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EDITORIAL

150 YEARS OF THE ACADEMY AND 60 YEARS OF THE JOURNAL RAD – MEDICAL SCIENCES

Marko Pećina

It is a true pleasure for me to be able to present to you the 36th issue of the journal RAD (Monographs) of the Croatian Academy of Sciences and Arts – Medical Sciences; even more so since this year, the Croatian Academy of Sciences and Arts celebrates its 150th anniversary (it was founded in 1861). In this same 2011, we celebrate 60 years since the publication of the first issue of the journal RAD – Medical Sciences (prepared by the Academy Department of Medical Sciences) in 1951.

In front of you, dear readers, there is volume 36/509; this means that between 1867 (when the initial issue of the journal RAD of the Croatian Academy of Sciences and Arts was published) and the present day, 509 volumes have been published in this Academy edition. The Department of Medical Sciences itself has so far – though in discontinuity – published 36 volumes since its first volume of 1951. In the last six years, our journal has managed to keep the continuity and join the relevant international databases. This achievement makes us very proud. The present volume 36/509 introduces papers from the symposium entitled *Chronic Heart Failure and Mechanical Circulatory Support*, which was held in Zagreb on 26 March 2010, in co-operation between the Academy Department of Medical Sciences and the Department of Cardiac Surgery, Dubrava University Hospital, Zagreb.

We cordially thank our guest editor, Prof. Željko Sutlić, MD, PhD, associate member of the Croatian Academy of Sciences and Arts, for his great effort regarding the compiling of the symposium papers.

In conclusion, I would like to repeat my argument from one of the previous editorials: *For any journal, the continuity is one of the most important proofs of both its good name and its credibility*. It is therefore with great pleasure that I present to you RAD 36 (2011), the seventh volume of our journal, which has been continually published annually or semi-annually since 2006. On behalf of the Editorial Board, I can promise you that we will continue enhancing the quality of the papers published in RAD of the Croatian Academy of Sciences and Arts – Medical Sciences.

SYMPOSIUM

CHRONIC HEART FAILURE AND MECHANICAL CIRCULATORY SUPPORT

Guest Editor
ŽELJKO SUTLIĆ

CHRONIC HEART FAILURE AND MECHANICAL CIRCULATORY SUPPORT

Željko Sutlić

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Mechanical heart and circulation support devices have become a standard in the treatment of patients with chronic heart failure, particularly the ones who require long-term circulation support. The use of these devices has so far significantly helped in the optimisation of the treatment and will eventually gain even better results. The interest for this type of therapy is rapidly increasing, in Croatia as well as worldwide. We had hence decided to organise a symposium entitled *Chronic Heart Failure and Mechanical Circulatory Support* at the Croatian Academy of Sciences and Arts in Zagreb, in co-operation between the Academy Department of Medical Sciences and the Department of Cardiac Surgery, Dubrava University Hospital. The Symposium was held on 26 March 2010 at the Academy Palace.

Experts from two Croatian university hospitals (Dubrava University Hospital and Zagreb University Hospital Centre), together with several experts from Germany and England, presented the basic and clinical aspect of short-term and long-term mechanical circulatory support. The Symposium was organised with generous help of the respected company *Thoratec*.

The Symposium resembles the aim of the Academy, especially the one of the Department of Medical Sciences, i.e. endeavouring to get incorporated into the modern technological trend, typical for the 21st century.

We warmly thank the members of the Department of Medical Sciences of the Croatian Academy, as well as the Department's former Secretary and the current President of the Croatian Academy of Sciences and Arts, Zvonko Kusić. Finally, our thanks also go to the Editor-in-Chief of the Academy's journal *Rad*, Marko Pećina, Fellow of the Croatian Academy, for his effort in editing this issue of the Journal.

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LONG-TERM MECHANICAL CIRCULATORY SUPPORT: SURGICAL TECHNIQUES

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Summary

Long-term mechanical circulatory support has become a valid treatment option for end stage heart failure. In selected patients' cases, this therapeutic option has been proven to improve survival, both as a bridge to transplant and as a destination therapy. In this article, we address implantation technique, strategies to prevent excessive bleeding, right heart failure, and driveline and pocket infection.

Key words: heart failure; mechanical circulatory support; surgical technique

Devices

Left ventricular assist devices (LVADs) are classified as either pulsatile or non-pulsatile (continuous), based on the nature of the flow they produce. The pulsatile pumps have a mechanical pusher plate or sac that propels blood mechanically or pneumatically, whereas continuous flow pumps are rotary devices that establish continuous flow. Furthermore, continuous flow pumps are either centrifugal or axial flow, where centrifugal pumps utilize a rotating disk that spins blood in a circular motion to create centrifugal force to pump blood; an axial flow pump consists of a spinning rotor that propels blood alongside the native circulation.

Pulsatile devices, such as Thoratec VAD system, allow left, right, or bi-ventricular assistance to patients with end stage heart failure. The VAD are prosthetic ventricles, which are composed of blood sacs inside a hard plastic casing. A pressure/vacuum system allows the air to enter the casing around the blood sac. This expansion and contraction of the air sacs allows the VAD to fill and eject blood, and provides the body with blood flow similar to that of the native heart. It has been FDA-approved both as a bridge-to-transplant therapy and for post-cardiotomy recovery from

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open-heart surgery. Thoractec pVAD is a paracorporeal device – the pump chamber is outside the body, thus allowing the use on patients of small body size.

Most of the currently widely implanted devices are the axial-flow rotary devices (such as Thoratec Heartmate II; BerlinHeart INCOR; MicroMed DeBakey VAD; HeartWare HVAD) that possess several advantages over the older devices, including their small size, ease of implant, durability and silent operation. However, since the device implant still requires open-heart surgery and the use of the cardiopulmonary bypass, patients may potentially develop complications related to the surgery.

Surgical technique

Although there is a whole range of different devices available on the market, the operative technique has been standardized with the following steps: mediastinal exposure with the creation of the device pocket; outflow graft anastomosis to the ascending aorta; placement of device inflow cannula at the left ventricular apex; de-airing of the device; and device start followed by weaning from cardiopulmonary bypass (CPB) support.

The patient is prepared for open-heart cardiopulmonary bypass surgery as usual. The sternum is opened, and prior to heparinization, a pre-peritoneal LVAD pocket is created in the left upper quadrant. We try to develop the plane above the posterior rectus sheet and to size the pocket according to the device mannequin. It is of utmost importance to perform meticulous pocket hemostasis, because the pocket will be inaccessible after the definitive pump placement.

To minimize the bypass time, it is possible to perform aortic anastomosis first with the use of aortic side-biting clamp. The graft is precloted, measured, trimmed, and sewn using 4-0 Prolene sutures with additional reinforcing Teflon strips. To prevent additional bleeding, fibrin glue is generously applied over the entire anastomosis line.

The heart is cannulated in the usual fashion, via the aorta and a single atrial venous cannula. CPB is instituted to allow the placement of the left ventricular apical inflow cannula. We tend to do it in normothermia on a beating heart, with the operating field being flooded with carbon dioxide. The left ventricular vent is placed via the right superior pulmonary vein to both maintain a dry operative field and additionally help de-airing the heart.

The heart is lifted and a specialized coring knife is used to create the apical core. Exact site and direction of coring should be carefully selected to avoid deviation into the septum. Like in all axial-flow pumps, there is a risk of generating negative intraventricular pressure and collapsing the ventricle. Therefore, inflow cannula positioning and ventricular preload are crucial to avoid potential suction events. Trabeculations that may impinge on the cannula should be excised and possible

mural thrombi completely removed. Afterwards, 12-15 braided polypropylene 2-0 sutures with medium-sized Teflon pledgets are equally spaced around the ventricular opening, passed through the sewing ring of the inflow cuff, and tied. Additional running Prolene 3-0 suture with circular Teflon strip and abundant fibrin glue can be used for the reinforcement of anastomosis. The cannula is brought down to the ventricle, secured to inflow cuff and attached to the LVAD body.

The LVAD driveline is passed through the abdominal rectus muscle and subcutaneous tissue using the appropriate stylet to the skin of the upper abdomen. We routinely try to lengthen the subcutaneous part of the driveline by passing it first through the auxiliary skin incision at the right upper quadrant, and afterwards to the final exit spot, slightly to the left from the median line and above the patient's belt line. By this maneuver, the potential route for infection spread from the driveline exit wound to the device pocket is significantly extended.

The heart is allowed to fill with blood and the device is de-aired through its outflow part. The previously de-aired outflow graft is then attached and secured to the device body. An additional venting hole is placed in the outflow graft. The complete evacuation of air is confirmed with transesophageal echocardiography and the device is started. The patient is then weaned from the CPB.

We routinely place a Gore-tex pericardial membrane over the anterior mediastinal structures and secure it to the pericardial edges to minimize the risk of injury during the planned reoperative sternotomy. Chest tubes are placed in the opened pleural cavities and in the mediastinum – next to the apical inflow cannula and LVAD pocket, and retrosternally, over the pericardial membrane. After the hemostasis is achieved, the chest is closed in the standard fashion.

Bleeding prevention

Excessive mediastinal bleeding is common after mechanical circulatory support device implantation, occurring in up to 40% of patients; it can lead to massive transfusions and re-exploration. Many risk factors predispose excessive bleeding in this subset of patients, including the compromised nutritional status and hepatic dysfunction due to chronic heart failure; extensive surgical dissection; reoperations; prolonged cardiopulmonary bypass; and coagulopathy, due to interactions between the circulating blood and the artificial surfaces.

Therefore, a special attention should be paid to the meticulous hemostasis of all surfaces. Some of the procedural steps, such as pocket creation and driveline tunneling, should be done prior to the heparin administration. We also routinely use a cell saver for intraoperative blood salvage, administer tranexamic acid in optimal doses to efficiently inhibit fibrinolysis, and use fibrin glue to reinforce suture lines.

Thromboelastography is routinely used both preoperatively and after the protamine administration to guide the possible coagulopathy treatment.

Right ventricular failure prevention

Right ventricular failure is a dreaded complication after the VAD implantation, with an extremely high mortality (up to 40%). Some intraoperative measures also contribute to the right ventricular failure prevention. Mean arterial perfusion pressure during implantation should be kept above a mean of 70 mmHg to provide the RV protection. Cardioplegic arrest should be used only in selected cases. The left ventricle, the assist device, the outflow graft and the ascending aorta should be meticulously de-aired to avoid a possible air embolization of right coronary artery. Excessive bleeding and massive transfusions impair the right ventricular function; it should therefore be avoided at all costs. Finally, left ventricular assist device speed should be adjusted to prevent an excessive shifting of the interventricular septum to the left side, which regularly impairs the right ventricular function.

Infection control

Clinical experience has shown that the LVAD infection rates can be minimized by optimizing the implant techniques and wound care; appropriate antibiotic prophylaxis; avoiding infections in indwelling catheters; maximizing patients' nutritional status; and optimizing glycemic control. There are several additional intraoperative and postoperative considerations that are important for infection control. The size of the preperitoneal device pocket should be minimized, whilst the length of the driveline passed through the abdominal wall muscle should be maximized. The sterility of all implantable materials should be vigorously monitored, while the number of people circulating the operating room should be limited to the necessary minimum. It is of utmost importance to immobilize the percutaneous driveline exit site, possibly by using an additional 2-point holder or a stabilization belt. Postoperatively, the exit wound dressing should be changed daily through the initial weeks, and subsequently on a 2- or a 3-day basis. The wound should be cared with chlorhexidine. Any signs of exit wound infection should be aggressively treated by daily re-dressing using hydrogen peroxide and povidone-iodine, combined with a targeted antibiotic therapy.

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Sažetak

Dugotrajna mehanička potpora cirkulaciji: kirurške tehnike

Dugotrajna mehanička potpora cirkulaciji postala je provjerena metoda u liječenju završne faze srčanog zatajenja. Kod odabranih bolesnika, dokazano je da poboljšava preživljenje, bilo kao potpora do transplantacije ili destinacijske terapije. U članku opisujemo tehnike ugradnje, strategije u cilju smanjenja prekomjernog krvarenja, zatajenja desnog srca te infekcije oko mjesta izlaska kabela za napajanje.

Ključne riječi: zatajenje srca; mehanička potpora cirkulaciji; kirurška tehnika

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CONSIDERATIONS FOR EXERCISE THERAPY WITH SHORT-TERM AND LONG-TERM MECHANICAL CIRCULATORY SUPPORT

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Summary

Once a mechanical circulatory support (MCS) system has been inserted the physiotherapists' role is crucial to prepare the patient either for transplantation, for upgrade to long-term MCS or for device explant. There are numerous considerations for rehabilitation that should be addressed in order to provide a safe and effective exercise programme. This paper highlights considerations for exercise in both short-term and long-term MCS devices.

Key words: physiotherapy; exercise; mechanical circulatory support; MSC; Ventricular assist device; VAD

Introduction

Currently there is a lack of evidence regarding exercise-training protocols for people who have mechanical circulatory support (MCS) devices implanted for end-stage heart failure. Of the papers that have described rehabilitation most are post-left ventricular assist device (LVAD) insertion; many are single case studies, have less than 10 subjects, or are retrospective analysis [1,2,3].

The use of short-term extracorporeal MCS has brought about new challenges to Physiotherapy once patients are haemodynamically stable in the intensive care unit (ICU). Short-term MCS devices are being inserted more frequently and in a wide variety of clinical situations. Usually these patients are confined to bed in the ICU. Prolonged immobility is known to dramatically affect functional capacity, which can adversely affect post-insertion outcomes and increase ICU length of stay.

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There are many versions of long-term LVADs available and the exercise capacity will depend on the ability of the device to deliver an output that matches the intensity of exercise required.

The following considerations are based on the limited available evidence and clinical experience gained at Harefield Hospital, UK.

Considerations for exercise with short-term MCS

The main objectives of mobilising patient's who have short-term MCS devices in-situ are to: improve respiratory function; re-educate balance mechanisms; improve peripheral vascular tone; facilitate normal movement patterns and prevent further deconditioning. Prior to mobilising patients who have short-term MCS devices in-situ a thorough risk assessment needs to be conducted. The patient must be haemodynamically stable on the MCS, must be awake, alert and able to follow commands.

An echocardiogram must be performed to assess for thrombus formation and the activated partial thromboplastin time must be within the range set by the surgical/medical team. Knowledge of the surgical procedure is imperative, as it must be known if the cannulae have been well secured prior to any attempt at mobilisation.

A method to secure the device cannulae to the patient needs to be in place to reduce the amount of movement produced when mobilising from the bed. The securing method should also help reduce the gravitational pull of the cannulae as the patient stands up. The patient must be able to tolerate sitting in the full chair position in the bed for an adequate amount of time with no drop in device flows or reduction in mean arterial pressure before progressing to mobilising out of bed with greater challenge on the cardiovascular system. Prior to more dynamic mobility the patient may need time to improve their peripheral vascular resistance to prevent venous pooling and reductions in device flows when they are in a position with greater gravitational effects.

A team of appropriately trained staff should be present for the mobility session. One member of the team to be responsible for all invasive lines/infusions and tracheostomy tube if necessary; two physiotherapists to facilitate normal movement/balance and to assist with the use of equipment; one perfusionist/ventricular assist device (VAD) team member per short-term device and one member of the surgical team if there are any concerns with the cannulae.

The exercise sessions should be progressed by improving normal movement patterns and exercise tolerance. A mixture of cardiovascular exercise and muscle resistance work should be incorporated into the rehabilitation programme. The device flows are not adjusted during the mobility session, as the peripheral vascular

resistance would not be able to be fully assessed and also to prevent any thromboemboli that may exist being dislodged by the change in flow dynamics.

The patient should not sit out of bed in case they suffer from venous pooling causing reduced device flow. If this does happen it may be unsafe to use a hoist to transfer the patient back into bed due to the position of the cannulae. The patients can sit in the full chair position in the bed, exercise from the bed and then return to the full chair position in the bed to avoid the necessity to sit out of bed. The cannulae need to be constantly assessed during the mobility session as they may exhibit an increased amount of movement ("chattering") caused by suction of the ventricles, which may lead to permanent damage.

Consideration for exercise with long-term MCS

The mechanism of non-pulsatile devices means that it is extremely difficult, if not impossible at times, to measure an accurate blood-pressure, oxygen saturation or heart rate using non-invasive means. It should not be assumed that the pump rate of the pulsatile devices is equal to the heart rate. Hypotension and low device flows are one of the most common problems. The patient must be well educated regarding the normal flow values so that they are able to take appropriate action when required.

Excessive movement of the driveline at the abdominal incision can cause micro-trauma, which can increase the chances of infection and cause pain. The driveline needs to be immobilised sufficiently to prevent shearing and torsion injury [4]. Driveline pain and infection can severely limit physical therapy, as it is not advisable to exercise when an active infection is present. The pain from the micro-trauma can also affect normal movement patterns. The position of the driveline through the abdominal wall causes the patient not to be able to perform any specific abdominal exercises. This driveline position also limits use of exercise machines that involve movement of the upper limbs and the lower limbs simultaneously or any movements that cause repeated twisting of the trunk.

The underlying condition requiring LVAD insertion and post-operative effects will affect the degree of exercise tolerance at any time. Each patient with an LVAD will require an individual assessment and exercise programme. The programme will be designed around physical limitations and the ability of the LVAD to affect exercise capacity.

Exercise prescription for long-term VADs

Treadmill exercise testing with a modified Bruce, Naughton or modified Naughton protocol has been used safely with this patient group [5,6]. The modified Wa-

ssermann ramp protocol for a cycle ergometer has also been used to assess maximal exercise capacity [6]. Treadmill exercise with a workload of 3-5 METS for 20-30minutes has been shown to be safe and effective [3].

Exercise should not be stopped suddenly and should include a "cool-down" period to prevent problems with venous pooling. Hypovolaemia will cause reduced device flows, which may result in feelings of light-headedness. When exercising for a prolonged period, patients should be encouraged to increase their fluid intake to avoid dehydration.

There is a lack of studies that have published any contraindications to exercise for patients with MCS. Only one study [7] has published any contraindications to exercise for LVAD patients and these are stated as contraindications at 4-6weeks post-surgery. These include: onset of angina; a drop in systolic blood pressure (BP) below resting BP; an increase in systolic BP exceeding 200mmHg; ECG changes; oxygen desaturation <85%; a drop in LVAD flow <3litres/minute and a rating of >13 on the Borg RPE scale at sub-maximal workloads. These contraindications are however extremely difficult to establish with non-pulsatile devices as it is difficult to gain accurate measurements by non-invasive means of BP, hear rate or oxygen saturations. On some non-pulsatile devices the device flows are not available to view if the patient is on portable batteries (Heartmate II). Together these limit the accurate assessment of the effect that the exercise is having on the patient.

Conclusion

Physiotherapy input is essential for patients requiring MCS to combat physical deconditioning that occurs with heart failure and with prolonged periods in bed on the ICU after device insertion. Separate considerations are implicated for exercising patients with short-term and long-term MCS. A thorough risk assessment should be conducted in order to establish a safe and effective exercise programme.

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Sažetak

Prijedlog programa vježbanja bolesnika s dugotrajnom i kratkotrajnom mehaničkom potporom

Nakon ugradnje mehaničke potpore srcu i cirkulaciji (MSC) važna je uloga fizioterapeuta u dobroj pripremi pacijenta za eksplantaciju uređaja, transplantaciju ili ugradnju dugoročnog MSC-a. Kako bi program vježbanja bio siguran i efektivan za pacijenta, potrebna je dobra priprema fizioterapeuta. Što je sve potrebno razmotriti kod fizioterapije pacijenata s ugrađenim kratkoročnim odnosno dugoročnim MCS uređajem prikazano je u ovom članku.

Ključne riječi: fizioterapija; vježbanje; mehanička potpora srcu i cirkulaciji; MSC; VAD

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SHORT-TERM MECHANICAL CIRCULATORY SUPPORT

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Summary

Heart failure continues to be an ever-growing public health concern. The continued aging of the population has contributed to the increasing incidence and prevalence of heart failure. Mechanical circulatory support is used to treat patients with advanced heart failure. A mechanical pump is surgically implanted to provide pulsatile or non-pulsatile flow of blood to supplement or replace the blood flow generated by the native heart. The main purpose of a mechanical circulatory support is to unload the failing heart and help maintain forward cardiac output and vital organ perfusion. A big variety of devices exists: from the percutaneous and short-term support, which can be used in the operating room or the cath-lab and afterwards in the intensive or coronary care units, to the internal and long-term devices, which can be used as a bridge-to-recovery or cardiac transplant, or as definitive therapy in patients with contraindication to cardiac transplant. This treatment involves not only the cardiac surgeons, but also the cardiologists, anaesthesiologists, intensivists and perfusionists. Appropriate patient selection represents the critical determinant of successful outcomes with the VAD therapy. The predictive risk stratification is extremely important for achieving the minimal peri-operative mortality rate. As VAD technology progresses, the collaboration of multidisciplinary teams composed of engineers, scientists, physicians, and nurses will continue to refine the technology and improve patient care and operation outcomes. Advances in device design will allow for an easier implantation and create smaller, more efficient, durable, and reliable units.

Key words: ventricular assist device; heart failure; mechanical circulatory support

Heart failure continues to be an ever-growing public health concern. The continued aging of the population has contributed to the increasing incidence and prevalence of heart failure [1]. Mechanical circulatory support is used to treat patients with advanced heart failure. A mechanical pump is surgically implanted to provide pulsatile or non-pulsatile flow of blood to supplement or replace the blood flow generated by the native heart. Types of circulatory support pumps include pneumatic

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and electromagnetic pumps. Rotary pumps are also available. Investigators and the medical device industry have been pursuing the development of mechanical cardiac support for more than four decades. Mechanical circulatory support has significantly evolved over the last years. It is now a real and useful therapeutic option not only for the treatment of cardiogenic shock, but also for advanced chronic heart failure, and even preventively in high-risk cases of percutaneous coronary intervention and cardiac surgery. The main purpose of a mechanical circulatory support is to unload the failing heart and help maintain forward cardiac output and vital organ perfusion. Originally introduced as a temporary bridge-to-recovery and then as a bridge-to-transplantation, the mechanical circulatory support has evolved into permanent or "destination" therapy for a growing number of patients with refractory heart failure [2]. A big variety of devices exists: from the percutaneous and short-term support, which can be used in the operating room or the cath-lab and afterwards in the intensive or coronary care units, to the internal and long-term devices, which can be used as a bridge-to-recovery or cardiac transplant, or as definitive therapy in patients with contraindication to cardiac transplant. This treatment involves not only the cardiac surgeons, but also the cardiologists, anaesthesiologists, intensivists and perfusionists. Indications for device support continue to evolve from day to day. Patients considered for mechanical circulatory support are not able to sustain adequate systemic oxygen delivery to maintain normal end-organ function despite maximal medical therapy. Haemodynamic criteria for device implantation include: systolic blood pressure lower than 80 mm Hg; mean arterial pressure lower than 65 mm Hg; cardiac index lower than 2.0 L/min/m^2; pulmonary capillary wedge pressure higher than 20 mm Hg; and systemic vascular resistance over 2,100 dynes-sec/cm [3]. The decision to implement mechanical circulatory support must be made with consideration to the ultimate goal of therapy. Mechanical circulatory support always represents a kind of a bridge (bridge-to-: decision, recovery, transplant, conventional treatment, death; or, finally, bridge-to-nowhere). As mentioned above, indications for mechanical support are continuously evolving, and herein we present some of them.

