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Review

Durable Mechanical Circulatory Support for Refractory Heart Failure

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Abstract

Advanced heart failure is a complex clinical condition that markedly impairs patient survival and the quality of life. Indeed, the prognosis of patients with stage C/D heart failure who do not respond well to medical therapy is very poor. Durable mechanical circulatory support was developed to extend the life of patients with advanced heart failure who are deteriorating despite guideline-directed medical therapy. Moreover, alongside heart transplantation, durable left ventricular assist device therapy is presently the mainstay of advanced heart failure treatment. Several recent studies have proven that durable mechanical circulatory support can extend the life expectancy of patients with advanced heart failure and dramatically improve their quality of life. Thus, this review aimed to provide an overview of indications and types of durable mechanical circulatory support devices available for clinical use. Second, this review consolidates current knowledge regarding survival rates, adverse events, and quality of life for patients after left ventricular assist device implantation. The paper aimed to provide a comprehensive overview of outcomes associated with left ventricular assist device therapy, underscoring the benefits and challenges patients face. Finally, we will briefly examine the future of durable mechanical circulatory support and devices that might enter clinical practice after feasibility trials.

Keywords

heart failure; mechanical circulatory support; ventricular assist device

Introduction

Heart failure (HF) is a common but complex life-threatening clinical syndrome primarily affecting the cardiovascular system; however, HF also promotes consequences for all organs and organ systems in the body. HF is generally caused by any structural or functional inability of the heart to fill with or eject blood. The mortality rate of HF varies with the severity of the disease. The functional status of patients with HF is often described using the New York Heart Association (NYHA) classification, with the disability severity ranging from I to IV. Several stages have been noted, from A to D, in the evolution of HF, as outlined by the joint guidelines of the American College of Cardiology and the American Heart Association [1]. This staged system, in contrast to the NYHA classification, emphasizes the progressive nature of HF and defines the appropriate therapeutic approach for each stage. The 5-year survival of patients with stage D HF is less than 20% [2].

An estimated 64.3 million people suffered from HF worldwide in 2017; thus, HF has been defined as a global pandemic [3]. The prevalence of HF is influenced by various factors, including lifestyle, pre-existing health conditions, and, in particular, age [4]. As the aging global population continues to increase, the burden of HF is expected to rise substantially, making it a predominant health concern in the older adult population [5]. The epidemiology of HF underscores its significant impact on public health. Some patients with stage C/D HF do not respond well to optimal medical therapy or certain forms of device-based treatments, and these patients have a very poor prognosis. Heart transplantation (HT) remains the gold standard for patients suffering from advanced HF with a 1-year survival of about 90% and a median survival of almost 13 years [6]. Unfortunately, only a minority of patients will be offered this therapy due to the chronic shortage of potential donors. The number of HT has plateaued worldwide until the recent introduction of donation after circulatory death [7]. In 2023, an estimated 10,115 heart transplants were performed worldwide based on the data from the Global Observatory on Donation and Transplantation [8].

Patients who are not HT candidates might benefit from durable mechanical circulatory support (MCS) with a left ventricular assist device (LVAD) or total artificial heart (TAH). Severely diminished life expectancy and quality of life associated with advanced HF patients can be improved using durable LVADs. Further, a large discrepancy exists between the number of patients suffering from advanced HF needing durable MCS and those receiving this treatment. Among the 6.7 million Americans over the age of 20 living with HF, about 5% may progress to the advanced stage D form of the disease annually [9,10]. It was estimated

that at least 300,000 patients are suffering from advanced stage D HF in the US [9]. While novel organ preservation techniques and donations after circulatory death have recently increased HT volumes, primary LVAD implantations have decreased [10]. In 2022, 6185 US patients received a primary LVAD or a cardiac allograft [11,12], meaning many eligible patients were deprived of a lifesaving therapy. Therefore, practitioners in the HF community need to raise awareness of possible MCS treatment options for patients suffering from advanced HF who are not responding well to guideline-directed medical therapy.

The Society of Thoracic Surgeons (STS) Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) is a registry of patients receiving MCS for advanced HF in certified centers in the US and Canada. The main objective of the INTERMACS registry is to facilitate patient selection for MCS to improve outcomes with current and future devices. Seven widely used INTERMACS patient profiles were devised to describe the disease severity in patients receiving MCS for advanced HF [13]. These profiles facilitate the collection of outcome data, empowering patients and caregivers to make informed decisions about potential device therapies. Ambulatory patients with advanced HF, significant symptoms, and recent hospitalizations are at high risk of death or requiring MCS. INTERMACS profiles help identify these patients who may benefit from MCS devices [14].

This review aimed to assess the current state of durable MCS, evaluate the most recent survival and complication data, and explore emerging technologies that may improve outcomes in patients with advanced heart failure.

Indications

Heart transplantation is a lifesaving procedure for patients suffering from end-stage HF. However, patients face significant waiting times before a suitable donor heart becomes available. Therefore, strategies to manage patients during this waiting period are crucial, given the acute shortage of donor organs. Indeed, durable MCS with LVAD should be considered the primary treatment option for patients with stage D HF, in addition to HT. International guidelines recommend LVAD therapy for patients with reduced left ventricular ejection fraction (LVEF) and functional NYHA class IV symptoms, even when optimal medical and device treatments have been implemented, and these patients are considered dependent on inotropes or temporary MCS [15,16]. Durable LVAD is also recommended for those advanced HF patients not requiring inotropes or temporary MCS. Moreover, durable LVAD support is recommended to reduce the risk of death and improve symptoms in cases when HT is contraindicated and in the absence of other surgical options. Guidelines for the diagnosis and treatment of acute and chronic heart failure outline that the lack of severe right ventricular dysfunction is crucial for the success of durable LVAD support [16]

