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Editorial

Current Perspectives on Durable Ventricular Assist Devices

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Introduction

Heart failure (HF) is a heterogeneous clinical syndrome presenting a global health challenge. The HF treatment landscape is continuously being revised. Novel agents target multiple drivers of HF progression such as autonomic nervous system dysregulation, iron deficiency, cardiac fibrosis, cellular remodeling, and inflammation. Continuous improvements in device therapy, such as cardiac resynchronization or percutaneous interventions, improve HF symptoms. However, for refractory HF, heart transplantation (HT) and mechanical circulatory assistance (MCS) remain the best options. The former is the gold standard but is limited by donor organ shortage. Strategies to increase the donor pool include donation after circulatory death, ex vivo perfusion and use of marginal donors [1,2]. Recently, genetically engineered pig cardiac xenotransplantation has been performed. This strategy has, to date, yielded a prohibitive mid-term mortality [3]. Genetically engineered pig hearts have thus far not reversed the poor outcomes of xenotransplantations observed over the past 6 decades [4]. Survival of propensity-score matched LVAD patients is comparable to heart transplantation out to three years, far surpassing survival curves for those with refractory heart failure symptoms on oral medical therapy alone [5,6]. Durable LVADs, therefore, remain the standard of care for patients deemed unsuitable for transplantation or in need of a bridge to transplant.

Durable Mechanical Circulatory Assistance

Implantable VADs have evolved from pneumatically-driven pulsatile devices prone to mechanical failure to magnetically levitated continuous-flow systems. The HeartMate 3 (Abbott) has been shown to have lower incidences of death, disabling stroke and mechanical device failure per patient-year in comparison to older generation devices [7]. Notwithstanding the increased morbidity burden of the contemporary LVAD recipients in comparison to their historical controls, patient outcomes are getting better [8]. Post_LVAD improvements in the 6-minute walk test, NYHA class, as well as across multiple quality-of-life scoring systems validate MCS as the best HT alternative [7]. Pharmacological management of patients with durable VADs is complimentary to mechanical support and should parallel treatment strategies for non-surgical HFrEF patients. With lacking LVAD specific data on the use of renin-angiotensin-aldosterone system inhibitors, β-blockers, mineralocorticoid antagonists, angiotensin/neprilysin inhibitors, and sodium-glucose cotransporter 2 inhibitors, one must rely on non-LVAD data to guide medical management in this patient population.

Patient Selection

Each candidate should be evaluated for the end-goal of MCS. The treatment strategies include bridge to transplant, bridge to candidacy, or destination therapy. It is paramount that device implantation precedes irreversible end-organ damage. Multiple scoring systems have been developed to risk stratify durable MCS candidates, but their efficacy is limited. There is no substitute for good clinical judgment.

Adverse Events

The VAD morbidity burden is linked to hemocompatibility-related adverse events and those which occur independently of activation of the coagulation cascade. The former include pump thrombosis, stroke, and bleeding while the latter include right ventricular failure, infections, outflow-graft twist occlusion and arrhythmias [7].

Hemocompatibility-Related Adverse Events

The low incidence of pump thrombosis in the magnetically levitated HeartMate 3 device has led to a reduction in antithrombotic management. The ARIES-HM3 trial has shown that warfarin alone is noninferior to its combination with aspirin in terms of safety, with the added benefit of reducing bleeding events [9]. While pump thrombosis has become a rarity, stroke and bleeding remain serious hemocompatibility-related complications even with the latest generation device [7].

Right Ventricular Failure

LVAD optimization and adequate decongestion take central stage in the immediate postoperative period. In some cases, this may lead to unmasking of incipient right ventricular failure (RVF). The impact of LVADs on RV function is the result of a complex interplay between their beneficial and deleterious effects. The benefits of reductions in pulmonary artery, RV and right atrial pressures are offset by increases in RV preload and a decreased contribution of the interventricular septum to RV function. The incidence of post-LVAD RVF varies from 5–44%. The absence of a universally accepted definition of RVF undermines its effectiveness as an outcome metric. Management of RVF requires timely addition of RV support in the setting of resistance to escalating pharmacological therapy. Inhaled or i.v. pulmonary vasodilators are important adjuncts to treatment of this syndrome. Planned biventricular assist device implantations for patients at high risk for RVF have superior outcomes than those who are initially fitted with an LVAD and then underwent rescue RVAD implantation [10]. Durable biventricular support has been employed for extended periods of time with acceptable results utilizing existing technology [11,12].