1. Cardiogenic shock associated with acute myocardial infarction (AMI) complicates clinical presentation of 6 to 20 % of patients suffering from AMI, and is reported with a mortality rate between 70-80 % [4].

2. Postcardiotomy cardiogenic shock is experienced by 2 to 6 % of patients undergoing coronary or valvular cardiac procedures [5]. Special consideration should be given to patients with severely impaired ventricular function undergoing high-risk cardiac procedures. Transplant evaluation should be initiated pre-operatively, and the procedure should be performed with an LVAD „back-up".

3. Chronic cardiac failure. In this subgroup of patients, short-term mechanical support can be instituted as a bridge-to-transplantation. The normalisation of haemodynamics and the maintenance of the end-organ function decrease post-transplant mortality [6].

4. Myocarditis is characterised by an unpredictable clinical course, and short-term mechanical circulatory support (especially biventricular support due to biventricular disease involvement) presents the chance for a bridge-to-recovery.

Of note, there are some reports of device implantation in patients suffering from ventricular arrhythmias refractory to medical therapy [7].

Appropriate patient selection represents the critical determinant of successful outcomes with the VAD therapy. The predictive risk stratification is extremely important for achieving the minimal peri-operative mortality rate. Aiming the optimal risk/benefit ratio, some reports have sought to identify the predictives of risks and benefits [8]. The timing of intervention is an important determinant of the clinical outcomes. For example, the optimisation of patient status with diuresis; the correction of coagulation abnormalities; the pulmonary rehabilitation; and the implementation of intra-aortic balloon pump may be useful. It is obligatory to control systemic sepsis or bacteraemia, due to a high risk of device contamination. On the other hand, the mentioned treatments and procedures may lead to unnecessary postponements, which may further lead to a marked increase in mortality [9-10]. Contraindications for device implantation, such as irreversible end-organ damage and unrecoverable neurologic injury, have to be considered as well.

THE COMPONENTS OF THE MECHANICAL CIRCULATORY SUPPORT

Ventricular assist devices (VAD) used in the outpatient setting are implanted devices placed through a median sternotomy typically during cardiopulmonary bypass. VAD is connected to the heart by an inflow cannula that decompresses the ventricular cavity and an outflow cannula that returns blood to either the ascending aorta or the main pulmonary artery. The pumping chamber of the VAD is implanted sub-diaphragmatically to a pre-peritoneal or intra-abdominal position, or it may be situated in a para-corporeal position outside the body. Smaller devices are being developed for thoracic implantation, some with outflow to the descending aorta.

THE PHYSIOLOGY OF VADS

VADs support the failing heart by unloading the ventricle and generating the flow to the systemic and / or pulmonary circulation. This creates parallel pumping

chambers that compete for the same venous return (pre-load), and face the arterial resistance (after-load) of their respective pulmonary and systemic vascular beds. Under optimal conditions, the native ventricle is a passive conduit, through which the mechanical pump fills throughout the cardiac cycle, and the decompressed ventricle should contribute little to the systemic cardiac output. If a ventricular stroke volume is generated, and the aortic / pulmonic valve leaflets are seen to open on echocardiography, either the return of the native ventricular function or an inadequate decompression of the native ventricle and device dysfunction should be suspected. Isolated right ventricular dysfunction, requiring insertion of a right ventricular assist device (RVAD) to support the failing ventricle, is a rare event. Cases have been reported postcardiotomy after an acute myocardial infarction, coronary artery bypass grafting, and valvular surgery. More commonly, an RVAD may be inserted around the time a left ventricular assist device (LVAD) to provide biventricular assistance is placed. Unlike a single VAD, biventricular mechanical devices create a complex system with two independent pumps, one of them right-sided and the other one left-sided. The left atrial venous return is normally greater than the right atrial pre-load, because of the bronchial circulation; overall, the left-sided output (LVAD plus native left ventricle) must always be greater than the right-sided output (RVAD plus native right ventricle), or else, pulmonary oedema may develop. In addition to navigating complex biventricular cannula insertion anatomy, native right and left ventricular function may also recover at different rates.

CHANGES IN THE VENTRICULAR FUNCTION AFTER IMPLANTATION

The histological and biochemical signs of recovery of mechanically supported myocardial tissue are an issue of inquiry. Although a VAD's main purpose is to assume the pumping function of the heart, the reduction in myocardial stretch after the VAD decompression may lead to a recovery process referred to as reverse ventricular remodelling [11]. Improvement in intrinsic myocyte function may occur due to alterations in abnormal gene expression; changes in collagen content; regression of cellular hypertrophy; and reduction in myocytolysis and inflammatory cytokines [12-15]. Although such changes may occur, most patients do not fully recover and are ineligible for explantation [16]. To help promote reverse remodelling, efforts are underway to assess the use of disease-altering pharmacological regimens in VAD patients. At the present time, all patients who appear to be bridge-to-recovery candidates are restarted on neuro-hormonal antagonists, which are then up-titrated to published guidelines as tolerated. In 2006, Birks et al. reported on the successful re-

versal of remodelling in selected VAD patients with non-ischemic cardiomyopathy treated with clenbuterol [17].

DEVICE SELECTION

The anticipated treatment endpoint must be considered when choosing a specific device. In this article, short-term mechanical support devices are described. These include counter-pulsation and centrifugal, axial, and pneumatic pumps. These devices, which are easily implemented, aim at providing either a short-term bridge-to-recovery or a short-term bridge-to-more permanent assistance or transplant as destination therapy.

Intraaorticsed pre-operatively as an adjunct to high-risk percutaneous interventions or coronary artery bypass grafting. Contraindications for IABP use are aortic insufficiency, aortic dissection and severe aortic and peripheral vascular atherosclerosis. The latter concerns the pre-operative use; it is however possible to insert the balloon via the ascending aorta during surgery.

The iVAC 3L™ is a mid-range minimal heart circulatory assist device that effectively generates up to three litres per minute. The iVAC 3L™ off balloon pump (IABP), first described in 1968 [18], is the most common form of short-term mechanical circulatory assistance. Couner-pulsation, provided by balloon inflation within the descending thoracic aorta during diastole with deflation at the onset of systole. The result is reduction in myocardial work through after-load reduction, and improvement in myocardial oxygen supply through the augmentation of diastolic blood pressure and coronary perfusion pressure [19]. IABP counter-pulsation timing is performed from the ECG or the arterial waveform. IABP counter-pulsation is used today in a variety of clinical settings, including the cardiogenic shock associated with myocardial infarction; the postcardiotomy shock; the mechanical complications of infarction, such as acute mitral regurgitation and ventricular septal defect; the post-infarction angina; and for the treatment of ventricular arrhythmias in the setting of ongoing ischemia. IABP has also been u ers critical haemodynamic support in the case of left ventricular failure, or during high-risk revascularisation procedures with potential postcardiotomy weaning complications, as a cost-effective bridge- to-decision or bridge-to-bridge solution. The use of device ensures a fast and cost-effective implementation, due to a universally adaptable design that fully integrates with any standard IABP console. Patients have faster post-operative mobility with subclavian or axillary artery access. With the increase in more complex and higher risk cases, the incidence of postcardiotomy failure has now begun to rise. Currently, about 6 % of patients develop postcardiotomy ventricular failure. The iVAC 3L™ is indicated

for OPCAB procedures (recovery support); postcardiotomy weaning complications; cases of cardiogenic shock; acute myocardial infarction. At 3 l/m, the iVAC 3L™ does the job when an IABP is insufficient for the demand, and a higher-cost and more complicated LVAD may not be warranted. The iVAC 3L™ provides the cardiologist and cardiac surgeon with additional life saving options, and opens previously not available procedural possibilities. The use of this device unloads the left ventricle and increases circulatory blood flow; reduces the myocardial workload allowing the heart to rest and heal; potentially avoids the need for inotropes during CPB weaning; lowers the anticoagulation requirements; increases the coronary artery and end-organ perfusion; and finally, lowers the risk of haemodynamic deterioration. The iVAC 3L™ incorporates a patented rotating two-way valve, which is connected to an extracorporeal dual chamber membrane housing via a 21 Fr. lumen catheter. It can be used with any standard IABP driver unit and does not require dedicated hardware. When the heart is in the systolic phase, the blood flows from the ventricle through the catheter tip and is aspirated into the membrane housing. During the diastolic phase, the membrane pushes the blood back through the catheter, subsequently opening the valve and delivering the blood to the aorta through the side outflow port. The device directly unloads the heart by active aspiration from the left ventricle and simultaneously creates a pulsatile flow in the ascending aorta. The use of this device provides many advantages, such as: the aortic blood-flow increase; the mean arterial blood pressure improvement; the myocardial perfusion increase; the after-load reducement; the end systolic LV volume reducement; and the myocardial demand decrease by reducing the cardiac work.

Centrifugal pumps have been used both for intra-operative cardiopulmonary bypass and as a means of providing right, left, or biventricular mechanical circulatory support. They have following advantages: wide availability, the ease of use, and relative low cost when compared to other devices. Disadvantages include the need for systemic anticoagulation with resultant bleeding complications. The progressive development of interstitial oedema secondary to capillary leak and the inability to ambulate and rehabilitate these patients limit this technology to short-term support. Some of the most commonly used pumps are the Biomedicus Biopump (Medtronic Bio-Medicus, Inc., Eden Prairie, Minn); the Sarns centrifugal pump (3-M Health Care, Ann Arbor, Mich); and the St. Jude Lifestream centrifugal pump (St. Jude Medical, Inc., St. Paul, Minn).

The Levitronix CentriMag short-term LVAS comprises a single-use centrifugal pump, a motor, and a primary drive console. Compared to other devices, the Levitronix LVAS is unique insofar that it is designed to operate with no mechanical bearings or seals. This is possible since the motor magnetically levitates the impeller,

achieving rotation with no friction or wear. The Levitronix CentriMag is a continuous-flow, centrifugal-type rotary blood pump that is placed outside the body (extracorporeally). The pump housing and the rotor are made of medical-grade polycarbonate, designed for single use. The only moving component within the pump is the impeller, which is magnetically levitated and rotated in a contact-free manner. The centrifugal pump design permits the rotation of the impeller at lower speeds, while still achieving the desired flow rates. The pump can rotate at the speeds from 1,500 rpm to 5,500 rpm, and can provide the flow rates of up to 9.9 litres per minute. The Levitronix pump causes very little damage to the blood, as it contains no bearings or seals – components known to cause haemolysis and promote thrombus formation. Moreover, the pump does not contain any flexing sacs, diaphragms, or valves, minimising thereby the risk of component failure and device-related adverse effects.

The extracorporeal membrane oxygenation (ECMO) utilises a centrifugal pump in combination with a membrane oxygenator to provide complete cardiopulmonary support in the setting of circulatory and respiratory failure. The successful use of ECMO in the paediatric population has been well described [20]. The outcome of ECMO for the treatment of cardiac failure in the adult population is more limited.

The TandemHeart percutaneous VAD (CardiacAssist, Inc., Pittsburgh, Penn) utilises a centrifugal pump that pumps blood from the left atrium to one or both femoral arteries. The left atrial catheter is placed percutaneously via a trans-septal puncture [21].

The Impella Recover device (Impella CardioSystems AG, Aachen, Germany) is a miniature axial flow pump designed for short-term right, left, or biventricular support. The device is able to generate flows of up to 4 to 5 L/min at the rotational speeds of between 28,000 and 32,000 rpm. The device has the advantage of being easily implanted and having minimal requirement for anticoagulation. The device can be placed percutaneously and positioned with echocardiographic guidance [22].

The Abiomed BVS 5000i (Abiomed Cardiovascular, Inc., Danvers, Mass) is a device for acute postcardiotomy failure. It is a dual-chambered, pneumatically driven extracorporeal pump, designed for short-term cardiac support. The dual chamber polyurethane blood sacs fill passively, with pneumatically driven ejection. The configuration mimics that of the native atria and ventricles. The device is capable of generating a pulsatile flow of up to 6 L/min. The ease of implantation, operation, weaning, cost-effectiveness, and widespread availability have made it one of the most commonly used devices in the setting of acute cardiac failure. The indications for its use have expanded beyond the postcardiotomy setting, to include the cardiogenic shock associated with acute infarction; myocarditis; and temporary right ventricular support in association with long-term LVAD implantation.

The MAQUET Heart Lung Support (HLS) system including CARDIOHELP and the disposable HLS Set and HLS Cannulae is a very light and small life support system. The portable system provides extracorporeal life support (ECLS), to replace or support the patient's circulation and respiration, the so-called cardiopulmonary support. The device is light enough to be carried by one person, and compact enough to be transported in a helicopter or vehicle. With its disposables, its integrated sensors and its software versions, the CARDIOHELP life support system opens up new possibilities for patients requiring veno-venous ECLS or veno-arterial ECLS, as well as for CO_2 removal and the use of minimal extracorporeal circulation (MECC). Vessel access is needed to link the extracorporeal life support (ECLS) system to the patient. Special HLS Cannulae can be gently percutaneously inserted into appropriate veins and arteries for cardiac support and/or respiratory assistance. Some authors reported in observational study that extracorporeal cardiopulmonary resuscitation (CPR) has a short-term and long-term survival benefit over patients with conventional CPR in patients with in-hospital cardiac arrest of cardiac origin [23].

The AB5000 Circulatory Support System provides temporary support for one or both sides of the natural heart in circumstances where the heart has failed, giving the patient's heart an opportunity to rest and potentially recover. The AB5000 Ventricle is vacuum-assisted technology with clear housing to allow clinicians a view into the device. It uses the same cannula as the previously described BVS 5000 Blood Pumps, allowing for a seamless transition of devices without requiring any additional surgical procedure. Unlike other ventricular assist systems that can require multiple drivers for a single patient, patients on the AB5000 Ventricle require only a single console – regardless of their condition. The AB5000 Console is designed to allow patients to leave their hospital rooms and walk within the hospital and on hospital grounds. Multiple studies have shown that patient ambulation, or walking, assists the recovery process greatly. The ease of use and the transport capability of the AB5000 System make it an important option for both regional and local cardiac centres, and enable a patient to be transported to a more advanced cardiac centre if necessary.

POST-OPERATIVE MANAGEMENT AND COMPLICATIONS

In the immediate peri-operative period, proper device function and meticulous post-operative care must be ensured in order to maintain adequate end-organ perfusion. Antibiotic prophylaxis begins pre-operatively, and is usually continued for 48 to 72 hours post-operatively. 24 to 36 hours after implantation, systemic anticoagulation with heparin and warfarin is initiated. Patients should be weaned

from mechanical ventilatory support as soon as feasible. Diuretics are administered early in the post-operative course, since many of these patients are in a chronic volume-overloaded state. Peri-operative renal insufficiency is usually managed with the early institution of continuous veno-venous haemofiltration for the optimisation of fluid balance. Since the publication of the landmark REMATCH (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure) trial in 2001, refinement in devices and the adoption of best practice management techniques have improved the short- and long-term patient care [24,25]. Peri-operative complications include haemorrhage; right ventricular failure; sepsis; air embolism; and kinking of conduits. The most common late complications are mechanical device failure, neurological events, and infection [2,26,27].

Herein, we describe some of the most common complications:

Mediastinal bleeding following left ventricular assist device implantation is relatively common and may be related to systemic anticoagulation or the potentially acquired von Willebrand disease [28]. The predisposing factors include hepatic congestion and dysfunction related to chronic heart failure; compromised nutritional status; the use of pre-operative anticoagulation; extensive surgical dissection; re-operative procedures; prolonged cardiopulmonary bypass; and coagulopathy secondary to interactions between the circulating blood elements and the artificial device surfaces [29]. Of note late bleeding and tamponade can occur due to the requirement of systemic anticoagulation.

Sepsis due to infection is the leading cause of death in patients receiving ventricular assist devices[2]. Infections in LVAD patients can affect different components of the device and can vary in severity. Patients can also develop infectious complications at sites remote from the device such as in the respiratory, gastrointestinal, or genitourinary tracts, as well as from indwelling intravenous and central lines. Other patient factors, which may increase the susceptibility to infection, include generalised debilitation and malnutrition, diabetes, renal failure, and immunologic derangements associated with T-cell death seen after device implantation [30]. VAD infections can occur at any time, but most frequently, they occur between 2 weeks and 2 months after the implantation. Bacteria that are able to form biofilm, such as Staphylococcus, Pseudomonas, or Enterococcus, predominantly cause device-related infections. The frequent use of broad-spectrum antibiotics increase susceptibility for fungal infections, which are associated with the highest risk of death [31].

Implanted mechanical devices are susceptible to thromboembolic events due to their unique properties. The foreign surfaces of VADs can activate the immune system, platelets, and the coagulation cascade. In addition, the blood-contact surfaces

of VADs, along with the turbulent blood flow, increase the risk of shear stress on the blood and thrombi formation. Intracranial haemorrhage, syncope, seizure, brain abscesses, and encephalopathy have all been reported. These data mostly originate from the bridge-to-transplantation experience, and may not apply to destination therapy patients, who are generally older, and have more comorbidities and longer implantation periods. Not all devices have the same neurological event rate, and design modifications incorporated in the newer generation of VADs, including the use of novel biologic materials, textured coatings, and a single moving part, are believed to reduce the risk of thrombus formation. All device patients are maintained on aspirin, mainly for its anti-inflammatory effect, and most devices require anticoagulation with heparin and warfarin. The vigilant control of anticoagulation parameters is necessary to balance the risk of thrombus formation with the threat of late mediastinal bleeding.

Approximately 20 % of patients undergoing left ventricular assist device placement will suffer from post-operative right heart failure [32]. Predicting which patients will manifest right-sided failure can be difficult. The post-operative right ventricular failure has a significant effect on the clinical outcomes, leading to increased length of stay in the intensive care unit; increased 30-day mortality following the LVAD implantation; and a lower bridge-to-transplantation rate. Clinically, the onset of the right ventricular failure can be sudden, and may occur at the onset of an LVAD device initiation. The blood product transfusion has been shown to have adverse effects on pulmonary vascular resistance [33]. The use of aprotinin has been shown to decrease the blood loss, the incidence of the right VAD implantation, and the peri-operative mortality in patients undergoing LVAD placement [34].

A significant proportion of patients undergoing the device placement experience a multi-system organ failure that carries a high mortality in patients. Patients undergoing the VAD implantation have a high incidence of comorbidities, and many manifest significant end-organ dysfunctions pre-operatively. Some may not recover the organ function following the device implantation. Other patients may manifest multi-system organ failure as the end result of complications related to device implantation. These include surgical trauma, prolonged cardiopulmonary bypass times, peri-operative bleeding, and sepsis.

Device failure is an ever-present concern in patients with mechanical circulatory assistance. Both cardiac catheterisation and transesophageal echocardiography have been described as useful tools for the diagnosis of device malfunction.

Immunologic effects and allosensitization are derived from the interaction between prosthetic device surfaces and circulating blood elements. A number of alterations are seen in the T-cell function. T cells in LVAD patients demonstrated an

increased susceptibility to activation-induced cell death. Another aspect of the immunologic disturbance that is seen is the B-cell hyper-reactivity. The overall clinical effect of these changes is two-fold. First, patients demonstrate progressive defects in cellular immunity, with a resultant increased risk of infection. Second, B-cell hyperreactivity ultimately leads to allosensitization to human leukocyte antigens. Untreated allosensitization is associated with prolonged pre-transplant waiting times, as well as an increased risk of acute rejection. When sensitisation develops, immunomodulation with intravenous immunoglobulin therapy in conjunction with cyclophosphamide has proven to be effective in reducing alloreactivity, and reducing the risk of acute rejection [35].

CONCLUSION

Mechanical circulatory support has emerged as an important therapeutic option in the treatment of both acute and chronic heart failure of various aetiologies. As VAD technology progresses, the collaboration of multidisciplinary teams composed of engineers, scientists, physicians, and nurses will continue to refine the technology and improve patient care and operation outcomes. Advances in device design will allow for an easier implantation and create smaller, more efficient, durable, and reliable units. Active areas of investigation include the effects of mechanical unloading on ventricular remodelling, as well as the potential use of device support in conjunction with other modalities, such as gene therapy; pharmacotherapy; and stem cell implantation to promote myocardial recovery.

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Sažetak

Kratkotrajna potpora cirkulaciji i izmjeni plinova u krvi

Zatajenje srca s porastom incidencije i prevalencije u sve starijoj populaciji polako postaje javno zdravstveni problem. Mehanička cirkulacijska potpora se koristi kao oblik liječenja u skupini bolesnika s uznapredovalim zatajenjem srca. Mehanička crpka se kirurški implantira kako bi osigurala, bilo pulsatilni, bilo nepulsatilni protok krvi koji služi kao supplement ili kao zamjena protoku krvi kojeg bi trebalo generirati srce. Glavni cilj i namjena mehaničke cirkulacijske potpore je volumno rasteretiti srce u terminalnom zatajenju i pomoći u održavanju protoka vitalnih organa održavajući minutni volumen. Prisutna je široka paleta uređaja: od onih koji se mogu perkutano implantirati, uređaja za kratkoročnu potporu koji se mogu koristiti u operacijskoj sali, u laboratoriju za kateterizaciju kao i u jedinici intenzivnog liječenja do potpuno implantibilnih uređaja za dugoročnu potporu. Uređaji mogu biti korišteni kao terapija premoštenja do oporavka ili do transplantacije srca ili, u pojedinim slučajevima, uređaji predstavljaju definitivnu terapiju, npr. kod bolesnika u kojih je kontraindicirana transplantacija. Ovaj oblik liječenja ne uključuje samo kardiokirurge, već i kardiologe, anesteziologe kao i perfuzioniste. Pravilna trijaža bolesnika predstavlja ključnu točku uspjeha u ishodu liječenja volesnika s mehaničkom cirkulacijskom potporom. Prijeoperacijska stratifikacija rizika je iznimno važna u minimaliziranju stope perioperacijsakog mortaliteta. Istovremeni tehnološki razvoj, kao i multidisciplinarna suradnja konstruktora uređaja, znanstvenika, liječnika i ostalog medicinskog osoblja dovest će do unaprijeđenja cjelokupnog procesa liječenja ove skupine bolesnika. Daljnji tehnološki razvoj ide u smjeru pojednostavljenja procesa implantacije, s manjim, efikasnijim, trajnijim i još više pouzdanijim uređajima.

Ključne riječi: mehanička cirkulacijska potpora; zatajenje srca

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POSTOPERATIVE MANAGEMENT OF PATIENTS AFTER VAD IMPLEMENTATION

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Summary

After the implantation of the left ventricular assisted device (LVAD), patients are admitted in intensive care unit (ICU). During the period of first several days, the goal of the postoperative care is to stabilize the patients' hemodynamics. Monitoring the continuous cardiac output, filling volumes and outflow resistance is necessary for the proper functioning of the pump. The use of pulmonary artery catheter and the transesophageal echocardiography are primary procedures. During the operation of the left ventricular support, the measuring of proper ventricular function and the early recognition of its dysfunction is important for a positive outcome. Further potential complications in connection with these patients are an increased risk of hemorrhage and thromboembolism. The infection of drivelines and devices in the early postoperative period occurs in up to 40 % of these patients. In case of a cardiac arrest, a special procedure has to be performed in patients in whom LVAD was implanted. Finally, we have shown the anesthesiologic management in cases when patients with LVAD have to undergo noncardiac surgery.

