# Mechanical Support of the Circulatory System

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Heart failure is an emerging public health epidemic with continuously increasing repercussion in the population. According to modern epidemiologic data 0.4-2% of the European population suffers from heart failure[1], while generally in ages over 65 years the incidence of heart failure is up to 10% of the population[2]. Despite the current progress in the pharmaceutical management of these patients, mortality remains high (about 50% in 4 years), while more than 50% of patients with severe heart failure die in less than one year[1].

## Introduction

The application of heart transplantation from C. Barnard in 1967[3], and its establishment due to N. Shumway with the entry in the clinical practice of cyclosporin in the eighties, gave a new prospect in the management of end-stage heart failure. Current results from the application of heart transplantation are satisfactory (annual survival 80%, 5 year survival 70%, 10 year survival 50%)[4]. Nevertheless, the continuously decreased heart donation the last years led to the need for alternatives.

Xenotransplantation with use of pig hearts is an attractive idea, particularly in societies that transplantation does not constitute a widely acceptable ethics. Thus, patients that do not fulfill the criteria for heart donation and patients that have the indication for redo transplantation may acquire a prospect in their treatment. However, the clinical application of this idea delays due to the difficulties of confrontation of the super-acute (from minutes to hours) rejection of the donored heart, as well as from the fact that currently the mean survival of the animals with orthotopic xenotransplantation is only one month[5].

On the contrary, the successful application of cardiac assist devices as bridge to transplantation, particularly in cases that end up with the improvement of the patient's status before the transplantation, led to a continuously increasing need for application of these devices. This policy, in combination with the lack of heart donors, leads research in designing new devices for permanent, and not only short-term, circulatory support.

After the first experiments of scientists as A. Kantrowitz, H. Shumacker, M. DeBakey, W. Kolff in the fifties[6] and the extensive clinical application over the last decades, currently these devices of circulatory support and especially the left ventricular assist devices (LVADs) are used in cardiac surgery mainly for post-pericariotomy cardiogenic shock. This status of acute heart failure is usually installed due to transmural mycardial infarction or severely stunned myocardium on the ground of decreased myocardial energy reserve and it is accompanied by high mortality (>50%).

## Short-term circulatory support devices

Generally, 5% of patients that undergo cardiac operation need support with intra-aortic baloon pump (IABP)[7], a percutaneous device for circulatory support,

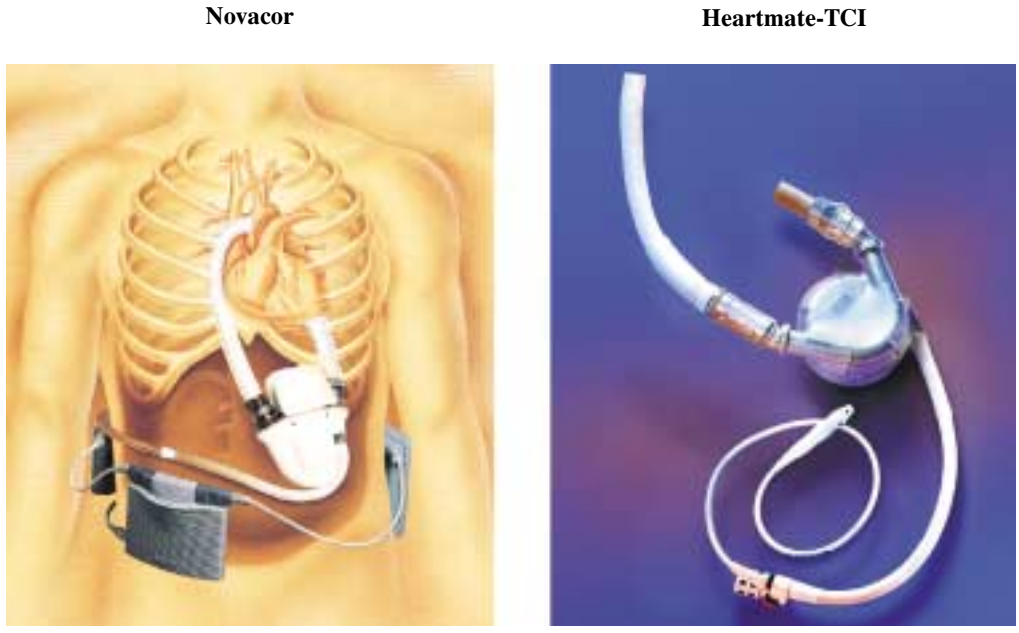


**Figure 1.** The devices for mechanical circulatory support that first entered the clinical practice.

that was designed due to the experimental work of Professor Moulopoulos[8]. From these patients 1/3 may need further LVAD for myocardial support, when postpericardiotomy cardiogenic shock is established[7].