Bridge to Transplantation

Mechanical circulatory support with a durable LVAD was designed to extend the survival of advanced HF patients [15,16]. Several modes of indication exist for durable MCS. Indeed, in patients eligible for HT, durable LVAD can be used under the indication of bridge to transplantation (BTT). Some patients eligible for HT might benefit from durable support while on the waiting list: waiting times vary greatly between countries, and patients often spend months on the waiting list. In those patients, durable MCS is intended to reduce mortality risk and preserve organ function while on the waiting list. The 2021 European Society of Cardiology Guidelines for the diagnosis and treatment of acute and chronic heart failure recommend long-term MCS (class of recommendation: IIa; level of evidence: B) in patients with advanced HF and reduced ejection fraction refractory to optimal medical and device therapy as a bridge to HT to improve symptoms and reduce the risk of HF hospitalization and the risk of death [16].

In October 2018, the Organ Procurement and Transplant Network lowered the urgency of waiting lists for stable patients on durable LVAD [17], ultimately reducing how often durable MCS is used for BTT indication in the US [18]. Based on the STS INTERMACS 2022 Annual Report data, the BTT indication for durable LVAD support has reduced to about 5% of all patients receiving MCS, while the destination therapy (DT) indication rose to 81% [18]. Patients with cardiogenic shock or temporary MCS were prioritized over durable MCS patients because these patients exhibited lower death rates while waiting for HT.

Generally, durable support with a continuous flow LVAD for patients on the HT waiting list is offered when risks outweigh the benefits of medical therapy. Patients receiving durable LVAD support must be compliant, and the treatment goal must match the wishes of each patient. Moreover, it is paramount that the patients being considered for LVAD therapy can maintain the device in an outpatient setting. In addition to the compliance and capabilities of the patient to maintain the device in an outpatient setting, several other factors influence the decision to place a durable LVAD. The severity of HF, perioperative risks, and the likelihood of major complications are all important factors to consider in the decision-making process. Additionally, the expected benefits of using an LVAD to improve survival and quality of life compared to alternative therapies are also considered.

Bridge to Transplant Candidacy

Bridge to transplant candidacy is indicated in patients with a potentially reversible ineligibility for HT. The typical clinical scenario in which this strategy has proven very use-

ful is when the patient has a prohibitively high pulmonary vascular resistance, which will decrease with durable LVAD support. Other contraindications for HT may resolve with additional medical management or improve with better perfusion provided by a durable MCS device. Similarly, the decision to undergo durable MCS device implantation is determined by the risks and benefits of device placement compared to guideline-directed medical therapy. However, in setting a bridge to decision (BTD) strategy, the likelihood that contraindications to transplantation will resolve should also be considered. Some of the conditions that could typically be resolved using the BTD strategy are pulmonary hypertension, diabetes control, obesity, substance dependency, and renal dysfunction.

Traditionally, irreversible liver or renal dysfunctions have been considered contraindications for HTs among advanced HF patients. More recently, combined heart–liver or heart–kidney transplantations have been considered in these patients. The convergence of heart and kidney failure significantly affects patient morbidity and mortality, necessitating innovative treatment strategies. In patients with advanced cardiac disease and concurrent renal dysfunction, traditional management often proves inadequate. Thus, simultaneous heart and kidney transplantation has emerged as a promising approach to address both organ failures together, potentially improving patient outcomes and quality of life. Research shows that simultaneous heart and kidney transplantation offers superior survival rates at five years post-transplant compared to isolated heart transplants for HF patients with renal dysfunction [19]. Hence, simultaneous heart and kidney transplantation represents a significant advancement for treating patients with both cardiac and renal failure.

LVAD therapy is a well-established treatment modality for advanced HF; however, whether outcomes are different based on the intended goal of therapy remains unclear, although it stands to reason that outcomes should favor HT eligible versus HT-ineligible patients. About 29% of patients are listed for HT after two years of the BTD strategy [20]. In the same study, patients were classified into three groups depending on the likelihood of being listed for HT with the BTD strategy. It was shown that in the likely, moderately likely, and unlikely groups, roughly 50%, 15%, and 10%, respectively, were transplanted after 24 months of follow-up. Based on data from the Multicenter Study of MagLev Technology in Patients Undergoing MCS Therapy With HeartMate 3 (MOMENTUM 3) trial, which involved 1020 patients randomly assigned to either the HeartMate 2 LVAD or HeartMate 3, LVAD patients who underwent implantation of the HeartMate 3 device and whose primary objective was the BTT or BTD strategy had a two-year mortality rate of approximately 15% and a two-year transplant rate of 40% [21].

Bridge to Recovery

Mechanical circulatory support with durable LVAD may induce left ventricular (LV) reverse remodeling, leading to myocardial recovery. This effect is associated with LVAD responders and the possibility of weaning from durable support in select patients. The survival of patients successfully weaned from durable LVAD support was reported to be similar to that of the International Society for Heart and Lung Transplantation (ISHLT), which was followed by HT [22]. Several studies have been conducted on myocardial recovery, and the data from single-center [23], multicenter studies [24], and reports from registries are encouraging [25,26]. The only prospective, multicenter, although nonrandomized study, the Remission from Stage D Heart Failure (RESTAGE-HF) study, explored the effect of durable MCS with LVAD alongside standardized pharmacological therapy on weaning rates from LVAD [24]. The primary endpoint was achieved in 40% of patients, and this was defined as the proportion of patients with sufficient improvement of myocardial function to reach criteria for explantation within 18 months of standardized therapy with sustained remission from HF at 12 months after explantation. However, these were preselected patients suffering from nonischemic cardiomyopathy at a younger age—the mean age of the population was 35 ± 11 years. Patients suffering from acute myocarditis and post-partum cardiomyopathy are known to have a greater chance of myocardial recovery [27].

