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Left ventricular assist devices as destination therapy in stage D heart failure

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1   Introduction

Mechanical circulatory support (MCS) has increasingly become an important management opportunity for patients with stage D heart failure (HF) with remarkable impact on patient survival and quality of life. Early clinical trials have demonstrated improved outcomes of durable left ventricular assist device (LVAD) support compared with optimal medical management.[1] As technology advanced, continuous flow LVADs outperformed pulsatile flow devices in clinical trials and the field migrated to HeartMate (Abbott Laboratories, Abbott Park, IL) and HeartWare (Medtronic, Minneapolis, MN) devices due to their clinical superiority. Among the continuous flow devices, axial flow and centrifugal flow with magnetic levitation (MagLev) designs were subsequently investigated in clinical trials with promising findings. Compared with a survival rate of 54% with the first-generation pulsatile-flow HeartMate XVE LVADs, survival has improved to 76% and 83% with implantation of the second-generation axial-flow HeartMate II and the third-generation centrifugal-flow HeartMate III LVADs respectively, after two years of follow-up post LVAD implantation.[1,2] Furthermore, minimal invasive procedures as alternatives to sternotomy for device placement, such as lateral thoracotomy, have been explored to improve postoperative recovery and long-term outcomes. Presently, the Food and Drug Administration (FDA) approved devices include the axial flow HeartMate II, centrifugal flow with passive MagLev design of HeartWare, and centrifugal flow with a fully MagLev design of HeartMate III. All of these devices are FDA approved for patient who are supported with an LVAD while they await heart transplantation (HT) [bridge-to-transplant (BTT)] as well as for patients who are ineligible for HT and, therefore, patient will require LVAD support for life [destination therapy (DT)].

In addition to marked advancement in device technology, surgical techniques and patient management, further improvement in patient survival following LVAD implantation has been achieved through an improved patient selection approach. This article focuses on patient selection, LVAD-associated complications, and future techniques and directions in this field with greater emphasis on the elderly patients who have more comorbidities, yet have no other therapeutic options for treatment of their advanced heart failure, and therefore need more carful assessment of the risk versus benefit of LVAD utilization in this population.

2   Patient selection for LVAD support

Renewed emphasis has been placed on appropriate patient selection for MCS, including LVAD. Delineating whether a patient will qualify for LVAD as BTT or DT is based on a myriad of factors and multidisciplinary discussion of candidacy. Many patient considerations and device considerations are synonymous for both BTT or DT utilization as clinicians must determine that device implantation is feasible both medically and surgically, that an implantable durable device confers an advantage to other treatment modalities, that patients have the support structures in place to enable success with the device, and most importantly, that the patient is amenable to LVAD support after being made aware of the risks and benefits. Undergoing a thorough evaluation with multidisciplinary input and engagement is necessary for success.

Age is certainly a consideration, as many centers will not consider HT in patients who exceed 65 to 70 years of age. Therefore, older patients beyond the age of 70 are generally considered for LVAD implantation as DT. The selection criteria for DT LVAD were constructed based on the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure and HeartMate II

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with no specific age limit.[3,4] Therefore, advanced age is not a contraindication to LVAD although significant comorbidities and frailty are more common in the elderly population and this may adversely affect outcomes post LVAD. Indeed, age has been shown to be an independent predictor of mortality and length of stay after LVAD implantation.[5,6] However, with careful selection and appropriate management of complications in addition to good surveillance follow-up and social support, a selective group of elderly patients can still gain remarkable benefit from LVAD support. Table 1 summarizes the main inclusion criteria for LVAD implantation as DT based on clinical trials. Most MCS and transplant centers use these criteria driven from clinical trials in conjunction with hemodynamic information, such as elevated left-sided filling pressures and low cardiac index (< 2.2 L/min per m^2) to determine eligibility for LVAD.