Devices as the centrifugal pump of Biomedicus, the centrifugal pump with oxygenator (Extracorporeal Membrane Oxygenator - ECMO), the AB-180, the ABIOMED BVS 5000, as well as percutaneous devices for myocardial support are already used for this purpose in the clinical practice with very good results. The most serious complications from these devices are diffuse bleeding from heparinisation of the patient, infections and acute renal failure[9].

## Devices for medium-term support of the heart

With regards to chronic heart failure, the use of LVADs and Total Artificial Hearts (TAHs) was always a field that attracted the interest of the surgeons as well as of the patients. The first LVAD implanted successfully in human by M. DeBakey in 1966[10] and the first total artificial heart (Liotta-TAH) presented in the clinical practice by D. Cooley in 1969[11]. Since the sixties, the last four decades the idea of the replacement of the failing heart with a device/mechanical heart was always in the limelight. After the primary efforts, the first LVAD that was approved for clinical application from FDA (Food and Drug Administration) and was implanted in USA was Novacor (Baxter) in 1984 and then HeartMate–TCI (ThermoCardio Systems Inc) 1986[7] (Figure 1). The first artificial heart Jarvik 7 - TAH was implanted in human in 1982, it was renamed as Symbion - TAH and in 1990 stopped its clinical application, which was restarted in 1992 with the name of CardioWest - TAH[12].

## Indications

Currently, the indications for the use of the LVADs are as bridge to myocardial recovery (BTR) or as bridge to bridge for recovery or transplantation (BTB) or as bridge directly to the transplantation (BTT).

## Types of LVADs

These devices are totally implantable or are placed paracorporeal, which is out of the body of the patient but next to it or extracorporeal, which is out of the patient's body and far from it. They provide pulsatile or continuous (axial) flow, using pusher-plate system the former or centrifugal pump or rotor system the latter (Diagram 1). The energy that is used is pneumatic or electric. The use of electric energy instead of pneumatic made possible the discharge of the patients from the hospital and their