Physiological effects of LVAD therapy involve continuous pressure and volume unloading of the left ventricle, which is responsible for LV reverse remodeling. This, in turn, leads to improved cardiac structure and function. Guideline-directed medical therapy and durable LVAD therapy further enhance cardiac outcomes [28]. Patients who experience improved cardiac function while receiving support exhibit improved clinical outcomes [29].

Left ventricular reverse remodeling and myocardial recovery associated with durable MCS with LVAD spans from positive effects (responders) to no effect (non-responders) [30]. Left ventricular markers of recovery following durable MCS with LVAD are defined by certain degrees of LVEF improvement and LV dimension reduction. Based on published data, responders, defined by an LVEF $>40\%$ with normal left ventricle dimensions, are reported in about 10% of durable LVAD patients. Partial responders, an LVEF $<40\%$ with normal left ventricle dimensions, are reported in about 30% of cases, and non-responders in about 60%, without a significant improvement in systolic function [30].

The incidence of myocardial recovery following durable MCS varies, as do the rates of relapse into HF after device removal. The largest published repositories of durable MCS implants report a low recovery rate of approximately 1% [26,31]. Meanwhile, identifying pa-

tients who experience myocardial recovery involves assessing clinical, hemodynamic, and echocardiographic parameters. Centers that have implemented protocols for systematically evaluating myocardial function after LVAD implantation have observed higher rates of myocardial improvement than the general LVAD patient population. Several recovery assessment protocols have currently been developed. The Harefield and Berlin groups are two European centers with the most experience in LVAD explantation for recovery [32,33]. These protocols employ various combinations of functional capacity measurement, imaging studies, and biomarkers to determine the candidacy for LVAD explantation or decommissioning. Patients undergo serial assessments, with recovery defined by echocardiographic, hemodynamic, and physiological markers of cardiac performance at normal and minimal pump speeds for up to 15 minutes. Longer periods of minimal pump speed are not recommended due to blood stasis and potential thrombus formation. A heparin bolus is administered before low pump speed testing while patients are in the target international normalized ratio (INR) range. Recovery assessments are halted if the patient develops symptoms during low pump speed studies.

LVAD recovery remains an under-evaluated and under-promoted strategy for durable MCS therapy. Known predictors of myocardial improvement with durable LVAD support are younger patients with a shorter period of HF and nonischemic etiology [34]. The incidence of myocardial recovery among these preselected patients might be as high as 50% [22]. Therefore, a bridge to recovery strategy, which is underutilized in the realm of advanced HF durable device therapies, should be considered in all young, advanced HF LVAD candidates with an underlying nonischemic cardiomyopathy.

Destination Therapy

Select patients with advanced HF who are not transplant candidates and unlikely to become candidates for transplantation could potentially become candidates for durable MCS as a DT. Indeed, DT, specifically durable LVAD implantation, is offered to patients whose benefits outweigh the procedural risks.

The Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial, conducted in 2001, demonstrated that using a left ventricular assist device in end-stage HF patients who were ineligible for HT resulted in clinically meaningful survival benefits and improved quality of life compared to medical therapy [35]. Subsequently, several prospective trials have explored the outcomes of durable LVADs.

A large registry showed that patients implanted with LVAD for DT had one-, two-, and three-year survival rates of 80%, 71%, and 61%, respectively [36]. In a subgroup of patients with a DT indication in the more recent MOMENTUM 3 trial, death occurred in approximately 22% of patients at two years, and 14% of patients in whom it was initially implanted as a DT underwent transplantation [21]. Conversely, approximately 5% of patients initially listed as DT had undergone transplantation based on registry data [20]. Thus, DT may be administered as a viable option in advanced HF patients who are not transplant candidates and unlikely to become candidates for transplantation.

Outcomes of Left Ventricular Assist Device Therapy

Historically, MCS design focused on providing a device that could entirely replace the heart [37]. Later, it was established that much simpler LVADs were more efficient and reliable than the options available for heart replacement. Early pulsatile LVADs were used for initial clinical trials to demonstrate the efficacy of MCS as a long-term therapy for HT ineligible patients [35]. Meanwhile, a breakthrough only later emerged for the patients suffering from advanced HF, once continuous flow LVADs were developed [38]. These devices almost entirely replaced the pulsatile ones, mainly since survival was observed to improve alongside an association with fewer adverse events and minimal malfunctions [39].

The HeartMate 3 (Abbott Laboratories, IL, USA) durable LVAD is available for clinical use in the US and Europe. Comparatively, its predecessor, the HeartMate 2 (Abbott Laboratories, IL, USA), is rarely used today. In addition to the HeartMate devices, another continuous flow durable LVAD, the HeartWare HVAD (Medtronic Inc., MN, USA), was also approved for clinical practice. However, the HeartWare HVAD was removed from the market in 2021 due to device malfunction, higher stroke rates, and mortality [40].

Survival

LVAD therapy has become a cornerstone treatment for patients with advanced HF. Durable LVAD therapy requires frequent monitoring, stringent follow-up, testing, and self-care. This is important to manage device-related complications and residual HF symptoms, as well as safely operate the device. For the long-term success of durable MCS therapy, it is paramount to prevent and timely treat common complications such as stroke, infection, and gastrointestinal bleeding, as well as chronic conditions (e.g., chronic kidney disease or diabetes). Lifelong maintenance of anticoagulation is also vital for the good functioning of the device. Self-care through education is crucial for battery management and driveline wound maintenance.