Keywords: LVAD; hemodynamics; TEE; LVAD; noncardiac surgery

After the implementation of ventricular assisted device (VAD), patients are admitted to the intensive care unit (ICU). Recommendations for anesthetic approach during the surgery suggest the use of total intravenous anesthesia (TIVA), in order to minimize the hemodynamic impact; e.g. TIVA technique using an opioid; benzodiazepine such as midazolam; and long-acting muscle relaxant. Halogenated anesthetic agents may be used as supplementation to intravenous anesthesia, but only in patients who can tolerate them hemodynamically. In many centers, as well

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as in ours, there is no advantage to attempting a "fast-track" approach, since these patients are required to remain intubated overnight or longer, regardless of the type of device implanted. During this period, it is important to stabilize the patients' hemodynamics and coagulation, and perform the transesophageal echocardiography to check VAD and heart function.

Hemodynamics

In all the patients undergoing the implantation of VAD, continuous hemodynamic monitoring has to be implemented. It is recommended to implant a catheter for measuring both the continuous cardiac output (CCO) and the mixed venous saturation (SvO_2). The hemodynamic management of an LVAD patient is important, as the pump function of each device depends on both the filling volume and the outflow resistance. HeartMate, Novacor, and Thoratec pumps all exhibit sensitivity to changes in the preload, especially when functioning in the "fill-to-empty" mode. While these devices exhibit no Starling effect with respect to stroke volume or stroke work, they can only pump the volume delivered to them, and inadequate filling will result in a decreased flow through a decrease in the stroke rate. Thus, the maintenance of an adequate preload is of crucial importance. Direct decreases in the pump flow occur when the preload declines, as a consequence of a decreased venous return secondary to an increased venous capacitance, alterations in the body position that reduce the venous return (lateral decubitus or reverse Trendelenburg position), inadequate administration of intravenous fluids, or uncontrolled surgical bleeding. The preload sensitivity of these devices suggests that the invasive monitoring of RV and pump filling pressures using a central venous, pulmonary artery catheter, or two-dimensional transesophageal echocardiography is necessary. Negative inotropic drugs and factors that can reduce RV output by increasing pulmonary vascular resistance (such as hypoxemia, hypercarbia or acidosis) should be avoided. Progressive increases in the central venous pressure and RV dilatation, combined with simultaneous reductions in LVAD output (or thermodilution-derived cardiac output), are highly suggestive of RV dysfunction and may require an intervention with either positive inotropic drugs (milrinone, dobutamine, or levosimendan) or selective pulmonary vasodilators (inhaled nitric oxide or prostaglandins).

Right-sided circulatory failure

Right-sided circulatory management is the key for successful postoperative care in patients with left ventricular assist device (LVAD). The strategies include the maintenance of chronotropy in the right ventricle (RV) and the decreasing of the

pulmonary vascular resistance. Inhaled nitric oxide may be invaluable in the early management of patients with LVAD, because its vasodilatative effect on pulmonary vasculature without the systemic hypotensive effect is more potent than other pulmonary artery vasodilators. Further approaches include the use of a phosphodiesterase inhibitor (most frequently milrinone), nesiritide or levosimendan, usually in combination with a systemic vasoconstrictor. In these patients, vasopressin has an advantage over other alpha-adrenergic agonists, as it possesses minimal vasoconstrictive effects on the pulmonary vasculature. The use of other systemic vasoconstrictors in patients with LVAD is common, as the systemic arterial vasodilation commonly occurs due to various reasons.

Hemorrhage

Postoperative hemorrhage is common in these patients. The preoperative heart dysfunction leads to hepatic congestion and renal dysfunction, both leading to imbalances in the platelet function and the coagulation cascade. An additional exposure of blood to foreign surfaces of cardiopulmonary bypass can exacerbate postoperative bleeding. In the intensive care unit, the prevention of bleeding is provided with warming the patient and with replenishing of platelets and other factors of the coagulation cascade. It is important that in patients, who are transplant candidates, transfusions of platelets and erythrocytes should be given through leukocyte filters to prevent develop antibodies against future donated organs. Fresh frozen plasma and cryoprecipitate do not have a high leukocyte content, and they do not need filtration.

Thromboembolism

Thromboembolism is associated with all current assist systems. The patient with a Novacor or Thoratec device is chronically treated with warfarin, except HeartMate IP/XVE, which appears to have the lowest overall thromboembolic rate and is generally maintained with chronic aspirin therapy alone.

Infection

Device-related infections are the most common cause of morbidity in the chronically supported patients. Driveline and device infections occur in up to 40 % of these patients. The vast majority of these infections may be managed with chronic antibiotic therapy until transplantation. The infection of the blood contacting surfaces of the device (valves or diaphragm) necessitates device change.

Cardiac arrest

In case ventricular tachycardia or ventricular fibrillation occur, it is important – though that device provides given cardiac output – to terminate these rhythm disturbances, primarily due to extreme oxygen consumption. If external defibrillation/cardioversion is used, it is important not to disconnect the percutaneous lead from the system controller and not to stop the pump prior to delivering the shock. The percutaneous lead should only be disconnected in cases where open-heart defibrillation is required. In the event the LVAD stopped operating and blood were stagnant in the pump and conduits for more than a few minutes (depending on the anticoagulation status of the patient), a risk of stroke and/or thromboembolism would exist if the device were restarted. Retrograde flow might occur during pump stoppage. During cardiopulmonary resuscitation (CPR), external chest compressions should be avoided. External chest compressions pose a risk due to the location of the outflow graft on the aorta and the inflow conduit in the left ventricular apex. Dislodgement could lead to fatal hemorrhage. It is necessary to use clinical judgment when deciding whether to perform external chest compressions in these cases.

Management of the VAD patients for noncardiac surgery

These patients can be very ill, and surgery can be contemplated early after VAD implantation. After weeks or months after implantation, patients may safely undergo noncardiac surgical procedures, with attention on several details. Anesthetic induction with sedative–hypnotic drugs, which increase venous capacitance (thiopental, propofol), or rapid administration of other vasoactive drugs, which produce selective dilation of the venous circulation, may produce acute hemodynamic decompensation in the LVAD patient, because the pump blood-flow decreases during these conditions. As a result, hypertension should be specifically avoided, because the emptying of the LVAD is reduced by increases in the arterial pressure. Incomplete LVAD ejection does not only decrease the forward flow, but rather promotes the blood stasis within the device and increases the risk of thrombus formation, even in the presence of systemic anticoagulation. Acute increases in the sympathetic nervous system activity and its consequent effects on the arteriolar tone, produced by laryngoscopy, intubation, or surgical stimulation, represent an important goal in the perioperative management of these patients. These may be avoided by the assurance of adequate anesthetic depth, using volatile anesthetics in combination with an opioid or by the judicious administration of arterial vasodilators to treat increases in the arterial pressure. In the absence of hypertension, most cases of low LVAD flow can be corrected by volume expansion, though RV dysfunction must also be

considered. The management of anticoagulant therapy is another major issue that requires attention in the perioperative care of the LVAD patient. Patients with a Novacor or Thoratec device, chronically treated with warfarin, should be converted to intravenous heparin therapy before elective surgery, similar to patients with a mechanical prosthetic valve. The heparin should be discontinued during the immediate preoperative period and resumed when the risk of postoperative bleeding diminishes. During emergency circumstances, the withdrawal of oral anticoagulants may not be accomplished before surgery, and the transfusion of fresh frozen plasma is required. Patients with HeartMate device are generally maintained with chronic aspirin therapy alone, and excess perioperative bleeding may require platelet transfusion to obtain adequate hemostasis.

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Sažetak

Postoperacijsko liječenje bolesnika s mehaničkom potporom srca u jedinici intenzivnog liječenja

Nakon ugradnje lijevostrane srčane potpore (LSP), bolesnici se zaprimaju u jedinicu intenzivne medicine. Tijekom ovog razdoblja od nekoliko dana, osnovni cilj poslijeoperacijskog liječenja je stabilizacija bolesnikove hemodinamike. Praćenje kontinuiranog minutnog volumena, tlakova punjenja i sustavne rezistencije je neophodno za ispravno funkcioniranje LSP-a. Uporaba plućnog arterijskog katetera s kontinuiranim mjerenjem minutnog volumena te transezofagijska ehokardiografija su primarni postupci. Za vrijeme rada LSP, praćenje funkcije desne klijetke te rano uočavanje njene disfunkcije od krucijalnog su značaja za dobar ishod bolesnika. Daljnje moguće komplikacije u ovih bolesnika su povećani rizik od krvarenja, kao i od nastanka tromboembolija. Incidencija infekcija u ovih bolesnika je visoka, i kreće se do 40%, osobito infekcije kanila. U slučaju zastoja rada srca, primjenjuju se posebni postupci oživljavanja, koji se razlikuju od uobičajenih algoritama. Na kraju, prikazane su i specifičnosti anesteziološkog postupka u ovih bolesnika ukoliko postoji potreba za nekardijalnom operacijom.

Ključne riječi: LVAD; hemodinamika; TEE, LVAD i nekardijalne operacije

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INITIAL CLINICAL RESULTS WITH THE LEVITRONIX CENTRIMAG MECHANICAL ASSIST DEVICE AT THE UNIVERSITY HOSPITAL REBRO ZAGREB

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Summary

Background: The management of end stage heart failure has been revolutionized by the use of mechanical circulatory support. The Levitronix Centrimag ventricular assist device (VAD) is designed for short-term cardiac assistance as a bridge to a more permanent solution to the hemodynamic problem. It has been used as bridge-to-transplantation, bridge-to-bridge, bridge-to-recovery, and bridge-to-decision.

Methods: In the period between September 2008 and November 2009, six patients received mechanical cardiac assistance with the Levitronix Centrimag device at our institution. In one patient, the indication was postcardiotomy cardiogenic shock. In the remaining five patients, the device was implanted electively, due to progressive decompensation of chronic heart failure unresponsive to medical therapy.

Results: The patient having received a biventricular assist device (BIVAD) in the postcardiotomy setting was 65 years of age. His ejection fraction and EuroSCORE were 20 % and 25, respectively. His NT-pro-BNP was 9,428 pg/ml and his pre-implantation lactate was 8.8 mmol/L. The mean age in the group of patients, in whom the VAD was placed due to decompensated severe heart failure (DSHF), was 46 ± 11 years. Their ejection fraction and logistic EuroSCORE were 16 ± 2 % and 28 ± 7, respectively. The preoperative serum lactate and NT-pro-BNP concentrations were 1.7±0.8 mmol/L and 9577 ± 3674 pg/ml, respectively. Of these, three patients had evidence of end organ dysfunction. The low cardiac output was responsible for acute renal failure, requiring renal replacement therapy in one patient. Neurocognitive dysfunction and renal failure not requiring dialysis was seen in another. The third patient had long standing

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primary hepatic insufficiency. A reversal of end organ dysfunction was seen in the former two patients, whereas the hepatic insufficiency was not caused by hemodynamic compromise and was, therefore, not relieved by circulatory support. The single patient, who had suffered from postcardiotomy cardiogenic shock, died shortly after receiving mechanical circulatory support. Three of five patients, in whom Levitronix Centrimag was placed electively, were successfully transplanted. The remaining two died of septic complications. In the cohort of patients, in whom ventricular assistance was placed due to DSHF, two required BIVAD placement, and three left ventricular assist devices (LVAD).

Conclusion: The Levitronix Centrimag VAD is useful in supporting circulation in patients with acute decompensation of congestive heart failure. It may also be used in patients with postcardiotomy shock. It is an imperative for the device to be placed before irreversible organ dysfunction occurs as the aftermath of malperfusion.

Keywords: Levitronix Centrimag; ventricular assist device

INTRODUCTION

The progress in pharmacological therapy has yielded significant improvements in the care of patients with heart failure. This has further been facilitated by the utilization of devices such as cardioverter/defibrillators and cardiac resynchronization therapy [1]. While heart transplantation remains an excellent therapeutic option for patients with terminal heart failure, it is available only to a minority of potential transplant candidates due to a shortage of organ donors [2]. The discrepancy between the number of heart transplantations and the number of patients, who could benefit from this form of therapy, provides a fertile milieu for the development of mechanical assist devices. Ventricular assist devices are now viable options for patients with severe heart failure symptoms as bridge-to-transplantation, bridge-to-decision, bridge-to-recovery, or as destination therapy. Various mechanical assist devices differ widely in the intended recipient patient populations. The Centrimag device (Levitronix, Waltham, MA, USA) is a contemporary adjunct to the available spectrum of short-term mechanical assist devices. It has been utilized in patients with refractory cardiogenic shock for either univentricular or biventricular support [3,4]. It has also been used for the purpose of extracorporeal membrane oxygenation [5]. The Levitronix Centrimag device is a new generation pump that offers hemodynamic support with reduced blood trauma. It does not contain rotating bearings or seals. It is also devoid of flexing valves or diaphragms. When compared to older generation centrifugal pumps, this technical design allows for longer circulatory support. Its dominant feature is a magnetically levitated rotor, which is not in contact with the housing of the device.

PATIENTS AND METHODS

In six patients, short-term mechanical circulatory support was instituted using the Levitronix Centrimag device between September 2008 and November 2009 at the University Hospital Rebro Zagreb. The records of these patients were reviewed. In one patient, the device was implanted in the setting of prolonged postcardiotomy cardiogenic shock. In five patients, the indication for ventricular assistance was decompensated severe heart failure (DSHF). These patients were analyzed separately, since the clinical settings were quite different. The patient in postcardiotomy shock received biventricular assist device placement (BIVAD). Of the five elective patients, who suffered from decompensated severe heart failure, three underwent solely left ventricular assistance, whereas in the remaining two a BIVAD was placed.

Technical considerations

The components of the Centrimag system include a centrifugal blood pump, a motor, a console and a flow probe. The magnetic force, generated by the motors, levitates the impeller in the pump housing in addition to creating the torque that translates into unidirectional flow out the device. The priming volume is 31 ml.

Implantation technique

The device was inserted through a median sternotomy in all patients. In three patients, the Centrimag was implanted for biventricular support, and in the remaining three patients, only the left ventricle was assisted. In three patients, the device was implanted with the use of cardiopulmonary bypass (CPB). The decompression of the heart made the placement of the left atrial and pulmonary artery cannulae simpler in those cases. In the remaining three patients, the Centrimag was implanted without CPB. All patients received a bolus dose of heparin, in order to achieve an activated clotting time greater than 450 seconds prior to the implantation. Antifibrinolytic therapy with tranexamic acid was administered to every patient. All cannulae were placed through two 2/0 Prolene purse-string sutures, reinforced with Teflon pledgets. The sizes of individual cannulae were tailored to the patient body surface area. Intraoperatively, heparin was fully reversed with protamine after the ventricular assistance had commenced.

Postoperative management

Anticoagulation with intravenous heparin was started 12-24 hours after the implantation of the Centrimag, provided that the chest tube output was minimal. The

target ACT was 180 to 200 seconds. Once the patients achieved hemodynamic stability in the intensive care unit, their sedation was discontinued, and subsequently, they followed the standard protocols for weaning off mechanical ventilation.

RESULTS

Six consecutive patients, undergoing Centrimag ventricular assistance, were included into our study. The patient demographic data are presented in Table 1. The patient, who underwent the salvage placement of the Centrimag device in the setting of postpericardiotomy shock, is presented isolated from the remaining five patients, since his clinical scenario differed greatly from the remaining patients. Irreversible organ dysfunction was likely present at the time of the ventricular assist

Table 1. Preoperative patient characteristics

	PCS*	DSHF**
N	1	5
Age (yrs)	65	46±11
Gender (n/%)		
Male	1 (100)	4 (80)
Female	0 (0)	1 (20)
Ejection fraction	20	16 ± 2
EuroSCORE	25	28 ± 7
DDRF	0	1 (20)
Non-DDRF	0	1 (20)
Hepatic failure	0	1 (20)
Neurocognitive dysfunction	0	1 (20)
Inotropes	1 (100)	5 (100)
Sodium ion (mmol/L)	135	127±9
Bilirubin	40	29±22
Alkaline phosphatase (IU/L)	119	178±245
Alanine aminotransferase (IU/L)	143	171±271
Urea (mmol/L)	12	12±5
Creatinine (mmol/L)	109	154±116
Mechanical ventilation	1 (100)	0 (0)
Lactate (mmol/L)	8.8	1.7±0.8

PCS = Postcardiotomy cardiogenic shock
DSHF = Decompensated severe heart failure
DDRF = Dialysis-dependant renal failure

device placement, which was instituted as salvage therapy. The patient was reoperated for bleeding on multiple occasions, due to a severe and resistant coagulopathy, and died within 24 hours of placing the device.

In the cohort of patients with decompensated severe heart failure (n=5), the mean duration of support was 21±23 days. The mean duration of ventilatory support was 14±6 hours. All patients remained in the intensive care unit for the duration of the ventricular assistance. One patient had to be taken back to the operating room 8 days after the implant procedure for bleeding. She was found to have an iatrogenic intercostal artery injury after a pleural tap had been performed. This was unrelated to the placement of the device. There were no permanent strokes.

Three of these five patients suffered from some degree of end-organ dysfunction prior to the placement of the device. In one patient, in whom the renal function recovered after the placement of the Centrimag as an LVAD up to a point where he could be weaned off renal replacement therapy, it was dialysis-dependant renal failure. The neurocognitive function in a second patient also improved upon the institution of Centrimag support. This patient also had non-dialysis-dependant renal failure, which did not show any significant improvement following VAD placement. The hepatic failure, seen in another one of the patients, did not improve with the

Table 2. Perioperative data

	PCS*	DSHF**
N	1	5
Duration of VAD support (days)	1	21±23
Mechanical ventilation (hrs)	20	14±6
Lactate POD 1 (mmol/L)	> 15	1.2±0.4
BIVAD	1 (100)	2 (40)
LVAD	0	3 (60)
Off pump placement	0	3 (60)
Duration of CPB (min)	281	37±20
Cerebrovascular incident	Unknown	0 (0)
DDRF	1 (100)	0 (0)
Bleeding (resternotomy)	1 (100)	1 (20)
Mortality	1 (100)	2 (40)
Bridge to transplantation	0 (0)	3 (60)

VAD = ventricular assist device
BIVAD = biventricular assist device
POD1 = postoperative day 1
CPB = cardiopulmonary bypass
DDRF = Dialysis-dependant renal failure

hemodynamic support. This patient suffered from hemochromatosis and had intrinsic liver failure. He underwent successful heart tranplantation after having been supported on the Centrimag for 11 days, and is currently being evaluated for liver transplantation. Three of the five patients with decompensated severe heart failure underwent heart transplantation. There were no deaths following the transplant procedure. The remaining two patients on Centrimag support, who were not transplanted, died. One died after 9 days of Centrimag LVAD support of pulmonary complications that progressed to septic shock. The device was supporting the second patient in this cohort, who died, for 62 days. She was initially found to have a panel reactive antibody (PRA) titer in excess of 90 %. The process of desensitization included the treatment with plasmapheresis, intravenous immunoglobulins and rituximab. Unfortunately, the PRA titer remained high, and the patient ultimately developed a sepsis with subsequent multiple organ failure, which led to death. Detailed perioperative data are presented in Table 2.

DISCUSSION

The challenges of heart transplantation include organ donor shortages; complex immunobiologic responses leading to acute rejection; complications of immunosuppressive treatment; and organ failure due to chronic rejection and allograft vasculopathy [1]. The limitations of transplant surgery have invoked innovations in VAD designs, making devices increasingly more appealing for the management of severe heart failure. The ventricular assist devices vary greatly, in terms of duration of intended support; type of flow augmentation; levels of possible ambulation; hence, they are designed for various patient populations. The Levitronix Centrimag is a short-term VAD, designed as a bridge-to-recovery, bridge-to-decision, bridge-to-bridge or bridge-to-transplantation [4,6]. We have found its versatile design simple to operate and useful in the settings of both uni- or biventricular failure. It has the ability to reverse end-organ dysfunction, provided that the potential for its recovery still exists. The level of ambulation these patients can achieve is limited, but physical therapy is nevertheless critical to the successful management of these patients. We have instituted the Centrimag support as a bridge-to-transplantation in five patients, and as a bridge-to-decision in the scenario of postcardiotomy shock in one patient. Three patients were successfully transplanted and have been discharged home. Our small series illustrates the feasibility of using the concept of short-term mechanical assistance in patients with severe decompensated heart failure as a bridge-to-transplantation, allowing for recovery of end-organ function secondary to malperfusion. This, in turn, allows for the transplant procedure to be performed

in optimal conditions for the patients. The device certainly has the potential to be used in the postcardiotomy failure scenario. It is paramount, however, to institute circulatory support prior to the development of irreversible end-organ damage.

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Sažetak

Rezultati ugradnje Levitronix Centrimag mehaničke potpore srcu u Kliničkom bolničkom centru Zagreb

Uvod: Liječenje terminalne faze srčanog popuštanja je revolucionarizirano uvođenjem mehaničke potpore srcu. Levitronix Centrimag je uređaj dizajniran u svrhu kratkoročne hemodinamske potpore prije nego što trajnije rješenje cirkulatornog problema postane moguće. Do sad se primijenjivao kao podrška srcu do transplantacije srca, do oporavka srčane funkcije ili do ugradnje trajnijeg oblika mehaničke potpore srcu.

Metode: U periodu između rujna 2008 i studenog 2009 Levitronix Centrimag je u našoj ustanovi ugrađen u 6 bolesnika. U jednog bolesnika radilo se o postkardiotomijskom sindromu niskog minutnog volumena. U preostalih pet bolesnika ovaj je oblik mehaničke potpore srcu ugrađen elektivno radi progresivnog kliničkog pogoršanja bolesnika u terminalnoj fazi srčanog popuštanja koje je postalo rezistentno na konzervativnu terapiju.

Rezultati: Bolesnik u kojeg je indikacija za mehaničkom potporom srcu bila postavljena hitno u postkardiotomijskom srčanom popuštanju bio je 65 godina star. Imao je ejekcijsku frakciju od 20% dok mu je logistički EuroSCORE bio 25. Prijeoperacijski NT-pro-BNP bio je 9428 pg/ml dok su serumske vrijednosti laktata prije implantacije Centrimaga bile 8.8 mmol/L. Prosječna dob u skupini bolesnika u kojih je indikacija za mehaničku potporu srcu bila progresivna dekompenzacija srčane funkcije bila je 46 ± 11 godinu. Navedeni bolesnici su imali prosječnu ejekcijsku frakciju od 16 ± 2% dok im je logistički EuroSCORE bio 28 ± 7. Prijeoperacijske vrijednosti serumskog laktata i NT-pro-BNP bile su 1.7±0.8 mmol/L i 9577 ± 3674 pg/ml. U troje bolesnika bila je evidentna kompromitacija funkcije nekog od ostalih organskih sustava. U jednog bolesnika se radilo o akutnom renalnom zatajenju ovisnog o hemodijalizi, u drugog o neurokognitivnoj disfunkciji praćenog sa bubrežnim zatajenjem ali bez potrebe za dijalizom. U trećeg bolesnika radilo se o primarnoj hepatalnoj insuficijenciji. U prva dva bolesnika došlo je do poboljšanja organskih funkcija nakon uspostave mehaničke potpore srcu, dok u trećeg bolesnika nije došlo do promjene hepatalne funkcije budući da ista nije bila uzrokovana malperfuzijom. Bolesnik u kojeg je mehanička potpora srcu stavljena zbog postkardiotomijskog kardiogenog šoka je umro. Troje od pet bolesnika kod kojih je Levitronix Centrimag ugrađen radi dekompenzacije kroničnog zatajenja srca su uspješno transplantirani. Preostalo dvoje bolesnika je umrlo od septičnih komplikacija. U kohorti bolesnika u kojoj je mehanička potpora srcu ugrađena elektivno, dvoje bolesnika je zahtijevalo potporu oba ventrikula dok je u troje ugrađena potpora samo lijevom.

