

Destination Mechanical Circulatory Support: Proposal for Clinical Standards

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Mechanical circulatory support device (MCSs) have evolved during the past 2 decades to become accepted bridging therapy for patients with irreversible hemodynamic deterioration while awaiting cardiac transplantation.¹ More recently, based on the results of the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) study,² MCS therapy has become available as permanent or destination therapy for a restricted population of patients with advanced heart failure (AHF) not thought to be appropriate transplant candidates. The potential proliferation of new devices and the possible expansion of the target populations bring new responsi-

bilities. Unlike pharmaceutical trials that have included thousands of patients, trials with MCSs will continue to be performed on a relatively small scale because equipoise for randomization can be undermined by the unmasked nature of mechanical support, the logistics of study finances, and the continuous device improvements—all of which constrain trial size and duration. Currently, insufficient evidence beyond REMATCH criteria exists for refining potential long-term MCS therapy candidate cohorts, and application of this challenging therapy is complicated further by the degree of institutional commitment, surgical expertise, multidisciplinary skills, available devices, and overall experience required for the successful application of mechanical circulatory support.

The REMATCH trial was a landmark study that demonstrated the benefit of MCSs in patients with AHF not eligible for transplantation. Patients supported with MCSs had significantly better survival at 1 year than did patients with advanced end-stage heart failure who were treated medically (many with long-term parenteral inotropes). Although a survival benefit was clear, it was only over a 2-year time period, and morbidity was substantial, particularly with respect to infections, neurologic events, and pump malfunctions.

These observations force us to consider carefully patient selection and the infrastructure of centers with strategies developed to provide this type of care. In the United States, the Food and Drug Administration (FDA) approval of the HeartMate

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device for chronic therapy occurred on November 25, 2002. Based on previous experience with newly marketed devices, procedures, and surgical techniques, 2 trends are likely after FDA approval: First, centers will begin to place devices into patients with a less dismal prognosis than the prognosis of those randomized in REMATCH. Second, the expansion of centers will lead to establishment of startup MCS D programs with less experience than established long-term MCS D centers and will lead to centers without on-site heart transplantation capabilities. Indeed, although the vast majority of implantable MCS D currently are placed in patients admitted to heart transplant centers, in time new "permanent MCS D" centers without these more expanded services may develop. These trends may decrease the survival benefit from destination MCS D therapy. In the worst case scenario, a detectable survival benefit may no longer exist in post-approval long-term MCS D implant practice, implying that destination MCS D therapy results only in switching the mode of death. Instead of dying of refractory heart failure, transplant-ineligible patients with AHF who receive mechanical support would die of infection, coagulopathies, neurologic events, or catastrophic device malfunction. Although observation of 129 patients in the REMATCH trial provided definitive evidence of benefit for this specific population, the trial neither adequately identified subsequent target populations nor defined centers in which the next phase of implementation should occur. The most appropriate suggestion may be that "destination MCS D centers" should resemble those participating in REMATCH. The immediate risks of uncritically generalizing REMATCH results may be device implantation in patients less likely to benefit.

Viewing this potential development within a social science perspective, it is important to avoid repeating history. We have to bear in mind the problems that led to a moratorium on cardiac transplantation in the 1970s and on artificial heart implantation in the 1980s, after an initial series of Jarvik-7 total artificial heart implantations.

To ensure high-quality and maximally effective destination MCS D services, a systematic strategy should be developed including 1) documentation of all destination MCS D implantations in an appropriate registry to facilitate risk-factor identification and the development of predictive models; 2) translational research on the impact of MCS D therapy on innate and adaptive immune responses, infection, coagulopathies, neurologic

dysfunction, and nutritional status; 3) expeditious and coordinated improvement of management practices; and 4) development of reimbursement rules and development of center standards for hospitals desiring to perform long-term MCS D therapy by regulatory bodies, such as the Centers for Medicare and Medicaid Services in the United States. Given the multidimensional challenge of the post-REMATCH era, a continuous collaborative strategy is in the best long-term interest of MCS D centers, manufacturers, regulatory agencies, and payors/insurers.