Multiple studies have indicated significant improvements in survival rates for patients receiving LVAD therapy with the current generation of technology. The one-year

survival rate for patients implanted with a centrifugal-flow LVAD is between 85% and 90%, with two-year survival rates exceeding 70% [18,39,41]. These rates are markedly higher than those for patients with stage D HF who were treated using medical management alone [42]. Patients with stage D HF experience poor quality of life, high symptom burden, and face a median life expectancy of only 6–12 months [43]. Standard medical therapy is insufficient for these patients. Moreover, the survival of patients on medical management is very poor, particularly those requiring inotropes. Thus, the mortality rate of patients with stage D HF requiring inotropes exceeds 70% within a year of diagnosis [44]. The high mortality rates of cardiogenic shock and advanced stage D HF support the use of durable LVAD therapy.

Over the last two decades, continuous flow LVAD pumps have improved survival rates (Fig. 1, Ref. [35,41, 45–49]). In the seminal publication of the REMATCH trial, the 1-year survival rate was reported to be 52% with the pulsatile LVAD (HeartMate XVE, Abbott Laboratories, IL, USA) compared to 25% in the control group [35]. The MOMENTUM 3 evaluated the HeartMate 3 LVAD, the leading continuous flow device on the market today [39,41]. Patients were recruited for the trial between 2018 and 2022, and those patients with advanced HF were randomly assigned to receive either the centrifugal-flow pump (HeartMate 3) or axial-flow pump (HeartMate II) as a bridge to transplantation or DT. The 1-year and 5-year survival rates were 87% and 58%, respectively, for patients receiving the HeartMate 3 compared with 84% and 44%, respectively, for patients receiving the HeartMate II [50]. These findings suggest improved survival may also be associated with enhanced functional status and reduced hospitalization rates. Certain patients may benefit more from the advanced features of the HeartMate 3, particularly its reduced pump thrombosis rates, which can contribute to better overall outcomes. Presently, the HeartMate 3 arm in the MOMENTUM trial has accomplished the best survival results for LVAD therapy in a clinical trial setting. These results observed in the MOMENTUM 3 trial were validated by analyzing "real-world" data from the STS INTERMACS [18,40] and ELEVATE [45,51] registries. Reduced adverse events, such as pump malfunctions, strokes, or bleeding complications, further corroborate the improved long-term survival of the HeartMate 3 device. The latest report from the ELEVATE registry suggests a 5-year survival rate of 63% for primary implants and a stroke-free survival rate of 58% [51]. Devices that enhance longevity also have the potential to reduce the overall cost of care by minimizing the necessity for subsequent interventions or hospitalizations.

Long-term survival following LVAD implantation varies based on several factors, including the patient's overall health status, the etiology of HF, and the presence of comorbid conditions. Comprehensive evaluations before implantation, including renal and liver function assessments, help guide clinicians in optimizing patient survival post-implantation. Five-year outcomes from the MOMENTUM 3 trial showed that the survival free of a major stroke in the HeartMate 3 group was 58% [50]. The real-world ELEVATE registry long-term 5-year data demonstrate a survival rate exceeding 60% in the primary implant cohort and significant improvements in both quality of life and functional capacity [51]. A recent analysis from the STS INTERMACS registry indicated that while survival rates remain elevated at two years post-implant, these rates begin to decline after the five-year mark, with approximately 50% of patients surviving post-5 years [36]. The STS INTERMACS registry data that included patients on LVAD support, patients with an initial bridge to transplantation or bridge to candidacy strategy, had five-year survival rates of 52% and 51%, respectively, and patients with an initial destination therapy strategy had a five-year survival of 44% [36]. Notably, advancements in device technology and management protocols have contributed to improved long-term survival rates, particularly for those patients transitioning from LVAD to heart transplantation.

Another important consideration in survival rates is the transition from supportive therapy with an LVAD to definitive treatment, such as heart transplantation. Research has shown that patients who undergo LVAD implantation to facilitate transplantation generally demonstrate better outcomes. Patients bridged to transplant with LVADs have survival rates similar to HT recipients, with overall survival rates exceeding 80% at one-year post-transplant [52]. This underscores the importance of using LVADs not only as a treatment modality for end-stage HF but also as a viable strategy for extending life while awaiting suitable donor hearts.

Adverse Events

Adverse events profoundly impact the quality of life of patients and carry a significant mortality burden. Adverse events can broadly be categorized into hemocompatibility-related and hemocompatibility-independent events. The former includes stroke, bleeding, and thrombosis, while the latter combines right ventricular failure (RVF), infection, and aortic regurgitation. Patient factors, device characteristics, and support duration influence the complication risk.

High readmission rates related to adverse events in patients on durable LVAD support remain an issue. Pump thrombosis, while very rare with the latest HeartMate 3 device, remains a critical complication that can lead to impaired outcomes, including strokes. Thus, strategies have evolved to mitigate this risk, focusing on individualized anticoagulation therapy to reduce thromboembolic events effectively. Anticoagulation therapy, essential for preventing thrombosis in patients on durable LVAD support, predisposes patients to bleeding complications. The burden of non-surgical bleeding events is a leading morbidity among