Zaključak: Levitronix Centrimag pruža efikasnu hemodinamsku potporu bolesnicima sa kompromitiranom srčanom funkcijom. Neophodno je započeti sa mehaničkom potporom srcu prije nego što se pojave ireverzibilne disfunkcije ostalih organskih sustava.

Ključne riječi: Levitronix Centrimag; mehanička potpora srcu

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TAKE THE BEST – HOW TO CHOOSE THE RIGHT DEVICE?

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Summary

An increasing number of patients suffering from end-stage heart failure require VAD implantation as either a bridge-to-transplantation or destination therapy. The choice of the right device depends upon the medical urgency; the need of uni- or biventricular support; the duration of support expected; and the institutional availability. Patients with multi-organ failure and unclear neurological situation can be supported with rotary pumps/ECMO first, and in case of recovery, a paracorporeal system can be connected to the previously implanted cannulas. In stable patients qualifying for left ventricular support, an intracorporeal system of the second generation can be implanted, allowing freedom of movement for 6-8 hours before recharging becomes necessary, and support intervals exceeding 1 year. Restrictions are given by the need of high-dose anticoagulation and a certain complication rate, especially in the first 3 months (bleeding, thromboembolism, infection, mechanical failure). The survival rate after the primary LVAD implantation is 74 % after 12 months and 55 % after 24 months; this is significantly better than the survival rate after RVAD, BVAD or TAH.

Keywords: cardiac failure; mechanical assist device; heart transplantation

Considering cardiac support, the selection of the best device for individual patients in their particular situations is a major challenge, besides technical issues and postoperative management. This is especially the case if long-term support is required. The patients' outcome after the implantation of a ventricular assist device (VAD) is affected by their health status, including medical urgency, the need for inotropes, the extending of end-organ failure, the right ventricle function, coagulation disorders, the suspicion of infection, severe myocardial necrosis, and previous cardiac surgery. Elective patients suffering from chronic heart failure without myocar-

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dial necrosis, with no or low-dose inotropic support and intact end-organ function, are at low risk. Patients in acute low cardiac output following myocardial infarction, resuscitation or cardiac surgery, requiring high doses of inotropes and with imminent multi-organ failure (MOF) are exposed to high risk after a VAD implantation. One of the most critical factors for implant success, however, is the age. According to Deng et al. (J Heart Lung Transplantation 2005), 41 % of patients ≤ 65 years were still alive 12 months after a VAD implantation, while 20 % had undergone heart transplantation. In contrast, the one-year survival rate of VAD patients > 65 years was only 26 %, and none of these patients had a transplant option.

Nowadays, a variety of VADs are commercially available. They are categorized into extra-/ paracorporeal devices (ECMO, Excor, ThoratecPVAD, Medos, Abiomed), intracorporeal systems and fully implantable total artificial hearts (Cardiowest TAH). The intracorporeal systems of the first generation were large displacement pumps (Novacor, Heartmate I), followed by the second-generation impeller pumps (Incor, Heartmate II, DeBakey LVAD, Jarvik Heart). The centrifugal technique (Heartware, Terumo, Coraid) is yet to be established on the market.

For device selection, several issues have to be considered. In many institutions, the costs determine the availability and the spectrum of mechanical support systems. A special expertise with one or the other device improves the results, but also influences the support strategies. Eventually, the device selection is based on the clinical setting to optimise the resources. Most patients are provided with a left-ventricular assist device (LVAD). Due to the inability of the current allocation system to provide donor hearts in time, and the consequently longer waiting periods, there is a clear trend towards the use of implantable systems. In the US, the Heartmate II device has the most widespread use, whereas in Europe and Asia, the BerlinHeart Incor is equally favoured. It may well be that all miniaturized LVADs serve the same purpose alike, provided that the implant team has the necessary expertise. The impeller devices have a low weight, allowing 5,000-10,000 rotations per minute, and generate the pump flow up to 6 l/minute. The INCOR system operates without any mechanical contact and ensures a wear-free long-term support for patients with terminal heart failure. A driveline is connected to a double-battery power pack, allowing the system to operate for 6-8 hours before recharging becomes necessary. During the past years, the number of implantations has dramatically increased, and the support intervals exceeding one year are no longer an exception.

Paracorporeal devices were primarily designed for biventricular use, i.e. for combined left and right heart failure. In fact, there is still no implantable biventricular rotary pump available today. Another suitable indication for paracorporeal systems are patients with multi-organ failure, as they demand higher pump flows than

urgent cases. A third indication is a borderline patient with a high risk of failure, who compromises the clinical budgets. Especially for the latter cases, new strategies have been developed to optimise the financial resources. Patients presenting with unclear neurology in an emergency situation are placed on ECMO first, for a short-term support as a bridge-to-decision. If recovery from MOF is doubtful but the patient is awake, two rotary pumps may be used as well. After the stabilisation of end-organ function, the rotary pumps/ECMO are converted to a biventricular assist device (BVAD). To simplify the conversion, we recommend the use of four implantable cannulas (right atrium / pulmonary artery; left ventricular apex / aorta) during the initial procedure. Later, the BVAD can easily – under mild sedation – be connected on ICU. The main problem associated with a paracorporeal device is its suitability for short- and medium-term support only, as well as the risk of ascending conduit infection.

Apart from multi-organ failure (MOF), the main early complications include bleeding and right heart failure (in case of an LVAD placement), thromboembolism occurs mid-term, and infection usually later. Therefore, meticulous surgical hemostasis during surgery is mandatory. After the cessation of cardiopulmonary bypass, heparin is completely antagonised and restarted only after 6-24 hours, if there is no evidence of bleeding (PTT ~ 60-80 seconds). Aspirin is added after the normalisation of platelet function, and the daily dosage is adjusted (100-200 mg max.) to the results of aggregometry. For hospital discharge, the patient is placed on warfarin (INR 2.0-4.0). In cases of aspirin resistance or embolic events under aspirin medication, clopidogrel or dipyridamol is added to achieve the adequate inhibition of the platelet function.

If severe right heart failure is present, the use of two paracorporeal pumps is recommended. After the LVAD implantation, right ventricular failure is responsible for approximately 30 % of early deaths. In cases with only mild to moderate right heart insufficiency, pharmacological intervention is sufficient. After the implantation, the LVAD flow should be increased gradually to avoid the right ventricular overload. Additionally, the right ventricle can be stimulated by inotropes, and pulmonary vascular resistance can be lowered specifically by the systemic application of PDE-5-inhibitors, prostaglandins and nitrates and/or by the inhalative application of prostaglandins and nitric oxide. A temporary support with a centrifugal pump is possible, too; however, it hinders patient mobilization.

The occurrence of neurological events depends on a patient's condition, the anticoagulation regime, and the VAD system. The average risk varies between 5 and 30 %, and it is highest during the first three months. However, asymptomatic thromboembolism is not infrequent, predominantly in the liver, spleen and kidney.

VAD-related infection is a major limitation of the long-term support, and it is responsible for approximately 20 % of the deaths after the first month after the LVAD implantation. Besides the highly aseptic surgery, daily careful wound dressing of the cannulas and driveline ports is mandatory. A proper fixation of the driveline closely to the skin outlet facilitates the healing and prevents the driveline infection as well. In case of an infection, the early onset of antibiotic therapy, as well surgical wound care, are imperative. In rare cases, an exchange of the VAD system or urgent heart transplantation remains the only option.

Results with VADs strongly depend on patient selection. Accordingly, a careful and individualized patient and VAD selection improve the results and lower the costs. The overall outcome data are best documented in the US INTERMACS Registry. From June 2006 to March 2009, a total of 1,092 patients on LVAD were reported there. The survival rate after the primary LVAD implantation was 74 % after 12 months and 55 % after 24 months (event death, censored at transplant or recovery). These are significantly better results than with the survival after the RVAD, BVAD or TAH (six-month survival rate of approximately 50 % in all instances). The following problems/complications after the VAD implantation were reported: major bleeding events; thromboembolism; infection; right ventricular failure on LVAD; persistent ventricular fibrillation on LVAD; and inadequate mobilisation possibility of the patient.

In conclusion: with the current VAD systems, good results may be obtained with a low complication rate and a high quality of life during support. The implantable and miniaturised VAD systems allow for increasing the support intervals and paving the way for destination therapy.

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Sažetak

Najbolji izbor – kako izabrati odgovarajući uređaj?

Sve veći broj pacijenata u terminalnoj fazi zatajivanja srca zahtijevaju ugradnju mehaničke potpore srcu i cirkulaciji, kao premoštenje do transplantacije srca ili kao destinacijska terapija. Odabir odgovarajućeg uređaja ovisi o kliničkom stanju pacijenta, potrebi za jednostrukom ili dvostrukom ventrikularnom potporom, očekivanom trajanju ugrađene potpore i mogućnostima institucije. Pacijentima s multi organskim zatajenjem i nejasnim neurološkim smetnjama može se prvo ugraditi rotacijska pumpa/ECMO, te u slučaju oporavka., parakorporalni uređaj može biti povezan s ranije implantiranim kanilama. Kod stabilnih pacijenata, predodređenih za ugradnju potpore lijevom ventriklu, moguće je ugraditi intrakorporalni uređaj druge generacije, koji dozvoljava slobodno kretanje 6-8 sati do punjenja baterija i podupire intervale preko jedne godine. Ograničenja nastaju zbog potrebe za visokim dozama antikoagulacijske terapije i pojave određenih komplikacija, posebno u prva tri mjeseca nakon implantacije (krvarenje, tromboembolija, infekcija, mehaničke nepravilnosti). Stopa preživljenja 12 mjeseci nakon ugradnje LVAD-a je 74% i 55% nakon 24 mjeseca što je značajno bolje nego preživljenje nakon ugradnje RVAD, BVAD or TAH.

Ključne riječi: zatajivanje srca; mehanička potpora srcu; transplantacija srca

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LONG-TERM MECHANICAL CIRCULATORY SUPPORT FOR PATIENTS WITH TERMINAL STAGE OF CONGESTIVE HEART FAILURE: A CASE REPORT

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Summary

Despite recent advances in treatment, the number of people with heart failure continues to grow; this is associated with high mortality and morbidity rates. Heart transplantation is very limited due to the lack of the adequate number of heart donors, and medical therapy remains palliative. He use of ventricular assist devices (VADs) has led to improved survival rates for patients with severe heart failure. Originally introduced as a temporary bridge-to-recovery, and later as a bridge-to-transplantation, VADs have evolved to permanent or destination therapy for patients with terminal stage of congestive heart failure[1]. In this paper, we report of our patient with dilatative cardiomyopathy, to whom – due to the end-stage heart failure, and for the first time in Croatia – a device for paracorporeal long-term mechanical left ventricular support (pVAD) was implanted.

Keywords: congestive heart failure; heart transplantation; mechanical circulatory support; left ventricular assist device (LVAD)

Introduction

Heart transplantation today has become a standard method of treatment for improving the quality and extending the life of patients in the terminal stage of systolic heart failure. However, due to the lack of adequate number of donors, heart transplantation is available only to a small number of such patients. In the last two decades, the development of mechanical circulatory support, i.e. devices for long-term paracorporeal mechanical left ventricular support, has significantly improved survival chances for patients with systolic heart failure. The mechanical support of

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the left heart (LVAD-left ventricular assist device) brings new possibilities into the treatment of terminal stage of congestive heart failure. The application of an LVAD was approved in the U.S. in 1994 as bridging to transplantation in individual critically ill patients [1]. Today it is applied in patients refractory to optimal medical therapy as a *bridge-to-transplantation*, as well as a *bridge-to-recovery*, and as a *destination therapy*. The key randomized study REMATCH (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure) concluded that mechanical circulatory support with pulsatile flow dramatically reduced the mortality by 48% in 129 patients who were not eligible for heart transplantation [2]. This paper surveys the patient with heart failure to whom for the first time in Croatia- a device for paracorporeal long-term mechanical left ventricular support was implanted.

Case report

The first Thoratec LVADs was implanted in a 41-year-old man with a history of dilatated cardiomyopathy, most probably due to myocarditis caused by cardiotropic viruses. Anamnestic data show as that at the beginning of 2007, he was suffering from heavy respiratory infection with fever, cataral symptoms and poor general condition, treated with azythromycin. During that year he was several times hospitalized on the grounds of cardiac decompensation, symptoms of dyspnea and intolerance to activity. In December 2007, echocardiograpy showed a global heart dilatation with severely reduced left ventricular ejection fraction (LVEF) of 20%, and severe mitral regurgitation. The right heart chateterisation showed moderate pulmonary hypertension PAP 35 mmHg, TPG 5 mmHg, RVSP 56 mmHg, pulmonary vascular resistance PVR 1,0 wood units, RVSW-I 8,05 gm^*m/m^2. Coronarography showed no significant coronary arteries disease. Due to terminal stage of congestive heart failure, patient was listed for heart transplant. In October 2008, invasive cardiac procedure was repeated, and it indicated progression of disease with LVEF 15%, and severe mitral regurgitation.

A team of cardiologists and cardiac surgeons recognized the patient as a candidate for LVAD implantation as a bridge-to-transplant. The procedure of LVAD implantation was successful, with normal patients postoperative recovery. For anticoagulant therapy, varfarin was used, ordinary INR controlling, with target value from 2.5 to 3.5, and antiplatelet therapy with aspirin 150 mg daily. After implantation of the mechanical assist device, clinical status of patient was progressively better. A control echocardiograpy indicated increase of LVEF on 32% with good contraction of the back wall of LV and minor mitral regurgitation. In December 2008, after physical rehabilitation, the patient was discharged home with LVAD.

After one month a device control was performed. In the patient, a brief eyesight failure with regular neurological status was noted. The head CT indicated ischemic vascular lesion near the occipital horn of the left lateral ventricul, showing that the patient was suffering from CVI caused by microembolism. The echocardiograpy proved regular function of the device without thrombotic mass. Further continuous echocardiograpy controls showed a significant improvement of global systolic function of left ventricular, LVEF 40 % with minimal aortic and mitral regurgitation with no significant pulmonary hypertension.

Four months after the LVAD implantation, we noted a significant improvement in LVEF and general condition. Due to a potential complication arising from the device usage, as a cerebrovasculary microembolism or infection, it was indicated to remove LVAD. An increase of LVEF to Teiholtz from 37% to 46% vs Simpson from 38% to 50%, was noted after a dobutamine stress testing. An excercise testing also was performed.

The explantation of LVAD was successfully performed in March 2009. The postoperative period was followed by subfebrility, an acute renal insufficiency and the retrosternal collecting of minor volume of liquid which was confirmed by MSCT examination of thorax. Hemocultures were positive to *Stenotropomonas maltophillia* and were successfully treated with systemic antibiotics. The renal function was substituted by hemodialysis. The operatition wound above the distal part of sternum was opened because of secretion, and it was treated daily and healed per secundam. The echocardiograpy revealed a dilatation of both ventricles, with a decrease of LVEF to 30% and RVEF to 35%, with moderate mitral regurgitation. Due to the medicament therapy, the patient was hemodynamically stabile and afebrile, and was hence discharged. The patient was feeling generally well until July 2009, when the symptoms of heart failure occurred. He was hospitalized in a poor general condition, with high temperature, a significant rash on the body and the extremities, with the staphylococci sepsis suspected. The laboratory tests indicated increased inflammation parameters, increased values of bilirubin, and positive hemoculture test to *Staphylococcus aureus*. Antibiotic treatment was prescribed. The progression of the end stage heart failure started in August 2009. The echocardiograpy proved massive mitral and tricuspid regurgitation on the basis of dilatation of ring, the dilatation of both ventricles with LVEF and RVEF of 15%. The patient became rhythmically and hemodynamically unstabile with the development of cardiorespiratory arrest. Upon applying all measurement of CPR and implantation of intraaortic balloon pump, the patient became stabile, and on the same day listed on the transplantation list with a high-urgency status. Eventually, the patient fell into a septic shock with a multi-organ failure, and despite the vasoactive and innotrop medicaments, the patient got into a cardiorespiratory arrest and died. The pathology examination confirmed septic shock as the cause of death.

The characteristics of the left ventricular assist device

Ventricular assist devices that are in use today differ by their basic mechanical characteristics; by the type of blood flow they create (continuous or pulsatile); by their positioning (intercorporal, paracorporal or extracorporal); and their ability to assist one or both ventricles.

In our case, Thoratec paracorporeal left ventricular assist device LVAD was used. Thoratec pVAD is a mechanical circulatory assist device to left ventricle, enabling pulsatile blood flow and consisting of three components: the device for blood, which has cardiac output of 65 mL and can produce a pulsatile flow of 1.3 to 7.1 L/min; the inflow and outflow cannula, which connects the device to the left ventricle and the aorta; and the external console, which starts the device pneumatically. The device is positioned paracorporeally, outside the body. The device can be used for the left or the right ventricular support or as a biventricular support for either a short or long term, or as destination therapy. It is necessary to use anticoagulant or antiplatelete therapy, because tromboembolism is associated with all devices.

Discussion

Heart failure continues to be a fatal disease, despite the advances in treatment, with only 35% surviving 5 years after the first diagnosis [3]. Systolic heart failure today is treated with medicaments, by heart transplantation or by a mechanical assist device, which has significantly improved treatment results and substantially changed the natural course of the disease. Only two researches have so far compared patients with advanced heart failure not eligible for transplantation, treated by optimal medicament therapy and mechanical circulatory support. The results of these researches have indicated that the survivals, the function capacity and the quality of life were notably better in patients treated with pulsatile mechanical heart support [3,4]. A wider use of mechanical assist devices is limited due to the price of the device; the size of the pump; possible complications; and the limited durability of the pump.

The indication for device therapy is the presence of heart failure in patients approved for transplantation [5]. As devices become more prominent, the indications expanded, so today, patients with acute decompensation of chronic heart failure; myocarditis; ventricular arrythmias; postcardiotomy failure; or acute myocardial infarction can be successfully treated with an assist device [6].

Patients to whom mechanical support is applied, are categorized in four groups. First group includes bridge-to-recovery patients, whose chances for recovery of function of the ventricle are significant as it is suffering from either a postcardiotomy shock or acute myocarditis. The second group includes patients, in whom

acute cardiogenic shock is developed in the institution not having transplantation or long term mechanical assist device possibilities. The group, in which VAD as a bridge-to-transplant is used, includes patients on the list for heart transplantation, where mechanical support is used for the stabilisation of hemodinamical status. The fourth group includes patients, for whom the mechanical assist device is a destination therapy. The removal of LVAD can be considered once the heart function is significantly recovered.

In our patient's case, it was proved by repeated echocardiography with the application of dobutamine stress test, as well as ergometry. The most frequent causes of death in patients with implanted LVAD are as follows: haemorrhagical cerebrovascular insult; right ventricle failure; multi-organ failure; and ishemical cerebrovascular insult. Despite the extreme negative outcome, the treatment with the mechanical left heart support has contributed to the improvement of cardiac function and reduced the NYHA stage with improvement of the general condition, after which the patient was fully mobile and discharged from hospital.

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Saţetak

Rana klinička iskustva sa dugoročnom potporom (Thoratec)

Unatoč novijim dostignućima u liječenju kongestivnog zatajivanja srca, broj ljudi sa srčanim popuštanjem kontinuirano raste što dovodi do povećane stope mortaliteta i morbiditeta.

Transplantacija srca je često ograničena zbog nedostatka broja adekvatnih donora, a medikamentozna terapija ostaje palijativna. Korištenje mehaničke cirkulacijske potpore (LVAD-left ventricular assist device), kao standardne terapije u liječenju završne faze zatajivanja srca značajno je poboljšalo ishod liječenja.

Mehanička potpora lijevom ventriklu, prvotno primjenjena kao metoda privremenog premoštenja prema ozdravljenju (bridge-to-recovery), zatim kao premoštenja do transplantacije (bridge–to-transplantation), danas se primjenjuje kao trajna opcija liječenja bolesnika s terminalnom fazom srčanog zatajivanja.

U ovom radu prikazan je slučaj bolesnika s dilatativnom kardiomiopatijom, kojem je po prvi puta, u Republici Hrvatskoj, zbog zatajivanja srca ugrađena parakorporalna mehanička potpora lijevom srcu.

Ključne riječi: kongestivno zatajivanje srca; transplantacija srca; mehanička cirkulacijska potpora; mehanička potpora lijevom ventriklu

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INTRAOPERATIVE TRANSESOPHAGEAL ECHOCARDIOGRAPHY AND ANESTHETIC CONSIDERATIONS IN PATIENTS WITH VENTRICULAR ASSIST DEVICES

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Summary

A ventricular assist device (VAD) is inserted to provide mechanical circulatory support. A VAD can rest the myocardium and allow it to recover from stunning or hibernation, while maintaining vital organ perfusion (*bridge-to-recovery*). If myocardial recovery cannot occur, the goal is to support the patient to transplantation (*bridge-to-transplantation*), or, if the patient is not a transplant candidate, to enhance the quality of life for a limited period of time (*destination therapy*).

Perioperative transesophageal echocardiography is a major component of patient management, and it is important for surgical and anesthetic decision-making. In addition to the standard examination, device-specific pre-, intra-, and postoperative considerations are essential to the echocardiographic evaluation. These include: (a) the pre-VAD insertion examination of the heart and large vessels, in order to exclude significant aortic regurgitation, tricuspid regurgitation, mitral stenosis, patent foramen ovale or other cardiac abnormality that could lead to right-to-left shunt after the left VAD placement, intracardiac thrombi, ventricular scars, pulmonic regurgitation, pulmonary hypertension, pulmonary embolism and atherosclerotic disease in the ascending aorta; and to assess the right ventricular function; and (b) the post-VAD insertion examination of the device and reassessment of the heart and large vessels. The examination of the device aims to confirm the completeness of the device and heart deairing, cannulas alignment and patency, and the competency of the device valves using two-dimensional, and color, continuous and pulsed wave Doppler modalities. The goal of the heart examination after the implantation should be to exclude the aortic regurgitation or an uncovered right-

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to-left shunt, and to assess the right ventricular function, the left ventricular unloading, and the effect of the device settings on the global heart function.

Keywords: transesophageal echocardiography; ventricular assist device; right-to-left shunt; cardiopulmonary bypass.

INTRODUCTION

Over the years, the ventricular assist device (VAD) therapy has become an increasing option for patients with end-stage heart failure. High implantation costs, as well as long postoperative length of stay in debilitated patients' cases, make the VAD therapy [1-4] complicated.

In the multidisciplinary approach, the cardiac surgeons and the heart failure team evaluate potential VAD candidates together, starting immediately after the admission to hospital, to identify the optimal timing for the VAD implantation. Special attention is paid to not delaying the VAD implantation as to prevent the end-organ dysfunction, such as renal failure, hepatic failure and intubation.

VADs are used when pharmacological manipulations and intraaortic balloon pump counterpulsation fail to improve the cardiogenic shock or less severe low-output states that are worsening. In general, VADs are pumps that collect blood returning to the heart and eject it downstream of the failing ventricle.

Typically, for the left ventricular support, blood is drained from the left atrium or the left ventricular apex to the pump, and returned to the ascending aorta. For the right ventricular (RV) support, blood is drained from the right atrium or the RV to the pump and returned to the main pulmonary artery. The goal is either to decompress the acutely ischemic and failing ventricle (thereby reducing its oxygen demand), so it can recover, or to provide a long-term support for a chronically failing ventricle as either a bridge-to-transplantation or destination therapy.

