. Recent data shows significant reductions in stroke and gastrointestinal bleeding in LVAD recipients, but infections remain a major concern. LVAD-mediated immune dysfunction has been reported in previous studies. Increasing LVAD utilization as destination therapy has shown improved long-term survival but the risk of infections with prolonged duration of LVAD support remained underexplored. In this article, we provide an overview of the infection risks associated with prolonged duration of LVAD support.

**Keywords:** LVAD infection; Risk of infections post LVAD implantation; VAD infection; VAD specific infections; VAD related infections

## About the study

Heart failure is a leading cause of health and economic burden globally. In the United States of America, more than 6 million Americans are living with heart failure [1]. This number increased from the 5.7 million people reported in the American Heart Association (AHA) 2016 report. AHA worrying projections indicate up to 8 million people will have heart failure in the United States of America by the year 2030 [2]. In Europe, 17.2 patients per 1000 population are living with heart failure [3]. Globally, an estimated 26 million people are living with heart failure, but these numbers are considered underestimated due to poor reporting of data from low and middle-income countries [4]. Despite advancements in treatment options heart failure mortality remains high, and up to 50% of patients will die within 5 years of diagnosis. Heart transplantation is the definitive therapy for stage D heart failure but due to organ shortage, most patients die waiting for an organ transplant. Mechanical Circulatory Support (MCS) is an alternative treatment for patients with stage D heart failure. The most common type of MCS used is the Left Ventricular Assist Device (LVAD). Post-LVAD survival with newer Continuous Flow (CF) LVAD implantation is now comparable to heart transplantation, reported >80% one-year and >50% five-year survival [5]. LVAD can be used as a bridge to transplantation (BT), destination therapy (DT), or a bridge to decision. Interagency Registry for Mechanical Assisted Circulatory Support (INTERMACS) was established in 2005 to monitor outcomes after an FDA-approved mechanical circulatory device implantation [6]. The Overarching goal of INTERMACS is to improve the life expectancy and quality of life of patients with advanced heart failure on MCS. Over the last decade, LVAD device types and indications have drastically changed. The most recent INTERMACS 2022 report showed 81.1% of LVAD implanted as destination therapy and 92.7% of LVAD were fully magnetically levitated [7]. INTERMACS 2022 reported a significant reduction

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## Short Communication

in stroke and gastrointestinal bleeding in LVAD recipients, but infections remain a major concern [7].

The International Society of Heart and Lung Transplant (ISHLT) defined LVAD infections in the following three categories as shown in the Table 1 [8]:

Table 1: LVAD Infections types as per ISHLT definition.	
<b>VAD-Specific Infections</b>	• Pump infections
	• Cannula infections
	• Device pocket infections
	• Driveline infections
<b>VAD-Related Infections</b>	• Bacteremia,
	• Central venous catheter associated bloodstream Infections
	• Infective endocarditis
	• Mediastinitis
<b>Non-VAD Infections</b>	• UTI
	• Pneumonia
	• Skin and soft tissues infections
	• Clostridium difficile infections
	• Others

- Ventricular Assist Device (VAD) specific infections:** Infections specific to VAD and do not occur in non-VAD patients e.g., pump, cannula, pocket, or driveline infections.
- VAD-related infections:** Infections not specific to the VAD device but need special attention due to the presence of a VAD e.g., mediastinitis, bloodstream infections, and infective endocarditis.
- Non-VAD infections:** Infections not affected by or not related to VAD, e.g., UTI, pneumonia.