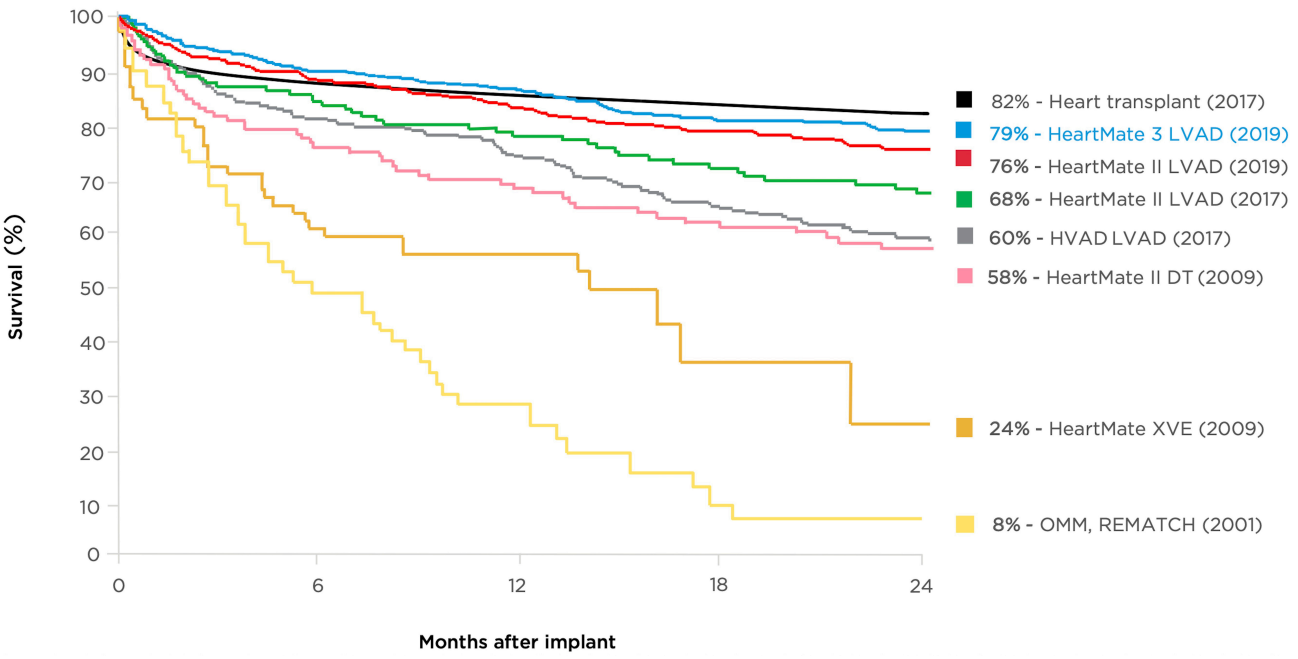

Fig. 1. Historical survival rates with durable left ventricular assist device support. The yellow and brown lines depict the survival associated with optimal medical therapy and pulsatile left ventricular assist device technology [35]. Eight years after the completion of the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure trial [35], pulsatile technology was replaced in favor of smaller continuous flow pumps, which translated into a dramatic improvement in survival as illustrated by the purple [46], green [47], and red curves [41]. The latest generation continuous flow pump, the HeartMate 3 (Abbott Laboratories, IL, USA), is associated with a 2-year survival of 83% [45], which now parallels that of heart transplantation [48]. Reproduced with permission from Netuka *et al*. [49]. Reproduced with permission of European Medical Group LTD trading as European Medical Journal, Copyright © 2025. All rights reserved. Abbreviations: DT, destination therapy; HVAD, HeartWare® ventricular assist device; LVAD, left ventricular assist device; OMM, Optima Medical Therapy; REMATCH, Randomized Evaluation of Mechanical Assistance for treating Congestive Heart Failure.

patients on LVAD. Historically, a pooled analysis of the HeartMate II and HeartWare HVAD reported that significant gastrointestinal bleeding events occur in about 20% of patients within the first year of LVAD implantation [53]. Moreover, based on the STS INTERMACS 2020 Annual Report data, one of the primary complications associated with LVAD therapy includes major bleeding at a rate of 0.5 events per patient–year [36]. In a subgroup of patients from the MOMENTUM 3 trial, after 24 months of follow-up, gastrointestinal bleeding was at 29% and bleeding requiring surgery at 11% [21]. Significant bleeding events occurred in almost 40% of patients at 2 years after LVAD implantation, reinforcing the complexities in managing these patients [21].

Traditionally, antithrombotic therapy for durable LVAD support has been vitamin K antagonists in combination with low-dose aspirin as an antiplatelet agent, although without any conclusive evidence of efficacy and safety. Recently, an international, randomized study of aspirin vs. placebo with vitamin K antagonists in HeartMate 3 LVAD carriers found that avoiding aspirin as part of an antithrombotic regimen is not inferior to a regimen containing aspirin [54]. The same study also found that avoiding aspirin does not increase thromboembolism risk and is associated with reduced bleeding events.

Direct oral anticoagulants (DOACs) are recommended over warfarin in patients with venous thromboembolism or nonvalvular atrial fibrillation; however, only a few small trials have explored the efficacy of DOACs in LVAD carriers [55,56]. The dabigatran trial was terminated early due to an increase in thromboembolic events in the dabigatran group among the HeartWare HVAD carriers [55]. Meanwhile, a small, randomized trial assessed the effect of apixaban in HertMate 3 patients [56]—the primary outcome of which was a composite of death or major hemocompatibility-related adverse events. The results of this study were encouraging, suggesting that apixaban anticoagulation is feasible and could be tested in a larger trial [56].

Stroke is one of the most dreadful adverse events associated with durable LVAD support. With older generation devices, the stroke rate has been reported as 0.12 events per patient–year [36]. A centrifugal continuous flow rotary pump, the HeartWare HVAD, although without total magnetic levitation of the internal rotor, was removed from the market due to increased incidence of stroke and device mal-

function associated with the device [40]. Stroke rates have decreased over the years, yet contemporary devices must be much less prone to stroke or malfunction. The rate of pump malfunction is about 0.01 event per patient–year of support, and the risk of stroke is about 0.04 event per patient–year of support after the initial 6 months [39,41,50,57]. In a subgroup of patients from the MOMENTUM 3 trial, device thrombosis was reported after 24 months of follow-up at 2%, and disabling stroke was reported at 6% [21].

