The Place of Assist Devices in the Treatment of Heart Failure

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Abstract

Ventricular assist device (VAD) surgery, "surgery" because of the high specificity of the procedure requiring adequate diagnostic possibility and organisation of the surgical and medical team has become an effective and dynamically developed option for treatment of end-stage heart failure (HF). The first implantation of a total artificial heart in a human was done by Cooley on April 4, 1969 in the United States and since that time the dynamic evolution from the concept of saving the lives of patients has converted into optional implantation of VAD. This procedure is not only applied as a last step but also as the treatment of choice when transplantation is not advocated or contraindicated. The Deutsches Herzzentrum Berlin (DHZB) under Professor Hetzer's supervision and leadership started a VAD surgery programme immediately after the foundation of the institution and a team of specialists is responsible for taking care of these special patients and also caring for them as outpatients.

The first implantation of an artificial heart as "Bridge to Transplantation" was done by R. Hetzer in July 1987. Between 04/1986 and 04/2008 a of total 1554 transplantations and 1243 VADs were implanted. The youngest recipient of a VAD was 8 days old and the oldest 71 years old. VAD surgery today incorporates several basic options: 1) assist device as a supporting tool for conservative surgery (reconstructive surgery in the severely diseased heart, heart infarction surgery, coronary bypass surgery, reconstructive surgery in heart infarction complications); 2) supporting options for transplantation programme: a) bridge to transplant, b) bridge to recovery after graft failure, c) bridge to re-transplant after graft failure; 3) independent sector of the assist device programme: a) "Bridge to Recovery" programme; b) permanent non-biological cardiac replacement (destination therapy); 4) paediatric assist device programme.

Paediatric surgery was established and developed in DHZB and continues to receive special attention as the results are very good and spontaneous recovery in children can be achieved in a substantial number of cases. This is a very encouraging message for the future of independent use of VADs which we also observe in adults.

Streszczenie

Wraz ze wzrostem odsetka przeżywalności chorych obserwuje się zwiększenie częstości występowania niewydolności krążenia (NK). Na tle całego wachlarza metod leczenia NK, które nie wyszły wciąż z obszaru eksperymentalnego, leczenie przy użyciu wszczepiania komór jawi sie nierzadko jako jedyna opcja ratująca życie chorego. W ostatnich latach stosowanie sztucznych komór serca (SK) zostało ugruntowane, a opcje użycia znacznie rozszerzone. W klasycznym ujęciu SK stosuje się w przypadku konieczności pomostowania do przeszczepu serca. Opcja ta stosowana jest w sytuacjach, gdy chory zakwalifikowany do przeszczepu nie jest w stanie dożyć momentu transplantacji, gdyż znaczne pogorszenie sytuacji hemodynamicznej pacjenta nie rokuje na utrzymanie przy życiu w oparciu o klasyczne leczenie. Dlatego program transplantacji jest znakomicie wspierany przez program, który można dziś określić „chirurgią sztucznego serca" (CSS). W taki sposób „chirurgia sztucznego serca" funkcjonowała jako pierwotna opcja zastosowania sztucznego serca, tj. jako pomostowanie do transplantacji, zapoczątkowane w 1986 r. w klinice Cliveland. Operacja ta wykonana była 15 lat po pierwszym wszczepieniu sztucznego serca u człowieka jako *total artifitial heart* (TAH), kiedy to po usunięciu chorego serca dokonano wszczepienia sztucznych komór. Operację tę wykonał Cooley w 1969 r. W 1988 r., dwa lata po operacji w Cliveland, pierwszego wszczepienia sztucznego serca w Niemczech dokonał (także w opcji udanego pomostowania do transplantacji) prof. Hetzer w DHZB w Berlinie. Ten sam operator w Berlinie zapoczątkował program wszczepiania sztucznego serca u niemowląt i małych dzieci. Ponadto, jako pierwszy na świecie, funkcjonowanie tego programu zapoczątkował udaną operacją pomostowania do, także udanej, transplantacji u dziecka w 8. dniu życia. Wskazania do pomostowania do transplantacji opierają sie na ocenie klinicznej oraz zastosowaniu następujących kryteriów hemodynamicznych: 1) obecność kwasicy metabolicznej; 2) zmniejszony indeks serca <2,0 l/min/m^2; 3) zaburzenie perfuzji obwodowej stwierdzanej w badaniu przedmiotowym; 4) spadek utlenowania krwi <40%; 5) oliguria (<1 ml/kg/min); 6) konieczność zwiększania zawartości tlenu u chorych z wentylacją mechaniczną