The interaction between LVAD biomaterial and the immune system may lead to long-term immune dysfunction. Previous reports have suggested increased susceptibility to infections post LVAD implantation due to impairment in cellular immunity [9]. T-cells from LVAD recipients showed higher levels of activation and proliferation in comparison to T-cells from matched stage D heart failure patients without LVAD. Increased T-cell activation and proliferation in LVAD recipients lead to T-cell apoptosis and cell death [10]. Decreased T-cell mediated cytokine response was noted in LVAD recipients compared to heart failure controls without LVAD [10]. In LVAD recipients, IL-6 levels declined to below pre-implant levels six weeks post-LVAD implantation [11]. Leukocyte counts declined significantly below pre-operative levels two months post-LVAD implant [12]. Several studies have reported LVAD-mediated immune dysfunction [9-13]. Despite laboratory evidence suggesting LVAD-mediated immune dysfunction, there is a paucity of data showing increased infections in LVAD recipients compared to matched patients with stage D heart

failure. Increasing LVAD utilization as DT shows impressive long-term survival but the risk of infections with prolonged duration of LVAD support is not well explored. Candida infections 3 months post LVAD implantation were noted in 28% of LVAD recipients compared to 3% of patients with stage D heart failure without LVAD ( $p=0.0029$ ) [10]. Cytomegalovirus (CMV) reactivation post-LVAD implantation was suggested due to the selective loss of Th1 cytokine producing CD4 lymphocytes [14]. Several other studies reported CMV reactivation in LVAD recipients [14-18]. However, CMV reactivation in LVAD recipients may only be a surrogate for critical illness in this patient population as CMV reactivation is common among critically ill patients [19,20]. CMV reactivation rate post-LVAD implantation was noted at 3.8% in LVAD recipients compared to 16-35% reported in critically ill non-immunocompromised patients [15]. The incidence of infections decreased from 3.2 infections/1000 days of LVAD support during the first year post-LVAD implantation to 0.78 infections/1000 days of LVAD support during the third year of post-LVAD implantation [21,22]. Indicating risk of infections significantly decreased with prolonged duration of LVAD support. Recent data indicating decrease in infections with prolonged duration of LVAD support may be explained due to improvement in LVAD patient care, better infection control practices, and improvement of heart failure with MCS leading to enhanced immune function. Despite improvements in MCS outcomes, the accessibility and affordability of MCS face constraints due to substantial hurdles in the execution of MCS initiatives as shown in the Table 2.

<b>Patient selection</b>	• Severity of heart failure
	• Comorbidities
	• Overall benefit to the patient
<b>Timing of implantation</b>	• Waiting too long may cause irreversible organ failure
	• Too early intervention may expose patients to unnecessary risks
<b>Ethical consideration</b>	• Requires significant resource allocations
<b>Device selection</b>	• Type of device selection, LVAD versus Total Artificial Heart
	• Type of heart failure, anatomy, age, and anticipated duration of support
<b>Surgical expertise</b>	• Requires high level of surgical skills and experience
<b>Post-operative management</b>	• Requires post implantation specialized care
	• Regular monitoring, anticoagulation, and device troubleshooting are essential for optimal outcomes

<b>Infections and complications</b>	• Infections
	• Bleeding
	• LVAD Thrombosis
<b>Costs</b>	• Challenging for patients and healthcare systems to afford the associated costs with MCS
<b>Bridge to transplantation</b>	• Coordinating timing of transplantation
	• Organ availability
<b>Patient and caregiver education</b>	• Patient and caregiver thorough education regarding MCS device
	• Lifestyle adjustments
	• Potential complications
	• Emergency protocols
<b>Devie durability</b>	• Requires device maintenance
	• Device failure can be life threatening
<b>Patient quality of life</b>	• Patients face physical and emotional stress post implantation.
<b>Long term outcomes</b>	• Long-term outcomes undetermined
<b>Reimbursement and regulations</b>	• Regulatory approval and reimbursement vary by region and country affecting access and affordability
<b>Research</b>	• Continued research and innovation are necessary to develop more advance technology

**Conclusion**

Over the past decade, LVAD device types and indications have drastically changed. LVAD is now increasingly used as destination therapy with improved long-term survival. Despite laboratory evidence suggesting LVAD-mediated immune dysfunction, there is a paucity of data showing increased infections in LVAD recipients compared to matched patients with stage D heart failure. Further studies are needed to study the effect of LVAD-mediated immune dysfunction on the risk of infections.

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