Identification of appropriate timing to proceed with LVAD is another important consideration which can be determined by the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) classification (Table 2).[7,8] As the spectrum of advanced HF with NYHA III-IV symptoms is wide and outcome post LVAD can be predicted based on the INTERMACS profiles, the addition of this classification can further improve patient selection for LVAD. For instance, outcomes in patients with INTERMACS 1–2 (unstable patients despite inotropic support) are inferior to those with INTERMACS 3 (stable patients on inotropes)

which indicates a need for hemodynamic stabilization of the former group with temporary MCS prior to proceeding with durable LVADs for better outcomes.[9,10] Additionally, an analysis of the ROADMAP study found that LVAD therapy remains superior to medical management for INTERMACS class 4 but not class 5–7 patients.[11] While patients were more likely to survive with LVAD in class 4–7, patients in class 5–7 who underwent LVAD did not have improvements in quality of life and actually experienced higher rates of rehospitalization compared to class 5–7 patients who were medically managed.[11] Based on these data, LVAD implantation should be considered typically in all INTERMACS 3 patients, patients with INTERMACS 1–2 who ideally show hemodynamic improvement with temporary support as well as selective highly motivated patients with INTERMACS 4–7 who may have survival benefit and improved functional capacity, yet accept the risk of LVAD-related complications and rehospitalization.

Several preoperative risk models have been suggested based on clinical data involving patients with LVAD to predict morbidity and mortality post device implantation. Identification of patients at high risk for LVAD based on these scores may affect negatively on the decision to implant an LVAD. While these scores are generally helpful tools for identifying patients at very high risk who may be considered as futile implant candidates, they should not be the only determinants for inclusion or exclusion patients for

Table 1. Selection criteria for LVAD implantation as destination therapy.

New York Heart Association class IIIb-IV heart failure symptoms for 45 of the preceding 60 days despite optimal medical therapy or patient is dependent on IABP for 7 days or on inotropes for 14 days or more.
Left ventricular ejection fraction less than 25%.
A peak exercise oxygen consumption (peak VO$_2$) of 14 mL/kg per minute or less unless patient is unable to perform the test or on continued need for IV inotropic or IABP support.
Patients are not eligible for heart transplantation.

IABP: intra-aortic balloon pump; LVAD: left ventricular assist device.

Table 2. INTERMACS classification.

INTERMACS profile	NYHA class	Description
1	IV	Crash and burn: critical cardiogenic shock. Includes life-threatening hypotension, organ hypoperfusion, or elevated lactate.
2	IV	Sliding fast on inotropes: declining organ function or inability to restore volume on inotropes.
3	IV	Inotrope-dependent, stable: at home or in hospital. Stable blood pressure and organ function on inotropes but unable to wean due to recurrent heart failure.
4	IV	Resting symptoms at home on oral therapy: stable but diuretic doses fluctuate often.
5	IV (Ambulatory)	Housebound: exercise intolerant. Comfortable at rest but symptoms occur with minimal activity. Often have evidence of volume overload and/or renal dysfunction.
6	IIIb	Walking wounded: exertion limited. Meaningful activity limited. No evidence of volume overload.
7	III	Advanced class III.

INTERMACS: Interagency Registry for Mechanically Assisted Circulatory Support. NYHA: New York Heart Association.

LVAD support. For example, the HeartMate II score is an initial tool for predicting post LVAD survival that can be discussed with the patient and family during evaluation of LVAD candidacy.[12] Age is one variable included in this score but other variables that can be assessed and optimized prior to LVAD implantation, such as albumin and kidney function, are important factors. Risk stratification based on the HeartMate II score can differentiate mortality risk (low: < 1.58, medium: ≥ 1.58 and ≤ 2.48, and high: > 2.48) at 90 days, as well as at one and two years post LVAD, based on the following formula: $0.0274 \times$ age (years) $- 0.723 \times$ albumin (g/dL) $+ 0.74 \times$ creatinine (mg/dL) $+ 1.136 \times$ International Normalized Ratio (INR) $+ 0.807 \times$ (0 or 1, if center volume is ≤ 15 or > 15, respectively). The risk of mortality post LVAD is not merely determined by the abovementioned variables and other clinical factors should be taken into consideration when evaluating patients for LVAD. Global IMACS data[13] comprising more than 14,000 patients from 35 countries demonstrates that congenital heart disease and the need for biventricular support are most closely correlated with early mortality. Thus, assessment of right ventricular (RV) function pre-LVAD should be an important consideration. Because it is responsible for the majority of morbidity and mortality after LVAD, several score models have been proposed to improve prediction of RV failure postoperatively, such as the Michigan score (also called Right Ventricular Failure Risk Score), Utah, Pitt and EUROMACS. Among the parameters associated with poor RV performance post LVAD are high right atrial (RA) pressure, high RA pressure to pulmonary capillary wedge pressure (PCWP) (RA/PCWP) ratio, and low RV stroke work index (RVSWI).[14] Recently, preoperative pulmonary artery pulsatility index (PAPi: defined as the difference between systolic and diastolic PA pressure divided by the mean RA pressure) is associated with RV failure after implantation of continuous flow LVADs, with PAPi < 1.85–2.0 indicates high risk of RV failure with high sensitivity and specificity that even exceed the performance of other hemodynamic parameters.[15,16] A recent external validation analysis including 94 patients supported with a continuous flow LVAD, Michigan RVF score, which emphasizes preoperative hemodynamic derangement and target end-organ dysfunction (Table 3), performed the best compared with other RV failure predictive scores and was also the best predictor of in-hospital and 3-year mortality post LVAD implantation.