As is the case with the diseased native heart, normal or slightly increased intravascular volume and normal or slightly decreased vascular resistance are necessary for the VADs to function optimally. Hypovolemia will delay the VAD filling with each pump cycle, which may decrease the overall pump output, leading thereby to hypotension.

Transesophageal echocardiography (TEE)

Transesophageal echocardiography (TEE) is an important tool in the perioperative management of patients undergoing VAD implantation. TEE has been shown to provide critical information on the diagnosis of preinsertion abnormalities, and the evaluation of postinsertion function [5,6].

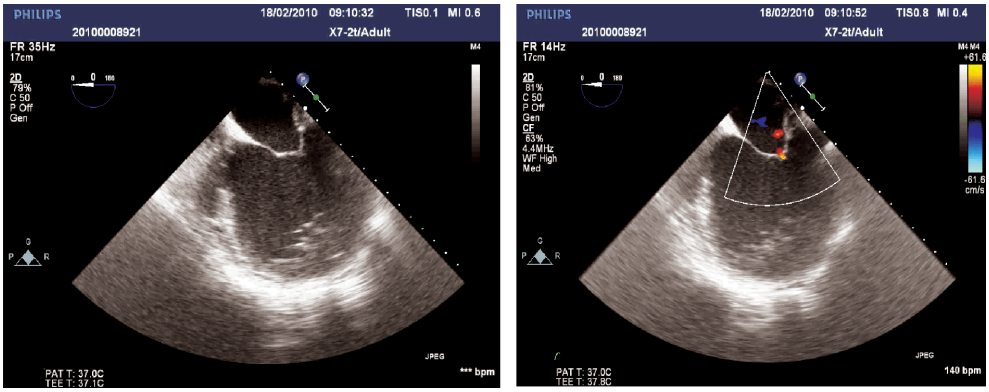

Fig. 1: Mid-esophageal two-chamber view, showing dilated overloaded left ventricle in a patient with dilated cardiomyopathy.

The echocardiographic assessment of patients undergoing the VAD insertion involves aspects pertaining both to a general echocardiographic examination and to specific considerations associated with the VAD. As in most echocardiographic assessments, a comprenhensive examination is required [7-10].

DEFECTS CREATING INTRACARDIAC SHUNTS

Patent Foramen Ovale

The investigation of a Patent Foramen Ovale (PFO) should always be performed before and after cardiopulmonary bypass (CPB) for the implantation of a VAD. Since a PFO is common (27,3 % in one study) [11], meticulous care should be taken to identify its presence.

In the pre-CPB period, the examination of the interatrial septum of the patient with LV failure will often show a rightward deviation [12], indicative of an increased LA pressure surpassing the RA pressure. Because of this factor, the investigation of a PFO with color Doppler echocardiography may clearly show a left-to-right shunt. The TEE assessment for a PFO after the VAD insertion can be started early, while weaning from the CPB, and a PFO can be potentially detected even before complete separation. Early detection is important, as the presence of a PFO requires the return to a CPB for closure.

Other Septal Abnormalities

Traumatic atrial septal defects (fossa ovalis) can occur intraoperatively and also produce profound hypoxemia in the setting of increased right-to-left atrial pressure gradient with the LVAD support [13].

Finally, ventricular septal defects, particulary postinfarct, are a potential cause of significant shunting, before and after the VAD placement.

VALVULAR AND ASCENDING AORTIC DEFECTS

Aortic valve

Normal functioning of the LVAD during full support usually prevents the systolic opening of the native or prosthetic aortic valve, given the increase in the aortic-to-LV pressure gradient, due to the suction of the blood from the LV through the inflow cannula and its propulsion into the aorta through the outflow cannula.

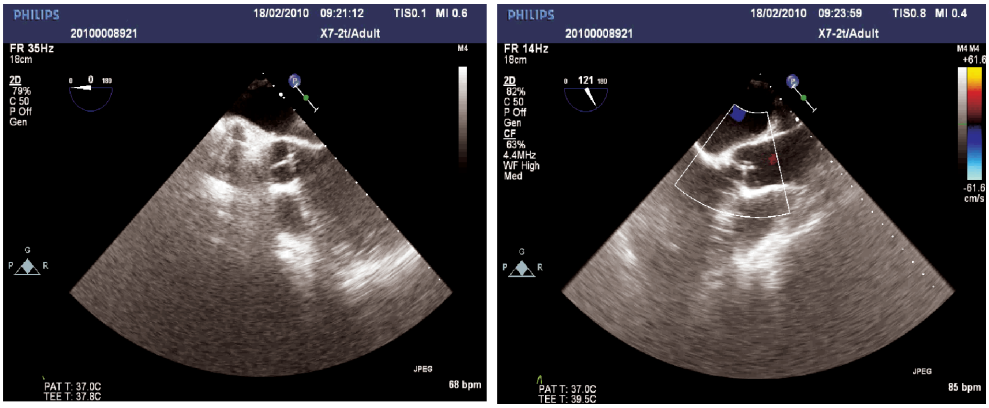

Fig. 2: Mid-esophageal short (SAX) and long axis view (LAX), showing normal aortic valve in the preinsertion period.

Aortic Insufficiency

The diagnosis of significant pre- and postoperative Aortic Insufficiency (AI) is crucial in patients receiving an LVAD. The presence of AI reduces the forward flow produced by the LVAD, due to the regurgitation of the LVAD-supported flow into the LV cavity. Aortic competence should also be assessed during the CPB by intraoperative TEE, before the insertion of the LVAD [14], when transvalvular gradients are closer to those to be observed after the LVAD insertion. The identification of severe and, possibly, moderate AI should indicate the need for surgical correction [15].

In patients with no previous aortic insufficiency, the incidence of AI after the LVAD insertion is low [16], and it may become present months later [17, 18]. Mechanisms producing the post-LVAD AI include endocarditis [19], aortic dissection [20, 21], and aortic leaflet prolapse or perforation.

Aortic Stenosis

Preoperative Aortic Stenosis (AS) is usually not critical to LVAD recipients, since pulsatile devices typically generate full cardiac output and, thus, the systemic blood flow does not depend on antegrade flow through the aortic valve. In VADs that provide partial or variable support, such as axial flow devices, the intermittent opening of the aortic valve occurs and contributes to a global cardiac output. Consequently, patients with severe AS may not be good candidates for such devices.

Ascending Aorta

The ascending aorta should be examined to detect abnormalities before performing the end-to-side anastomosis of the outflow cannula. A mid-esophageal (ME) ascending aortic long-axis view should be used to locate and classify the structural abnormalities in the ascending aorta. The aortic arch and the descending aorta should be assessed with the same goal. Atheromata with thickness > 5 mm and/or protruding and/or mobile components are associated with an increased risk of cerebral embolic events during the cardiac surgery.

Tricuspid Regurgitation

Functional Tricuspid Regurgitation (TR) is a common finding in patients with heart failure. Adequate RV function is essential after an LVAD insertion to optimize the LVAD filling. The presence of significant postoperative TR can significantly contribute to the RV dysfunction and the development of a low output state. Given that LVAD insertion produces the unloading of the LV and a decrease in the PA pressure, it might be expected that TR would be reduced post-insertion. Some authors have found this true, but not others, who reported an acute worsening in TR after the LVAD insertion. The fact that an isolated implantation of an LVAD does not produce a consistent change in the degree of perioperative TR is likely associated with a combination of factors, including the leftward shift of the interventricular septum, produced by the LVAD; an increase in the PA pressure and the RV dysfunction due to the inflammatory response to surgery, CPB and blood transfusion; and an increase in preload to the RV due to an increased left-sided output, delivered by a functioning LVAD in lieu of the previously failing left heart. Leftward interventricular septal shift is more pronounced in LVAD patients, who are hypovolemic and have higher VADs flows.

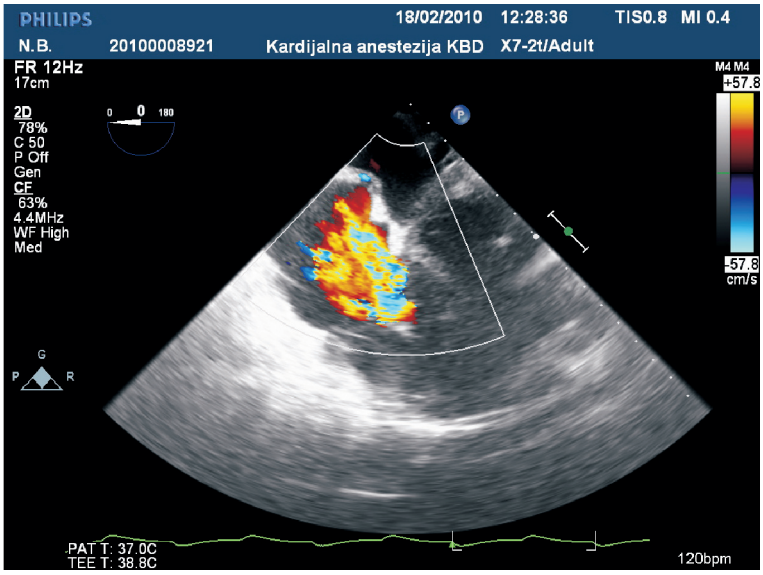

Fig. 3: Massive tricuspid regurgitation after the LVAD insertion.

MITRAL VALVE

Mitral Regurgitation

Functional Mitral Regurgitation (MR) is a significant and common complication of end-stage heart failure and cardiomyopathy [22,23]. A central jet on the color Doppler image, which has been reported to be of at least moderate severity in 39 % of the patients in a retrospective study of patients with advanced systolic heart failure, characterizes this form of MR. The insertion of a LVAD leads to reduced LV size, an improved coaptation of the mitral valve leaflets and, ultimately, a decreased preexisting MR. The persistence of significant MR post-LVAD insertion may indicate inadequate LV decompression.

Mitral Stenosis

Mitral Stenosis (MS) is a rare finding in patients scheduled for an LVAD insertion. Significant MS restricts the filling of the LVAD, leading to low device output and, consequently, to low cardiac output. RV failure can also occur due to increased pulmonary vascular resistance (PVR).

Pulmonic Valve

Pulmonic valve lesions are relatively rare in patients receiving a VAD. Pulmonic insufficiency more than moderate would be an important finding in those patients.

In patients receiving only an LVAD, it would compromise the RV function through volume overload.

VENTRICULAR ASSESSMENT

Right Ventricle

The RV dysfunction is a well-recognized and serious condition that may occur in LVAD recipients. As the output of the native RV determines the preload of the LVAD [24], a decrease in RV function will translate into a reduction in the LVAD output. Reports suggest that at least 9-33 % of patients suffer severe RV failure after the LVAD insertion [25-30] and may require an RVAD. This decision is often needed when a CPB is discontinued, because the RVAD insertion should be performed early after the development of severe RV failure following LVAD implantation.

Left Ventricle

The evaluation of the LV function pre-LVAD insertion will show depressed function with either a dilated or normal size ventricle, depending on the cause of heart failure. The LV ejection fraction (LVEF) for LVAD insertion is typically <25-30 %. Significant diastolic dysfunction is also usually present and diagnosed with PW Doppler of the transmitral inflow, combined with PW Doppler of the pulmonary veins or with tissue Doppler. Severe LV dysfunction increases the risk of apical thrombus formation. Apical thrombus, when present, is often located near the inflow cannula insertion site. Thus, the preoperative interrogation of the LV for the presence of thrombus is an essential part of the echocardiographic examination.

THE ASSESSMENT OF VAD COMPONENTS

Cannula position

Inflow cannula. The inflow cannulas and their orientation within the RA, the LA or the ventricles can be visualized on two-dimension imaging. The inflow cannula to an LVAD may originate from the LA or the LV. The most common origin is the apex of the LV and, in this case, the cannula should be aligned with the LV inflow tract, i.e. with the mitral valve opening, and not abutting any wall.

Outflow cannula. The outflow cannula for an LVAD or an RVAD is visualized with two-dimensional imaging. A long axis view of the ascending aorta at the level of the right PA will usually show the outflow cannula anastomosis to the ascending aorta. The ascending aorta should also be checked for the presence of calcification, plaque, or dilation, which could modify the placement of the cannula.

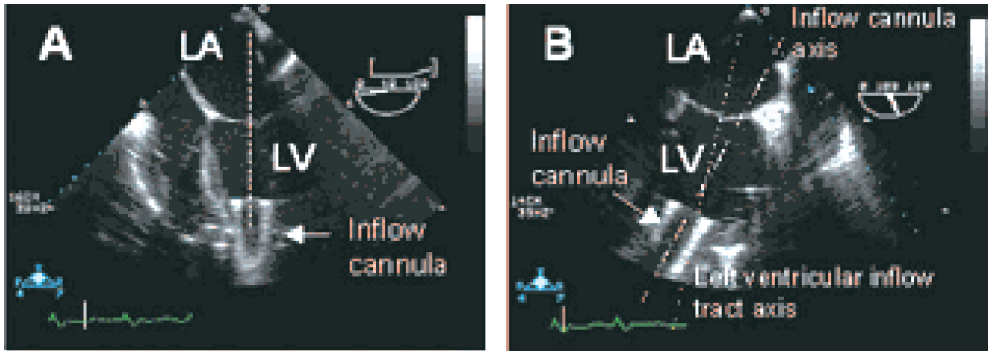

Fig. 4: The alignment of the left ventricular assist device (LVAD) inflow cannula, mid-esophageal four-chamber view (A). The ideal axial alignment will optimize blood flow to assist the device. A small angle is observed between axes for the two-chamber view (B). LA = left atrium; LV = left ventricle.

Thromboemboli

The presence of intracavitary thrombi requires extra care during cannulation, as there is a risk of embolism. The incidence of thromboembolic complications after the LVAD support varies significantly in different reports between 5 % and 47 %. The use of TEE allows for the identification of mobile LV thrombi adjacent to the LVAD inflow cannula, and the LV outflow tract.

Anesthetic Considerations in Patients with Ventricular Assist Devices

In the end stage of cardiac failure, patients inevitably have mild to severe pulmonary hypertension and may be on chronic inodilator therapy with dobutamine

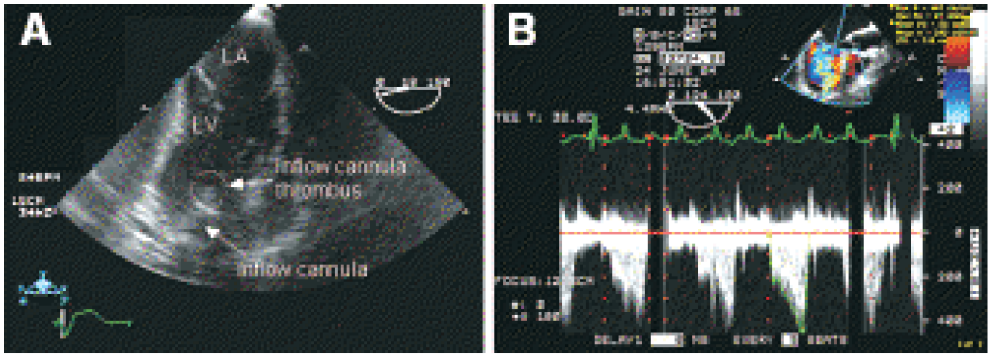

Fig. 5: (A) Echodense structure at the inlet of the inflow cannula compatible with a thrombus. The obstruction of the inflow cannula can produce an increase in the velocity at the inflow cannula (B). LA = left atrium; LV = left ventricle.

and/or milrinone; they furthermore suffer from substantial hepatic, renal and pulmonary insufficiency. Some may have an IABP in place and be already mechanically ventilated or on intermittent or continuous hemodialysis. Many of these patients are reops (prior coronary revascularization, valve surgery, AICD), and require therefore the anticipation of major bleeding and/or the incision of vital structures during opening, dissection and cannulation.

In anticipation of the potential for massive blood loss, large bore central venous access is obtained together with pulmonary artery catheterization. A rapid infusion blood-warming device is primed to ensure the ability to give fully warmed blood and blood products at the volumes of 250-1000 mL/min. Blood and blood products (e.g. 6 units of packed red blood cells, 6 units of fresh frozen plasma, 12 units of platelets) are readied in preparation for post-CPB coagulopathy. Early transfusion may reverse factor deficiency before vicious cycles (bleeding → DIC → bleeding) develop.

The anesthetic regimen should acknowledge the tenuous hemodynamic state and compromised drug elimination capacity of these patients; for example, cisatracurium should be used instead of vecuronium.

Aprotinin, a kallikrein and serine protease inhibitor, which has antifibrinolytic and platelet sparing effects on the CPB, may be used, as it has been proven to decrease the blood loss, the blood requirement and perioperative mortality. Some advocate priming the CPB circuit with fresh frozen plasma to decrease the dilution of clotting factors in patients with preoperative coagulopathy, and maintain the levels of antithrombin III, avoiding thereby consumptive coagulopathy.

Transesophageal echocardiography (TEE) is essential not only to monitor the LV filling and the RV function throughout the case, but also to exclude the presence of an atrial septal defect (ASD), the patent foramen ovale (PFO), aortic regurgitation or mitral stenosis. These lesions must be repaired prior to the separation from the CPB; with an ASD or a PFO, a right-to-left shunt may commence, as the left-sided filling pressures are decreased when the LVAD support begins.

Adequate LVAD output during the separation from the CPB requires aggressive volume loading, since the LVAD decompresses the LV and the left atrium. The RV dysfunction is treated with inodilator drugs (milrinone, dobutamine), whilst excessive systemic vasodilatation, causing systemic hypotension, is treated with norepinephrine and/or vasopressin. Severe pulmonary hypertension may induce an acute RV failure and responds well to inhaled nitric oxide, 10-20 ppm, which has markedly decreased the requirement for emergency placement of an RVAD to come off the CPB in the OR.

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Sažetak

Intraoperacijski TEE i anesteziološko liječenje bolesnika s mehaničkom potporom srca

Uređaj za mehaničku potporu srcu (eng. VAD) se ugrađuje radi pružanja mehaničke potpore srcu i cirkulaciji. Njime se osigurava oporavak miokarda nakon *stunninga* i *hibernacije,* i u isto vrijeme održava perfuzija vitalnih organa (eng. bridge-to-recovery). Ukoliko se miokard ne može oporaviti od oštećenja tada je cilj ovakve terapije pružiti potporu bolesniku do trenutka transplantacije srca (eng. bridge-to-transplantation), ili ukoliko bolesnik nije pogodan za transplantaciju, poboljšati mu kvalitetu života u ograničenom vremenu (*ciljna terapija*).

Perioperacijski TEE je glavna metoda u liječenju i nadziranju takvih bolesnika koja pruža brojne informacije i kirurgu i anesteziologu, olakšavajući pri tom donošenje važnih terapijskih odluka. Uz osnovni standardni pregled, za ehokardiografsku procjenu su važni i za uređaj specifični pre-, intra- i postoperacijski ehokardiografski pregled. To uključuje: (a) pregled srca i velikih krvnih žila prije postavljanja VAD uređaja, kako bi se isključila značajnija aortna regurgitacija, trikuspidna regurgitacija, mitralna stenoza, otvoreni foramen ovale i druge abnormalnosti koje bi mogle dovesti do D-L shunt-a nakon postavljanja VAD-a, stvaranja intrakardijalnih tromba, ventrikulskih ožiljaka, plućne regurgitacije i hipertenzije, plućne embolije i aterosklerotske bolesti u uzlaznoj aorti. Važno je i procijeniti funkciju desnog ventrikula, i (b) pregled uređaja nakon postavljanja VAD-a i ponovna procjena srca i velikih krvnih žila. Cilj pregleda uređaja je potvrditi ispravnost uređaja, izvršenog srčanog odzračivanja; potvrditi ispravan položaj kanila i njihovu prohodnost, kompetentnost valvula i to uporabom dvodimenzionalnog, obojenog, kontinuiranog i pulsnog doplera. Cilj pregleda srca nakon implantacije je isključiti aortnu regurgitaciju ili neprepoznati D-L shunt, i procijeniti funkciju desnog ventrikla, odterećenost lijevog ventrikla i općenito učinak različitih podešavanja uređaja na globalnu srčanu funkciju.

Ključne riječi: transezofagusna ehokardiografija; uređaj za mehaničku potporu; desno-lijevi shunt (D-L); izvantjelesni krvotok

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ECHOCARDIOGRAPHIC EVALUATION OF PATIENTS WITH HEART MATE II CONTINUOUS FLOW VENTRICULAR ASSIST DEVICE

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Summary

Echocardiography plays an important role in evaluating patients both before and after the implantation of mechanical circulatory support devices. It consists of a standard examination expanded to specific aspects of ventricular assist devices. The scope of examination varies according to the type of the device, the method of implantation and the localization of the inflow and outflow cannulas. This article is focused on the echocardiographic examination of patients undergoing the implantation of the HeartMate II (Thoratec) – a continuous-flow ventricular assist device. It provides a review of all the important parts of the examination, including the preoperative, the intraoperative and the postoperative examination. The utilization of transthoracic and transesophageal echocardiography is presented. The methods of diagnosing the malfunction of the device are also discussed. The author emphasizes that the assessment of a patient with a mechanical assist device is a complex and an interdisciplinary challenge, where echocardiography is crucial in the assessment of the patients with mechanical circulatory support devices.

Key words: echocardiography; ventricular assist device

The echocardiographic examination is crucial in assessing the diagnosis and monitoring of the clinical status of patients with heart failure. Its role is especially important in patients with advanced heart failure. The idea of using mechanical circulatory support has improved significantly in recent years. Ventricular assist devices (VAD) are used more and more often in the treatment of patients with end stage heart failure. Echocardiography plays an important role in assessing the patients treated with mechanical circulatory support devices.

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In general, the echocardiographic examination of the patient before and after VAD insertion consists of a standard examination expanded to specific aspects of VAD. The scope of examination varies according to the type of the device, the method of implantation and localization of the inflow and outflow cannulas. This article is focused on the echocardiographic examination of patients undergoing the implantation of the Heart Mate II (Thoratec) – a continuous flow ventricular assist device.

The use of echocardiographic examination concerns all phases of device implantation. It includes:

- Preoperative examination and qualification to VAD implantation (TTE, TEE);
- Perioperative examination (TEE);
- Early postoperative monitoring in the intensive care unit (TEE, TTE);
- Long-term follow-up (TTE, TEE).

To attain these goals, the echocardiographic examination should be focused on:

- Assessment of the left ventricle (LV);
- Assessment of the right ventricle (RV);
- Identification of intracardiac shunts;
- Assessment of the valves;
- Identification of intracardiac thrombi;
- Assessment of the aorta;

After device implantation:

- Deairing of the heart and the device;
- Assessment of the alignment of the inflow and outflow cannula;
- Left ventricular unloading;
- Right ventricular function;
- Assessment of the flow pattern in the inflow and outflow cannula;
- Reassessment of the aortic valve, intracardiac shunts and aortic dissection.

The assessment of the preoperative status of the patient should answer the following questions:

- Is the patient really a candidate for VAD implantation?
- What type of VAD device should be implanted according to the heart functional status?
- Are there concomitant diseases impeding device implantation present?

The evaluation of the pre-VAD patient is a multidisciplinary approach, where an echocardiographer should confirm myocardial dysfunction being the cause of the existing heart failure. Next, the assessments of the ventricular function and the

anatomical structure of the heart allow choosing the appropriate type of the device. The identification of coexisting pathologies permits an appropriate planning of operation scope.

The assessment of the left ventricle

The size of LV, wall thickness and diastolic function should be assessed. The evaluation of the insertion site in the apex of the left ventricle including wall thickness, the presence of scar and thrombi should be performed.