Since approval of the HeartMate device for long-term therapy occurred on November 5, 2002, decisions regarding reimbursement strategies are beginning to be established. Because such decisions will significantly influence which centers perform chronic MCS D implantation and will affect the overall health care impact of this therapy, it is appropriate for expert societies such as the International Society for Heart and Lung Transplantation (ISHLT) to provide funding agencies, such as the Centers for Medicare and Medicaid Services, in the United States with recommendations for selecting centers to perform destination MCS D implantation and to receive reimbursement. The ISHLT is uniquely positioned to develop recommendations because it provides an international framework with many diverse medical and surgical experts available for consultation who are involved in AHF and MCS D therapy. In collaboration with other professional societies, such recommendations could be tailored to the individual requirements of different countries. By their nature, any set of guidelines will somewhat limit use of this technology, especially in the early implementation phase. Although limited deployment of destination MCS D technology may seem counterproductive to those interested in more immediate expansion of this new technology, consistent optimization of outcomes from the start and appropriate patient selection eventually will provide the highest likelihood for acceptance by the public, by regulatory bodies, and by the cardiology community at large.

In suggesting policies for identifying centers that would qualify for long-term MCS D implantation programs, our over-riding commitment is to the protection and benefit of the individual patient. In this regard, the patient could most obviously receive harm from this complex therapy if the medical and surgical personnel and the institutional team did not have sufficient expertise. However, given the limited mid- and long-term efficacy data, it also is important

to prevent the use of this therapy in patients with AHF who could be treated more appropriately with medical therapy, heart transplantation, or other surgical therapies short of MCSD. If institutions or individuals make decisions for implantation who are not truly experienced and expert in the allocation of therapies for patients with AHF failure, proliferation of this therapy may result in the inappropriate use of MCSDs in patients who are “too well” (needlessly subjecting them to expensive and unproven long-term therapy) or “too ill” (those with multisystem dysfunction and a decreased probability of successful outcome).

IDENTIFYING CENTERS TO PERFORM DESTINATION MCSD IMPLANTATIONS

- **Option I:** *Restrict long-term MCSD implantation to REMATCH-participating heart transplantation centers. Rationale:* Only centers that participated in REMATCH will have the expertise to perform at the same level to ensure comparable outcomes.
- **Option II:** *Restrict long-term MCSD implantation to heart transplantation centers currently using MCSD as bridge to transplantation. Rationale:* Only centers that bridge patients with MCSD to cardiac transplantation will have the expertise to perform at levels that ensure outcomes comparable to those of REMATCH.
- **Option III:** *Use a staged approach: Stage I: Restrict long-term MCSD programs to hospitals as defined in Option II. Stage II: Expand long-term MCSD therapy to hospitals with established long-term cooperation with regional cardiac transplant programs and that meet a minimum set of established requirements for training and infrastructure. Rationale:* In Stage I, care must be taken that destination MCSD centers most closely match REMATCH centers to achieve outcomes/benefits similar to those of REMATCH. If Stage I is completed successfully, center inclusion can be broadened.
- **Option IV:** *Offer long-term MCSD programs to all interested hospitals that have cardiac surgery programs, with assessment of center-specific outcomes on an annual basis and continued approval based on achieving a target outcome level. Rationale:* All centers that perform cardiac surgery should have the opportunity to initiate programs and should be subjected to the same procedural algorithms.
- **Option V:** *Enforce fulfillment of a minimum set of requirements for training of physicians, surgeons, and other personnel and infrastructure, before initi-*

ating long-term MCSD programs in all interested centers, with assessment of center-specific outcomes on an annual basis and continued approval based on achieving target outcomes. Rationale: Fulfilling a set of minimum requirements (defined below) will maximize the likelihood of satisfactory performance and outcomes, balanced with the goal of disseminating the new therapy for the benefit of the large AHF population not eligible for heart transplantation.

ISHLT PROPOSAL FOR MINIMUM REQUIREMENTS FOR MCSD CENTERS

The ISHLT Board of Directors recommends Option V for identifying centers to perform long-term MCSD implantation, accompanied by strict and well-defined requirements for surgeon, physician, and center expertise. This option would provide patient safeguards in terms of requirements yet allow flexibility in terms of technology dissemination if and when justified, based on available evidence. The ISHLT proposes the following minimum requirements for destination MCSD centers:

1. A MCSD center should have an established heart failure program directed by specialized heart failure cardiologists who have extensive experience in advanced heart medical therapy,³ in the care of patients after heart transplantation, and in the care of patients receiving mechanical circulatory support as a bridge to transplantation with a potential for long-term use. At least one heart failure cardiologist must have expertise in managing all of these modalities and in appropriate allocation of specific therapies to individual patients, as determined by severity of heart failure and response to alternative therapies. Her/his experience must have been obtained at a heart failure, transplant, and ventricular assist-device bridging center in which the cardiologist had personal experience caring for 10 or more patients receiving MCSD support with the potential for therapy including out-of hospital care chronic (>2 months) support and patient ambulation. **Rationale:** Only with in-depth cardiologic understanding of the broadest spectrum of available medical, interventional, and surgical heart failure treatment options (including transplantation) can the potential benefit of long-term MCSD implantation be estimated. Specialized physicians working in transplant centers or established AHF centers who take care of patients with AHF on a

routine, full-time basis and who are involved in the daily decision-making about allocating medical, surgical, and transplant therapies would provide the best guarantee that new long-term MCS D therapy is implemented appropriately. Thus, long-term MCS D centers are expected to have cardiologists actively involved in AHF care who can responsibly allocate long-term MCS D therapy to appropriate patients.

2. The MCS D center must have established surgeons who are personally experienced and expert in implanting and managing MCS D devices with the potential for destination therapy. At least one surgeon in the MCS D center must work or have worked at a heart transplant, heart failure, or MCS D-bridging center and should have documented expertise in implantation, in peri-operative and post-operative management, and in removal of such devices. Her/his experience must include being the primary implanting surgeon of at least 10 MCS Ds which have the potential for chronic (>2 months) support and patient ambulation. **Rationale:** Appropriate surgical expertise in implantation and in surgical management of such devices is critical to optimizing surgical outcomes and to minimizing preventable surgical complications, which would be more likely if devices were implanted by surgeons with inadequate experience and expertise.
3. Other participating physicians, surgeons, and non-physician staff and faculty should have adequate training through educational fellowships and programs conducted at established long-term or bridge-to-transplant MCS D centers. **Rationale:** Only with sufficient expertise in bridge to transplantation or in long-term MCS D implantation can satisfactory outcomes be expected.
4. The center should have an established infrastructure for infectious disease management, post-MCS D nursing, and post-MCS D social work, with written protocols for pre-, intra-, and post-operative MCS D management, including end-of-life situations. **Rationale:** Only if these components are established in a long-term MCS D program can a maximum benefit from this new mode of therapy be expected.
5. The center must report volumes for the long-term mechanical support program and must report outcomes at 1 month, 6 months, and 12 months that meet or exceed previously established target volumes and outcomes for all such programs. **Rationale:** By comparing a center's outcomes and implant volume with agreed-upon

minimum numbers of procedures performed and reasonably expected outcomes for long-term MCS D support, a center's ability to deliver this therapy safely and effectively can be determined.

6. The MCS D center should have a quality-assurance program that includes participation in a national or international MCS D database such as the ISHLT-MCS D database. **Rationale:** Quality assurance programs constitute a major source of quality control for disseminating this new therapy. Because the mid- and long-term outcomes of MCS D therapy are uncertain, participation in a large national or international database committed to outcome research is critical.
7. The center should have an AHF-related research and teaching program. **Rationale:** This new mode of therapy implies an obligation to society to provide research to improve outcomes and to provide specific teaching programs to disseminate knowledge and skills about AHF management. Although these program components may enhance patient care, they also are highly desirable for overall evaluation and dissemination of this new mode of therapy.

Based on the above criteria, we envision that centers currently performing bridge-to-transplant MCS D implantation in an established AHF and heart transplant program probably would be able to meet these requirements immediately. Similarly, cardiologists and cardiac surgeons experienced in MCS D surgery, transplantation, and AHF therapy who have relocated to a non-transplant heart failure center would likely justify inclusion of their new center as a MCS D center if the appropriate infrastructure and personnel training were in place. If MCS D destination therapy is deemed efficacious for a sufficiently large sub-set of patients with AHF, additional centers wishing to provide this therapy could qualify by fulfilling the above requirements through the acquisition of appropriate surgical and cardiologic personnel (see requirements above) or through appropriate training. Finally, we recommend that coverage for these procedures be provided only to facilities meeting MCS D center criteria as outlined above and that these payments be adequate to meet reasonable cost requirements.

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