Besides assessment for RV failure, frailty assessments can also offer insights into mortality. INTERMACS data indicates frail patients had higher one year mortality compared to their non-frail counterparts.[17] Mortality was also

Table 3. Right ventricular failure risk score (Michigan score) for predicting right ventricular failure post LVAD implantation.

Significant variables in the model	Points for the presence of each variable
Vasopressor requirement	4
AST ≥ 80 IU/L	2
Bilirubin ≥ 2.0 mg/dL	2.5
Creatinine ≥ 2.3 mg/dL	3
Risk score (sum of points)	**Risk of right ventricle failure, likelihood ratio (95% CI)**
≤ 3 points	Low risk: 0.49 (0.37–0.64)
4.0–5.0 points	Intermediate risk: 2.8 (1.4–5.9)
≥ 5.5 points	High risk: 7.6 (3.4–17.1)

AST indicates aspartate aminotransferase. CI: confidence interval; LVAD: left ventricular assist device.

noted to be higher in those who were too ill to complete gait speeded testing pre-LVAD.[17] Moreover, identification of risk factors for renal failure pre-LVAD can aid in appropriate patient selection and mitigate the risk of dialysis post-LVAD. It has been well established that elevated creatinine pre-LVAD confers increased risk of renal failure post-LVAD. Recently, proteinuria has also been implicated as another risk factor that can portend renal dysfunction post-LVAD[18,19] and all-cause mortality and need for dialysis.[19] The significant negative impact on quality of life with dialysis coupled with reduction in survival with renal failure post-LVAD highlights the importance of renal failure risk factor utilization to ensure appropriate patient selection for durable LVAD.[20] A recent study from our institution involving 358 patients supported with LVAD has confirmed the importance of pre-LVAD kidney function and proteinuria as independent predictors of in-hospital renal replacement therapy after LVAD with dialysis requirement found to be associated with poor prognosis including higher risk of in-hospital and long-term mortality as well as higher risk of LVAD-associated morbidity.[21] Therefore, a detailed preoperative assessment and optimization of renal function prior to LVAD implantation may be useful in risk stratification and patient selection.

Psychosocial milieu and support are also important determinants.[22] Many centers require a trained caregiver be present for a period of time following LVAD implantation. Abstinence from substance and alcohol abuse is typically mandatory for LVAD support. Important psychosocial determinants that influence success with long term LVAD support include adherence and compliance, mental health, knowledge and capacity, and coping mechanisms in addition to existing social constructs.[22] Patients with limitations in any or multiple of these areas have reduced capacity to

succeed with LVAD therapy. Early engagement of social services and psychiatry to assess, adequately address and treat concerns is helpful.

Device utilization has migrated toward pairing pump selection with a careful analysis of a patient's medical and surgical history. Presently, HeartMate II, HeartMate III, and HeartWare are all FDA approved for either BTT or DT indications and are the contemporary devices used currently in practice, thus limiting insurance dictation of pump selection and leaving the decision to the LVAD team. Table 4 summarizes the main characteristics of these devices compared with other adult durable MCS devices for advanced HF. The initial ENDURANCE trial[23] comparing HeartWare and HeartMate II devices was followed by a supplemental trial[24] which controlled for blood pressure to reduce stroke risk and demonstrated noninferiority of HeartWare to HeartMate II for TIA/stroke and superiority in a composite of freedom from death, disabling stroke, and pump exchange. Additional size advantages allow for intrapericardial HeartWare placement and recent FDA approval for lateral thoracotomy approach for device implantation[25] offers sternal sparing options for patient who are candidates for HT with shorter hospital length of stay and fewer episodes of thrombosis. The MOMENTUM trial[26] comparing HeartMate III to HeartMate II devices demonstrated superiority of the HeartMate III to the HeartMate II device with regard to survival and freedom from both disabling stroke and exchange or removal for pump thrombosis with remarkable and sustained benefit seen at two years of follow-up.[2] For these reasons, the HeartMate II has been largely replaced by HeartWare and HeartMate III for primary device implantation. However, there remain indications for use of Heart-Mate II, particularly in patients who require an exchange of

the device for another HeartMate II in the event of hemolysis/thrombosis but for whom replacement with an alternative device is not feasible.

