Benefits of DuraHeart™: 'a bridge to life' when treating end-stage heart disease

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“Newer devices were linked with better survival ... Third-generation left ventricular assist devices using more reliable technology such as DuraHeart™ are expected to perform even better.”

Currently, over 5 million American adults are afflicted with heart failure [1]. Although medical therapy has improved the outcomes for these patients, the prognosis of severe heart failure is still dismal. The 1-year mortality rate of those with end-stage heart failure exceeds 50% [1,2]. Heart transplantation is the gold standard treatment for end-stage heart disease. However, only a small number of patients can receive this therapy owing to the lack of donor hearts, while other patients are ineligible owing to coexisting medical conditions.

“...both the HeartWare and the DuraHeart have sophisticated software algorithms ... When determining the optimum treatment for patients with end-stage heart failure, newer left ventricular assist devices such as DuraHeart will provide a strong option...”

Implantable left ventricular assist devices (LVADs) have emerged as a viable therapy for use either as a ‘bridge to transplantation’ (BTT) or a ‘destination therapy’ (DT). Traditionally, LVADs had several limitations including large pump size, high infection rate, mechanical failures and thromboembolic events. The first-generation LVADs were large pulsatile, volume-displacement pumps. The second-generation models became much smaller and used axial flow with blood-immersed bearings. The latest third-generation models have a centrifugal pump using magnetic or hydrodynamic levitation of the internal impeller to avoid mechanical contacts inside the device housing. These new devices

promise better outcomes for patients with end-stage heart disease leading to the expanded use of LVAD therapy.

DuraHeart™ (Terumo Heart Corporation, MI, USA) is the world’s first third-generation LVAD. This device uses a magnetic levitation system that enables the impeller to float without any contact inside the blood chamber. It also has a back-up hydrodynamic bearing, in case of failure of the magnetic system. This new technology is designed to reduce thromboembolic events and achieve long-term durability. The DuraHeart was first implanted in Europe in 2004 and evaluated in a clinical trial [3]. In the USA and Canada, the clinical evaluation of this device has only recently begun.

Durability of DuraHeart

DuraHeart has mainly been used in European countries. In European trials of DuraHeart, 68 patients with advanced heart failure who were eligible for heart transplant were implanted with a DuraHeart device from January 2004 to July 2008 [3]. Of those, 33 patients were enrolled in the conformity mark in European Economic Area (CE-mark) study and 35 patients were enrolled in a postmarket study. Median age was 58 (range: 29–74) years. Mean support duration was 242 ± 243 (19–1148) days. A total of 35 patients (51%) remain alive with ongoing support, 18 transplanted, one explanted and 14 died during support. Kaplan–Meier survival rate was 81% at 6 months, 77% at 1 year and 61% at 2 years. In 33 CE-mark trial patients, the most frequently occurring adverse event was infection. In total, 58% of patients contracted an infection, but only six patients suffered device-related infections such as driveline or device pocket. This was

Keywords

- DuraHeart™ ■ heart failure
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a 90% reduced infection rate as compared with the first-generation LVAD (0.4 vs 3.49 per patient year) and was comparable to the small second-generation device (0.4 vs 0.37). There were no pump mechanical failures, pump thrombosis or hemolysis. This clinical trial demonstrated that DuraHeart is a safe and reliable device with long-term durability.

Expanded indication of LVAD implantation

Left ventricular assist device implantation is an option for patients with end-stage heart disease awaiting heart transplant. BTT therapy using LVADs began in the early 1980s [4]. Although there are no randomized trials comparing BTT therapy with medical therapy for heart transplant candidates, some retrospective studies have demonstrated significant benefits of LVAD therapy. Frazier *et al.* reported outcomes of BTT therapy using the first-generation LVAD, HeartMate® VE (Thoratec Corp., CA, USA) [5]. A total of 67% of patients survived to heart transplantation and 4% to device explantation for cardiac recovery. However, there were significant adverse events related to large pulsatile devices, including infection (in 40% of patients), bleeding (in 11% of patients) and thromboembolic events (in 6% of patients). Using the second-generation LVAD HeartMate II (Thoratec Corp., CA, USA), Pagani *et al.* presented an evaluation of 281 patients undergoing BTT therapy with HeartMate II [6]. At 18-month follow-up, 56% of patients had received heart transplantation, 21% required ongoing LVAD support, 2.5% underwent device explantation for recovery and 20% of patients had died. A total of 16% of patients had device-related infections such as driveline or device pocket. Device thrombosis was observed in only four patients. As LVADs evolved from the first to the second generation, BTT therapy improved survival rates of patients to heart transplantation.