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Currently the DHZB has 36 surviving patients with idiopathic dilated cardiomyopathy among 83 patients weaned from VADs since 3/1995 after an average of 333 days of support. The figure for post-weaning 10-year survival with native hearts has reached 70.7±9.2%, which is better than the life expectancy after heart transplantation. Including post-transplant survival for patients with recurrent heart failure (successfully transplanted patients) the overall 5- and 10-year survival is even better than transplantation and reaches 79.1 and 75.3% respectively.

There are several diseases in infants and adults that are potentially treatable surgically on the basis of a VAD or when a "stand-by" assist device is taken into account. This is promising news when VAD surgery is reaching a higher standard on the basis of new technological developments. Regardless of the highly developed technologies and standards, the human aspect should rank first.

Key words: ventricular assist device, heart failure.

Od tego czasu wskazania do SK w chirurgii znacznie poszerzono. W DHZB w latach 1986–2008 wykonano 1554 przeszczepy serca, w tym 46 powtórnych transplantacji. W tym samym czasie dokonano 1243 wszczepień sztucznego serca, korzystając z osiemnastu rożnych typów sztucznych serc. Program chirurgii sztucznego serca stał się w znacznym stopniu programem uniezależnionym od transplantacji. Obecnie wszczepienie SK wykonuje się w następujących opcjach chirurgicznych: 1) przy wspomaganiu chirurgii „konserwatywnej" w takich działach, jak: chirurgia rekonstrukcyjna, gdzie wydolność serca jest bardzo obniżona (EF≤25%), w tzw. chirurgii ostrego zawału serca, także z bardzo upośledzoną funkcją krążenia, a nawet u chorego w stanie wstrząsu kardiogennego – aby podać działy najczęściej wymagające wspomagania CSS; 2) przy wspomaganiu transplantacji, w której wyróżnia się obecnie podgrupy: a) pomostowanie do transplantacji, o którym już wspominano; b) tzw. pomostowanie do czasu powrotu funkcji serca do normy (dotyczy kardiomiopatii rozstrzeniowej, jak również ostrego ciężkiego zapalenia mięśnia sercowego określanego jako *fulminant myocarditis*). W tym dziale osiągnięcia DHZB są wyjątkowe, ponieważ dokonane były jako pierwsze w świecie, a podjęte w marcu 1995 r. Od tego czasu 36 chorych z grupy 83 z kardiomiopatią rozstrzeniową żyje bez potrzeby stosowania SK po odłączeniu od wspomagania. Chorzy ci średnio po 333 dniach wspomagania z użyciem SK i skutecznego leczenia farmakologicznego, dzięki skutecznej dekompresji i odciążeniu lewej komory, cieszą się trwałą poprawą funkcji serca do wartości zbliżonej do normy lub normalnej. Ten dobry, choć nadal ograniczony w kontekście ogólnym, wynik leczenia z użyciem SK napawa optymizmem; 3) w chirurgii sztucznego serca: a) pomostowanie do czasu powrotu funkcji serca do normy (*recovery ad integrum*), o którym powyżej wspomniano; b) stosowanie SK jako leczenia docelowego. Opcja ta to wspomaganie wszczepieniem SK w sytuacji, w której istnieją przeciwwskazania do transplantacji, a zastosowanie tej opcji daje szansę na zapewnienie godnego życia w następnych latach.