Infection rates, especially those associated with the driveline, are notable concerns for LVAD patients. A systematic review highlighted that 30–40% of patients experience major infection post-implantation [58]. Such infections can significantly hinder rehabilitation and affect long-term transplant eligibility. Based on the STS INTERMACS 2020 Annual Report data, major infections associated with LVAD therapy were reported at a rate of 0.57 events per patient–year [36].

Quality of Life

Quality of life is a crucial factor in evaluating the effectiveness of LVAD implantation. Research suggests that patients generally experience substantial improvements in their quality of life after LVAD surgery. A registry study that analyzed changes in the quality-of-life visual analog scale among patients undergoing LVAD implantation for dilated cardiomyopathy (destination therapy) revealed a remarkable improvement from approximately 35 points to approximately 75 points [59]. Various instruments, such as the Kansas City Cardiomyopathy Questionnaire (KCCQ) and the Short Form Health Survey (SF-36), have demonstrated notable improvements in quality-of-life aspects. The MOMENTUM trials also provided valuable insights into the outcomes of LVAD implantation. Indeed, the functional capacities of patients in the MOMENTUM 3 trial exhibited significant improvements [51]. Moreover, these patients demonstrated enhanced exercise tolerance and reduced symptom burden, which can significantly improve their daily lives by enabling them to engage more fully in social and physical activities. These improvements were also evident in functional capacity as measured by the NYHA functional classification system. The average six-minute walk distance increased from 137 to 320 meters, and health-related quality of life was assessed using the KCCQ [21]. The improvements observed in patients implanted with the HeartMate II device were comparable to those with the HeartMate 3. The treatment groups had no significant differences in functional status test results or quality-of-life measures.

Right Ventricular Failure

Right ventricular failure (RVF) is a critical complication that can emerge in up to 40% of patients following LVAD implantation [47,60], although not all patients require a right ventricular assist device (RVAD) [61]. The hemodynamic changes induced by LVAD support can significantly affect right ventricular performance. The pressure and volume load of the left ventricle are reduced, alleviating stress on the left ventricle while increasing the volume load on the right ventricle. Indeed, RVF can ensue if the right ventricle, which may already be compromised due to pre-existing heart failure or pulmonary hypertension, cannot adapt to these changes.

Risk factors for developing RVF after LVAD implantation include preoperative right ventricular dysfunction, severe pulmonary hypertension, and a history of right ventricular myocardial infarction, among others. Preoperatively, echocardiographic and hemodynamic assessments of RV function are crucial for identifying high-risk RVF patients. Additional risk factors identified during the intraoperative phase, such as prolonged cardiopulmonary bypass time, can further exacerbate this complication. Extracorporeal membrane oxygenation and dialysis in the preoperative period are associated with RVF postoperatively [62]. End-organ dysfunction and overall preoperative disease severity have been associated with the use of RVAD following LVAD implantation [62]. Echocardiographic markers of RVF are related to the degree of tricuspid regurgitation and left ventricular dilation; hemodynamic indicators include right atrial pressure, reduced pulmonary artery pulse pressure, and low cardiac output.

A proactive approach is crucial to prevent RVF. Several predictive scoring systems have been developed, although with modest discriminatory power when applied to external populations [63]. More recently, the STOP-RVF calculator effectively stratified RVF risk among LVAD candidates [60]. The STOP-RVF calculator was designed to aid in selecting and treating patients requiring durable MCS. Moreover, optimizing medical management before surgery, such as administering inotropic agents to enhance right ventricular (RV) contractility and utilizing pulmonary vasodilators to reduce pulmonary artery pressures, may reduce the incidence of RVF following LVAD. In patients identified as high-risk for RV failure, consideration of biventricular assist devices (BVADs) may be warranted [61]. Once RVF develops on LVAD, timely and effective management becomes imperative. Medical interventions include diuretics to manage fluid overload, inotropes to bolster RV function, and adaptive strategies such as adjusting the settings of the LVAD to achieve a balance in flow dynamics. In severe cases, temporary mechanical support using RVAD may be employed, offering critical support while allowing the RV to recover.

Aortic Regurgitation

New aortic regurgitation after LVAD implantation is associated with increased mortality and cardiac rehospi-

talization due to hemodynamically inefficient circulation [64]. Conventional semi-quantitative echocardiography often underestimates aortic regurgitation in durable LVAD carriers. Several factors contribute to aortic regurgitation after LVAD, including older age, longer circulatory support duration, lack of aortic valve opening, elevated blood pressure, and suboptimal outflow graft anastomosis [65,66]. Therefore, preventive measures should be implemented in all durable LVAD carriers to reduce the chance of aortic regurgitation progression. Precise assessment of aortic regurgitation at implantation is crucial. Strict criteria should be followed when addressing aortic regurgitation during LVAD implantation, as even mild degrees at implantation may later progress to moderate or severe regurgitation, posing a significant problem for these patients. Meanwhile, patients on LVAD with only moderate aortic regurgitation can experience severe congestive HF symptoms. In cases when only trace aortic regurgitation appears during LVAD implantation, preventive measures and medical management are warranted. Preventive measures include reducing LVAD flows to maintain aortic valve opening during each cycle and maintaining low blood pressure. Therefore, even mild aortic regurgitation should be surgically addressed during LVAD implantation. While direct comparisons of surgical options specifically aimed at addressing aortic regurgitation during LVAD implantation are lacking, bioprosthetic aortic valve replacement is likely superior to valvuloplasty or complete oversewing of the valve.

