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EDITORIAL

Mechanical Circulatory Support for the Failing Heart – Progress, Pitfalls and Promises

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Heart failure remains the dominant cause of death in industrialised countries, with most of the disease occurring in the elderly [1]. In Australia, it is the most common cause for hospitalisation and is associated with significant morbidity, mortality and immense costs for the hospital system. Efforts to shift care into the community have been successful with heart failure management programs, however more than $AUD1B is spent on inpatient hospital heart failure care annually [1]. However, a significant proportion of patients suffer heart failure throughout the entire span of life from infancy, through adolescence, into adulthood and older age. It is these younger patients with severe heart failure who remain the current focus of advanced therapies including mechanical circulatory support, with medical therapy having made significant inroads into the stabilisation and management of less severe forms. For suitable patients, heart transplantation remains the treatment of choice [2], but continues to be limited by donor shortages throughout the world despite focussed medical, societal and governmental efforts to increase awareness and donation rates [3]. With persistently high rates of waiting list deaths for those on the heart transplantation list despite implantable defibrillators, cardiac resynchronisation and optimal medical therapy, mechanical circulatory support (MCS) has been successful in bridging critically ill patients, who previously would have been expected to die, to subsequent transplantation [4,5]. The success of MCS and the shortage of organ donors, has resulted in most heart transplant waiting lists having 40-50% of patients waiting on a chronic mechanical support device [6]. Here we review the significant progress of MCS in the last decade and foresee that, with ongoing improvements, it is feasible that destination therapy will become an accepted part of advanced heart failure management in some patient groups and that the next decade will bring the first clinical trial of mechanical organ replacement versus human organ transplantation.

What devices are available for use? There have been significant changes in the MCS field with three generations of left ventricular assist devices (LVADs) on the market. As seen in Figure 1 (from [7]), first-generation pulsatile LVADs, such as the 1998 HeartMate XVE (Thoratec Inc, Pleasanton, Calif, US) which represented 80% of chronic implants in 2006, are no longer implanted. Rather, second and third generation continuous flow LVADs (cfLVADs) have increased from 1% in 2006 to 97% of chronic implants in 2013 [7]. They have proved to be more durable and reliable although not without their own problems, with the two most commonly implanted pumps worldwide being the centrifugal-flow HeartWare Ventricular Assist System (HVAD) (HeartWare International Inc, Framingham, MA, US) and the axial-flow HeartMate II (HMII_ (Thoratec Inc, US)). (The centrifugal flow VentraCor LVAD, designed and manufactured in Australia, failed as a result of financial stress rather than significant design flaws, and was largely superseded by the HeartWare HVAD pump.) Short term biventricular support is available with external pump drivers including the pulsatile Thoratec paracorporeal VAD (PVAD) or venopulmonary artery extracorporeal membrane oxygenation (VPA-ECMO) with external centrifugal pumps in combination with an LVAD, but make up less than1% of total pump implants. Chronic biventricular replacement is available with the Syncardia total artificial heart (TAH), with a gradual increase to nearly 3% of implants. The Syncardia is a pulsatile pump and uses an external pneumatic driver, recently updated for increased mobility. Recently the concept of implanting two cfLVADs has been suggested, with some promise, although a formal