Podsumowanie: Stosowanie sztucznego serca pozwala na ratowanie życia chorego, a także na przedłużanie życia w sytuacji, w której żadne inne środki nie są już dostępne. Chirurgia sztucznego serca może zapewnić godne życie chorym przy braku alternatywnych i skutecznych sposobów leczenia krańcowej niewydolności krążenia.

Słowa kluczowe: sztuczne serce, sztuczna komora.

Introduction

Aging of the general population seems to be a continual trend of our days. In parallel with this development, "semi-effective" treatment methods for heart failure, which used to be lethal, have become available and this has paradoxically led to a situation in which more and more patients suffer from chronic forms of heart failure. Thus, heart failure resistant to the classical medical means has become a major clinical problem everywhere and is likely to continue to be a growing field of clinicians' activity over time. Semi-effective methods of treatment mean that we are armed with plenty of methods to help patients suffering from heart failure, but that their quality of life is far from satisfactory after this traditional treatment.

Methods recently developed, such as myocardial replacement therapy, have, after the first enthusiasm, returned to the stage of medical trials with only potentially "good perspectives". Cardiac resynchronization therapy, which is widely accepted clinically, can be regarded only as "bridging to the next option," shifting advanced heart failure into a later period in the great majority of patients. The trend is that more and more patients who would have died from heart diseases receive life prolongation for a limited time after which, however, although all the other organs are in

good condition, heart failure returns as the main problem to be solved. The aim of this article is to document that today the realistic possibility exists of supplementing the diseased heart chamber by implantation of an assist device for univentricular or biventricular support or of removing the native heart and implanting an artificial substitute (total artificial heart, TAH).

The first replacement of total artificial heart into humans was done by Cooley on April 4, 1969 [1]. The idea of developing a mechanical substitute for the heart was first born of the need to save the lives of patients suffering from acute illness rather than to help patients with chronically diseased hearts. Application of a total artificial heart in an animal model at the Cleveland Clinic was reported in 1958 [2]. Successful bridge to transplantation with mechanical cardiocirculatory support was first performed in 1986 [3].

The first application in Germany as a "bridge" to transplantation of an artificial heart (known as the Bücherl heart after its developer) was by R. Hetzer in July 1987. At the same time Hetzer organized a special team at the Deutsches Herzzentrum Berlin (DHZB) to work on the further development of a ventricular assist device. The team reduced the discovery-to-delivery gap in introducing new technology. There were periods when the 24-hour-a-day activity of the team working on this issue kept us aware that new developments can really save patients' lives. The life could often be saved in cases where the illness progressed to the stage of "no return"; in the literature this haemodynamic situation is known as "true decompensation" [4]. Patients suffering from true cardiac decompensation could be saved only by mechanical support; even transplantation cannot be performed when the haemodynamic condition is disastrous and metabolic acidosis persists.

In July 1988 a product invented and developed by the Berlin team (Berlin Heart Excor VAD) led to successful bridge to transplantation. In October 1990 bridge to transplantation was successfully performed in an 8-year-old boy as the first procedure worldwide in a child. From the beginning, the most fascinating aspect of the assist device programme was the possibility of assist device implantation in infants and new-born children. It was observed that the severely diseased heart can recover after myocarditis treatment and biventricular support and that weaning from the assist device is sometimes possible. This discovery led to the idea that the process of weaning might be taken into account as a real treatment option. The first two (consecutive) patients for weaning were prospectively considered to be candidates for weaning before mechanical support was implanted on the basis of criteria accepted in our institution. The patients were successfully weaned from the assist device and are still alive 14 years later. Unfortunately, until today our scientific knowledge of weaning remains severely limited, so that it is not a prospective alternative in the treatment of heart failure; evidence-based criteria in this respect are still lacking. For this reason selection for weaning is undertaken after mechanical support is in place when the clinical development demonstrates such a possibility, although it is not prospectively assessable. Criteria for weaning were first established on the basis of DHZB experience and published in 1997 [5].

