TESTIMONY

to the

MEDICARE COVERAGE ADVISORY COMMITTEE

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Presented by
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On behalf of the
AMERICAN COLLEGE OF CARDIOLOGY
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INTRODUCTION

The American College of Cardiology (ACC) appreciates the opportunity to testify today regarding Left Ventricular Assist Devices (LVAD) for Destination Therapy.

The ACC is a 28,000 member non-profit professional medical society and teaching institution whose purpose is to foster optimal cardiovascular care and disease prevention through professional education, promotion of research, development of standards of care, and formulation of healthcare policy. The College represents more than 90% of the cardiologists practicing in the United States.

My name is Dr. James Kirklin and I am a professor of surgery and Director of Cardiothoracic Transplantation at the University of Alabama at Birmingham. I am a member of the ACC Committee on Advanced Heart Failure/Heart Transplantation. I also serve as editor of the Journal of Heart and Lung Transplantation, the official publication of the International Society for Heart and Lung Transplantation.

BACKGROUND

On November 5, 2002, the United States Food and Drug Administration (FDA) approved the HeartMate device for chronic implantation (Destination Therapy) in selected patients with refractory advanced heart failure. However, decisions regarding coverage strategies are not yet established. Since such decisions will have a significant impact upon the selection of centers which will perform Mechanical Circulatory Support Device (MCSD) implantation as well as on the overall healthcare impact of this therapy, it is appropriate for expert professional societies to provide recommendations for the selection of centers to perform destination MCSD implantation. The document provided to you entitled "Destination Mechanical Circulatory Support-Proposal for Clinical Standards," was developed by members of the International Society for Heart and Lung Transplantation (ISHLT) with input from and collaboration with members of national cardiologic and cardiac surgical organizations. It has been endorsed by the ISHLT Board of Directors. The ACC's and AHA's Committees on Advanced Heart Failure/ Heart Transplantation agree with the ISHLT document.

LEFT VENTRICULAR ASSIST DEVICES (LVADs) FOR DESTINATION THERAPY: QUESTIONS FOR THE MEDICARE COVERAGE ADVISORY COMMITTEE

Voting Questions

1. *Is the evidence adequate to support LVAD use in patients meeting the Randomized Evaluation of Mechanical Assistance for the Treatment of Heart Failure (REMATCH) trial criteria? In your assessment of the evidence, please consider the appropriateness of endpoints, patient selection criteria, and the management and extent of complications. Are the actual 2-year survival data consistent with the Kaplan-Meier survival in the REMATCH article?*

The REMATCH trial was a landmark randomized multicenter clinical trial in which patients with persistent class IV heart failure symptoms for at least 90 days despite optimal medical therapy who were not eligible for heart transplantation were randomized to receive either continued medical therapy or MCSD support as definitive therapy. The highly significant doubling of survival at one year in this extremely ill population validates the effectiveness of this therapy in non-transplant patients. In addition to the improvement in survival at one year from 25% (medical therapy) to 52% (MCSD therapy), quality of life was significantly improved in the MCSD group. The patient population was one of the highest risk groups of advanced heart failure patients, as indicated by their generally advanced age (68 years in the medical group and 66 years in the MCSD group), class IV symptoms, and a majority on continuous inotropic therapy (72% in the medical group and 65% in MCSD group).

Although serious adverse events were more common in the MCSD group (many device-related), the improvement in survival occurred despite these complications. With technological improvements and development of methods to neutralize or prevent these potentially lethal events, the survival advantage would be expected to increase in the future. Although the survival of two years was low with MCSD therapy (23%), this was still nearly three times the survival with medical therapy. Among somewhat younger patients with refractory advanced heart failure not eligible for heart transplantation, the expected two-year survival would be higher.

2. *If the evidence is adequate, what is the size, if any, of the overall health effect of LVADs compared to optimal medical management for these patients? (See MCAC document "Recommendations for Evaluating Effectiveness" for categories of effectiveness).*

Given this significant survival advantage and improved quality of life in the REMATCH group, MCSD therapy would likely be **substantially more effective** than medical therapy.

Discussion Questions

1. *REMATCH showed increased survival in device recipients, but the survival advantage diminished over time and was associated with severe complications and increased hospitalization. Does the expectation of a relatively short extension of life and limited improvement in the quality of life justify the risks of LVAD implantation?*

Although the extension of life was generally less than 2 years in REMATCH (the only study which has addressed truly chronic implants), the major cause of death in the MCSD group was infection, a potentially preventable event which accounted for 40% of the overall MCSD deaths. The REMATCH trial itself provided some insights into possible reduction of device related mortality. The authors noted a 25% decrease in relative risk of MCSD deaths per year when survival was adjusted for the date of entry into the trial. Furthermore, infection (the major cause of MCSD mortality) was significantly reduced at two REMATCH centers that routinely utilized a patient harness designed to minimize movement of the drive-line at the skin exit site. In another multi-center controlled study of MCSD as a bridge-to-transplant, device-supported patients had a major increase in survival to transplant (71% vs. 36%, $p = .001$) compared to "control" patients (supported with inotropic agents with or without intra-aortic balloon pump support). Although this study does not provide data about longevity, it does support the superiority of MCSD's to medical therapy in this critically ill patient population.

