Impact of Mechanical Circulatory Support on Posttransplant Outcomes

Todd F. Dardas, MD, MS

KEYWORDS

• Heart transplant • Mechanical circulatory support • Temporary circulatory support • Artificial heart • Survival • Risk factors • Health utility

KEY POINTS

- Mechanical circulatory support is not associated with reduced posttransplant survival in most cases.
- Significant reductions in transplant survival may occur following left ventricle assist device (LVAD) support complicated by infection, total artificial heart, and extracorporeal life support.
- Continuous-flow LVAD support is associated with an increased risk of posttransplant vasoplegia syndrome.

INTRODUCTION

Mechanical circulatory support (MCS) devices allow for myocardial recovery, serve to stabilize end-organ function before definitive therapy, act as permanent support, provide a bridge to transplant (BTT), and dramatically increase the likelihood of surviving cardiogenic shock. When used as part of a BTT strategy, MCS may extend life to the median survival of heart transplant, which is currently more than 12 years. However, MCS devices are associated with complications that may prevent transplant or reduce posttransplant survival. For those truly in need of MCS, the potential gain in survival of MCS far outweighs the alternative of waiting for a transplant unsupported. Accordingly, ventricular assist device (VAD) support at listing is present among 25% to 40% of candidates in recent series.[1,2] Experience with MCS before a transplant is growing rapidly; as more experience accumulates, the advanced heart failure community will reduce the risk of mortality and morbidity attributable to MCS. This article focuses on posttransplant outcomes specifically associated with selected MCS devices.

DURABLE DEVICES

Left Ventricular Assist Devices

Each left VAD (LVAD) generation has achieved lower mortality than prior generations, and high-quality prospective trials have established the efficacy of durable LVADs as BTT.[3–5] Declining mortality among LVAD-supported candidates (43% mortality in 2005–2006 decreasing to 8% in 2015–2016) and increasing prevalence of MCS at the time of listing (increasing from 10% to 35% prevalence between 2005–2016) suggest increasing experience and improved efficacy.[1] Mortality for status 1A registrants declined dramatically over the same time, and this decline is partly attributable to LVADs used as rescue therapy. Thus, the use of LVADs as BTT is well accepted; the advanced heart failure community is responsible for identifying and managing risk factors contributing to higher rates of posttransplant outcomes.

Disclosure: Research grant (International Society for Heart and Lung Transplantation/Medtronic).
Department of Medicine, University of Washington, 1959 Northeast Pacific Street, Box 356422, Seattle, WA 98195, USA
E-mail address: tdardas@uw.edu

Cardiol Clin 36 (2018) 551–560
https://doi.org/10.1016/j.ccl.2018.06.009

Posttransplant mortality

Early experience with pulsatile-flow LVADs (PF-VADs) as BTT suggested no association between LVADs and posttransplant mortality.[6–9] In the PF-VAD era, mortality was similar between VAD- and non–VAD-supported recipients after adjusting for severity of illness, donor-recipient mismatches, and cold ischemic time.[6–9] Consistent with high rates of infectious complications encountered with pulsatile devices available at the time, these reports describe a higher risk of first infection and dying of infection after transplant among PF-VAD–supported recipients.[8,9] Early comparisons between pulsatile and continuous-flow (CF) devices suggested equality between the two modalities with regard to posttransplant survival.[10]

CF devices have proven more reliable with fewer complications and improved survival compared with pulsatile devices and, accordingly, have replaced pulsatile devices as the mainstay of durable MCS. In the CF era, mortality has decreased for registrants in general and among persons initially supported with LVADs.[1,11] However, increasing survival among registrants obligatorily increases the number of prevalent registrants and exacerbates the supply-demand mismatch of donor hearts, resulting in scrutiny of even small differences in mortality as programs attempt to optimize the utility of each donor. Given the obligate need for repeat surgery and high burden of complications, posttransplant outcomes with durable LVADs will remain of great interest.

Several reports address posttransplant mortality among LVAD-supported transplant recipients when compared with unsupported recipients in the CF-VAD era and found no clinically significant difference in posttransplant mortality (**Table 1**). Weiss and colleagues[12] reported no significant increase in posttransplant mortality for persons supported with the HeartMate II (Abbott Corp, Abbott Park IL) (multivariable hazard ratio [HR] 1.22; 95% confidence interval [CI] 0.87–1.72). Dardas and colleagues[13] reported posttransplant survival for MCS and non-MCS registrants from the Organ Procurement and Transplantation Network (OPTN) registry. This report suggests an increase in posttransplant morality among persons with implantable LVADs using elective time (HR 1.2, 95% CI 0.88–1.3) and among LVADs with complications (HR 1.2, 95% CI 0.99–1.4), though neither were statistically significant when compared with a reference group of recipients supported with dual inotropes and intra-aortic balloon pumps (IABPs). Trivedi and colleagues[14] noted clinically nonsignificant differences in 3-year survival among registrants transplanted from status 1B with an LVAD using elective status 1A time (84%), status 1B LVADs (85%) and status 1A VAD-supported patients with complications (78%, $P = .01$). Donneyong and colleagues[15] used a time-dependent Cox model with propensity matching to evaluate the effect of HeartMate II support before transplant compared with no support. When adjusted for donor, recipient, and propensity to receive LVAD support, the investigators found that 30-day (HR 1.23; 95% CI 0.79–1.95) and 30- to 365-day (HR 1.31; 95% CI 0.85–2.01) mortality rates were higher among the LVAD-supported group, though statistical significance was not met. Higher risk among LVAD-supported recipients was not seen in the large, pooled International Society of Heart Lung Transplant (ISHLT) adult heart transplant Registry analysis (sampled from 2004–2008), which demonstrated a relative risk (RR) of 1.16 (95% CI RR 0.82–1.65) for CF-VADs compared with no inotropes at transplant and an RR of 1.19 (95% CI RR 0.84–1.69) when CF-VADs were compared with those without inotropes or MCS.[16] Posttransplant mortality was not significantly increased in a modern ISHLT Registry analysis (2005–2015), which demonstrated only 2% absolute risk reduction for inotropes when compared with pretransplant CF-VAD support.[2] Although there are differing mortality signals among LVAD-bridged patients, most data suggest no decrement in survival among recipients transplanted from durable LVAD support (**Fig. 1**).

The exception is LVAD-supported patients with complications. Quader and colleagues[17] reported 14% posttransplant mortality at 1 year among those recipients with device complications and 10% mortality among recipients with CF-VADs without complications. Although these complications were not further delineated in this investigation, most reports have found a higher risk of posttransplant mortality among patients with device infections. Concern for recrudescent infections among device-supported recipients is justified given the obligate need for posttransplant immunosuppression and the high frequency of infections encountered during VAD support. Although pump-related infections may resolve with explant at transplant, resistant organisms and/or deeply seated infections at relatively impenetrable sites may not resolve or recur in the presence of immunosuppression. Reports from the CF-VAD era indicate variable signals toward increased posttransplant mortality following LVADs complicated by infection. John and colleagues[18] reported a nonsignificant decrease in 1-year survival posttransplant survival between those persons without a percutaneous lead infection (89%) when compared with those with a percutaneous lead infection (75%, $P = .07$). In