The assessment of the right ventricle

The assessment of the right ventricular function is a most important clinical problem, as the right heart failure occurs after LVAD implantation in up to 33 % of patients [1]. This is especially important in patients with axial flow pumps, while severe right ventricular failure requires the implantation of RVAD device, which nowadays means a pulsatile flow device. A few successful cases of right and left ventricular support with two axial flow pumps were reported lately. In patients with advanced heart failure, the severely impaired left ventricular function causes the decrease of the right ventricular preload. Under a decreased preload, the right ventricular function can be apparently preserved, yet under VAD support, the rapid increase of cardiac output causes an increase of preload of the right heart, and the right ventricle failure can become apparent despite the usually concomitant reduction of the right ventricular afterload. The right ventricular dysfunction is difficult to predict because of its multifactorial origin. The echocardiographic evaluation of the right ventricle is difficult because of its complex anatomical structure. There are no uniform, echocardiographic methods for the assessment of the right ventricle function. The semiquantitative evaluation includes the visual estimation of the RV size and contractility using 2D TTE and TEE images. The longitudinal function, defined as tricuspid annulus to RV apex motion, and free wall contractility are assessed.

The most often used quantitative parameters are as follows:

- Right ventricular end diastolic diameter – RVEDD (mm);
- Global right ventricular fractional area change – RV-FAC (%);
- Regional right ventricular fractional area change – RVOT fs (%);
- Maximum derivate of the right ventricular pressure – dp/dt max;
- Tricuspid annular plane systolic excursion – TAPSE (mm);
- Right ventricular systolic pressure – RVSP (mmHg);
- Pulmonary acceleration time – Acc (ms).

The grading of the RV dysfunction including both semiquantitative and quantitative methods of RV assessment was proposed (2). Grade I includes patients with moderately increased RVEDD, RV-FAC 30-35 %, RVOT fs 20-40 %, RVSP 30-50 mmHg, moderate to severe tricuspid insufficiency, Acc < 90 ms and TAPSE 10-15 mm. In this group of patients, RV failure after VAD implantation is less probable. Group II consists of patients with RV-FAC < 25 %, RVOT fs < 20 % and TAPSE < 10 mm. The systolic pressure in the RV is diminished and mild tricuspid insufficiency can be observed. In this group of patients, excessive pharmacological support is necessary; however, the right ventricular assist device implantation may be required. The third group consists of patients with evident RV dilatation (RVEDD > 80 mm) and dysfunction, who require RV mechanical support. The decision in most cases is difficult and is made in the operating theatre after the discontinuation of the cardiopulmonary bypass (CPB), or in the short time after the starting of the support of the left ventricle [2,3].

The identification of intracardiac shunts

The most common shunt observed is Patent Foramen Ovale (PFO); this shunt occurs in up to 27 % of patients [4]. The methods of examination do not differ from the standard examination; however, the examination of a patient with advanced heart failure requires several remarks. First and foremost, the LV dysfunction with elevated left-side pressures will unmask left to right shunt, which can be easily recognized with color Doppler (Fig. 1). In case of an increase in the right-side pressures, left to right shunt may not be visible despite the use of echocardiographic contrast and Valsalva maneuver. The latter must be used with caution in a patient with advanced heart failure. The assessment of the continuity of the interatrial septum should be repeated after the introduction of CPB and after starting the VAD device. Significant shunts must be closed at the time of operation. The exploration of other possible sites of intracardiac shunts should not be omitted.

The assessment of the valves

The evaluation of the aortic valve is a very important part of preoperative examination. Aortic insufficiency, when significant, can reduce the VAD forward flow. The assessment of the degree of regurgitation does not differ from standard examination. In patients with severe left ventricular dysfunction and elevated left ventricular and diastolic pressure, as well as diminished pressure in the aorta, the severity of aortic regurgitation can be underestimated. Repeated examination after introduction of CPB allows the estimation of the aortic valve function under increased pre-

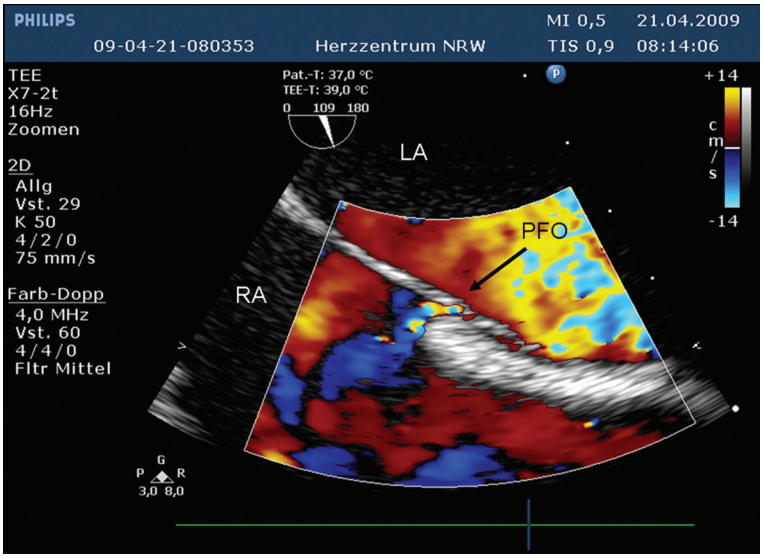


Fig. 1. 2-D and Color Doppler transesophageal echocardiographic examination. Patent Foramen Ovale with left to right shunt. LA – left atrium, RA – right atrium, PFO – Patent Foramen Ovale.

ssure. The inspection of the aortic valve should be repeated intraoperatively after starting the device following the implantation. The significant regurgitation requires surgical intervention and concomitant valve reconstruction, or the implantation of the bioprosthesis. The stenosis of the aortic valve, unless severe, does not require any additional intervention. The status of the aortic valve requires systematic evaluation during follow-up, because both regurgitation and stenosis can increase in time following VAD implantation. The tricuspid valve regurgitation is often observed in patients prior to VAD implantation. Its appropriate assessment is important, while the degree of tricuspid regurgitation can contribute to the right ventricular function after the implantation. The proper evaluation of the underlying mechanism (functional or organic) and a degree of regurgitation is crucial. The severe regurgitation requires surgical intervention. The degree of tricuspid regurgitation can change after LVAD implantation and depends upon many factors, such as right and left ventricular filling, and interventricular septum shift. Too excessive unloading of the left ventricle causes leftward shift of the interventricular septum and an increase in tricuspid regurgitation. The decrease in the pump speed causes an increase in the diameter of the left ventricle; the interventricular septum is moved to the right, and the tricuspid insufficiency diminishes. The mitral regurgitation is common in patients with heart failure, and although being frequently severe prior to the implantation, it decreases after unloading of the LV following VAD implantation. Persistent

high-grade mitral regurgitation may indicate an inadequate unloading of the left ventricle. Surgical intervention is uncommon. Mitral stenosis is rare; if significant, it requires surgical repair. Pulmonal valve regurgitation or stenosis, if significant, may impair right ventricular function. In those cases, surgical intervention is required [2,3].

The identification of intracardiac thrombi

Enlarged heart chambers, decreased global systolic function, regional wall motion abnormalities and atrial fibrillation contribute to the increased probability of thrombus formation. The most recent localizations are apex and left atrial appendage.

The assessment of the aorta

The echocardiographic examination of the ascending aorta allows identifying atherosclerotic changes in the aortic wall and choosing the proper site of distal anastomosis. The excessive atheromata are associated with an increased risk of thromboembolism. In case of aortic dissection, surgical intervention prior to VAD implantation is necessary.

Perioperative examination

The principle of the transesophageal echocardiographic examination during VAD insertion, before beginning of the CPB, does not differ from the preoperative examination. In cases in which TEE was not performed preoperatively, intraoperative TEE should confirm previous results, particularly those concerning intracardiac shunts and the presence of thrombi.

Inspection for presence of the air concerns both the heart and the device. The air is most frequently located in the apex of the left ventricle, in the left atrial appendage and in the left atrium near pulmonary veins. Both cannulas and the sites of anastomosis are also a potential source of air embolism.

The evaluation of the alignment of inflow and outflow cannulas should also be performed after chest closure. The inflow cannula should be directed toward the mitral valve and should not touch any wall (Fig. 2). The flow in the left ventricle and both cannulas can be estimated using Color Doppler and measured with both PW and CW Doppler. While assessing the inflow cannula, unidirectional and laminar flow without turbulence should be considered normal. PW measurements show a continuous pattern of flow with slight pulsatile increase in the flow velocity, synchronous with cardiac contraction (Fig. 3a, Fig. 3b). The continuous flow velocity signal from 0,6 to 1,2 m/s can be demonstrated. The maximal flow velocities of 1-2 m/s are considered normal [2,3,5]. The properly unloaded left ventricle has approximately

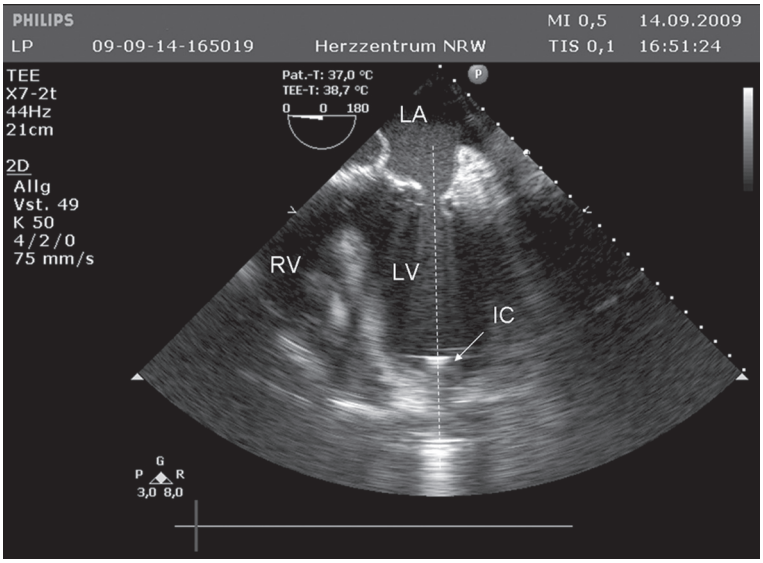


Fig. 2. 2-D transesophageal echocardiographic examination, 4 chamber view. The inflow cannula in the apex of the left ventricle. LA – left atrium, LV – left ventricle, RV – right ventricle, Arrow shows the inflow cannula – IC. Dashed line shows axis between inflow cannula and mitral valve.

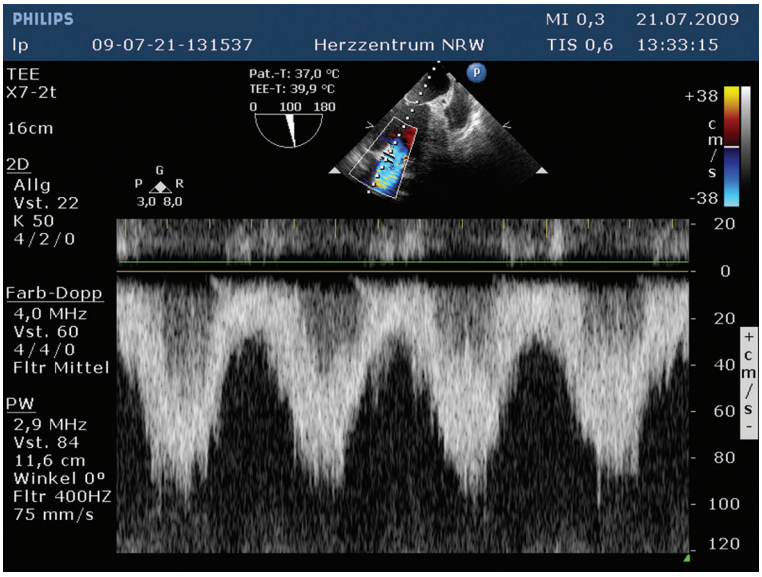
normal diameter, the aortic valve is permanently closed (Fig. 4) and the interventricular septum is in the neutral position. Intermittent partial aortic valve opening is acceptable and should decrease the risk of thromboembolic complications. The function of the right ventricle should be carefully monitored after VAD is started. The methods of assessing its function are similar to preoperative evaluation.

Early postoperative monitoring in the intensive care unit

The evaluation of VAD function in the intensive care unit early after implantation is performed according to the clinical status of the patient, with special attention being paid to bleeding and possible tamponade. The standard echocardiographic examination including the assessment of all mentioned earlier parameters should always be performed.

The assessment of the ventricular assist device during a long-term follow-up

The echocardiographic examination is an important part of a patient's status assessment during follow-up. Transthoracic examination is sufficient in most un-



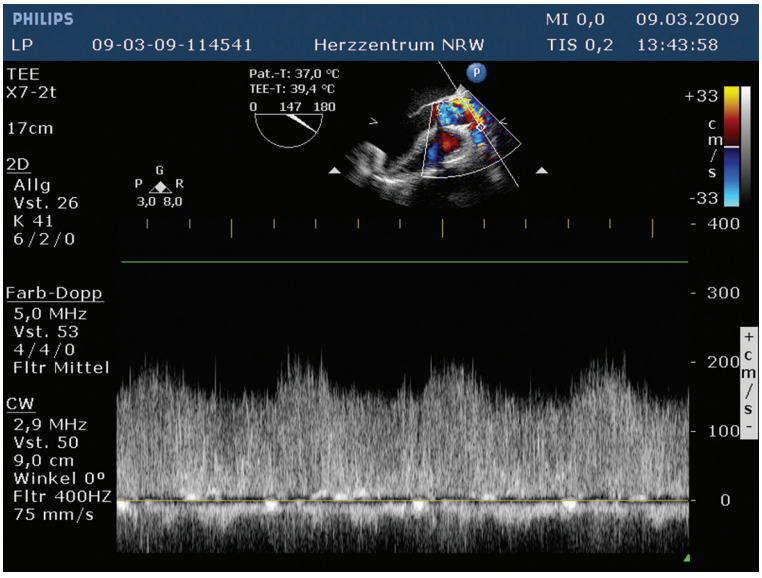


Fig. 3. PW and CW Doppler transesophageal echocardiographic examination. Flow velocity pattern across the inflow (a) and outflow cannula (b).

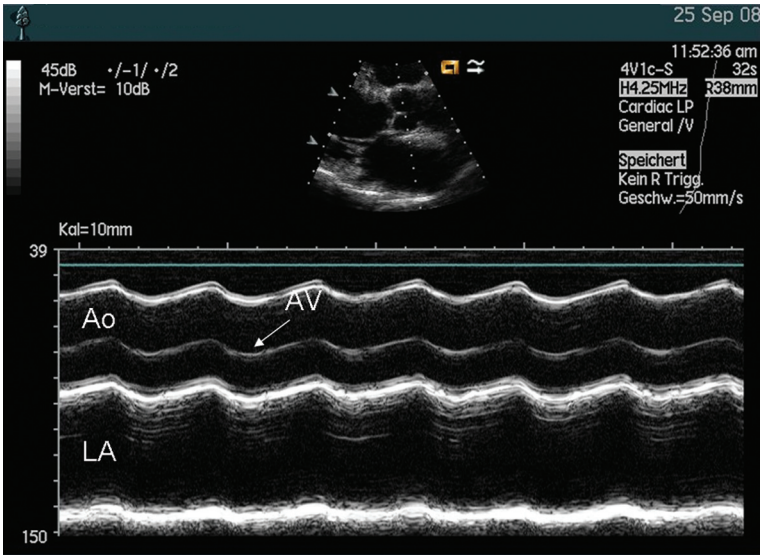


Fig. 4. M–Mode echocardiographic examination. AV remains closed both in systole and diastole. Ao – aorta ascendens, AV – aortic valve, LA – left atrium.

complicated cases. In special cases, transesophageal examination is necessary. The standard TTE examination should be performed including the cannulas alignment and the flow velocity pattern. The visualisation of the outflow cannula is often possible in the second right intercostal space (Fig. 5). Since the device flow is dependent on pre and afterload, as well as on the pump speed, the actual blood pressure and pump speed should be noted.

Ventricular assist device dysfunction

The continuous flow device malfunction is relatively seldom. In the group of 133 patients with the Heart Mate II device, pump replacement was necessary in 9 % of patients, but thrombosis was documented only in 5 cases (4 %). The breakage of the percutaneous lead was the main cause of malfunction [6]. As the direct evaluation of the pump is not possible with the use of echocardiography, the diagnosis of suspected pump thrombosis must be established indirectly, by the assessment of cannulas and ventricle function. Echocardiographic signs suggesting device malfunction include the dilatation of the left ventricle, a permanent opening of the aortic valve and interventricular septum shift to the right, suggesting the insufficient unloading of the left ventricle [7]. A lack of improvement after the adjustment of the pump speed suggests device dysfunction. The possible reasons for device malfunction include

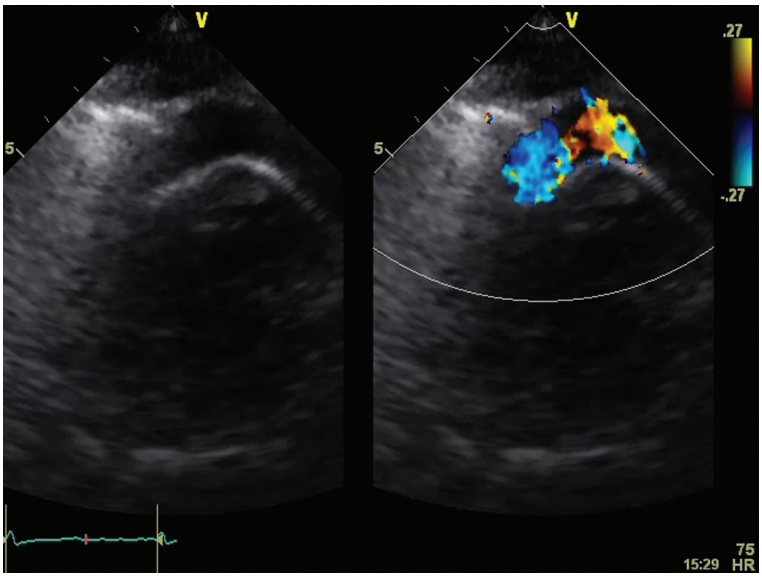


Fig. 5. 2-D and Color Doppler transthoracic echocardiographic examination, right parasternal view (second intercostal space). The outflow cannula with flow is visible.

inflow and outflow cannula obstruction, and flow obstruction inside the pump. Both transthoracic and transesophageal echocardiography can be useful methods of assessing VAD function.

Echocardiography is a powerful tool in assessing patients with mechanical circulatory support devices. However, one must remember that the assessment of a patient with a mechanical assist device is a complex, interdisciplinary challenge, and the echocardiographic examination should be taken into account only together with the analysis of the complete clinical data.

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Sažetak

Ehokardiografska procjena bolesnika s mehaničkom potporom srcu Heart Mate II

Ehokardiografija igra ključnu ulogu u kliničkoj prognozi pacijenta prije i poslije ugradnje uređaja za mehaničku potporu srcu i cirkulaciji. Ova metoda uključuje standardni pregled sa specifičnim pogledom na ventrikularni potporni uređaj. Područje pregleda ovisi o vrsti uređaja, metodi implantacije i smještaju ulazne i izlazne kanile. Ovaj članak opisuje ehokardiografski pregled pacijenta te što je sve potrebno sagledati prilikom preoperativnog, intraoperativnog i postoperativnog pregleda. Prikazan je način upotrebe transtorakalnog i transezofagijskog ehokardiografa. Opisuju se i metode dijagnosticiranja nepravilnog rada uređaja za mehaničku potporu. Autor naglašava kompleksnost dijagnostike pacijenata s ugrađenom mehaničkom potporom srcu i cirkulaciji te prikazuje ehokardiografiju kao neophodnu dijagnostičku metodu kod ovih pacijenata.

Ključne riječi: ehokardiografija; mehanička potpora srcu

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THE FIRST CLINICAL USE OF HEART MATE II LEFT VENTRICULAR ASSIST SYSTEM IN CROATIA AS A BRIDGE-TO-TRANSPLANT: A CASE REPORT

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Summary

Left ventricular assist systems (LVAS) are widely accepted nowadays as a successful tool for bridging the patients with end-stage heart failure to heart transplantation (BTT). The second generations of axial-flow devices, such as the HeartMate II, provide a safe and reliable, as well as an effective hemodynamic support in such patients, offering them an improved quality of life; they are furthermore associated with a very low rate of device malfunction or infection requiring device change. We report here of our first three patients with the implanted HM II LVAS as a BTT.

Key words: heart failure; LVAD; dilatative cardiomyopathy

Introduction

Currently, approximately 14 million people in Europe suffer from heart failure; this number is forecast to increase to 30 million by the year 2020 and is associated with high mortality and morbidity rates [1,2]. Nearly 40 % of heart failure patients will die within one year of their first hospitalization, whilst only 25 % of men and 38 % of women will survive more than five years following the diagnosis [2]. Heart transplan-

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tation is still the most successful treatment option for patients with advanced heart failure refractory to medical therapy. The REMATCH (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure) trail demonstrated a survival advantage for the left ventricular assist devices (LVADs) therapy over optimal medical management for patients with advanced heart failure, who were not eligible for transplantation [3]. LVADs are nowadays widely accepted as a successful tool for bridging the patients with end-stage heart failure to heart transplantation (BTT) [4]. As a consequence of limited donor availability, waiting lists for heart transplantation (HTx) are growing as are support durations for VADs in BTT programmes [5]. Although the first generation of pulsatile devices have shown good results as BTT device, they are – to a certain extent – limited in their design and mechanical durability. These limitations include a large pump size; the need for extensive surgical dissection for implant; a larger body habitus of the recipient; and audible pump operation [5,6]. The second generation of smaller axial-flow devices that produce a continuous flow, such as the HeartMate II (HM II), provide a safe and reliable, as well as an effective hemodynamic support in patients awaiting transplantation, with improved quality of life, and are associated with a very low rate of device malfunction or infection requiring device exchange.[7] In this paper, we report our first three patients with implanted HM II left ventricular assist system (LVAS) as a BTT.

The description of HeartMate II Left Ventricular Assist System

HeartMate II LVAS (Thoratec Corporation; Pleasanton, California) is an axial-flow rotary ventricular assist system composed of a blood pump, a percutaneous lead, an external power source and a system driver with a spinning motor as its only moving part (Fig. 1). The HM II has an electromagnetic motor contained in the pump housing and creates a magnetic field that spins the rotor and imports torque to its internal bladed impeller. No compliance chamber or valves are necessary, and a single driveline exits the right lower quadrant of the abdomen. The inlet cannula is placed in the apex of the left ventricle, and the outflow cannula is anastomosed to the ascending aorta. The small, 124 mL LVAS greatly reduces the amount of dissection required to crate a nesting pocket and is placed intraperitoneally or extraperitoneally. The pump is designed to spin at 6,000 to 15,000 rotations per minute and to produce as much as 10 L/min of cardiac output.