Recent VAD experience

The number of heart transplantations and the types and number of assist device implantations at our institution are given in Tables I and II.

Tab. I. Transplantation and Assist Device Programme, Deutsches Herzzentrum Berlin 04/1986-04/2008

	n
Heart transplantation, total	1554
– men	1257
– women	297
Re-transplantation, total	46
– acute	20
– chronic	26
Age	8 days–71 years
Assist device, total	1243

Tab. II. Types of assist device implanted at the Deutsches Herzzentrum Berlin 04/1986-04/2008

Bücherl TAH	2
Berlin Heart EXCOR	648
Novacor	116
TCI-HeartMate I	23
Abiomed	47
MicroMed DeBakey VAD I	40
Arrow LionHeart	6
Impella	33
Berlin Heart INCOR	169
Levitronix	48
Terumo DuraHeart	14
CardioWest TAH	42
Arrow CorAide	1
Thoratec HeartMate II	32
Combination	11
Jarvik 2000	7
VentrAssist	2
MicroMed DeBakey VAD II	2

Although the era of artificial cardiac support began at the end of the 1950s and its clinical use started at the end of the 1980s, and although the available devices have undergone significant technological improvements during the past decade, the option of the use of mechanical circulatory assist devices is not yet being fully exploited. The basic explanation lies probably not in the technical difficulties that have to be faced by the surgeon but in the need for a special team that must be able to solve the clinical and technical problems arising during the interaction between the assist system and the human body. Thrombotic and haemorrhagic complications are the leading clinical problems in this respect. These factors make the use of VADs as a clinical tool less attractive and more expensive, and it is mainly hospitals with a well-developed transplant programme that are incorporating assist device treatment.

VAD programmes

The basic options of a VAD programme are:

I. Assist device as a supporting tool for conservative surgery
   a) reconstructive surgery in the severely diseased heart (valve reconstruction surgery),
   b) heart infarction surgery (coronary bypass surgery, reconstructive surgery in heart infarction complications),

II. Supporting options for transplantation programme:
   a) bridge to transplant,
   b) bridge to recovery after graft failure,
   c) bridge to re-transplant after graft failure.

III. Independent sector of the assist device programme:
   A. "Bridge to recovery" programme
   a) recovery in postcardiotomy syndrome,
   b) recovery in chronic forms of heart failure (dilative CMP),
   c) recovery in acute heart failure (fulminant myocarditis).
   B. Permanent non-biological cardiac replacement (destination therapy)

IV. Paediatric assist device programme

Assist device as a supporting tool during surgery

First of all, having the option of VAD implantation available as a standby extends the indications for reconstructive surgery and renders this surgery more effective when it is undertaken in "borderline" patients. This includes those cases in which the results of surgery are limited by non-surgical factors that are known preoperatively. In some publications it is stated that among the contraindications to valve surgery (reconstructive surgery) is severely diseased myocardium (LVEF <30%) [6, 7]. The risk of severe haemodynamic instability in such patients leading to frank myocardial failure after mitral valve surgery is difficult to assess preoperatively and this limit for surgery (LVEF <30%) is probably considered the minimal Rubicon of myocardial performance to avoid risk of death. If necessary, an assist device can support the haemodynamics in the first critical postoperative hours and days. After such a period heart function usually recovers and the VAD can be removed. It would be trivial to state that ventricular assist implantation cannot help to overcome a poor operative result.

On the other hand, the possibility of supporting the failing circulation in urgent surgical situations, for example in postcardiotomy syndrome, illustrates how important it can be.

Supporting options for transplantation programme

Mechanical devices can keep patients alive until transplantation and this is an important role of mechanical circulatory support. In addition to the bridge to transplant option, VADs are also important when a newly implanted cardiac graft fails. In such situations support of the failing graft by an assist device for a very limited time can help to achieve myocardial recovery or, if that proves not to be the case, longer term assist support can return the patients to the option of "bridge to retransplantation". Although this life-saving procedure is followed only in rare exceptions, the option is very important to enable fully comprehensive medical treatment.