Biventricular Support

The excellent outcomes of isolated left ventricular support have not been duplicated in the biventricular failure setting [67]. Durable biventricular assist devices (BVADs) and total artificial hearts (TAHs) continue to have a higher mortality and morbidity burden than LVADs. Some patients develop RVF after LVAD implantation; when it grows, severe RVF usually occurs early, within days of LVAD implantation [68,69]. The etiology of RVF on LVAD support is multifaceted. A single parameter is insufficient for RVF prediction after LVAD implantation [70]. Biventricular assist device support duration is expected to be short if needed after LVAD implantation [71]. A United Network for Organ Sharing database study showed that 1% of LVAD patients were converted to durable BVAD support, and 0.2% to TAHs [72]. While the quality of life can be excellent for extended periods on BVAD support, abrupt and severe clinical deteriorations are always possible [73]. Therefore, continuous vigilance should be maintained in this unique patient population.

A total artificial heart is a durable MCS device designed to replace the function of a failing heart in patients with severe HF not amenable to treatment with LVAD. Currently, only the Syncardia Total Artificial Heart (SynCardia Systems, LLC, AZ, USA) and the Berlin Heart EXCOR devices are available. Other devices, such as BiVACOR (BiVACOR Inc., Houston, TX, USA) or Aeson (Carmat SA, Vélizy, France), remain under investigation. Additionally, the strategy of using two continuous-flow ventricular assist devices is still considered off-label, despite its widespread use. Compared to LVADs, TAHs are not used frequently. The clinical outcomes for dual HeartMate 3 devices vary across studies. For instance, one study reported a survival rate of 55% to 92% at 18 months [74,75]. Another retrospective analysis using the INTERMACS database revealed that the survival rates among patients with BVADs were 68% at 6 months and 62% at 12 months [76]. Notably, this study also identified 11 patients who died while the device was implanted, nine patients who survived to reach HT, and 18 patients who were alive on support at the average follow-up of 5 months.

One of the pioneering publications on the outcomes of TAH therapy in BTT was the trial conducted by Copeland [77]. This trial demonstrated an overall 1-year survival rate of 70% and a survival rate of 79% up to HT. Notably, at 1- and 5-year follow-ups, survival rates in transplanted patients reached 86% and 64%, respectively. However, compared to LVADs, outcomes from using TAHs are generally poorer. Nevertheless, in certain patients with biventricular failure, an artificial heart may represent the sole viable option. A comprehensive INTERMACS registry reported TAH outcomes up to two years post-implantation, revealed that 34% of patients died, 53% underwent heart transplantation, and 13% remained alive with their device intact [78]. In 2012, Copeland concluded his initial population follow-up by publishing outcomes at 10 years: compared to the initial findings, survival parameters deteriorated, with 68% of patients requiring a transplant and a decline in survival rates at 1, 5, and 10 years after HT from 78%, 60%, to 41%, respectively [79].

Timing of Referral

Delayed referrals remain a significant obstacle to achieving the full potential of this therapy. The proportion of INTERMACS 1 patients remains high in the most contemporary series of durable VAD implants [18]. In the ELEVATE registry, which provides contemporary real-world data of patients supported with the HeartMate 3 LVAD, 70% of patients were categorized as INTERMACS Profiles 1–3 [51]. Moreover, 12% of patients were on pre-LVAD temporary mechanical circulatory support [51]. Thus, wider dissemination of information about the benefits of LVAD therapy in comparison to optimal medical management is paramount. Similarly, a better understanding of outcomes among patients with higher INTERMACS Profiles, particularly among ambulatory patients, should aid in patient selection and expand referrals. Elective device implantation

among ambulatory patients is anticipated to result in lower complication rates and better overall outcomes, although this has not been confirmed in a randomized trial [80].

A critical piece of the puzzle remains the incentive to innovate, which is currently diminished by the lack of competition between manufacturers. Providing a device without a driveline, using transcutaneous energy transfer, would immensely impact the quality of life of LVAD patients and would certainly allow for wider adoption of the technology. The perception that patients with an LVAD are cumbersome to manage, in part due to driveline infection management, impedes the timely referral of patients. Notwithstanding delays in referrals, the outcomes of LVAD patients in the advanced stages of HF are significantly better than for patients treated noninvasively.

Scope Into the Future

Surgical management of advanced HF is at a crossroads. On the one hand, extensive efforts are being made to expand the pool of available donors for HT, including the ever-increasing use of donors after circulatory death. Furthermore, the allograft pool is being developed by including marginal donors, which was previously thought unacceptable. The potential of these strategies, albeit significant, will certainly fall short of the needs for HT candidates. This is why refinement and technical developments of novel mechanical circulatory devices are paramount. With the number of patients with advanced HF increasing in parallel to the ageing population, these demands are quite acute. Thus, reducing adverse events is the key to disseminating this management line. Indeed, increasing the hemocompatibility of the pumps and removing the driveline is an important first step.

Maglev technology has revolutionized the field of durable MCS support. Current benchmarks for patient outcomes have been set with this technology, although the incentive for innovation is lagging. Thus, the BrioVAD (BrioHealth Solutions, Burlington, MA, USA) system has recently been developed. This LVAD system is a fully magnetically levitated pump designed to provide short- and long-term mechanical circulatory support to the left ventricle [81]. A trial to evaluate the safety and efficacy of the BrioVAD is underway [81]. The maglev technology has also initiated further refinement in the VAD and the TAH arena by developing the BiVACOR device [82].