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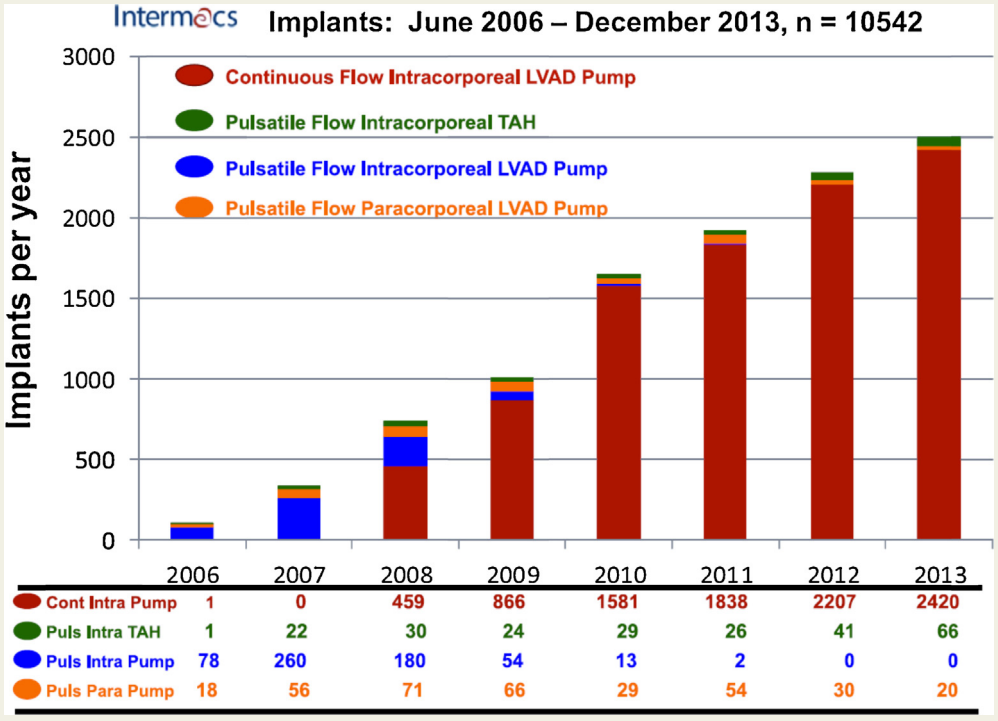

Figure 1 Primary adult implants in the INTERMACS registry by year of implant (from Ref [7]) (Kirklin et al., JHLT 2014).

trial of such configuration is yet to start. Devices implanted at St Vincent's over the last 30 years, since the inception of the mechanical and circulatory support program in 1994, are shown in Figure 2.

Most recently, LVADS have started down the route of miniaturisation with the recent development of the HeartWare Miniature Ventricular Assist Device (MVAD) and the centrifugal-flow HeartMate III. These newer devices are able to induce pulsatile fluctuations in flow through software manipulation of pump rotor speed, to try to, among other things, normalise vascular responses and encourage aortic valve opening [8].

What are the current indications for using these devices? Although LVADs were first approved for a bridge-to-transplant (BTT) indication, it was the landmark Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Cardiac Heart Failure (REMATCH) Trial in 2001 which suggested that these pumps could provide significant survival benefit compared with medical therapy in patients with end-stage heart failure (New York Heart Association Class IV) ineligible for transplantation [9]. This was followed up by a further study using the HeartMate II axial flow cfLVADs to show an even further improvement in outcomes [10]. Overall, the sixth INTERMACS annual report gives survival rates (for more than 10,000 patients in the database) of 80%, 70%, 59% and 47% after one, two, three and four years, respectively [7]. The subsequent approval for destination therapy (DT) by the United States Food and Drug Agency (FDA) in 2010 resulted in a massive uptake across the country, with non-transplant centres joining the more established programs to demonstrate excellent outcomes across a wide range of patients [7]. The almost exponential rate of increase in implantations has caused pause for thought from other countries, with the DT indication only approved specifically in USA. Other countries have tacit DT approval due to low transplant rates, meaning that patients are implanted with little realistic likelihood of transplantation. While both are approved for use in Australia, HMII and HVAD are indicated for BTT, they have a more general approval for management of severe heart failure without mention of transplantation. However, reimbursement for the cost of care for these patients is only linked to acceptance onto a transplant waiting list, meaning that DT therapy is not available in Australian public hospitals. An Australian destination clinical trial has been developed and is currently awaiting final approval to commence.

One of the indications that has proved challenging is ''bridge-to-candidacy'' for patients currently too unwell to be considered for heart transplant listing, but with the possibility of non-cardiac organ improvement, including rehabilitation, with subsequent reconsideration for transplant listing. Unfortunately these patients, by definition, have greater co-morbidities and are at greater risk of poor post-pump outcomes [7]. The hope of LVAD-induced ''recovery'' or remodelling has only been shown to occur in a very small cohort of carefully selected patients, despite aggressive medical therapies.

Which patients are selected for device implantation? With increased experience, many centres have developed strict eligibility criteria in considering potential LVAD patients.