Independent sector of the assist device programme

Artificial heart programmes nowadays include a rather small sector in which treatment is explicitly based on the use of a VAD.

In selected patients, especially those suffering from myocarditis and dilative cardiomyopathy, mechanical unloading can lead to myocardial recovery, as was reported from our institution previously [8]. However, as yet there are no reliable predictive criteria for patient selection in this respect. The option is still hampered by this lack of prospective criteria. Currently the DHZB has 36 surviving patients with idiopathic dilated cardiomyopathy among 83 patients weaned from VADs since 3/1995 after an average of 333 days of support. The figure for post-weaning 10-year survival with native hearts has reached 70.7±9.2%, which is better than the life expectancy after heart transplantation. Including post-transplant survival for patients with recurrence heart failure (successfully transplanted patients) the overall 5- and 10-year survival is even better and reaches 79.1 and 75.3% respectively. This is a very encouraging message for the future of independent use of VADs.

Patients suffered from dilated cardiomyopathy and had to be treated with an assist device to keep them alive. Assist support leads to decompression of the LV and optimal unloading of the left as well as right ventricle (by reducing LV filling pressure), which are optimal conditions for myocardial recovery. It seems that the level of the myocytes as well as the matrix is reflected by mass reduction of diseased heart muscle [9] and functional improvement of the heart. Reverse remodelling can be achieved, which not only has structural significance but also improves the haemodynamics. Pharmacological approaches and also myocyte restoration and replacement to induce reverse remodelling can be conjugated with trials as an aid to the assist device programme. Such trials are now underway in our own and other institutions. It is too early to speak of the results and a portion of scepticism should be kept in mind.

When we are able to predict which patients would be "suitable" for weaning in a prospective manner, this will open up the way for circulatory support as an independent and powerful method of treatment of heart failure, similar to the transplantation option.

Permanent non-biological cardiac replacement (destination therapy)

The second possibility that could lead to assist device treatment as an independent option is "destination therapy". In the final analysis, all of us will age and no medical means will make us immortal but, if patients are healthy except for their deficit in heart function, the VAD seems to promise a life with at least a minimum of comfort and where human dignity can be preserved until the end of that life.

Various assist systems are now able to improve physical conditions and offer the patient an acceptable quality of life for several years (Table II). Patients in whom transplantation is contraindicated (because of age or neoplastic disease) are candidates for mechanical support as destination therapy. However, we are in an era where biomedical science has revealed underlying mechanisms responsible for bleeding or thrombus formation when blood is exposed to fabric material. Unexpected complications of bleeding or thrombosis can cause serious clinical problems, and there are still many unanswered questions. The main limitation of artificial devices is not lack of performance or safety of the mechanical function but bleeding/thrombosis complications, both in young and in aging patients. More research has to be done to develop artificial material with surfaces that would be friendlier to the blood of the host after VAD implantation. If this is possible, VAD programmes will benefit significantly and there will be a chance to support the heart for almost unlimited time. Today it is difficult to assess how far away we are from achieving this. Currently, the importance of primary care clinicians, engineers and medical technicians in educating the patients on assist devices is a challenge. Organizational changes have been required to accommodate patients' ambulatory examinations and a 24-hour-a-day service in emergencies. We now have 72 patients up to five years with various modes of support on a VAD who are living at home. Some of these patients frequently require checks and the help of our specially trained medical and engineering personnel.

Paediatric assist device programme

VADs have an even more importance place in the treatment of paediatric patients than in that of adults. New therapies are needed to treat the ever-growing number of children with end-stage heart failure. The main indications are: low cardiac output following initially satisfactory weaning from CBP, acute myocarditis, sepsis syndrome, cardiac trauma, and severe post-transplantation rejection, end-stage congenital heart disease, DCM, and endocardial fibrosis. There are several diseases in infants that are potentially treatable surgically when a "stand-by" assist device is taken into account, as it was first used at the Deutsches Herzzentrum Berlin after the development of small implantable pumps for infants and young children (Berlin Heart paediatric device).