“Left ventricular assist device therapy has become more accessible and reliable than ever before.”

The success of LVAD implantation as BTT therapy has led to the implementation of DT. Improvements in LVAD reliability have enabled device implantation in patients with end-stage heart failure as a permanent therapy in transplant-ineligible patients. The Randomized Evaluation of Mechanical Assistance in the Treatment of Congestive Heart Failure (REMATCH) trial

was a landmark trial published in 2001 [7]. It was the first randomized study to compare LVAD implantation with medical therapy in patients with end-stage heart failure who were ineligible for heart transplantation. A total of 129 transplant-ineligible patients were randomized to DT using either the first-generation LVAD, HeartMate XVE (Thoratec Corp.) or medical therapy. The results led to the first US FDA-approved device for DT. Patients with LVADs demonstrated significantly improved 1-year survival rates with medical therapy from 25 to 52% and 2-year survival rates ranging from 8 to 23%. The positive results in the REMATCH trial were achieved even though the study employed the larger pulsatile-flow device. Therefore, newer generation devices were expected to have better results. The HeartMate II DT trial is the newest randomized trial to evaluate the second-generation LVAD as DT [8]. A total of 200 patients with end-stage heart failure, who were ineligible for transplantation, were enrolled and randomized in a 2:1 ratio; 134 patients received a small axial flow device, HeartMate II, and 66 patients received a large pulsatile device, HeartMate XVE. Patients with HeartMate II had significantly improved 2-year survival as compared with patients with HeartMate XVE (58 vs 24%; $p = 0.008$). One-third of the HeartMate XVE devices required replacement over the 2-year study period as compared with only 10% of HeartMate II devices. Newer devices were linked with better survival and quality of life in transplant-ineligible patients with severe heart failure. Third-generation LVADs using more reliable technology such as DuraHeart are expected to perform even better.

Future perspective of LVAD therapy

At present, the DuraHeart and HeartWare Ventricular Assist Device (HVAD; HeartWare Inc., MA, USA) are commercially available centrifugal LVADs. The HVAD is a smaller device with a displacement volume of 50 cc and weight of 145 g. The impeller is suspended within the pump housing using a combination of passive magnetic and hydrodynamic levitation systems. This pump is designed to be implanted in the pericardial space, directly adjacent to the heart. Implantation in the pericardial space is expected to lead to relatively short surgery duration and quick recovery time. By contrast, DuraHeart is designed to be implanted into the preperitoneal pocket. It cannot be implanted in the pericardial space because of its size (a displacement volume of 180 cc and weight of 540 g). However, since 2004, there has been more clinical experience with

the DuraHeart LVAD than with the HVAD. A reliable and durable DuraHeart LVAD promises long-term left ventricular support without device failures and thromboembolic events.

In the future, the key factors that will drive device selection are the durability and reliability of the device itself, as well as ancillary equipment. Peripherals such as batteries, cables and controllers are becoming increasingly smaller and more patient friendly. The smaller batteries are also capable of providing better longevity. Furthermore, the incidence of false alarms (observed commonly with the first-generation devices) is reduced. Although the HeartMate II controller continues to have issues with frequent alarm states (mostly not clinically significant), both the HeartWare and the DuraHeart have sophisticated software algorithms and, in the case of HeartWare, the controller can instruct the patient on how to resolve alarm codes.

When determining the optimum treatment for patients with end-stage heart failure, newer LVADs such as DuraHeart will provide a strong

option for either 'BTT' or 'DT' indications. However, further clinical investigation will be necessary to evaluate the benefits of these third-generation LVADs.

Left ventricular assist device therapy has become more accessible and reliable than ever before. Physicians must be aware of the option of mechanical ventricular support for end-stage heart failure. The optimal timing of referrals, before patients develop irreversible complications, is the key to the success of LVAD implantation.

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