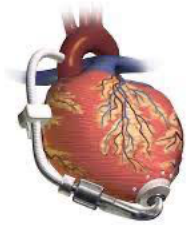

Good News and Bad News: The Cost of Mending a Broken Heart
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The approval of a new treatment protocol known as "destination therapy" highlights the realities of today's health economics. This article discusses the technology, the economics and the philosophy of the newly approved left-ventricular-assist systems.

A landmark decision

I am writing this article in the week before Christmas, a time traditionally associated with generosity and goodwill. For sufferers of congestive heart failure, and particularly those who are moving inexorably to the point of no return with end-stage organ failure, there has been some very good news recently, which could put them in a somewhat better frame of mind.

One year ago, the results of the clinical trial on Thoratec's Heartmate Left-Ventricular-Assist System, referred to as the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH), were published and the data was analyzed by the Food and Drug Administration (FDA).[1] Initially, in view of the risks of side effects associated with the device, it had approval only for patients who were seriously ill and it was still considered to be a "bridge-to-transplant." On 6 November 2002, however, the FDA announced that it was giving approval for the device to be used as a long-term, permanent treatment for end-stage congestive heart failure, including for those who, for a variety of reasons, do not qualify for heart transplantation.[2,3] This landmark decision to permit this new treatment protocol, which is now being referred to as "destination therapy," is extremely welcome, but there are consequential effects of this change of approval criteria that have to be explored with some urgency. This article discusses the good news and the bad news.

The results of the REMATCH

Let us consider for a moment the nature of the technology associated with Thoratec's Heartmate Left-Ventricular-Assist System and assess the clinical outcomes. Thoratec has developed electrically powered and pneumatically driven devices; REMATCH was concerned with the former and is designated the Heartmate VE LVAS, VE indicating the vented electric device. It is implanted in the abdomen and works in parallel with the patient's own heart. Blood is channeled into the device by means of a conduit attached to the left ventricle. Once blood empties into the pump, a control system triggers the pumping process and a polyurethane diaphragm pressurizes the chamber and forces the blood through an outflow conduit directly into the aorta. Two tissue valves, one on either side of the pumping chamber, control directionality of

blood flow. Titanium is extensively used in the structural components of the device. The blood contacting surfaces are textured through the use of sintered titanium microspheres in an attempt to stimulate the formation of a tissue layer, thereby improving blood compatibility. The implant is powered by two rechargeable batteries that are worn externally and attached to the system controller. Fully charged batteries last for approximately six hours and the patients can live a near normal lifestyle, at least from the cardiological point of view.

The Heartmate has been in clinical use as a bridge-to- transplant since the early 1990s and has a CE mark for this use. In the REMATCH clinical trial, 129 patients were randomly assigned to receive the LVAS (68 patients) or to be treated by medical management (61 patients).All patients had end-stage heart failure, classified as New York Heart Association Grade rv, with a series of strict physiological and hemodynamic inclusion criteria, and all were ineligible for transplantation. Once out of hospital, patients were monitored on a monthly basis, with the primary end-point being death from any cause. Enrolment took place between May 1998 and July 2001. The results were remarkable. The Kaplan-Meier curves (the plots that give percentage survival as a function of time) showed that there was a reduction of 48% in the risk of death from any cause in the group that received the LVAS, compared with the medically managed group, with a relative risk of 0.52.Thus, estimates of survival at one year were 52% in the device group and 25% in the medical therapy treated group, and at two years, 23% and 8%, respectively. Median survival was 408 days in the device group and 150 days in the medical therapy group. It was further shown that the benefits were greatest in the younger cohorts of patients. One year's survival in patients under the age of 60 was 74% for device-treated patients and 33% for medical therapy treated group. The corresponding figures for the 60-69 year old group were 47% and 15%, respectively. One interesting finding was that there was no difference in the quality of life index between the two groups. This is a matter of some significance because results from the first types of totally implantable artificial heart showed that prolongation of life was often achieved at an unacceptable quality of life.

All this is good news for prospective patients. So where is the bad news? This comes from two different directions, which may be related.