Indications

Indications for urgent VAD implantation are the following:
Metabolic acidosis;
Cardiac index <2.0 l/min/m^2;
Critical peripheral perfusion;
Mixed venous saturation <40%;
Oliguria (<1 ml/kg/min);
On respirator with mounting FiO_2;
Massively impaired cardiac function.

These indications reflect the investigations necessary to determine the metabolic and haemodynamic situation. A clinical situation that reflects clinical shock is the key to the investigation and invasive monitoring and echocardiography are the gold standards for preoperative diagnosis. Assessment of the patient's pulmonary condition requires serial X-ray investigation as well as blood gas analysis. Careful clinical investigation by an experienced surgeon is crucial to exclude contraindications and to settle the indications.

Serial ECG and regular blood analysis are mandatory in all patients considered candidates for assist devices. The complication rate is dependent on the preoperative haemodynamic situation, and the general rule "Poor clinical condition, poor outcome" should not be forgotten. Multiple organ failure is the major multifactorial cause responsible for negative outcome in patients on assist device systems [10].

"Bridge to next option"

As shown in Table II, there are a large number of assist device types, in some ways not many fewer than the types of cars being driven on the streets (Table II). This indicates how much effort has been undertaken worldwide to produce an optimal device. From the practical viewpoint assist device implantation can be classified into urgent and non-urgent implantation. Although assist device implantation is often performed as an urgent operation, there are several programmes which are based on surgery being planned in advance, if possible. An example is gradual worsening of a patient's haemodynamics, where the clinical situation progresses with time, making it possible to identify the risk of true decompensation and time surgery optimally. In such cases a long-term assist device is used. The urgent option is well illustrated by the slogan "bridge to next option". In many cases at the beginning it is not possible to assess the treatment options. Thus, at the beginning a short-term simple (and low-cost) system is used as a "bridge to next option" and during the next several days the day-by-day follow-up will clarify whether the patient will experience early recovery or whether a long-term option has to be pursued. The long-term options are given above: bridge to transplant, bridge to recovery where a longer period of time (months) will be needed, or destination therapy. It is important to find the best solution for the given patient. When long-term VAD treatment is needed, the short-term device should be replaced by an appropriate system.

Single versus dual chamber assistance

In the great majority of patients, and if assist implantation is undertaken before profound and long-lasting haemodynamic depression sets in and without a long period of metabolic acidosis, only single chamber (left ventricular) support is needed. The right ventricle can restore its haemodynamic performance after left ventricular filling normalizes under mechanical LV support. However, in up to 10% of patients unexpected RV failure will develop de novo, requiring RV support as well. This accompanying RV failure is difficult to predict on the basis of preoperative criteria.

Summary and perspectives

Although there is no alternative treatment which has results comparable to heart transplantation, assist device programmes are not only gaining more attention but are occupying an even more important place in the treatment of patients suffering from acute or chronic heart failure.

Currently, reverse remodelling with cardiac assist devices supported by novel therapeutic agents under trial to induce reversibility of the remodelling of the diseased heart seems theoretically promising. The researchers suggest, on the one hand, that pharmacological agents can induce restoration of the heart muscle [11] and that, on the other hand, cell seeding might help rebuild the muscle mass by natural growth and thus restore heart function. In such a case the selection of patients suitable for "restitutio ad integrum" after decompression and unloading would play a secondary role. Many controversies surround the issue of seeding cells to restore heart structure and function and there is a lack of animal and clinical trials to test whether any drugs possess the potential to induce clinical recovery in humans. After a very exciting time full of promises, the futuristic idea of "organ printing" as it was first published is now viewed more soberly. At the same time the idea of mechanical circulatory support has become more and more realistic in practical medicine and is now used not only to keep patients alive, but to keep them alive with their human dignity preserved.

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