2. *One REMATCH inclusion criterion was that a candidate for LVAD implantation for destination therapy could not be a heart transplant candidate. Should the evaluation to determine transplant candidacy be performed only by a heart transplant center that has been approved for Medicare reimbursement?*

The ISHLT proposal for clinical standards for MCSD center selection (see ISHLT document) recommends that potential MCSD patients should be evaluated by heart failure specialists who have extensive personal experience in evaluating patients for advanced heart failure medical therapy, transplantation, and MCSD-bridging therapy. In addition, they should have extensive experience and expertise in the management of patients receiving these therapies, as well as having surgeons who are experienced in transplantation and MCSD surgery participating in the evaluation process. This would usually occur at a Medicare-approved heart transplant center, but could occur at a hospital where the physicians and surgeons fulfill the requirements outlined in the ISHLT Proposal for Clinical Standards at a non-Medicare-approved heart transplant center or a non-transplant center where appropriate institutional resources and programs for Destination MCSD Therapy were in place.

3. *Initially, should there be specific facility (e.g. transplant center only) and personnel requirements that must be met to provide the patient with an optimal chance of successful LVAD implantation (e.g., adequate pre/post operative care, follow-up care, psychological support for patient/family, and end-of-life care)?*

We believe it is extremely important to have strict heart failure cardiologist, MCSD surgeon, and institutional requirements (as outlined in the ISHLT proposal) in order to maximize the likelihood of appropriate patient selection and outcome with this complex, expensive therapy.

The requirement for demonstrated expertise in the selection of patients, implantation techniques, and postoperative management of these patients is supported by the challenging nature of implementing MCSD therapy and the serious potential complications. Even in experienced centers, re-operation for postoperative **bleeding** occurs in 20% or more of patients after MCSD placement (Hampton, 2002). In the REMATCH trial, 42% of MCSD patients suffered bleeding complications (usually early after operation) within the first six months. Prevention of postoperative bleeding is particularly important because of its destabilizing effect on hemodynamics and its potentiating effect on postoperative infection.

With the large surface of the device and the current requirement for an external drive-line, patients with implantable MCSD have a high incidence of nosocomial bloodstream **infections** (reported at approximately 8 per one thousand device days at an experienced center), which are associated with increased mortality on device support (Gordon, 2001). The risk of death during MCSD support is increased about two-fold in the presence of gram-positive infections, five-fold with gram-negative infections, and ten-fold with fungal infections (Gordon, 2002). In the REMATCH trial, the probability of device infection was 28% by three months. Importantly, infection accounted for 41% of deaths in the MCSD group in REMATCH.

The potential for **device malfunction** is present throughout the life of the device, and requires expertise and experience for proper diagnosis and management, which may include device replacement in an often complicated surgical situation. Potential sources of device malfunction include inflow valve failure, erosions of the outflow graft secondary to kinking, rupture of pump lining, motor failure, and wear on bearings. These failure modes can be difficult to diagnosis rapidly and may be life threatening. In REMATCH, device failure was the second leading cause of death in the MCSD group, accounting for 17% of MCSD patient mortality. The need for expertise in outpatient MCSD management is underscored by the finding in REMATCH that no device failures occurred in the first twelve months, but the likelihood increased to 35% by 24 months, resulting in the need for device replacement in 10 of 38 MCSD patients who survived more than six months.

These important and potentially life-threatening complications underscore the challenges of this therapy. Even in experienced centers, with very experienced surgical, medical, and intensive care unit teams, successful reduction in the incidence and severity of these potential complications and their proper management requires labor-intensive and expert care. Achievement of favorable outcomes would be much less likely in the hands of inexperienced surgeons, MCSD physicians, and ICU personnel. As noted above, even with the already experienced centers of REMATCH, there was a 25% decrease in the relative risk of MCSD death per year when survival was adjusted for the date of entry into the trial.

4. *REMATCH results are based on LVAD implantation in 68 patients. Complete, timely, and accurate LVAD implant and outcomes data for destination therapy patients is critical to future Medicare coverage review and policy refinements. Should mandatory data reporting be required as a condition for Medicare reimbursement?*

Although this complex therapy holds great promise for a subset of patients with advanced heart failure, the mid- and long-term outcomes remain uncertain. Therefore, mandatory reporting of

outcomes data to a national or international database (such as the ISHLT MCSD Database) is critical for proper outcome analyses, risk factor assessments, and potentially patient-specific predictions.

RECOMMENDATIONS

In suggesting policies for identification of centers to perform chronic MCSD implantation, our overriding commitment is the protection and benefit of the individual patient. In this regard, the patient could most obviously receive harm if the medical and surgical personnel in the institutional team did not have sufficient expertise. However, perhaps equally important given the limited mid- and long-term efficacy data is prevention of the application of this therapy to patients with advanced heart failure who could more appropriately be treated with medical therapy, heart transplantation, or other surgical therapies short of MCSD. Thus, a major concern in the proliferation of this therapy is the inappropriate selection of MCSD for patients who are "too well" (thus needlessly subjected to an expensive and unproven long-term therapy) or "too ill" (with multisystem dysfunction and a low probability of successful outcome) if decisions for implantation are made by individuals or institutions not truly experienced and expert in the allocation of therapies for advanced heart failure.