The surgical procedure

We are describing the standard operative protocol that was – with a few differences – used in all three patient cases. A median sternotomy was performed, and a cardiopulmonary bypass (CPB) was instituted. The inflow cannula was first

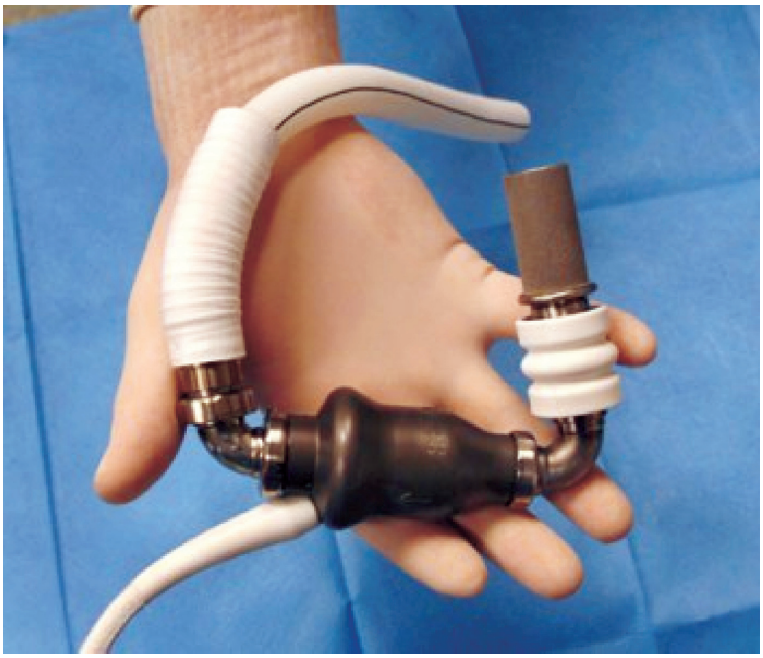

Fig. 1: LVAS

placed in the left ventricular apex after apical coring. Sutures were used to secure the sewing ring to the ventricle under direct visualization. The inlet cannula was inserted into the swing ring and secured. The outflow graft was then anastomosed via outflow conduit to the ascending aorta in an end-to-side fashion, and the pump was activated. The pump was placed parallel to the diaphragm in a previously made pocket within the muscles of the abdominal wall. Following de-airing, the patient was weaned from the CPB in the usual fashion.

Case report 1

The first HeartMate II was implanted in a 59-year-old man with a history of ischemic cardiomyopathy, glucose intolerance and renal insufficiency. Four years prior to the operation, he underwent a triple coronary artery bypass grafting with the aneurysmoraphy of the left ventricle due to two myocardial infarctions. Six months before the operation, his condition started to deteriorate due to the global cardiac decompensation and the impairment of the renal function with the New York Heart Association functional class (NYHA) III/IV. A control echocardiogram revealed an ejection fraction around 0.20, with global hypokinesis. In addition, he had extremely dilated left ventricle, dilated atria and moderate mitral regurgitati-

on. His estimated pulmonary artery pressure was 31 mmHg, pulmonary vascular resistance 1.57 wood units with an ejection fraction of the right ventricle 0.35. With aggressive conservative management, the patient was – prior to the operation – in NYHA class II with improved renal function and listed as a candidate for a heart transplant. In June 2009, he underwent the implantation of HeartMate II LVAS. Early after the operation, the patient was hemodynamically stable, however with a higher output on drainage tubes, which finally required a revision and hemostasis next morning. After the procedure, the patient was hemodynamically unstable on high-dosage inotropic agents, unresponsive to vasopressors, and with a progression to low cardiac output syndrome. Subsequently, he became rhythmically unstable and developed ventricular fibrillation, which could not be converted after multiple defibrillation and medication support. He transesophageal echocardiography revealed the akinesia of the right ventricle, with severe tricuspid regurgitation. The patient eventually succumbed to multi-organ failure on the 2nd postoperative day due to acutely developed right-heart failure. The autopsy revealed an acute myocardial infarction of the right ventricle.

Case report 2

The second HeartMate II was implanted in a 57-year-old woman with a history of dilated cardiomyopathy of unknown cause, which was diagnosed 10 years earlier. Within the last year, she was on several occasions admitted to hospital due to cardiac decompensation and minimal tolerance to any physical activity. The echocardiogram revealed an extremely dilated and hypokinetic left ventricle with ejection fraction 0.15, and severe mitral regurgitation. Her estimated pulmonary artery pressure was 45 mmHg, and her pulmonary vascular resistance was 2.7 wood units. Her right ventricle was moderately dilated with ejection fraction 0.35. The patient was listed for a heart transplant and was recognized as a candidate for HM II LVAS that was implanted in October 2009. The initial postoperative transthoracic echocardiogram revealed that the aortic valve was opening with lower pump speeds, so the pump rate was maintained at 9,500 rpm. The histological examination of the myocardial plug revealed myocyte hypertrophy, clusters of lipofuscin pigment without any sign of myocarditis. Early postoperatively, there was occurrence of gastrointestinal bleeding that was treated with endoscopical coagulation without further complications. We also noticed local infection around the percutaneous lead, with positive strains of *Corynebacterium spp* and *Staphylococcus aureus*; the infection was successfully treated with systemic antibiotics and aggressive wound care. On several consecutively preformed transthoracic echocardiographies, the ejection fraction of the left ventricle was around 0.40 with normal position and flow of inlet cannu-

la, paradoxical septal motion and moderate to severe tricuspid regurgitation. The anticoagulation treatment was started by intravenous heparin until we achieved international normalized ratio 2.5 – 3.5 with oral warfarin. The patient was given aspirin as well. No other significant clinical events occurred during the postoperative period, and she begun an aerobic exercise programme approximately 1 week following the operation. During the hospital stay, HM II was functioning properly, and the patient was a month and a half after the operation sent home. (Fig. 2) She remains in NYHA class I with no symptoms and is awaiting the transplantation more than 4 months after the implantation.

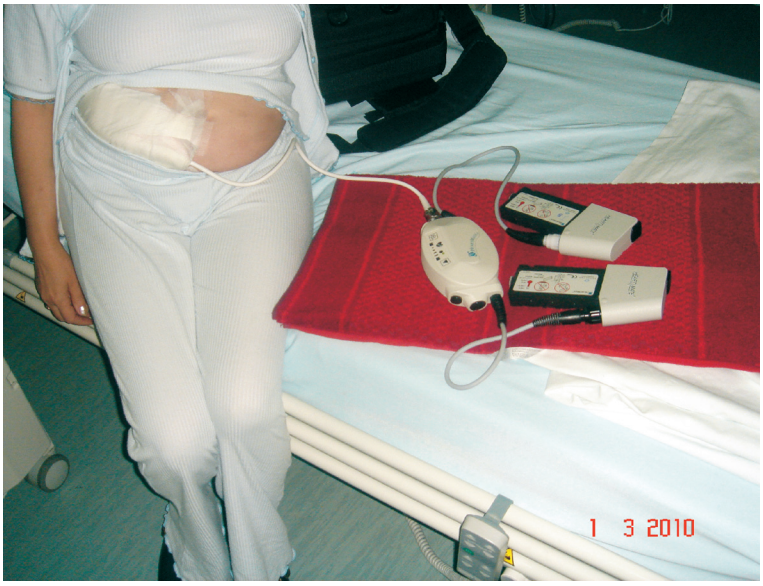

Fig. 2: Our patient with HM II

Case report 3

A 62-year-old woman with a history of hypertension, hyperlipidemia, diabetes and smoking also suffered an ischemic stroke 20 years ago, which was resolved completely. Two months prior to the implantation of HeartMate II LVAS, she was admitted to our hospital because of cardiac decompensation due to dilated cardiomyopathy of unknown cause. At that time, transthoracic echocardiography was used to reveal ejection fraction of the left ventricle around 0.20, with severe mitral regurgitation, without any apparent sign of pulmonary hypertension. A month before the implantation procedure, she was repeatedly hospitalized due to global heart decompensation and NYHA class III-IV. Despite optimal medical therapy,

the patient's clinical state started to deteriorate, and she had symptoms even while resting and with minimum exertion. In February 2010, she underwent the implantation of HeartMate II LVAS. Early after the operation, the patient was hemodynamically stable, the initial echocardiogram revealed occasional opening of the aortic valve, good position of the inflow cannula within the dyskinetic septum. Additional studies approximately three weeks after implantation revealed that the optimal pump speed was 8,800 rpm (4,4 L/min), which has been maintained since then. The patient was discharged home 4 weeks after the implantation. No adverse clinical events have occurred so far.

Discussion

A main therapeutic goal in treating patients with advanced heart failure is to enhance their quality of life and functional capabilities. Several studies showed that the implantation of a continuous-flow left ventricular assist device, as compared to pulsatile-flow device, has significantly improved the probability of survival free of stroke and reoperation due to device malfunction in patients with advanced heart failure, in whose cases the current therapy had failed, and who were ineligible for transplantation [3,8]. The continuous flow devices, such as HM II, are smaller than the previous ones and have fewer mobile parts, thereby increasing their mechanical durability. Regarding adverse events, according to *Laphor et al*., the bleeding remains a serious problem with incidences of more than 50 %, as are infectious complications of the drive-line, as noticed in our patient group, which – when well treated – are not life-threatening [9]. Therefore, the authors suggest a less aggressive anticoagulation protocol in view of a common absence of pump thrombosis. They also concluded that the HM II, while used for BTT, might also be used for destination therapy. We have presented the first three patients in Croatia to be supported with HM II as a bridge-to-transplant. One patient succumbed an acutely developed right heart failure, whilst the other two were, without any complications, more than 4 and 1 month post-implant respectively, successfully rehabilitated.

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Sažetak

Rana klinička iskustva sa dugoročnom potporom (Heart Mate II)

Uređaji za potporu lijevom srcu (LVAS – left ventricular assist system) su danas prihvaćeni kao uspiješno sredstvo za premoštenje bolesnika u završnom stadiju zatajivanja srca do transplantacije. Druga generacija aksijalnih pumpi, kao što je HeartMate II, pruža sigurnu i učinkovitu hemodinamsku potporu takvim bolesnicima, poboljšavajući kvalitetu života. Danas su ti uređaji povezani sa niskom inicidencijom malfunkcije ili infekcije koje bi zahtijevale zamjenu. Prikazujemo naša tri bolesnika kojima je ugrađen HeartMate II LVAS kao premoštenje do transplantacije.

Ključne riječi: HeartMate II LVAS; premoštenje do transplantacije; zatajivanje srca

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END STAGE HEART FAILURE – TRANSPLANTATION OR LVAD?

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Summary

Heart failure is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill or eject blood. According to the data from the International Society for Heart and Lung Transplantation registry, the half-life of patient survival after heart transplantation has progressively improved from 8.9 years in 1982 to a projected half-life of approximately 11 years from 2002 to 2006. The peak VO2 (VO2max) is the most objective assessment of functional capacity in patients with heart failure, and may be the best predictor of when to list a patient for cardiac transplantation. Mechanical cardiac support devices may be implanted in patients, in whose cases all other pharmacological therapies (oral medications and intravenous inotropes) for severe heart failure, as well as non-pharmacological support with intraaortic balloon pump counterpulsation, have failed. Left ventricular assist device provide support of the left ventricular function, causing reverse ventricular remodeling and permanent improvement of left ventricular function. End stage heart failure is not an end of life, since heart transplantation, better medications and devices, including ventricular assist devices implantations, offer patients a better quality and an appreciable extension of life.

Key words: heart failure; heart transplantation; LVAD

1 The definition of heart failure

Heart failure (HF) is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill or eject blood [1]. The most common cause of heart failure is the left ventricular systolic dysfunction (about 60%).

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The right ventricular systolic dysfunction is usually due to the left ventricular systolic dysfunction. However, it can also develop as a consequence of ventricular infarction, pulmonary hypertension, chronic severe tricuspid regurgitation, or arrhythmogenic right ventricular dysplasia. The diastolic left ventricular dysfunction has become a more common reason of heart failure. The American College of Cardiology and American Heart Association (ACC/AHA) have developed a classification of heart failure based upon the evolution and progression of the disease. Stage A includes patients at risk of developing heart failure, but who have no structural heart disease at present. The management strategy is the prevention of heart failure. Stage B includes patients with structural heart disease without symptoms. The management goal is the prevention of left ventricular remodeling leading to heart failure. Stage C includes patients with a structural heart disease with current or prior symptomatic heart failure. They may be treated with pharmacological therapy. Cardiac resynchronization therapy may be added. Stage D includes patients with severe refractory heart failure [1]. This classification system is a complement and does not replace the New York Heart Association (NYHA) functional classification. The important goal of it is that the risk factors and structural changes for the development of HF and the therapeutic interventions performed even before the appearance of the left ventricular dysfunction or symptoms should reduce the morbidity and mortality from HF.

The NYHA functional classification scheme is used to assess the severity of functional limitations, and it correlates fairly well with the prognosis.

2 Indication for transplantation

In the 2008 report from the Registry of the International Society for Heart and Lung Transplantation (ISHLT), it is estimated that annually, more than 5,000 heart transplants are performed worldwide (including more than 2,000 not reported) [2]. The majority of centers perform between 10 and 19 heart transplants per year. The average recipients' age ranges from 50 to 59.

The ACC/AHA and European Society of Cardiology (ESC) guidelines include the following indications for cardiac transplantation: [1,3].

Absolute indications:

1) Hemodynamic disorder due to HF
2) Refractory cardiogenic shock
3) Dependence on intravenous inotropic support to maintain organ perfusion
4) Peak VO2 lower than 10 mL/kg per minute
5) Severe symptoms of ischemia that consistently limit routine activity and are not

amenable to coronary artery bypass surgery or percutaneous coronary intervention
6) Recurrent symptomatic ventricular arrhythmias refractory to all therapeutical modalities

Relative indications:

1) Peak V02 of 11 to 14 mL/kg per minute (or 55 % predicted) and major limitation of a patient's daily activities
2) Recurrent unstable ischemia not amenable to other intervention
3) Recurrent instability of fluid balance/renal function not due to patient non-compliance with medical regimen

Insufficient indications:

1) Low left ventricular ejection fraction
2) History of functional class II or IV symptoms of HF
3) Peak VO2 over 15 mL/kg per minute (or over 55% predicted) with no other indications

Ventricular assist devices (VADs) can provide mechanical support to "bridge" selected patients to transplantation; especially those on the waiting list with a high level of mortality expectation.

3 Prognosis after heart transplantation

After transplantation, there is significant mortality prospect in the first six months, followed by a mortality rate of about 3.5 percent per year. According to the data from the ISHLT registry, the half-life of patient survival after heart transplantation has progressively improved from 8.9 years from 1982 to 1991 to 10.3 years from 1992 to 2001, and to a projected half-life of approximately 11 years from 2002 to 2006 [2]. The controlled trials of patients with stable NYHA class III to IV HF have demonstrated mortality benefit from medical management including angiotensin converting enzyme (ACE) inhibitor therapy, beta-blocker therapy, aldosterone antagonist therapy, implantable cardioverter-defibrillator (ICD) and cardiac resynchronization therapy (CRT); often a combination of CRT+ICD [4]. The predictors of death within two months of status 1 candidates included status 1A, mechanical ventilation, inotropic and intra-aortic balloon pump support, pulmonary capillary wedge >20 mmHg and serum creatinine >1.5 mg/dl, failed cardiac transplant, valvular cardiomyopathy, age >60 years, weight ≤70 kg, and lack of ICD on the day of listing. One-year survival for status 1 candidates improved from 49.5 to 69.0 percent; for status 2 candidates, it improved from 81.8 to 89.4 percent. The peak VO2 (VO2max) is the

most objective assessment of functional capacity in patients with HF, and may be the best predictor of when to list a patient for cardiac transplantation. The 2002 task force of the ACC/AHA recommended the use of exercise testing with ventilatory gas analysis for this purpose [5]. The others risk models are Heart Failure Survival Score (HFSS), including: presence or absence of coronary artery disease; resting heart rate; left ventricular ejection fraction; mean arterial blood pressure; presence or absence of an interventricular conduction delay on ECG; serum sodium; peak VO2; and an invasive version with pulmonary capillary wedge pressure. Seattle Heart Failure Model in contrast of HFSS included ICDs and CRT.

4 Indication for left ventricular assist device (LVAD)

In the 2006 Heart Failure Society of America (HFSA) guidelines, the 2005 ACC/AHA HF guidelines with 2009 focused update, and the 2008 ESC HF guidelines recommended [1,3] that patients awaiting heart transplantation, who have become refractory to all means of medical circulatory report, should be considered for a mechanical support device as a **bridge to** transplantation [6]. **Destination therapy** has been recommended for highly selected patients with severe HF refractory to conventional therapy, who are not candidates for heart transplantation, and particularly those who cannot have any approvement from intravenous inotropic support at an experienced HF center [6]. The 2008 ESC guidelines (although experience is limited) considered these devices for long-term use when no definite procedure is planned [3]. Mechanical cardiac support devices may be implanted in patients who have experienced no clinical improvement from pharmacological therapies for severe HF, including oral medications, and intravenous inotropes, and non-pharmacological support with intraaortic balloon pump counterpulsation. The main criteria for selection of patients are as follows: a) active heart transplant candidate; b) maximal inotropic support, with or without Intra-aortic balloon pump (IABP); c) systolic blood pressure <80 mmHg with a cardiac index below 2.0 L/min per m2 or a pulmonary capillary wedge pressure over 20 mmHg [7].

5 Prognosis after LVAD implantation

The LVADs are associated with the least morbidity and the best chance for rehabilitation and recovery before and after transplantation in patients requiring a prolonged support. An important consideration is that the device be implanted before developing secondary end-organ damage. In case of irreversible end-organ damage (especially renal dysfunction), there will be no improvement of a patient's clinical status. A screening risk score to predict operative mortality after device

implantation are as follows: indication for ventilator support (4 points); postcardiotomy shock (2 points); the implantation of temporary LVAD prior to HeartMate (2 points); central venous pressure >16 mmHg (1 point) and prothrombin time >16 seconds (1 point). A risk score >5 were associated with a significantly greater operative mortality than lower score (46 versus 12 percent). Patients with low (0 to 4), intermediate (5 to 7) or high (8 to 10) risk score had increasing mortality rates (8, 32, and 49 percent) and decreasing rates of successful bridging to transplantation (89, 65, and 49 percent) [8].

LVAD provide support of the left ventricular function only; the management of the right ventricular function is therefore very important, and the goal has to be the management of pulmonary vascular resistance. LVAD support reverse ventricular remodeling and cause permanent improvement in left ventricle function, causing regression of myocyte hypertrophy and fibrosis, improvement in myocyte contractility, restoration of beta-adrenergic receptors, normalization of calcium metabolism, altered expression of genes involved in processes such as myocyte metabolism and apoptosis [9-13]. This structural reverse remodeling is complete by about 40 days, with evidence of clinical benefit and an improvement in the quality of life [14]. These data suggest that human myocytes have the capability of undergoing beneficial functional and electrophysiological changes and an increase in contractility and hemodynamic improvement [12,13,15].

End stage heart failure is not an end of life, since heart transplantation, better medications and devices, including VADs implantations, offer patients a better quality and an apreciable extension of life.

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Sažetak

Terminalna faza zatajenja srca – transplantacija ili LVAD

Zatajenje srca kompleksni je klinički sindrom, a može se razviti kao posljedica bilo kojeg strukturalnog ili funkcionalnog poremećaja koji utječe na punjenje klijetki i ispumpavanje krvi. Prema podacima ISHLT registra, poluvrijeme preživljavanja nakon srčane transplantacije produžilo se s 8,9 godina u 1982. na oko 11 godina u razdoblju između 2002. i 2006. Vršni VO2 (VO2max) najobjektivniji je parametar u procjeni težine zatajenja srca i mogao bi biti najbolji prediktor stavljanja bolesnika na transplantacijsku listu. Mehanička srčana potpora indicirana je u bolesnika u kojih se farmakološkom terapijom (oralnom i parenteralnom) te nefarmakološkom s intraaortnom balon pumpom ne ostvari adekvatno poboljšanje kliničkog statusa bolesnika. LVAD potpora je lijevom srcu, a može dovesti do remodeliranja i trajnog poboljšanja funkcije lijeve klijetke. Terminalna faza zatajenja srca nije i kraj života jer transplantacija, noviji farmakološki pripravci i mehanička potpora, uključujući i VAD, bolesnicima omogućuju bolju kvalitetu i p***rodužetak života.***

Ključne riječi: zatajenje srca; transplantacija srca; LVAD

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ANTIMICROBIAL PROPHYLAXIS AND INFECTION CONTROL IN CASES OF MECHANICAL CARDIAC SUPPORT DEVICES

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Summary

Ventricular assist devices (VADs) for patients with severe heart failure are improving, and there are increasing numbers of implants, as device therapy enters the era of permanent use (i.e. destination therapy). The device-related infection of implanted pumps and sepsis remain important risk factors for death, and once infections are established on biomaterial surfaces, they usually persist despite prolonged antimicrobial therapy.

Biofilm forming is the crucial moment in the pathogenesis of many subacute and chronic bacterial infections, including the infections connected with a foreign body. Biofilm is a significant clinical problem. Its eradication by conventional antimicrobial agents is rather complicated, as it disposes of several mechanisms for developing resistance to antibiotics. The role of persisting cells is crucial in the context of the tolerance of bacterial biofilm towards antimicrobials. The mechanism for biofilm forming and the consequential antimicrobial resistances are the key to developing new therapeutic strategies.

Therefore, adherence to evidence-based infection control and prevention guidelines, meticulous surgical technique and optimal post-operative surgical site care form the foundation for VAD-associated infection prevention.

Keywords: ventricular assist device; infection; biofilm; antimicrobial therapy; prevention guidelines

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INTRODUCTION

The most frequent complications of ventricular assist devices (VAD) are bleeding, infection, thromboembolism, renal failure, haemolysis and neurological dysfunction. Bleeding and infection are the most prevalent and immediate complications [1].

Infection frequency in patients in need of a VAD is presumed to be over 35 % [2]. Within the first three months (peak in the third week) following the operation, 28 % of patients suffer from infections [3,4]. According to the *REMATCH trial* (the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure), the mortality caused by sepsis equals 41 % [5].

Besides the risk factors (gender; obesity; smoking; chronic obstructive pulmonary disease - COPB; Low Cardiac Output State; *Diabetes mellitus*; corticosteroid therapy; renal and hepatic insufficiency) [6] and the prevention of infections common for all cardiac surgical patients (urinary tract infection – UTI [7]; ventilated associated pneumonia – VAP [8]; catheter-related bacteraemia – CRB; sepsis), for patients with mechanical cardiac support devices, characteristic are also several additional specific factors. These factors are as follows: the prevention of infections connected with the mechanical cardiac support pump / device (VAD); the pre-, intra- and postoperative management; and the very origin of VAD infections related to biofilm forming.

MECHANICAL CARDIAC SUPPORT DEVICE (*Ventricular Assist Device – VAD*)

First generations of implantable pulsative VADs (*Heart Mate I*) had – though having enhanced the haemodynamics in cardiac surgical patients – also contributed to developing frequent infections (18–80 %) [3,9,10]. High infection frequency (among other factors) has initiated the development of new generations of rotational, non-pulsative pumps (*Heart Mate II*), the introduction of which aimed at reducing the infection frequency (by 13–27 %). Differences between the older and the newer pumps, in favour of the latter ones, are further manifested in the following: size and weight (1/7 smaller and 1/4 lighter); operation scale (as opposed to extensive operation and large haematoma at the pump site, the infection frequency is much lower when the pump is smaller); thinner, more flexible and impregnated cuffs have replaced the earlier inadequately immobilised, non-flexible and large drivelines that had often resulted in ascedental infections. Consequently, with regard to the pump site and the pump of the first generation itself, secondary infections and pump infections ending in bacteraemia had occurred more frequently, unlike *Heart-Mate-II*-related infections, which – according to Lahpor – do not exceed the range 0–3 % [11].

