Cardiac transplantation provides definitive management of severe heart failure in selected patients who have exhausted all other options. The results of transplantation have improved steadily as a result of improved immunosuppressive strategies, and advances in the therapy of post-transplant complications, such as infections and rejection, and in intensive care unit management (1,2). A severe donor shortage has limited the availability of donor hearts, resulting in prolonged waits for organs for patients with advanced heart failure and tenuous hemodynamics. This necessitated the development of left ventricular assist devices (LVADs) as bridges to transplantation to provide mechanical circulatory support for patients whose heart failure was refractory to other therapies, including inotropes (3). These devices are approved by the Food and Drug Administration (FDA) and are widely used. The first LVADs were pulsatile flow devices with an internal volume-displacement mechanism for pumping blood, powered by pneumatic or electric sources, and inflow and outflow valves. In many ways, these devices mimic the native circulatory systems that they were implanted to support with distinct periods of systole and diastole (4–6). LVADs improved survival in patients waiting for cardiac transplantation (3).

With >500,000 new cases of congestive heart failure diagnosed annually, cardiac transplantation remains an option for only a small fraction of these patients. By some estimates, as many as 200,000 patients who are not candidates for transplants would potentially benefit from mechanical circulatory support (7,8). This was the rationale for the REMATCH (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure) trial, which ushered in the era of destination therapy (9). This study demonstrated a significant improvement in survival for patients receiving pulsatile flow LVADs (Thoratec HeartMate, Thoratec Corporation, Pleasanton, California) compared with optimal medical therapy, which generally meant inotropic support. Improvements in functional class and quality of life were also noted.

Yet, the REMATCH trial also revealed the limitations of using pulsatile flow devices for long-term mechanical circulatory support. The 1-year survival for LVAD patients was only 52%, and device failure was frequent (9). Patients receiving LVADs also succumbed to device-related infections that were difficult to manage without device replacement. Of patients surviving 2 years with the pulsatile devices, 65% required replacement (10). The pulsatile devices’ large size also limited their use to larger patients. As a result of these limitations, the adoption of destination therapy for patients with refractory advanced heart failure who are not transplant candidates has been slow at best.

Several continuous flow pumps entered clinical trials within the past few years. These devices offered the potential advantages of smaller size, less extensive surgical procedures for implantation, and the rotary, continuous flow design that would improve durability and reduce the likelihood of device breakdown and malfunction (11–13). An initial experience of 133 patients receiving the HeartMate II continuous flow rotary pump LVAD as a bridge to transplant demonstrated a 75% 6-month and 68% 12-month survival with a significant improvement in functional class, 6-min walk test results, and quality of life (14). Complications included stroke, post-operative bleeding, right ventricular failure, percutaneous lead infection, and device thrombosis.

In this issue of the Journal, Pagani et al. (15) report the outcomes of 281 patients who have reached study end point or completed 18 months of post-operative follow-up in this bridge to transplant trial (ClinicalTrials.gov number NCT00121472). Patients at 33 centers in the U.S. who were waiting for cardiac transplantation and were United Network of Organ Sharing status 1A or 1B were enrolled with the HeartMate II LVAD implanted. Post-operative medical care was center specific. The primary end point was the percentage of patients who had received a cardiac transplant, had the LVAD explanted because of recovery of cardiac function, or who continued to have mechanical support with the LVAD at 18 months. The 281 patients included 18 months of follow-up for the original 133 patients reported previously (14). The population enrolled was particularly ill because a majority was receiving inotropic support, one third was supported by at least 2 inotropes, and 45% had intra-aortic balloon pump support.

At 18 months, 222 patients (79%) reached the primary end point of receiving a transplant, having the device explanted for cardiac recovery or ongoing mechanical circu-
latory support. Of these, 157 (56%) had undergone transplant, 58 (20.6%) were alive with LVAD support, 56 (20%) had died, and 7 (2.5%) had the device explanted for cardiac recovery. The median duration for mechanical support for all patients was 155 days. Overall patient survival with LVAD support was 82% at 6 months, 73% at 12 months, and 72% at 18 months. Major causes of death included sepsis (4%), stroke (4%), right ventricular failure (3%), device-related deaths (3%), and multigorgan failure (2%). Most of the deaths (77%) occurred within the first 6 post-operative months. Adverse events were frequent and included strokes (8.9%), localized device-related infections (30%), percutaneous lead infections (14%), and right ventricular failure (19%), most of whom needed inotropic support for at least 14 days. Most patients (59%) had at least 1 post-operative surgical procedure. Functional class, 6-min walk test, and quality of life were all significantly improved after 6 months of LVAD support compared with the pre-LVAD baseline. Hemodynamic support provided by the continuous flow LVADs was similar to that of pulsatile flow devices.

The study results suggest that comparable hemodynamic support and improvements in functional class, 6-min walk test results, and quality of life can be achieved with the continuous flow LVADs compared with the pulsatile flow devices but with improved survival compared to historical controls using the older LVADs (3,6,16,17). Adverse events, including infection, post-operative bleeding, right ventricular failure requiring right ventricular assist device support, and nonstroke neurological events were significantly less frequent with the continuous flow than the pulsatile flow LVADs when compared with historical control patients (3). There also were no mechanical failures related to the pumping mechanism in the continuous flow LVADs, although 11 patients required a pump exchange as the result of device thrombosis, infection, percutaneous lead fracture, or complications at the time of implantation. These results suggest that continuous-flow devices may not only provide more reliable methods of mechanical support for patients awaiting cardiac transplantation but may do this with fewer complications of infection and device failure.

Although the present study only involved the use of LVADs as bridges to transplant, the implications for destination therapy are apparent. Patients receiving LVADs permanently for mechanical support are even more in need of devices that are durable, less likely to fail, and less prone to infection as they have no backup therapy such as transplantation. The results of this study would at least provide preliminary evidence that continuous flow devices have advantages that would be appealing to patients receiving mechanical support for destination therapy.

There are limitations to this study, of which the most significant is the absence of randomization with a pulsatile flow LVAD approved by the FDA for bridge to transplant (such as the HeartMate LVAS) as a comparator. The results showing the superiority of the continuous flow devices compared with pulsatile devices using historic controls in studies ranging over a 10-year period (3,6,16,17). Comparison with the overall survival in the REMATCH trial may also not be entirely valid because the 52% annual survival in the LVAD group was for all comers and the REMATCH population by design included patients who were not transplant candidates (9).

However, there was a “learning curve” within the REMATCH study, with patients receiving LVADs later in the trial having better survival. This has also been observed in single-center results of destination therapy with pulsatile LVADs (18). Though the 18-month mortality in this cohort was 20%, rehospitalizations and surgical operations were still frequent occurrences in the present bridge-to-transplant study. Optimization of patient selection by use of recently published risk assessment scores may help reduce adverse events (19,20). Ultimately, the utility of continuous flow LVADs for destination therapy will be defined by the ongoing randomized trial comparing the HeartMate II to the HeartMate LVAS, which is the FDA approved device for destination therapy (ClinicalTrials.gov number NCT00121485).

**REFERENCES**


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