3 LVAD-associated complications

Despite the improvement in survival, functional capacity and quality of life, LVAD complications remain an Achilles heel of device implantation. With advancements in LVAD technology, the burden of complications has considerably decreased. Based on the second annual IMACS registry, with the vast majority of patients supported with continuous flow LVADs, infection (40%) and bleeding (35%) remain the most common LVAD-associated complications.[13] Furthermore, neurologic events and device thrombosis remain devastating complications with high morbidity and mortality. Gender-specific complications have been reported and give pause in device consideration. Female LVAD patients more frequently have major bleeding, arrhythmias, RV failure requiring RV support, and have worsened survival compared to male counterparts.[27] While LVAD thrombosis portends greater mortality in women, renal failure indicates higher mortality for men.[27] Patient size also conveys risk, particularly in the underweight and obese groups.[28] While survival is comparable regardless of body mass, obese patients are more likely to have device malfunction while underweight patients experience thromboembolic events more frequently.[28] Greater body mass index also correlates with increased infection risk as does younger age.[29] We have recently shown that diabetes is associated with increased risk of all-cause mortality and LVAD-related complications, including a composite of stroke, pump thrombosis, and

Table 4. Adult durable mechanical circulatory support devices.

Features	Evaheart	Jarvik 2000	HeartMate II	HeartMate III	HeartWare HVAD	SynCardia TAH
Company	Sun Medical Technology Research Corp	Jarvik Heart, Inc.	Abbott Laboratories	Abbott Laboratories	Medtronic, Inc	SynCardia Systems, LLC
CE approval	Approved	2000	2005	2015	2009	1999
Indication	BTT/DT	BTT	BTT/DT	BTT/DT	BTT/DT	BTT
Chamber supported	LV	LV	LV	LV	LV	LV+RV
Support capability	Years	Years	Years	Years	Years	Years
Flow type	Centrifugal, continuous	Axial, continuous	Axial, continuous	Centrifugal, Q2s washing	Centrifugal, Lavare cycle	Pulsatile
Flow capability, L/min	Up to 14	Up to 12	Up to 10	Up to 10	Up to 10	Up to 9.5 (for 70 cc), Up to 7.5 (for 50 cc)
Pump speed, RPM	1600–2200	8000–12000	6000–15000	2000–5500	1800–4000	100–130 BPM
Anticoagulation	+	+	+	+	+	+

BPM indicates beats per minute. BTT: bridge-to-transplant; CE: Conformité Européene; DT: destination therapy; LV: left ventricle; RPM: rotations per minute; RV: right ventricle.

device infection, despite improvement in glycemic control after LVAD implantation.[30]

3.1 Infection

Infections with LVAD is common ranging from 20% to 60% of patients and can manifest in a variety of ways ranging from driveline infections to bloodstream infections and LVAD pocket infections. The most frequent type of infection occurs at the driveline, with not surprisingly higher mortality rates with bloodstream infections.[29] As infection is associated with increased inflammation, it may further increase the risk of device thrombosis and ischemic stroke.[31] Most of the infection events can be treated successfully with antibiotics while it may need pump exchange in some cases, leading to increased length of hospitalization and mortality.