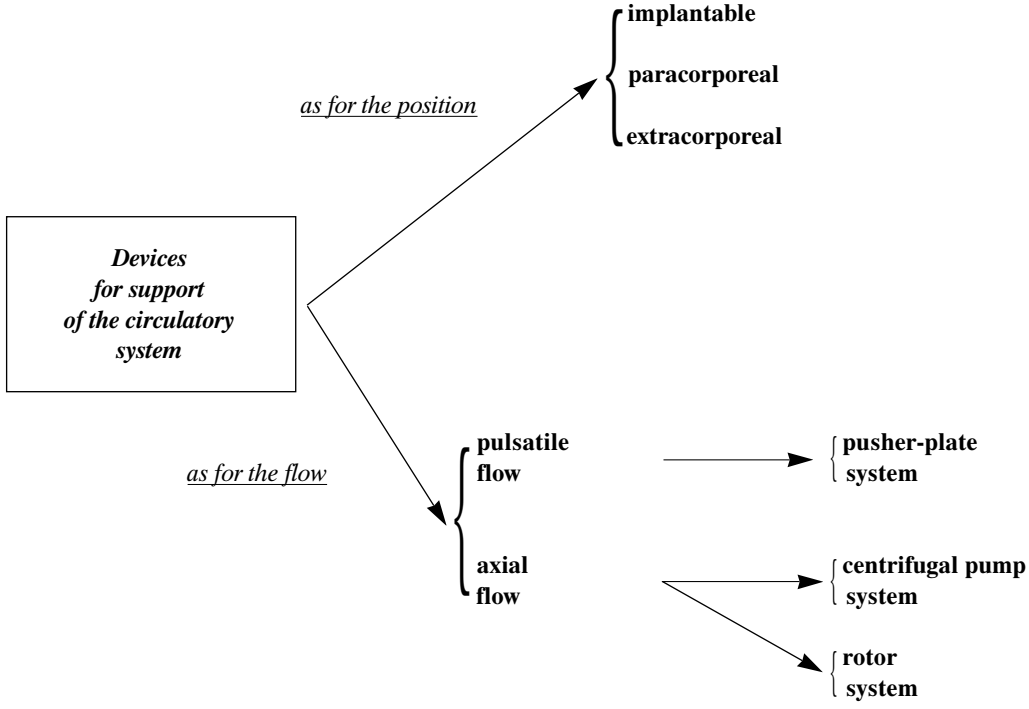


**Diagram 1.** Devices for support of the circulatory system.

return to an almost normal life. Recently, the application of a smaller size battery added independence and quality of life in these patients. The very new technology of Transcutaneous Energy Transfer (TET) to the implantable rechargeable battery of the device into the patient's body gave a new prospect in the field of LVADs and TAHs[13]. Thus, the driveline infection, which is one of the most serious and frequent complications of the myocardial assist devices may be minimised. Alternatively, to avoid this complication, Jarvik 2000 uses the skull mounted pedastal, utilising the knowledge and the technology of the cochliar implants. Since the loose connective and the subcutaneous addipose tissue are prone to the collection of bacteria, avoiding the driveline insertion from the abdominal wall where such conditions exist and use of the TET technique, is expected to decrease the infections[14] (Figure 2).

The trend of the designing of myocardial assist devices (LVADs, TAHs) is to be totally implantable and to use the system of transcutaneous energy transfer. There is also the trend of using the axial flow devices, which appear to have advantages against the other types of devices with pulsatile flow (Figure 3). The former devices have smaller size and are totally implantable, while they can be applied in most patients, even in patients with relatively small body mass indices. They are less noisy and require less energy, therefore they need smaller battery. Moreover, they do not need venting of their functional compartment.

## Complications

Despite the big progress of the last years in the technology of myocardial assist devices, the complications that accompany their use are noumerous. Mainly these are: bleeding from connection sites of the device with the heart or bleeding from the circulatory system (22-35%), tromboembolic events (7-28%), driveline infection (9-30%), infection of the implantation sheath (7-21%), endocarditis of the device (4%), etc[15].

## Total replacement of the heart (TAH)

As for the artificial heart, Jarvik 7-TAH that was implanted first in human in 1982, had as result 50% of patients to be bridged successfully to transplantation with longest interval of support 620 days[4]. This

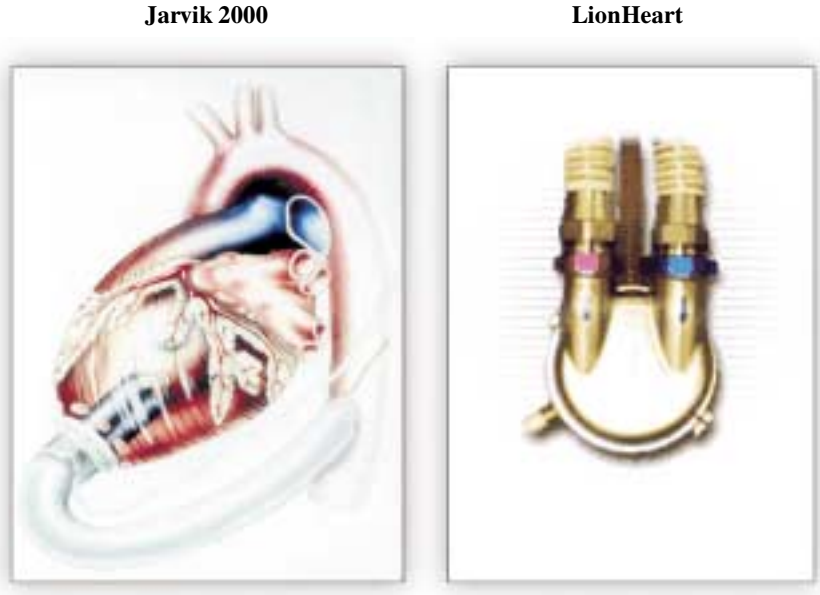


**Figure 2.** Modern devices for mechanical circulatory support.

device was renamed Nimbus and in 1990 stopped its clinical application, which restarted in 1992 as CardioWest. The main complications of TAHs are thromboembolic events and infections. Currently, CardioWest has offered 72% survival in a mean period of support of 24 months[16]. The new generation of TAHs has lately been presented in the clinical practice with very good experimental results. A-biocor-TAH was first implanted in the USA in June 2001, while PennState/3M-TAH is expected to enter shortly the clinical practice (Figure 4).

**Figure 3.** The current trent in mechanical circulatory support devices is to have small size as Jarvik 2000.

## Results

Currently, more than 40 devices already have been manufactured for the mechanical support of the circulatory system and they are in various stages of application, from the experimental to clinical level (Table 1)[17].