Infections in VAD Patients

Patients with implantable VADs are prone to infections and the risk is proportional to the duration of support. Infections can be classified as VAD-specific, VAD-related, and non-VAD infections. Predisposing factors include a skin-to-driveline interface, obesity, and diabetes [13]. Over a fifth of patients with durable LVADs will develop driveline infections [7]. This common complication significantly impacts patient quality of life. Bacterial biofilm formation on the driveline and pump surfaces complicates treatment, as biofilms are undetectable by immune cells and resist antibiotic penetration. Furthermore, there is no consensus on optimal antibiotic regimens for prolonged infections [14]. Device-specific infections challenge the conventional paradigm mandating removal of all infected foreign materials. In the setting of durable MCS this poses a formidable challenge.

Aortic Regurgitation

De-novo aortic regurgitation (AR) after cf-LVAD implantation produces a hemodynamically inefficient circulatory system. If the aortic valve is permanently closed, de-novo AR is a pancyclic event and is underestimated by conventional semi-quantitative echocardiography. Preventive measures include addressing AR at the time of LVAD implant, reducing LVAD flows to maintaining aortic valve (AoV) opening and treatment of hypertension. Replacement of mechanical aortic valves at the time of LVAD implant is mandatory, and surgical treatment of a valve with mild or greater AR should be strongly considered. While the absence of direct comparisons of surgical options aimed at addressing AR makes recommending the best option difficult, bioprosthetic AoV replacement is likely superior to valvuloplasty or complete oversewing of the valve. AR after LVAD implantation is associated with mortality and cardiac rehospitalization [15]. Variables associated with de-novo AR are age, duration of support, absence of AoV opening, hypertension and suboptimal outflow graft anastomosis angles [16,17]. Both surgical and transcatheter AVR may be considered in patients with significant post_LVAD AR.

Promoting Myocardial Recovery

Reverse cardiac remodeling associated with VAD-induced unloading is not synonymous with functional myocardial recovery. Only a minority of patients reach the stage where VAD removal is considered. A greater likelihood of recovery is seen in the settings of acute myocarditis and post-partum cardiomyopathy. Historically, strategies employed to enhance myocardial recovery included clenbuterol and mesenchymal stem cell injection at the time of LVAD implant [18]. More recently, a standardized aggressive pharmacological protocol intended to induce reverse remodeling coupled with frequent evaluation of native myocardial function has been shown to increase the chance of LVAD explantation [19].

Need for Continued Innovation

Notwithstanding the importance of current durable MCS options, one should not ignore their pitfalls. While transcutaneous energy transmissions have already been utilized in the obsolete AbioCor total artificial heart (Abiomed) and LionHeart 2000 LVAD (Arrow International), there are currently no totally implantable systems [13]. Total artificial hearts present only a small percentage of the entire mechanical assistance portfolio, but recent advancements in the field may reignite interest for this line of management.

Summary

Favorable trends in survival rates after durable MCS in the contemporary era highlight the need for careful multidisciplinary discussions to optimize individual patient outcomes. Heart failure management should be evaluated in the context of lifelong treatment. Durable VADs and HT are mutually complementary and not exclusive strategies, and as such provide the best possible outcomes for end-stage heart disease.

Author Contributions

HG made significant contributions to the conceptualization, writing - original draft and revision of the manuscript. KK made significant contributions to the provision of study materials, writing - original draft of the manuscript. All authors read and approved the final manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Conflict of Interest

The author declares no conflict of interest. HG serves on the editorial board of this journal. HG 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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