Mechanical Circulatory Support
New Data, Old Problems

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Mechanical devices to support the circulation in the presence of a “failing” heart were originally conceived as alternatives to biological replacement of the heart. Such alternatives are needed because of the problems inherent in allotransplantation. These have included the grossly inadequate supply of donor hearts, as well as the need for chronic immunosuppression and the myriad of complications attendant on its use. Thus far, however, such devices have been employed primarily as “bridges” to extend the survival of desperately ill patients until an appropriate donor heart becomes available. Although such use has been a productive endeavor in terms of gaining experience with the devices and prolonging some lives that would otherwise have been lost before a donor became available, it has not increased the numbers of donors and has simply shifted the population of those who receive donor hearts to include sicker patients. The rare use of a mechanical device to provide temporary support as a bridge to myocardial recovery from some original insult deserves note but thus far appears to involve very small numbers of patients.1,2

The Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) study, published in 2001,3 was the first and is still the only randomized, controlled study to compare the use of permanent or “destination” mechanical circulatory support (left ventricular assist device, or LVAD, and the specific model called the HeartMate vented electric device, from Thoratec Corp, Pleasanton, Calif) with optimum medical therapy for a group of transplant-ineligible patients. The trial was positive in terms of a statistically significant survival benefit at 1 year for patients randomized to the LVAD. The data from the trial led to Food and Drug Administration approval of the use of a modified HeartMate XVE LVAD for the purpose of destination therapy in 2002.

However, although the results of this landmark trial were statistically significant and led to the Food and Drug Administration providing an equally landmark decision that allowed destination LVAD procedures and outcomes since the Food and Drug Administration approved the HeartMate device for this purpose in November 2002. Three hundred nine such implants have been reported between the inception of the registry and December 1, 2006. Follow-up in this analysis extended for another year, until December 1, 2006. Two hundred eighty of these 309 patients consented to participate in the registry, and 222 of these had sufficient preoperative data for analysis. The reasons for this were likely several. First, the subset of patients aged >70 years showed less benefit or no benefit in the REMATCH trial, yet that group would likely be a major part of the target population for wider use of LVADs, especially in the transplant-ineligible population. The second and perhaps even more important reason was the high frequency of device failure (35% at 2 years, with the device actually requiring replacement in 10 of 68 patients) and the fact that most deaths were related directly or indirectly to device therapy. The poor quality of life for the LVAD patients who never really recovered after surgery and spent most of their remaining life in the hospital might well (in some unmeasurable way) outweigh the modest improvement seen in those who had prompt physiological recovery. The field was in a state of evolution, and it was clear that newer generations of more durable and complication-free devices were needed before widespread clinical enthusiasm would become evident. Third, the devices and their management are very expensive,4,5 and if a large population of patients were to become candidates for destination LVAD therapy, the burden on the healthcare system could be enormous. For better or worse, probably only the first 2 reasons have thus far limited clinical application.

So, what more have we learned, and what has actually happened in the clinical world since approval of the device? In this edition of Circulation, an article by Lietz et al6 presents data from the US Food and Drug Administration–mandated Destination Therapy Registry, which has required enrollment from participating US hospitals of destination LVAD procedures and outcomes since the Food and Drug Administration approved the HeartMate device for this purpose in November 2002. Three hundred nine such implants have been reported between the inception of the registry and December 1, 2005. Follow-up in this analysis extended for another year, until December 1, 2006. Two hundred eighty of these 309 patients consented to participate in the registry, and 222 of these had sufficient preoperative data for analysis. The analysis of these data helps clarify several important questions and may help guide the clinician in making decisions about referring or selecting patients for possible destination LVAD therapy.

The first important question, given the high LVAD mortality rate and device malfunction rate in the REMATCH trial, would be: Have results gotten better? Has a normal learning curve, pump modifications, or patient management changes led to better outcomes? The answer would seem to be “no” or “not much.” In a prior report of 42 patients who received implants at the 4 highest-volume centers participating in the Thoratec Destination Therapy Registry, there was

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an increase in survival and a decrease in adverse events, particularly in the incidence of sepsis, in patients who received implants in the post-REMATCH era. These patients, however, represented a minority (28%) of the total registry patients. In the entire registry group reported here, the 1-year survival rate of 56% among the destination LVAD patients is not dissimilar to the REMATCH group’s rate of 52%, although the 2-year survival rate of 30.9% in the more recent cohort is somewhat better than the 23% seen in REMATCH. However, these survival curves actually may not be as good as they seem, because the authors censored 47 patients at the time of transplant and an unreported number at the time of reimplantation with pumps other than the HeartMate XVE. Had these alternatives not been available, the survival rates might have been even worse. There was still a 27% in-hospital postoperative mortality rate in this more recent group. Also, in this more recent group, 24.6% of patients still required device replacement or died as a direct result of pump failure (10 deaths, 6% of all deaths), and the probability of device exchange or fatal device failure was a dismaying 72.9% at 2 years. Sepsis also remained a major cause of death, accounting for 17 (41%) of 41 deaths in the LVAD group in REMATCH and 29% of deaths in the current registry data. Although the overall percentages may be the same or a bit better than in the REMATCH group, it is clear that there is still a lot of room for improvement, room that newer generations of devices will hopefully fill with better durability profiles and lower complication rates.

The second important question would be: Given the terribly ill patient population enrolled in REMATCH (control survival rate 25% at 1 year and 8% at 2 years), are we still implanting the same patients, or have the results of REMATCH led to a predictable “indication drift” to less sick patients? The answer would seem to be that more recent patients are less sick. The average age of patients in the newer cohort was 60 years, whereas it was 67 years in the REMATCH group, and fewer patients in the recent group had underlying ischemic cardiomyopathy. Importantly, 47 (17%) of the destination LVAD patients in this registry ultimately underwent heart transplantation, which attests to the unspoken but real shift to the use of devices as bridges to transplant eligibility rather than end points in and of themselves. These patients on LVADs reversed their secondary organ dysfunction or their pulmonary hypertension or other comorbidities that had made them transplant ineligible. Presumably, none of the patients in the REMATCH trial became transplant eligible.

This use of LVADs as bridges to transplant eligibility would appear to be a sensible use of the technology and highlights the fact that declaring a patient transplant ineligible at 1 point in time is not necessarily a final judgment and is often one that cannot be made definitively until a period of mechanical support has provided time for recovery. However, this still does not answer the question of whether the devices are appropriate alternatives to biological replacement of the heart, ultimately in transplant-eligible patients. This question represents the true “elephant in the room” that is not discussed. Given the limited donor supply, the population of transplant-eligible patients represents the biggest future issue in the field, and we still have no data with which to guide their candidacy for permanent mechanical support.

Lietz et al’s primary contribution consists of the construction of a risk score from registry in-hospital mortality data after LVAD implantation that may guide the clinician in determining patients for whom such therapy would truly be of benefit. The risk score constructed from the “usual suspects” for postoperative risk is something of a self-fulfilling prophecy but does help in identifying patients for whom an implant would be futile, especially because the causes and severity of heart failure were similar between the high- and low-risk groups. Such valuable insights into patient selection, if disseminated and implemented, may better define the population who could benefit from destination therapy.

Disclosures

None.

References


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