Given the five options for identifying centers to perform destination MCSD implantation as outlined in the ISHLT document, members of the ACC's and AHA's Committees on Heart Failure/Transplantation favor **Option V**: **Enforce fulfillment of a minimum set of established requirements for physicians, surgeons, personnel, training, and infrastructure prior to initiation of chronic MCSD programs in all interested centers, with assessment of center-specific outcomes on an annual basis and continued approval based upon achievement of target outcomes.** We recommend that **Option V** be the system for identifying centers to perform chronic MCSD implantation, but with **strict and well-defined requirements for surgeon, physician, and center expertise**.

PROPOSAL FOR MINIMUM SET OF REQUIREMENTS FOR MCSD CENTERS

1. There should be an established heart failure program directed by specialized heart failure cardiologists who have extensive experience in advanced heart failure medical therapy, the care of patients following heart transplantation, and the management of patients receiving mechanical circulatory support as a bridge to transplantation with a potentially chronic MCSD. At least one heart failure cardiologist at the MCSD center must have expertise in management of all these modalities as well as appropriate allocation of specific therapies to individual patients as determined by severity of heart failure and a response to alternative therapies. His/her experience must have been obtained at a heart failure, transplant, and MCSD-bridging center in which he/she had personal experience caring for 10 or more patients on MCSD, including out-of-hospital, support of device types with the potential for chronic (greater than two months) support and patient ambulation.

Rationale: Specialized physicians working in transplant/advanced heart failure centers who take care of such patients on a routine full time basis and are involved in the daily decision-making process of allocating medical, surgical, and transplant therapies would provide the best guarantee that the new chronic MCSD therapy is implemented appropriately.

2. There should be established surgeons at the MCSD center who are personally experienced and expert at the implantation and management of MCSD. At least one surgeon at the MCSD center must have experience at a heart transplant, heart failure, MCSD- bridging center and have documented expertise at implantation, perioperative and postoperative management, and removal of such devices. His/her experience must include implantation as the primary implanting surgeon of at least 10 mechanical circulatory support devices which have the potential for chronic (greater than 2 months) support and patient ambulation.

   Rationale: Appropriate surgical expertise in the implantation and surgical management of such devices is of critical importance in order to optimize surgical outcomes and minimize preventable surgical complications which would be more likely if devices are implanted by surgeons with inadequate experience and expertise.

3. There must be adequate training for other participating physician, surgeon, and non-physician staff and faculty through educational fellowships and programs conducted at established chronic or bridge-to-transplant MCSD centers.

   Rationale: Only in the context of sufficient expertise of all personnel in bridge-to-transplantation or chronic MCSD implantation can satisfactory outcomes be expected.

4. There should be an established infrastructure for infectious disease management, post-MCSD nursing and post-MCSD social work, with written protocols for pre/infra/post-operative MCSD management, including end of life situations.

   Rationale: Only if these components are established in a chronic MCSD program can a maximal benefit be expected.

5. There will be required center reporting of chronic mechanical support program implant volumes and outcomes at one month, six months, and twelve months, which meet or exceed target volumes and outcomes for all such programs.

   Rationale: By comparing a center's outcomes and implant volume to an established minimum number of procedures performed and reasonably expected outcomes for chronic MCSD support, a center's ability to deliver this therapy safely and effectively can be examined.

6. There should be a Quality Assurance Program within the MCSD center, including participation in a national or international MCSD database such as that proposed by ISHLT.

Rationale: Because the mid- and long-term outcomes of MCSD therapy are uncertain, the participation in a large national or international database on MCSD therapy committed to outcomes research, such as the ISHLT MCSD Database, is of critical importance.

7. Advanced Heart Failure-related research and teaching programs should be in place.

Rationale: This new mode of therapy implies an obligation to society to provide research aimed at improving outcomes and refining appropriate patient selection as well as specific teaching programs to disseminate knowledge and skills about advanced heart failure management. Such programs are critical to the safe dissemination of this new mode of therapy.

CONCLUSIONS

Based on the above criteria, we envision that centers currently performing bridge-to-transplant MCSD implantation in the setting of an established advanced heart failure and heart transplant program would likely be able to meet these requirements immediately. Similarly, cardiologists and cardiac surgeons experienced in MCSD surgery as well as transplantation and advanced heart failure therapy who have relocated to a non-transplant heart failure center would likely justify inclusion of their new center as a MCSD center if the appropriate infrastructure and personnel training were in place. If MCSD Destination Therapy is deemed efficacious for a sufficiently large subset of advanced heart failure patients, additional centers wishing to provide this therapy could qualify by fulfilling the above requirements through the acquisition of appropriate surgical and cardiological personnel (see requirements above) or through appropriate training. Finally, it is our recommendation that coverage for these procedures only be provided to facilities meeting MCSD center criteria as outlined above.

The ACC appreciates the opportunity to testify before the MCAC panel on Ventricular Assist Devices for Destination Therapy.

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