With regards to the results from the use of these devices, there is 38-75% survival to transplantation and 33-59% survival to discharge of the patient from the hospital[18]. One of the really impressive results of these devices, apart from the support of the heart up to the transplantation (or permanently), is the functional improvement of the myocardium after long-lasting offloading of the left ventricle, mainly in cases of myocarditis but also in dilated myocardiopathy[19]. Thus, in up to 17% of patients that received LVAD successful removal of the device was achieved, since myocardial recovery has been established[20]. In the level of molecular biology it appears that the long-lasting myocardial offloading contributes in the improvement of myocardial hypertrophy, the decrease of excretion of natriodiouretic factor, the improvement of mitochondrial use of the intermediary substances of Krebs cycle, the improvement of intracellular calcium metabolism, the decrease of myocardial TNF, the change of gene expression of heart failure, the decrease of the phenomenon of cell apoptosis etc.

Comparing the use of LVADs with the pharmaceutical treatment solely in the end-stage heart fail-


**Figure 4.** The devices of total replacement of the heart, which are used in clinical practice (total artificial hearts).

**Table 1.** The main modern devices for support of the circulatory system.

| Devices having permision for clinical practice | Devices in clinical trial | Devices in preclinical phase | Devices in the laboratory phase - under developement |
|---|---|---|---|
| Novacor | Abiocor TAH | PennState TAH | TCI-HeartMate III |
| TCI-HeartMate | CardioWest TAH | Thoratec-IVAD | Novacor II |
| Thoratec | Jarvik 2000 | Terumo-ILVAS | CorAide |
| Berlin Heart | LionHeart | WorldHeart -HeartSaver VAD | Streamliner |
| Medos | Micromed -DeBakey | | HeartQuest |
| Toyobo | TCI-HeartMate II | | |
| Zeon | AB180 | | |
| | CardioVad | | |

ure, the primary results from the REMATCH study (Randomized Evaluation of Mechanical Assistance in the Treatment of Congestive Heart Failure) that started in 1998 were published recently. Annual survival in the two groups of patients was 52% and 25% respectively (p=0.002). Especially, in the subgroup of patients with age <60 years (which constitutes criterion for transplantation) annual survival was 74% (similarly with transplantation). Biennial survival was 23% and 8% respectively (p=0.09), while mean survival was 408 and 150 days, respectively[21]. After these results ThermoCardio Systems Inc applied in the FDA for the approval of using HeartMate –TCI, which was utilized in the study, as permanent myocardial assist device.

These very good preliminary results from the use of LVADs in heart failure do not only comprise the good prognosis of the patients, but also the improvement of the quality of their life, which is not recorded easily in studies but is obvious to those who deal with these groups of patients.

The cost of using the myocardial assist devices is high. It is calculated that for the implantation of such device about 190.000 dollars per patient are required, while the cost for the heart transplantation is roughly 175.000 dollars. Even if this money is lot, it should be compared with the high cost of the pharmaceutical treatment of the end-stage heart failure. Thus, the numerous and the long-lasting hospital admitions of these patients and the very expensive pharmaceutical regimes that are needed may utilize the 1-4% of the budget of a health system[22].

## Prospects

The last decade, particularly in the USA, there is the trend for the myocardial assist devices to be used increasingly as bridge to transplantation. From 1994,

when FDA gave permission for the clinical application of pneumatic LVADs as bridge to transplantation and from 1998, when permission was given for the same reason in the electric devices, more than 4000 appliances have been implanted worldwide. Because of the commercial competition and the huge economic interests that exist, the criteria for the entry in the clinical practice of a new device are strict. All the new devices according to the "Medical Device Amendments Act'' should be "secure and effective" as proved from "well designed controlled studies'' or "significant scientific testimonies''. Clinical studies should exist before the approval of the entry in the market (pre-marketing approval/ PMA) from the FDA. It is believed that soon there will be a balance as well as indications and principles will be placed in the whole process. Some devices will prevail as better and the other will stop to be therapeutic options.

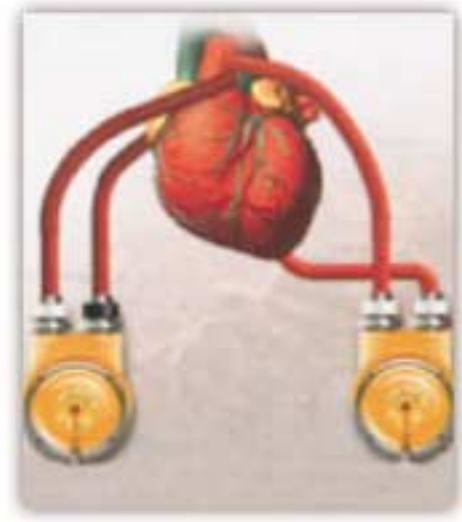

**Figure 5.** The popular mechanical circulatory support device Thoratec, which can be used for the support of both ventricles (LVAD + RVAD).