The materials and mechanics

Notwithstanding the prolonged life expectancy and maintenance of quality of life, those patients receiving the Heartmate experienced a significant number of adverse events, at a rate more than double that experienced by the control group. There was a predominance of infection, bleeding and device malfunction, and evidence of a high incidence of neurological events. Infection has always been a serious issue with any percutaneous device. Within three months of implantation, the probability of infection of the device was 28% and although many incidents were confined to the drive-line tract and pocket, fatal sepsis was common, accounting for 41% of the deaths in this group. The incidence of ischemic stroke was low, suggesting that few serious blood compatibility problems existed. This has been attributed to the textured titanium surface, although the clinical evidence for this is not clear. It is notable that bleeding was common (42% of device-treated patients had problems), which suggests that the anticoagulation regime may have erred on the side of caution with respect to clotting compared with bleeding. This delicate balance

between coagulation and hemorrhage was demonstrated further by the fact that the rate of neurological events in the device group was 4.35 times higher than in the control group, which suggests a significant problem of microemboli release and subsequent minor arterial blockages in the brain. As far as the device performance was concerned, no catastrophic fatal failure occurred, but the probability of device failure of some sort was 35% at two years, and it was necessary to replace the device in 10 cases.

All this shows that, although recognizing the tremendous clinical success achieved in the REMATCH trial, the well-known biomechanical and biomaterials problems have clearly not yet been completely solved. This is, however, a minor salutary lesson, rather than a major disaster, and we must look elsewhere for the real bad news.

The realities of health economics

The price of this success is high, precisely how high and how affordable remains to be seen. Costs are difficult to determine at this stage, but the median hospital cost for the procedure, including the device was US$142 000.[4] Taking the median survival time as 400 days, this implies an average additional cost (of living) of US$350 per day. At the present time, health insurers have not decided whether this "destination therapy" would be covered in the United States. The position in Europe would be variable because of the differences in the balance between public and private health insurance, but sums of this amount are bound to cause concern within the industry. The bad news is, therefore, that we could have a life-saving treatment modality that is unaffordable for the vast majority of potential recipients. The health-care sector has been here before, of course, with several examples of hugely expensive drugs and surgical procedures, but we have to wonder if any lessons have been learnt. It may well be that the cost of using the Heartmate could come down with the wider acceptance of the device and the procedure. There could even be some healthy competition with companies such as Arrow,[5] World Heart[6] and MicroMed [7] all having made significant progress with similar systems, but it is hard to see this making much difference. The average cost quoted above takes into account the costs associated with the high incidence of sepsis and resolution of this issue should bring the figure down.

The underlying problem here lies with the difficulties of matching the high costs associated with the development and evaluation of complex medical devices (and the corresponding delay in achieving any return from investment), with the downward pressure on healthcare costs and the reluctance of insurers to pay for the real costs of medical device related treatment. As many devices have become more complex and the requirements for testing become more onerous, the gulf is getting bigger. Even more significant is the trend towards more biologically active devices and the introduction of tissue-engineered products into clinical practice. This will exacerbate these difficulties, many of the products of the future requiring a pharmaceutical-size investment but reaping only medical-device size rewards. It was no wonder that the share price of Thoratec (THOR quoted on NASDAQ), which was around US$16 at the time of the REMATCH announcement has fallen in the last year; it has fallen further since the announcement of FDA approval in November 2002 (US$7.8 at the time of writing). The US market for heart-assist devices is estimated to be of the order of US$2.5 billion. This is a strange response from investors to a company about to lead the way into that market, even taking into account the current uncertainties of the market in general.

Commitment is the key ingredient

Having discussed the technology and the economics, we should finish on the philosophy. This situation has an immense ethical dimension. The artificial heart has been around for more than 30 years, but it has taken a long time to progress to the state we experience today. In the early years, investigators could only use the total implantable artificial heart in patients of such poor prognosis that they would have died immediately if they had not been fitted with the device. As an exercise in precaution, this was admirable. However, as a strategy for the ambitious development of new technologies, it was lamentable. It is an understandable strategy, probably an ethical one, but not a sensible one. Technology does not succeed without commitment and you cannot be committed if all the odds are deliberately stacked against you. As Goethe wrote, "Until one is committed, there is hesitancy ... the moment one definitely commits oneself, then providence moves all." So it is with the healthcare system we are discussing here: there has to be commitment from the whole system if this technology is really to succeed. Let us hope that the REMATCH trial and the boldness of the decision to approve this "destination therapy" will allow this technology to move much faster. The technical deficiencies that undoubtedly still exist will be resolved through the greater clinical experience. It is time for the good news-bad news scenario to be corrected.

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