Fully implantable MCS devices are designed to overcome the challenges posed by percutaneous drivelines, particularly the risks of infection and the need for frequent driveline exit site care. Previous iterations of these devices incorporating transcutaneous energy transfer (TET) technologies underwent feasibility clinical trials [83,84]. However, the production of these devices was discontinued due to adverse clinical outcomes, primarily related to hemocompatibility issues and thromboembolic events. Currently, under early clinical feasibility testing, the fully implanted ventricular assist system (FIVAS) is a combination of the coplanar energy transfer (CET) system (Leviticus Cardio, Ltd., Petach Tikva, Israel) and the Jarvik Heart LVAD (Jarvik Heart, Inc., NY, USA) [85]. This technology enables wireless resonance energy transfer while simultaneously providing more than 8 hours of LVAD support.

Groundbreaking innovations in bioengineering are underway, aiming to integrate biological components with mechanical systems. These advancements could enhance compatibility with the human body and improve patient outcomes. Biocompatible surfaces, for instance, could potentially reduce shear stress on blood in microcirculatory systems and maintain its rheologic properties. This could reduce the risk of thromboembolism and decrease the need for anticoagulation.

The potential of artificial intelligence (AI) to revolutionize MCS management is particularly noteworthy. Artificial intelligence can enable predictive analytics for complications, real-time monitoring, and personalized patient care, transforming how we manage these devices. Incorporating maglev technology and AI to replicate the natural blood flow of a healthy heart could revolutionize the field of MCS. Additionally, design changes to reduce the size of MCS devices could make them more suitable for truly minimally invasive approaches.

Socioeconomic and Ethical Considerations

Patient income, education, and employment status significantly influence their access to LVAD therapy. For instance, the higher costs associated with LVADs deter patients without sufficient financial resources or insurance coverage from considering this option. Additionally, patients in rural or low-income countries face challenges accessing specialized medical facilities or providers trained in LVAD selection and management. Furthermore, variations in coverage policies, out-of-pocket expenses, and reimbursement practices are crucial in shaping patient decisions. To address these disparities, healthcare systems and policymakers can implement initiatives that promote awareness of LVAD therapy, enhance provider education on equitable access, and actively work to overcome systemic barriers to care.

The ethical considerations surrounding durable LVADs as a DT are multifaceted and significant. One primary concern is the justification of patient selection, particularly in weighing the benefits of prolonged life against the potential decline in quality of life. Patients often face complications, extended hospitalizations, and significant lifestyle changes. Informed consent becomes paramount, requiring patients to fully comprehend both the procedural risks and the long-term implications of living

with an LVAD, including the potential for continuous dependency on medical care. Additionally, resource allocation raises ethical dilemmas, as LVADs are costly devices, prompting questions about accessibility and equity in treatment options across diverse socioeconomic groups. Furthermore, the emotional and psychological impacts on patients and their families must be considered. The decision to proceed with LVAD implantation may burden caregivers substantially and lead to complex end-of-life discussions. Thus, striking a balance requires a patient-centered approach prioritizing autonomy, transparency, and equitable access to care.

Long-term failures of LVADs and the need for replacements are critical considerations for patients and healthcare providers. As LVADs are mechanical, these devices have a finite operational lifespan. When an LVAD reaches the end of its mechanical life, patients may experience a decline in cardiac function, leading to potential complications such as heart failure symptoms, thrombosis, or pump malfunction. In such cases, patients may require urgent surgical intervention to replace the failed LVAD with a new device or, in some instances, consider transitioning to heart transplantation if the eligibility criteria are met. Several strategies are being explored to address the risk of LVAD failure and enhance longevity: Continuous monitoring of device parameters, such as flow rates, power consumption, and pulsatility, can provide early indicators of potential mechanical issues. Incorporating advanced diagnostics, including machine learning algorithms, may enable predictive analytics to foresee pump failure based on historical data and real-time metrics. Nonetheless, ongoing research into materials and engineering design improvements aims to enhance the durability and performance of LVADs, ultimately reducing the incidence of long-term failures.

Conclusions

Surgical management of advanced HF stands on two pillars. Firstly, heart transplantation remains the gold standard, but fails to meet the needs of potential recipients due to a profound lack of donors. Secondly, durable mechanical circulatory assistance provides a useful means to fill the gap between the number of potential heart transplant candidates and actual recipients. Nevertheless, recognizing the complementary nature of these two approaches is paramount in providing this challenging patient cohort with the best possible outcomes.

Abbreviations

AI, artificial intelligence; BTD, bridge to decision; BTT, bridge to transplantation; CET, coplanar energy transfer; DT, destination therapy; FIVAS, fully implanted ventricular assist system; HF, heart failure; HT, heart transplantation; INTEREMACS, Interagency Registry for Mechanically Assisted Circulatory Support; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVAD, left ventricular assist device; MCS, mechanical circulatory support; MOMENTUM 3, Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HeartMate 3; NYHA, New York Heart Association; REMATCH, Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure; STS, Society of Thoracic Surgeons; RVF, right ventricular failure; TAH, total artificial heart; TET, transcutaneous energy transfer.

Author Contributions

TK and HG conceptually designed this review article and contributed equally to its preparation. TK provided the first draft while HG reviewed it critically for important intellectual content. Both authors contributed to the editorial changes suggested during the review process, read and approved the final manuscript. They also agreed to be accountable for all aspects of the work.

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Conflict of Interest

The author declares no conflict of interest. Hrvoje Gasparovic is a member of the editorial board of this journal. Hrvoje Gasparovic declares that he was not involved in the processing of this article and has no access to information regarding its processing.

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