### Other devices of myocardial support - RVADs

Generally, with regard to other devices for myocardial support, roughly 90% of the patients with heart failure can be faced with LVAD, since heart failure of the right heart is improved indirectly with the offloading of the left ventricle and only 20-30% of the patients with LVAD are led to a non reversible pharmaceutically dysfunction of the right ventricle and may also require RVAD (Right Ventricular Assist Device) (Figure 5). On the contrary, in patients with biventricular failure use of TAH appears to be a better choice.

### Conclusions

In conclusion, assist devices of the circulatory system constitute an option for the end-stage heart failure treatment and are accompanied by good results. The very good prognosis and quality of life that is achieved from these devices render them as culprit in such cases, especially in countries that can bear the cost from their use. The very promising new generation of these devices (LVADs, TAHs) are currently the only substantial alternative in the declining internationally, due to the lack of donation, heart transplantation. The results from many clinical studies on these devices that are in progress internationally, are expected to change the methodology in the treatment of heart failure.

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The circulatory system, also called the cardiovascular system or the vascular system, is an organ system that permits blood to circulate and transport nutrients (such as amino acids and electrolytes), oxygen, carbon dioxide, hormones, and blood cells to and from the cells in the body to provide nourishment and help in fighting diseases, stabilize temperature and pH, and maintain homeostasis. Development of mechanical circulatory support systems The methods for providing mechanical circulatory support (MCS) have varied greatly. The evolution of MCS technology has been gradual, as the biological barriers to progress have remained constant and difficult. Clinicians and engineers have collaborated for many years to develop an array of devices that range from very smallâ€¦Â  Timeline showing the evolution of the various types of blood pumps used for mechanical circulatory support. CPB , Cardiopulmonary bypass; ECMO , extracorporeal membrane oxygenation; LVAD , left ventricular assist device; TAH , total artificial heart. Mechanical circulatory support devices/ventricular assist devices are considered medically necessary for long-term support in heart failure patients meeting the following criteria: â€¢ Are permanently or temporarily ineligible for heart transplant due to at least one of the following reasons (Mehra et al., 2016): o Diabetes with end-organ damage or persistent poor glycemic control (glycosylated hemoglobin [HbA1c] > 7.5% or 58 mmol/mol), despite optimal management o Irreversible renal dysfunction (eGFR < 30ml/min/1.73 m2) o.Â  Except as noted, authorization for the implantation of a MCSD will not be given if any of the following are present: â€¢ Heart failure that can be reasonably expected to recover without MSCD. Mechanical Circulatory Support. The Brief Statement below is provided to explain Indications, Contraindications, and Warnings/Precautions for the Medtronic mechanical circulatory support product. 3277. 2. HeartWare HVAD System. HeartWare HVAD System - International. Brief Statement: HeartWareâ„¢ HVADâ„¢ System. Indications for Use. The HeartWareâ„¢ HVADâ„¢ System is indicated for hemodynamic support in patients with advanced, refractory left ventricular heart failure; either as a Bridge to Cardiac Transplantation (BTT), myocardial recovery, or as Destination Therapy (DT) in patients for whom subsequent transplantation is not planned. Contraindications. The HeartWare System is contraindicated in patients who cannot tolerate anticoagulation therapy. Chronic mechanical circulatory support for inotrope-dependent heart failure patients who are not transplant candidates: results of the INTrEPID Trial. J Am Coll Cardiol 2007;50:741-7. 7. Samuels L, Holmes EC, Hagan K, Thomas MP, Garwood P. Incorporation of an in-line filter for ultrafiltration or hemodialysis to the Abiomed BVS5000 ventricular assist device. ASAIO J 2006;52:634-7. 8. Brown JL, Estep JD. Temporary Percutaneous Mechanical Circulatory Support in Advanced Heart Failure. Heart Fail Clin 2016;12:385-98.Â  Results following implantation of mechanical circulatory support systems: the Montreal Heart Institute experience. Can J Cardiol 2009;25:107-10. 50. Slaughter MS, Pagani FD, Rogers JG, et al.