

EDITORIAL COMMENT

Moving Beyond “Bridges”*

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Left ventricular assist devices (LVADs) have revolutionized the care of heart failure. They now provide another therapeutic option for many patients, transplant eligible or ineligible, with symptoms refractory to medical therapy and resynchronization therapy. For appropriately selected patients, LVADs offer improvements in both quality and length of life. The enthusiasm for LVAD use in the cardiovascular community is growing; >100 U.S. hospitals have met Joint Commission approval to provide LVADs for destination therapy (DT [i.e., permanent]) and the Thoratec Corporation estimates that >10,000 of their

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continuous flow Heartmate II VADs have been implanted worldwide. The fifth INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) annual report (1) provides details on 6,885 patients who had received 1 of the 13 Food and Drug Administration approved durable mechanical circulatory support (MCS) devices between June 2006 and June 2012 in 145 participating hospitals (114 of which are Centers for Medicare & Medicaid Services (CMS) approved for DT). Post-implant survival is very good; actuarial survival for continuous flow VADs is 80% at 1 year and 70% at 2 years. Furthermore, the post-implant survival difference between DT and bridge to transplant (BTT) patients has narrowed despite differences in risk profiles. In 2012, >40% of implants were designated as DT.

Although the original paradigm of MCS was to completely replace the function of the heart, the “assist” nature of such devices became the predominant clinical use of LVADs in the context of “bridging” patients for the short term to the definitive therapy of transplantation. This parlance has stuck and the LVAD as a “bridge” to either transplant, more time for evaluation (e.g., bridge to candidacy), or recovery has become part of the lexicon. In

contrast, the “DT” designation implies the lifetime or permanent intent of the therapy. Although apparently only semantic at first glance, the embrace of this lexicon by regulatory agencies has had significant impact for new device development, reimbursement decisions, and the assessment of clinical trials. This endorsement has in essence forced clinicians into the contemporary practice of stating their intentions with this therapy at the time of implant, for example, BTT or DT. Not surprisingly, it is difficult to make such polar decisions in a dynamic clinical situation and clinicians often default to the “no clear intent” strategy of bridge to candidacy (BTC).

However, an inherent limitation of such an approach is the attempt to predict the future. Exacerbating the issue is the lack of direct evidence that making such designations has a meaningful impact on patient outcomes and satisfaction, cost, or device development. It is in this context that Teuteberg et al. (2) report, in this issue of *JACC: Heart Failure*, on the current (and mandated) practice of designating intent strategy at the time of LVAD implant. In 1 of the most important reports to come from INTERMACS, these investigators confirm that such intended strategies commonly change over time, limiting the usefulness of these a priori designations.

The specific aims of the present study were: 1) to describe the characteristics of the various cohorts defined by the original intent strategies; and then 2) to describe what actually happened. The analysis was limited to patients receiving a primary continuous flow LVAD between March 2006 and March 2011. Three groups of patients excluded from the analysis: 1) those receiving a TAH or biventricular assist devices, 2) those implanted as a bridge to recovery, and 3) those implanted for reasons other than BTT or DT. Three intent strategies were described: 1) BTT; 2) permanent therapy, or DT; and 3) BTC. The BTT patients had to be either listed at the time of implant or listed within 24 h after implant. If listing did not occur within 24 h of implant, the patient was considered BTC. The INTERMACS investigators were also asked to further divide their predictions of BTC patients into those likely, moderately likely, or unlikely to be listed for transplant.

The primary analysis compared the outcomes of these intent strategies at 6, 12, and 24 months. A competing outcomes methodology was used to estimate the dynamic simultaneous probability of having 1 of 3 mutually exclusive events (e.g., death, transplant, or LVAD explant). In all, 2,816 patients were ultimately reviewed. Three important observations were made, as follows.

One, the most common pre-implant strategy was BTC at 42% (vs. 38% as BTT), reflecting the uncertainty of patient outcomes at the time of LVAD implant and an unwillingness to dichotomize future therapeutic plans. Twenty percent were initially designated as DT. However, there was a significant impact over time on the initial intent strategies. In 2008, BTT was the most common initial intent strategy (>50%); by 2011, BTT was the least common (<25%)

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behind BTC (43%) and DT (35%). The approval of the Heartmate II LVAD for DT use by the Food and Drug Administration in January 2010 certainly impacted this trend. Pre-implant strategy also appeared to be driven by comorbidities (e.g., diabetes mellitus, malnutrition, ascites) and social risk, in that the BTC/DT patients (who had more comorbidities) generally had similar degrees of ventricular dysfunction and hemodynamic derangements compared to the BTT patients.

Two, and not surprisingly, survival (alive with LVAD or transplant) paralleled the intent strategy because level of illness (e.g., more comorbidities) tracked with the intent strategy. One-year survival with BTT (77.7%) was better than BTC (70.1%), which was better than DT (60.7%). Clinicians were also reasonably savvy at predicting outcomes in the BTC groups, for example, the “likely to list” survival (73.7%) approached BTT survival (77.7%), and the “moderately” or “unlikely to list” survival (62.8% and 62.9%, respectively) was similar to DT survival (60.7%).