3.2 Bleeding events

Gastrointestinal bleeding (GIB) and epistaxis are the most common bleeding events while on LVAD and are major causes of readmission after LVAD implantation, occurring in 17% to 40% of patients.[32,33] In our institution, these bleeding events occur in 30% of patients and account for 26% of hospitalizations post LVAD implantation. The recurrent and prolonged hospitalizations associated with GIB, including repeated endoscopies and blood transfusions, adversely affect quality of life in the LVAD population. Recurrent bleeding requires reduction in anticoagulation, which increases the risk of pump thrombosis. The pathogenesis of GIB associated with LVAD has not been fully elucidated but it may be attributed to low pulsatility and LVAD-induced shear stress degradation of high molecular weight von Willebrand factor along with combined antiplatelet and antithrombotic therapy,[34,35] resulting in the development of arteriovenous malformation with high bleeding risk. Unfortunately, the development of a new magnetically levitated centrifugal CF-LVAD, HeartMate III, which was engineered to reduce shear stress and to create an intrinsic artificial pulsatility, has not resulted in reduction of GIB risk or severity.[2,26] Patients who bleed are also statistically more likely to have postoperative RV failure.[36] Treatment modalities range from scoping procedures, transfusions with careful watching, to medical treatment options including octreotide,[37,38] danazol,[39] and fish oil supplementation[40] with varying results and limited success. Therefore, new therapeutic strategies are still warranted to reduce the development of angiodysplasias and reduce the risk of bleeding in the LVAD population.

3.3 Neurologic events

Major neurologic events include ischemic and hemor-rhagic stroke which can have a devastating impact on quality of life for patients as well as negatively influence transplantability, mortality, and other factors relevant to both patients and providers. Based on the INTERMACS registry, patients supported with continuous flow LVADs had 1-year incidence of stroke of 11%. Risk factors for stroke include inadequate aspirin dose,[41] intra-aortic balloon pump support pre-LVAD, and cardiomyopathy etiology.[42] Strokes can occur throughout the continuum of LVAD support regardless of age of the patient but are more prevalent in female patients and in those with a hypercoagulable state such as infection or gastrointestinal bleeding.[42,43] Atrial fibrillation increases ischemic stroke risk whereas hemorrhagic stroke risks include suboptimally controlled blood pressure and elevated INR levels.[24,41]

3.4 Device thrombosis and hemolysis

Recent emphasis has been placed on adherence to guidelines designed to reduce risk of LVAD hemolysis/thrombosis. An unexpected increase in incidence of LVAD thrombosis[44] led to greater scrutiny and analysis of possible causes of this phenomenon. Appropriate surgical positioning and anchoring of the device, timely anticoagulation initiation, avoidance of hypertension, and avoiding lower LVAD speed settings were found to significantly reduce thrombosis to less than 2% when there was adherence to these guidelines.[45] Treatment for LVAD hemolysis/thrombosis has ranged from intensification of anticoagulation and INR goal ranges, to hospital admission for heparin or/and glycoprotein IIb/IIIa inhibitors,[46] to thrombolytic therapy with tPA administration.[47] Ultimately, patients may require device exchange or urgent transplantation to resolve severe cases of device thrombosis. According to the MOMEN-TUM 3 trial, and a subsequent secondary analysis of this trial, HeartMate III has resulted in a substantial decrease in risk of pump thrombosis requiring reoperation or medically managed pump thrombosis, and fewer nondisabling strokes compared with HeartMate II devices.[2,26,48] These promising results may be translated into a future reduction in serious pump thrombosis and stroke with increasing use of Heart-Mate III in lieu of HeartMate II and HeartWare LVADs in clinical practice.

3.5 RV failure

RV failure can occur early or late after LVAD implantation and may require varying degrees of support from inotropes and intensified diuresis to right ventricular assist devices (RVAD) support either for a temporary period of time or for long term support. Durable RVAD support offers additional challenges in the United States where the FDA

has not yet approved these devices for support. INTER-MACS defines RV failure to be elevated RA pressures greater than 16 mmHg either measured by right heart catheterization (RHC) or by dilated inferior vena cava or jugular venous distention in addition to evidence of venous congestion.[49,50] The significance of severe RV failure is manifested in greater risk of death and morbidity as patients requiring RVAD have increased incidences of bleeding as well as renal and hepatic sequelae. As outlined previously, preoperative predictive scores and pressure measurements obtained via RHC are utilized to calculate proclivity toward right heart failure (RHF). Specifically, the presence of higher RA/PCWP ratio, lower PAPi, or/and RVSWI confer greater risk of RV failure.[50,51] Maintenance of sinus rhythm, diuresis or renal replacement therapy, phosphodiesterase-5 inhibitors and inotrope support have all been employed to treat RV failure.

