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Review

New era for therapeutic strategy for heart failure: Destination therapy by left ventricular assist device

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Summary Until 2010, Japan had been using the Toyobo (Nipro, Osaka, Japan) extracorporeal left ventricular assist device (VAD) developed 30 years ago as a 2—3 year bridge to transplantation (BTT). In contrast, western nations started to use implantable VADs in the 1980s that allow in-home care as destination therapy (DT) as well as BTT. Designated in 2007 as ''medical devices in high demand,'' the 5 major implantable mechanical hearts are smoothly undergoing clinical testing. The HeartMate XVE (Thoratec Corp., Pleasanton, CA, USA) gained approval from the Ministry of Health in November of 2009, the DuraHeart (TerumoHeart, Ann Arbor, MI, USA) and EVAHEART (Sun Medical, Nagano, Japan) in December 2010, and obtained formal insurance reimbursement in April 2011. The Jarvik 2000 (Jarvik Heart Inc., New York, NY, USA) and HeartMate II (Thoratec) VADs are pending approval. On the other hand, the organ transplantation law allowing explantation of donor organs from brain-dead patients finally passed in July 2009 and was realized in July 2010. This law paved the way to pediatric heart transplants as well as a dramatic increase in overall organ transplantation cases. Because many juvenile patients awaiting donor organs need a VAD as a long-term bridge, development and clinical introduction of pediatric VADs capable of implantation is an exigency. Although expectations for transplants are high, the donor numbers are low. Therefore, the demand for implantable VADs capable of long-term home treatment is extremely high in Japan.

Contents

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Introduction

In Japan, the development of ventricular assist devices (VADs) began in the 1960s [1,2], but the preliminary models were only used for post-operative cardiac failure [3]. In those terms, VADs were not used as a ''bridge to recovery (BTR),'' but as a temporary measure for self-recovery of the heart [4—6]. It was not intended for long-term care for chronic heart failure caused by cardiomyopathy. Recently, the connotation of BTR has significantly changed [7—9], as it now refers to the recovery of the heart through various means of treatment, incorporating surgery [10,11], medicine [12—14], cardiac resynchronization therapy [15—18], apheresis [19], and regenerative medicine [20,17,21], and not just the use of VADs.

On the other end of the spectrum, the artificial heart project that started in the USA during the 1960s aimed to make a replaceable and implantable ventricular device that would be the ultimate alternative to heart transplantation [22]. Because of this prestigious objective, it took nearly 30 years until the completion of AbioCor in 2000 (Abiomed, Danvers, MA, USA) (Fig. 1) [23]. However, in the realm of long-term versatility, it is still far from perfection. Although the term ''destination therapy (DT)'' insinuates an impeccable alternative to heart transplantation, because of the limits to long-term use at this time, it refers to the care of elderly or unfit patients that are not reasonable candidates for transplant [24]. However, if mechanical heart treatment can surpass the 10-year survival rate for heart transplantation, it is a reasonable vision that VADs will be the most common form of cardiac failure care, excluding the youth [25,26].

Artificial heart treatment in Japan

In Japan, VAD treatment started in 1980 at the Mitsui Hospital [3] as a remedy for postcardiotomy heart failure (PCHF) and by November 2009, there has been 1128 cases (Fig. 2) [27]. The majority of those cases are extracorporeal VADs manufactured by the Japanese company, Nipro (Osaka, Japan) (Fig. 3). The first reported case that a VAD was used as a bridge to transplantation (BTT) occurred in 1992 at the Saitama University Medical School and the Osaka University Hospital for a patient with dilated cardiomyopathy [a Nipro left (L)VAD was used]. The latter case is the first successful BTT, when a 16-year-old male patient went from the University of Osaka to Texas in the USA and endured a 150-day bridge period. After the 1997 establishment of the Organ Transplantation Law, heart transplantation also started, with the first case occurring in 1999 at the University of Osaka. By July 2010 before the revision of the Organ Transplantation Law, there were only 69 heart transplants. Unfortunately, because the number of donors is severely limited, almost 90% of patients resort to VADs as a BTT and the average bridge period surpasses 800 days. Due to this fact, the use of implantable VADs with minimal complications is imperative. However, only about 20% of VAD patients survive the bridge period, and patients who continue to wait for donors are in virtually the same situation as having received DT, even if the initial purpose was a BTT. A majority of patients with extracorporeal VADs require hospitalization, which still constitutes DT, but with a tremendously low quality of life (QOL). Furthermore, many cardiologists are still uneasy about DT for patients who are not eligible for transplantation [28,29]. On the bright side, the successful implementation of implantable LVADs will allow patients to return home and work, raising the QOL. Branching from this, patients may be able to seek high quality DT as an alternative to transplantation in the near future. Four kinds of implantable LVAD which were submitted with the request document from the relevant academic societies about the highest medical needs, HeartMate XVE (1st generation), EVAHEART (2nd generation), DuraHeart (3rd generation), and Jarvik 2000 (2nd generation) in 2007 and one more added, HeartMate II (2nd generation), in 2011. The HeartMate XVE gained approval from the Ministry of Health in November of 2009, the DuraHeart and EVAHEART in December 2010 and obtained formal insurance reimbursement in April 2011. The Jarvik 2000 and HeartMate II VADs are pending approval. We have treated 20 patients with implantable continuous flow LVADs (EVAHEART: 8, DuraHeart: 8, Jarvik 2000: 3, HeartMate II: 1) (Fig. 4) since 2007 in the University of Tokyo Hospital and the clinical outcome of implantable LVADs is quite different from that of paracorporeal Nipro VAD (Fig. 5).

Implantable VAD use in destination therapy

In recent years, many Japanese academic conferences disputed the meaning of DT with the use of implantable LVADs. In 2008, the definition, ''long-term home treatment,'' was proposed and it has been generally accepted ever since [30]. In the past many total artificial hearts (TAH), such as the 1980 Jarvik 7 [31] and the 2001 AbioCor, underwent clinical trials [32] but none were able to achieve success in DT. Rather in the past 10 years, the use of implantable LVADs in DT for patients not eligible for heart transplants dramatically increased. In the 2001 HeartMate VE REMATCH study (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure) [33], the results showed that HeartMate VE LVAD treatment excelled over internal therapy. In 2002, the US Food and Drug Administration (FDA) approved the HeartMate VE for DT. Furthermore, in 2005, the HeartMate XVE study showed similar results, which certified increasing DT records (Fig. 6). In the USA, the HeartMate II underwent clinical trials for DT and