Three, and arguably most important, the intent strategy changed after implant (Fig. 1). At 2 years, just short of half (43.5%) of the BTT patients (not transplanted but still with an LVAD) were no longer listed. In contrast, nearly a third (29.3%) of BTC patients were listed. Moreover, 14.6% of the DT patients still on support at 12 months were considered for transplant. In fact, duration of support, even in the BTT group, exceeded 2 years in a substantial number of patients. Such a finding highlights the variable course in advanced heart failure when the therapeutic intervention is extreme, i.e., surgical implantation of an LVAD.

The analysis has limitations. The study is limited to INTERMACS patients, although most patients receiving LVADs in the United States are in the registry. Pre-implant strategies were not protocol defined and therefore subject to significant variability due to such factors as regional transplant practice, center LVAD volume, and clinician experience. Post-transplant survival was not broken down by primary intent strategy so the pre-implant intent strategy could not be gauged as a predictor of transplant outcomes.

Reasons for a change in strategy were also not delineated, although surrogate markers could have been used to explore this issue further. Comfort with the DT designation may have also been affected by the HeartMate II approval occurring in the middle of the sample period. Finally, there is no discussion of patient perceptions of the differences between their original implant intent and their ultimate outcomes and/or change in implant intent over time. The life-saving nature of a therapy is not the only relevant criteria in a patient’s choice of therapeutic options (3).

This straightforward yet important study brings to light an elephant in the room. Is it even relevant to have a strategic intent at the time of LVAD implant other than to extend survival and improve quality of life? In this analysis, nearly half of the patients could not be categorized as BTT or DT. The distinction between transplant and nontransplant candidates is arbitrary and poorly defined by hard evidence. The condition, advanced heart failure, is the same; the affected populations are not distinct. In either case, the patient is ill enough to need circulatory support to avoid death and/or undue suffering from severe heart failure. The predominant issue is the nature of the circulatory support, in other words, biologic (transplant) versus mechanical (LVAD), that can be offered at that moment. The primary practical difference in the therapies is availability. Therefore, for any patient with medically refractory heart failure, the next therapeutic option should be directed by the available therapies at hand and not contingent on what therapies might be available in the future. In some regions, donor availability may allow transplantation in a reasonable time-frame, for example, 1 to 2 weeks. In other places, LVAD implantation is likely more prudent. In either situation, delaying circulatory support rarely improves outcomes.

As noted by Teuteberg et al. (2), doing away with intent strategies would free investigators from having to conduct separate studies for patients with the same problem. Trial designs could also employ novel “control” groups like a contemporaneous INTERMACS cohort as used in the ADVANCE (HeartWare Ventricular Assist Device (HVAD) Bridge to Transplant Trial) trial (4).

Clearly, heart transplantation is fixed by donor availability which is immutable. Ultimately, one might envision a time when all patients who are ill enough to need MCS will be provided with it, and transplantation will be limited to those with either complications of MCS (5,6) or patient/physician preferences. To some degree, this paradigm is currently operational in that most patients are transplanted as status 1 candidates, and an increasing number of such patients are supported by an LVAD (7). Many BTT patients were in fact getting long-term LVAD support comparable to the DT cohort, yet remained transplant candidates. However, such a system will require a reassessment of the current heart transplant allocation scheme, which has been recognized (5,6).

The MCS field is moving quickly in both technologic terms (e.g., smaller devices [8], transcatheter power

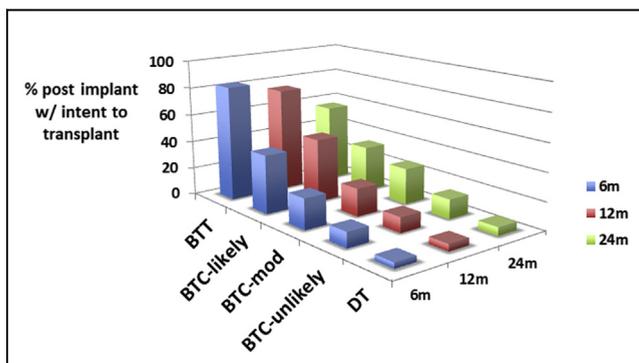


Figure 1 Bridge to Transplant Intent Over Time

Blue bars = 6 months; red bars = 12 months; green bars = 24 months. BTC = bridge to candidacy; BTT = bridge to transplant; DT = destination therapy.

sources) and management strategies (e.g., platform for adjuvant therapies [9]). But important challenges do remain. For example, only 30% of patients on LVAD support are truly free of a major adverse event (stroke, infection, device failure, bleeding) at 1 year after implant (1). We need to make sure that as this field rapidly evolves, labels do not usurp the ultimate goal and that patients are not defined by the nature of their therapies but by their individual situations and their personal choices.

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