3.6   Aortic insufficiency

Aortic insufficiency (AI) is present in up to 30% of continuous flow LVAD patients by one year of LVAD support and tends to be a progressive phenomenon, in part related to left ventricular offloading prompting fusion and remodeling of the aortic cusps.[52] Progression and development of AI is seen more often in hypertensive elderly patients after longer term LVAD support who have a smaller body surface area and closed aortic valve.[53] Targeting appropriate outflow graft to the ascending aorta angles can lower risk of AI progression.[53]

Patients implanted with LVAD as DT will maintain LVAD support for the duration of their life. Multisystem organ failure is the most frequent reason for death followed by RHF and cardiovascular concerns and ischemic or hemorrhagic stroke.[13] Patients electing to utilize hospice services when death is imminent may do so in the context of a hospital setting or at home pending patient and family wishes and level of care desired and needed to ensure comfort and dignity in passing. Ensuring that patients have determined a power of attorney and have completed an advanced directive can be very useful when addressing end of life concerns. For these and many other reasons, early and continued engagement of palliative care clinicians throughout the LVAD continuum is invaluable.

4   Cost-effectiveness of durable LVADs

HF afflicts approximately six million Americans, with 700,000 individuals newly diagnosed each year. Of the six million HF patients, nearly 250,000 have advanced HF who suffer from low quality of life, more frequent hospitaliza-

tions, and high mortality.[54] The US health care spends more than $26 billion with an expectation that this number will double by 2030.[55] Randomizes studies have shown that implantation of continuous flow LVADs achieve significant reduction in mortality with a 1-year survival approaching 80% among patients receiving DT LVAD, yet these devices are associated high cost and increased burden of complications. One study has shown that readmissions were more frequent after LVAD implantation than among patients on HF medical therapy.[56] Moreover, among 220 Medicare beneficiaries with HF, the cost of readmission was increased after LVAD as compared to this before LVAD implantation. Based on previous studies, it appears that LVAD in not cost-effective in patients with inotrope-dependent HF.[57,58] However, with the introduction of the second-generation devices and improved patient selection, the incremental cost-effectiveness ratio (an estimate of the cost-effectiveness of an intervention, defined as the difference in cost between two interventions, divided by the difference in their effect) per quality-adjusted life-year gained (a summary measure of health outcome for economic evaluation incorporating the impact on the quantity and the quality of life) has become more favorable. A recent study found that among patients with advanced HF who are not dependent on inotropes (ambulatory patients), the use of DT LVAD compared with medical therapy does not appear to be favorable by conventional thresholds, but may provide acceptable value in a selective group of low risk patients who have lower adverse events rates or in settings where LVADs can be managed at a lower cost.[59] Therefore, careful selection of appropriate patients and LVAD implantation at the right time when patients are expected to respond adequately is warranted to improve cost-effectiveness to LVAD therapy.

5   Summary and future directions

The use of LVAD as DT is becoming the most durable option to extend quality of life and survival in elderly patients with advanced HF who are not candidates for HT. Given the substantial shortage of HT donors, even among elderly who are eligible for HT, DT LVAD is becoming a promising durable treatment option for an increasing number of patients with expected long waiting time for HT.

There is an increasing interest in minimally invasive approaches for LVAD implantation which may reduce the risk of bleeding, RV failure, and shorten the time of postoperative recovery. The most common surgical strategy is partial sternotomy with left thoracotomy using central or peripheral cannulation for cardiopulmonary bypass. Off-pump im-

plantation is reasonable but requires more surgical skills and apical coring during rapid ventricular pacing to minimize risk. New generation devices, such as the HeartWare MVAD, are generally smaller and can be potentially implanted with a minimally invasive approach. Future studies will examine if these new surgical techniques result in better outcomes. Additional advances in LVAD technology include the transcutaneous energy transfer technology; a promising technology which will enable totally implantable (wireless) LVAD implantation and lower power requirements without skin penetration or need of percutaneous driveline. These future devices will further improve quality of life and minimize the risk of device infection in the LVAD population.

In summary, LVAD is a promising treatment for increasing number of patients with advanced HF refractory to medical therapy. However, LVAD is still associated with risk of adverse events and social burdens. Technologic evolution in the field of durable LVADs are needed to improve effectiveness and reduce LVAD-associated complications, readmissions, and cost. Besides improvement in LVAD technology, careful patient selection and appropriate timing of LVAD implantation are critical, particularly among elderly patients. Optimal cost-effective use of LVAD therapy requires stratification tools, appropriate resources, and multidisciplinary team work, all of which remain the key for achieving the most favorable outcomes.

Acknowledgments

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