PRE-, INTRA- AND POST-OPERATIVE MANAGEMENT

Pre-operative infection control includes the patient-related procedure and the setting of the central venous catheter, while following the CDC 2009, Guideline for the Prevention of Intravascular Catheter-Related Infections [12].

Full patient preparation for the operation comprises the following: eradication of chronic infections / focus; decolonisation of the skin by the means of antiseptic polyhexadine-based cleansing; eradication of the nasal carrier *Staphylococcus aureus* MRSA by applying antibiotic prophylaxis; elimination of superfluous medical devices (urinary catheter, central venous line, etc.); prevention of the aspiration of stomach content (in case of intubation) and decubitus; maintenance of oral hygiene; control of the blood glucose level accompanied by adequate diet [6].

The staff should maintain maximal hand hygiene (in accordance with the WHO Guidelines on Hand Hygiene in Health Care) both before and after the contact with a patient during all procedures, as well as pre-, intra- and post-operatively; this is of crucial importance for the prevention of hospital infections [13]. Antimicrobial prophylaxis is tailored to institutional surveillance cultures, and a patient's culture results in doses adjusted for renal and hepatic function: Vancomycin (15 mg/kg, i.v. one hour pre-operatively, every 12 x 48–72 hours) – covered gram-positive bacteria; Levofloxacin (500 mg i.v. Q12 x 48–72 hours) – for gram-negative bacilli / capable of penetrating into the area of inflammation (macrophages); Rifampicin (600 mg PO 1–2 hours pre-operatively, daily x 48–72 hours) – due to small molecule, capable of penetrating into the biofilm; Fluconazole 400 mg i.v. pre-operative and each day x 48h – covered *Candida* spp.; Mupirocin 2 % nasal ointment pre-operatively and twice daily x 5 days – decolonisation of the staphylococcal nasal carrier (REMATCH trial) [5].

The intra-operative infection control includes the operating room, the operating field and the mechanical cardiac support device / pump itself.

In the operating room, the staff hand hygiene has to be harmonised with the European norms – EN 12791: 2005 Surgical hand disinfection [13,14,15]; apart from limited movement of the staff in the room, it is also recommended to use a *HEPA filter* for maintaining ultra-clean air during the surgical implantation procedure [6, 16, 17].

The operating field, apart from prior antiseptic cleansing (with chlorhexidine or iodoform) and polyalcohol antisepsis, is to be covered with sterile coverings.

VAD itself should be opened only immediately before the operation; using meticulous surgical technique (careful haemostasis – avoiding the pump site haematoma), it is to be implanted and immobilised, and a drain should be placed [16].

In post-operative infection control, the most critical component is driveline immobilisation (care), as this is the place where the initial contamination – colonisation – infection (usually by the saprophyte flora of the patient's skin) most frequently occurs. It is therefore very important to instruct patients on the following issues: minimisation of driveline exit site trauma; importance of personal hygiene and life environment cleanliness; adequate diet and nutritional support [18]; and the control of blood glucose level [19]. It is further of major importance to terminate the peri-operative prophylaxis after 48 hours, and to introduce – in accordance with microbiological cultures – the antimicrobial therapy, with the aim of avoiding an increasingly frequent medical problem – the emergence of multiresistant organisms (Extended Spectrum Beta Lactamasis *Enterobacteriaceae* – ESBL; Vancomycin Resistant *Enterococcus* – VRE) [20,21].

Driveline exit site care includes: dressing technique; antiseptic cleansing; avoiding shower for the first 30 days (later using a special shower set); if any clinical signs of infection emerge, a surrounding skin swab after bandaging is taken, as well as the aspiration of the wound secretion for microbiological analysis, i.e. isolation and identification of agents with the accompanying sensitivity test.

INFECTION

Post-operative VAD infection includes the already mentioned driveline site on the skin, the VAD site, and the infection of the inner pump surface.

Infections may be caused in the following ways: by intra-operative inoculation (in the rarest number of cases); haematogenously (seldom) as a result of haematogenous spreading of catheter-related bacteraemia (CRB); as a consequence of secondary bacteraemia caused by either ventilated associated pneumonia (VAP) or urinary tract infection.

The most frequent late infection occurs however as a result of the spreading of the initial driveline colonisation to the pump site. It is an ascedental bacterial colonisation of the saprophyte flora not only to the driveline, but also to the inflow / outflow cannulas, accompanied by biofilm / glycocalyx forming. The colonisation becomes an infection spreading to the pump site, which – depending on the size – contains non-drained blood (haematoma), i.e. a potential medium for microorganisms. From the pump site, the infection spreads to the pump itself, i.e. further to the blood stream as bacteraemia / sepsis.

Except from VAD infections, in some patients, deep sternotomic wounds connected with purulent mediastinitis or a necrosome of the thoracic wall may develop.

Biofilm

According to the *National Institutes of Health,* biofilm production is regarded an important medical term, as it is a part of over 80 % of all the microbial infections in the human body [22].

It is in the nature of 99 % of bacteria to form biofilm, and the most common microorganisms, responsible for two thirds of infections connected with a foreign body, are biofilm-forming bacteria – staphylococci (*Staphylococcus aureus*, *S. epidermidis, S. lungdunensis),* followed by *Pseudomonas aeruginosa* and *Enterococcus* spp, and, in cases of fungus infections, *Candida* spp.

The mentioned saprophyte flora, which initiates the colonisation, consists mainly of staphylococci (coagulase-negative and *Staphylococcus aureus* / MRSA), which – within a very short time period (24 hours) – initiate the "good biofilm" forming, as protection from the pathogenic flora. A longer time period is needed for biofilm forming in gram-negative bacteria (e.g. *Pseudomonas aeruginosa*).

The majority of chronic infections are connected with the forming of biofilm adhered to the native tissue, the mucous surface or the wound tissue: e.g. cystic fibrosis and *Pseudomonas aeruginosa*; endocarditis of native valves; middle ear infection; periodontitis; etc.

However, biofilm is much more frequently an agent causing non-eradicated infections connected with a foreign body, i.e. the forming of extracelullar matrix (glycocalyx) at the surface of medical products (implants) in the human body; e.g. urinary catheters (10-30 %); mechanical ventilation (9-27 %); central venous catheter (3-8 %); vascular grafts and coronary bypasses (1-5 %); pacemakers (1–7 %); and other various kinds of implants / prosthetic devices – breasts, joints, intra-ocular lenses, etc. (1–3 %). According to Lynch [23], infection frequency associated with the implantation of the mechanical cardiac support devices (VAD) is the highest: 25–50 %.

In order to enable the direct visualisation of the three-dimensional structure of bacterial biofilm, the *Center for Genomic Sciences* has developed a new diagnostic protocol – the *Confocal laser scanning microscopy (CLSM),* based on 16S rRNA [24], and the *Fluorescence in situ hybridization (FISH)* method, which have in the recent years helped creating a better understanding of these types of infections [25].

Biofilm – depending on the sort, type and surrounding – consists of bacteria within and surrounding the glycocalyx. The bacteria at the bottom of biofilm (in anaerobic conditions) are the reason why the antibiotic therapy may be extremely resistant (low-level penetration of antibiotic / antifungal medications; protection from phagocytosis); biofilm-producing bacteria may be extremely difficultly cultivated by using the traditional microbiological methods [26].

The antimicrobial therapy in cases of infections associated with biofilm is based on the result of a conventional antibiogram of the planctonic bacteria. However, this sensitivity is not equal, even if the agents within the biofilm are. The bacteria within the biofilm are 100–1,000 times more resistant than the planctonic bacteria; the antibiotic is therefore active against the latter bacteria, but not against the biofilm; this makes the treatment of patients suffering from implant infection unsuccessful [27]. None of the so-far known antibiotics (except for peroral Rifampicin, which should always be combined with other antimicrobial drugs) have managed to be active against hibernating bacteria within the biofilm; only the new lypopeptide, Daptomycin, has been successful. Due to its extremely swift bactericidal acting by causing the bacterial membrane of the agent – gram-positive bacteria – to break, Daptomycin is antimicrobially active against the stationary bacterial phase of the agents, i.e. the biofilm [28,29].

AGENTS CAUSING VAD INFECTIONS

Staphylococcus aureus and coagulase-negative staphylococci (CoNS) are the most frequent agents of driveline exit site and pump site infections. In doubt of an infection, not only must the microbiological analysis be done without delay, but also the urgent direct gram-medication taken, so that the empirical antimicrobial therapy might be commenced as soon as possible. Agents causing infections in intra-vascular devices resulting in VAD bacteraemia are, apart from the already mentioned gram-positive cocci, *Candida, Pseudomonas aeruginosa* and other multiresistant microorganisms.

The prevalence of enterococcal device colonisation in Herrmann's study [17] may be explained by the high incidence of thromboembolism of small bowel arteries. Due to the virulent factors and primary pathogenic nature, infections caused by *S. aureus* usually develop in the early post-operative period as acute, and are accompanied by common inflammation symptoms. Infections caused by *Staphylococcus epidermidis* and other CoNS are in most cases – due to the low-level invasiveness of the agents and the slow development of the clinical inflammation symptoms – recognised only several months after the operation.

THERAPY

Apart from the surgical procedure (in case of the pump site infection, incision is obligatory) and the antibiotic therapy in the treatment of such infections, in cases of the presence of *Staphylococcus aureus,* aerobic gram-negative bacilli and *Candida* spp., the VAD implant has to be removed as well. The supportive surgical therapy is *Vacuum Assisted Closure – V.A.C.*, which accelerates wound healing and granulation production, and eliminates excess liquid from the wound surface and the skin lobe.

Table 1.

Supervision culture	Urine	Blood culture	Wound Tissue	Part of prosthesis	Bronchoaspirate Sputum	Others	Serology
30/10/2008 SURGERY							
☑					10/08 B*. *E.coli, P. aeruginosa*		☑
11/08 – MEROPENEM, VANCOMYCIN, FLUCONAZOLE							
					11/08 S†. *Candida albicans*	11/08 VC‡ *E.coli*	
			12/08 *St. epidermidis*				
		03/09 *Stenotrophomonas maltophilia*		03/09 *St. pidermidis*		03/09 D** *Corynebacterium*	
03/09 – VANCOMYCIN, CIPROFLOXACIN							
	04/09 *Proteus mirabilis*		04/09 *Corynebacterium*				
		07/09 *S.aureus*					
07/09 - CLOXACILLIN							
	08/09 *P.aeruginosa*				08/09 B. *P. aeruginosa*		
08/09 - MEROPENEM							

ABBREVIATIONS: ☑ – Satisfactory supervision culture; B* – bronchoaspirate; S† – sputum; VC‡ – top venous catheter; D** - top drain
10/08 – month/year

Table 2. M.B. – op. LVAD 18. 06. 2009. / exitus 20. 06. 2009.

Supervision culture	Urine	Blood culture	Wound Tissue	Part of prosthesis	Bronchoaspirate Sputum	Others	Serology
14/01/		☒	☒	☒		☒	☒
St. aureus N■							
	25/01/ *Morganella morganii* *Enterococcus faecalis*						
08/06 /							
St. aureus N■							
16/06/ CEFAZOLIN							
18/ 06 /09 SURGERY							
19/06/							
Enterobacter N■					19/06/ B*-		
cloacae					*P. aeruginosa*		
P.aeruginosa S§							
Enterococcus spp.							
19/06/ MEROPENEM							

ABBREVIATIONS: ☒ – No indications for taking; N■ – nose; B* – bronchoaspirate, S§ – skin (hurdle)
14/01/- day/month/

Table 3. S.B. – op. LVAD 28. 10. 2009.

Supervision culture	Urine	Blood culture	Wound Tissue	Part of prosthesis	Bronchoaspirate Sputum	Others	Serology
☑	10/09 E. coli	☒		☒	☒		☒
26/10/– 04/11/ – CIPROFLOXACIN **27/10/ – VANCOMYCIN**							
28/10/09 SURGERY							
						10/09 D Coagulasa negative staphylococci	
01 – 09/11/ – CEFAZOLIN							
			06/11/ *St.epidermidis*				
	11/09 *E.coli*		11/09/ *St.epidermidis*				
15 – 21/11/ – AMOXYCILLIN/ CLAVULANIC acid **23/11/ – 03/12/ – VANCOMYCIN**							
			22,23,24,26/11/ *St. epidermidis* 23,24,26 /11/ *Corynebacterium*				

ABBREVIATIONS: ☑ – Satisfactory supervision culture;☒ – No indications for taking; D** – top drain
10/09 – month/year; 26/10/ -day/month/

Table 4.

Supervision culture	Urine	Blood culture	Wound Tissue	Part of prosthesis	Bronchoaspirate Sputum	Others	Serology
☑	☑	☒	☒	☒	☒	☑ ☑	☒
17/02/ - VANCOMYCIN 1g in 20.00 h							
18/02/2010 – SURGERY							
18 – 21/02/ – VANCOMYCIN RIFAMPICIN FLUCONAZOLE							
22 – 24/02/ – CEFAZOLIN							

ABBREVIATIONS:
☑ – Satisfactory supervision culture; ☒ – No indications for taking; D** – top drain
17/02/ - day/month/

Along with a carefully chosen antimicrobial therapy according to the agent antibiogram, in cases of gram–positive cocci, which are also the most frequent, it is relevant to prescribe the antibiotic that is active against biofilm. In referential literature, there are frequent mentions of using Rifampicin in combination with Cloxacillin, Vancomycin, Linezolid or Fucidic acid in the staphylococcal biofilm therapy [30,31].

In his work, Beiras-Fernandez [2] mentions the currently most efficient antibiotic for treating multiresistant gram-positive biofilm-related VAD infections – the already mentioned Daptomycin. In a retrospective study, 9 patients suffering from post-implantation VAD infections were analysed. In as much as 83 %, infection agents were gram-positive cocci (33 % Methicillin Resistant *Staphylococcus aureus* – MRSA; 25 % *Enterococcus faecium;* 12,5 % Methicillin Resistant *Staphylococcus epidermidis* – MRSE; 12,5 % Methicillin Sensitive *Staphylococcus aureus* -MSSA); out of this number, in 66 %, catheter-related infections were present. Therapy with Daptomycin was empirically initiated in all cases. Successful outcomes were reported in seven subjects (78 %), with two patients succumbing due to multiorgan failure related to their heart condition prior to completing the therapy.

DUBRAVA CLINICAL HOSPITAL

In the Dubrava Clinical Hospital, four patients received mechanical circulatory support in the period between October 2008 and February 2010; one patient was implanted Paracorporal VAD, and the others Left VAD).

Prior to the VAD implantation, each of the hospitalised patients underwent, inter alia, microbiological screening: nose, pharynx, skin (axilla, inguinal region, anus / perineum) swabs, and urine culture. In accordance with a patient's clinical state and if indicated, following samples were taken pre- and / or post-operatively: haemoculture; bronchial aspirate / sputum; wound swab / tissue / part of a prosthetic device; other material – e.g. drain peak; drain content; central venous catheter peak; catheter-surrounding skin swab, etc. In some patients, serology to: *Cytomegalovirus, Ebstein Barr* virus and *Toxoplasmis* was indicated as well. The entire microbiological control and the samples taken (according to time periods) in all four cases may be seen in Tables 1–4. Usual peri-operative prophylaxis was prescribed routinely, in accordance with the REMATCH trial [5], except for substituting Levofloxacin (which is not registered in Croatia) by Ciprofloxacin, in cases where the control swabs were satisfying. Where not, the chosen antimicrobial therapy (see Tables 1–4) was introduced even prior to the operation, and changed during the post-operative stay in accordance with a patient's clinical state and the results of the microbiological analyses of the samples.

The final outcome of the medical treatment of the four patients with mechanical cardiac support device implants was that two of the patients died, while in the other two cases, the operations were successfully performed; in one of the latter cases, heart transplantation was consequently performed as destination / end therapy.

The first patient (G.K., Table 1), though the mechanical heart was removed by using intensive haemodynamic monitoring and applying carefully chosen, state-of-the-art antimicrobial therapy, died due to septic shock. The second patient (M.B., Table 2) also died, only two days following the operation, due to sepsis of unknown aetiology. The third patient (Š.J., Table 4) was released from hospital soon after the operation; the patient's general state was stable, all the control cultures were satisfying, and the patient received adequate and carefully chosen antimicrobial therapy based on the microbiological samples. The fourth patient (S.B., Table 3), with both pre- and post-operative states being stable, ended the hospitalisation in December 2009; eight months following the VAD implantation, in June 2010, heart transplantation was successfully performed.

CONCLUSION

Microbes are ubiquitous in the environment and pose a constant threat to the well-being of the patients with implanted VAD. The infection prevention and control according to the *Evidence based guidelines*, along with the regulation of the pre-operative risk factors, are therefore important factors in the context of patient prepara-

tion for the mechanical circulatory support. Meticulous surgical technique, optimal post-operative care of the surgical site and driveline immobilisation, avoiding the emergence of trauma, and applying healthy diet assure the success of the operation. Thanks to the today's correct approach in treating VAD infections and the new bactericidal antimicrobial medications, the outcome of the therapy applied in cases of patients with chronic LVAD infections has become successful in an increasing number of cases. In future, this will surely be further supported by enhancing the VAD hardware with antiseptic dressing and biomaterial resistant to biofilm forming, as well as by developing completely implantable systems with transcutaneous energy transmission to eliminate the need for percutaneous driveline. Such VAD technology will probably result in the reduction of morbidity by preventing the colonisation of microorganisms, leading consequently to the reduction of biofilm-related infections and the related unnecessary antibiotic therapy.

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Sažetak

Antimikrobna profilaksa i kontrola infekcije kod mehaničke potpore srca

Danas je sve većem broju bolesnika sa teškim zatajenjem srca, zbog napretka tehnologije omogućeno privremeno ili trajno liječenje uređajem (pumpom) za mehaničku potporu srca (VAD).

Infekcije implantiranih srčanih pumpi i sepsa ostaju važnim fatorom rizika za smrt. Kad se na površinama biomaterijala utvrdi postojanje infekcija one perzistiraju unatoč produljenoj antimikrobnoj terapiji.

Formiranje biofilma je presudni korak u patogenezi mnogih subakutnih i kroničnih bakterijskih infekcija, a osobito infekcija povezanih sa stranim tijelom. Biofilm je signifikantan klinički problem. Teško se eradicira konvencionalnim antimikrobnim lijekovima, jer posjeduje nekoliko mehanizma stvaranja antibiotske rezistencije. Perzistirajuće stanice imaju glavnu ulogu u toleranciji bakterijskog biofilma prema antimikrobnom lijeku. Mehanizam stvaranja biofilma i posljedične antimikrobne rezistencije biti će ključ za razvoj novih terapijskih strategija.

Dakle, poštivanje dokazima utemeljene kontrole infekcija uz smjernice za prevenciju istih, pedantna kirurška tehnika i optimalna njega postoperativnog kirurškog mjesta čine temelje za prevenciju infekcija povezanih s VAD-om.

Ključne riječi: VAD; infekcija; biofilm; antimikrobna terapija; smjernice za prevenciju infekcija

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OVERVIEW OF NEW MECHANICAL CIRCULATORY SUPPORT DEVICES

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Summary

Continuous-flow left-ventricular assist devices (LVADs) have emerged as the standard of care for advanced heart failure patients, who require long-term mechanical circulatory support. In this review, we describe in brief the basics of the development of various devices, both the old (pulsatile-flow) and the new (continuous-flow) devices. A clinical review of modern devices and their today's relevance are given in a brief outline.

***Keywords**:* assist device; heart transplantation

THE HISTORY OF THE MECHANICAL SUPPORT DEVICE DEVELOPMENT

Akutsu and Kolff are credited with the first reports on a successful experimental implantation of a total artificial heart (TAH) in 1958. Cooley used the TAH as a temporary support device until transplantation in 1969. The heart performed 64 hours of support. In 1982, Jarvik-7 TAH was used by Dr. Jarvik as a first permanent heart support device. Copeland and colleagues performed the first planned TAH implant as a bridge-to-transplantation (BTT). After having undertaken several trials and multiple studies, the FDA gave an approval for HeartMate I as destination therapy (DT) in 2002; for TAH (CardioWest) in 2004; for HeartMate II as BTT in 2009; and for HeartMate II as DT in 2010 (Table 1) [1].

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THE REQUIREMENTS FOR A SUCCESSFUL MECHANICAL SUPPORT DEVICE

Circulatory support systems are being developed to take over the pumping functions of the natural heart. Blood components must operate continuously, without maintenance, for years. Mechanical components are necessarily small and must operate without failing under highly stressed conditions. The development of these highly sophisticated devices is very demanding, and only the most qualified engineers are included in the process. Technologic barriers for successful Mechanical Circulatory Support that must be overcome are listed in Table 2.

Table 2. Technologic barriers for successful Mechanical Circulatory Support

• Development of specific materials
• Development of specific surfaces for blood-biomaterial interactions
• Blood pump designs
• Methods of storage of energy

Minimally six basic engineering disciplines are necessary for mechanical circulatory support system development (Table 3).

Table 3. Engineering disciplines necessary for mechanical circulatory support system development

• Mechanical	• Biomedical
• Electrical	• Manufacturing
• Software	• Quality engineering

The criteria for the selection of materials for mechanical support device must be chosen based on specific requirements for circulatory support (Table 4). [2]

Table 4. Criteria for selection of materials for mechanical support device:

• Structural strength
• Corrosion resistance
• Surface properties
• Toxicity levels

A major challenge for biomedical engineers is designing cost-effective long-term support, which should be small, efficient, quiet and capable of continuous use for ye-

ars of service without maintenance, while pumping blood in a hostile environment. The system should operate at least 5 to 10 years maintenance-free (Table 5).

The main objectives in mechanical circulatory support design are biocompatibility; reliability; functionality; cost. The components of biocompatibility are the avoidance of the mechanical compression of vital organ or tissues; the minimization of the need for surgical dissection; the avoidance of the migration of implanted elements; the avoidance of the damage to formed elements in blood; the avoidance of the pathologic stimulation of the coagulation system; the avoidance of heat and electrical damage to tissue; the anatomic compatibility; the avoidance of leaching toxic elements to the surrounding tissue [3,4].

Table 5. Special requirements for designing cost-effective long-term support:

- Small
- Efficient
- Quiet
- Capable of continuous use for years of service without maintenance
- Capable of pumping blood in a hostile environment
- The system should operate at least 5 to 10 years maintenance-free

A SURVEY OF PULSATILE AND CONTINUOUS-FLOW PUMPS

The blood pressure and flow can be generated by either positive displacement (pulsatile) or rotary (turbodynamic continuous-flow) pumps (Figure 1). Positive displacement (pulsatile) pumps propel fluid (blood) by cyclically changing the internal volume of the pumping chamber, similar to the native heart, and by moving a particular volume of blood with each ejection. The output requirement for a pulsatile configuration is a flow rate 5 to 10 L/min at a mean pressure of 100 to 150mmHg, and a rate less then 120 beats per minute.

Rotary pumps (also designated as turbodynamic) are characterized by a rotating component that has one or more impellers, which are supported within the pump by a bearing; they are powered either through a spinning shaft or magnetic forces that act on magnets within the impeller. The assembly comprised of all the rotating elements is called the rotor of the pump.

The hydrodynamic performance of rotary pumps with axial-flow design is determined by the speed of the rotor and the pressure difference across the inlet and the outlet orifices of the pump. As the difference decreases, blood flow through the pump increases with the increased speed of the pump. The relationship between the flow, the pump speed and the pressure is shown in Figure 2.

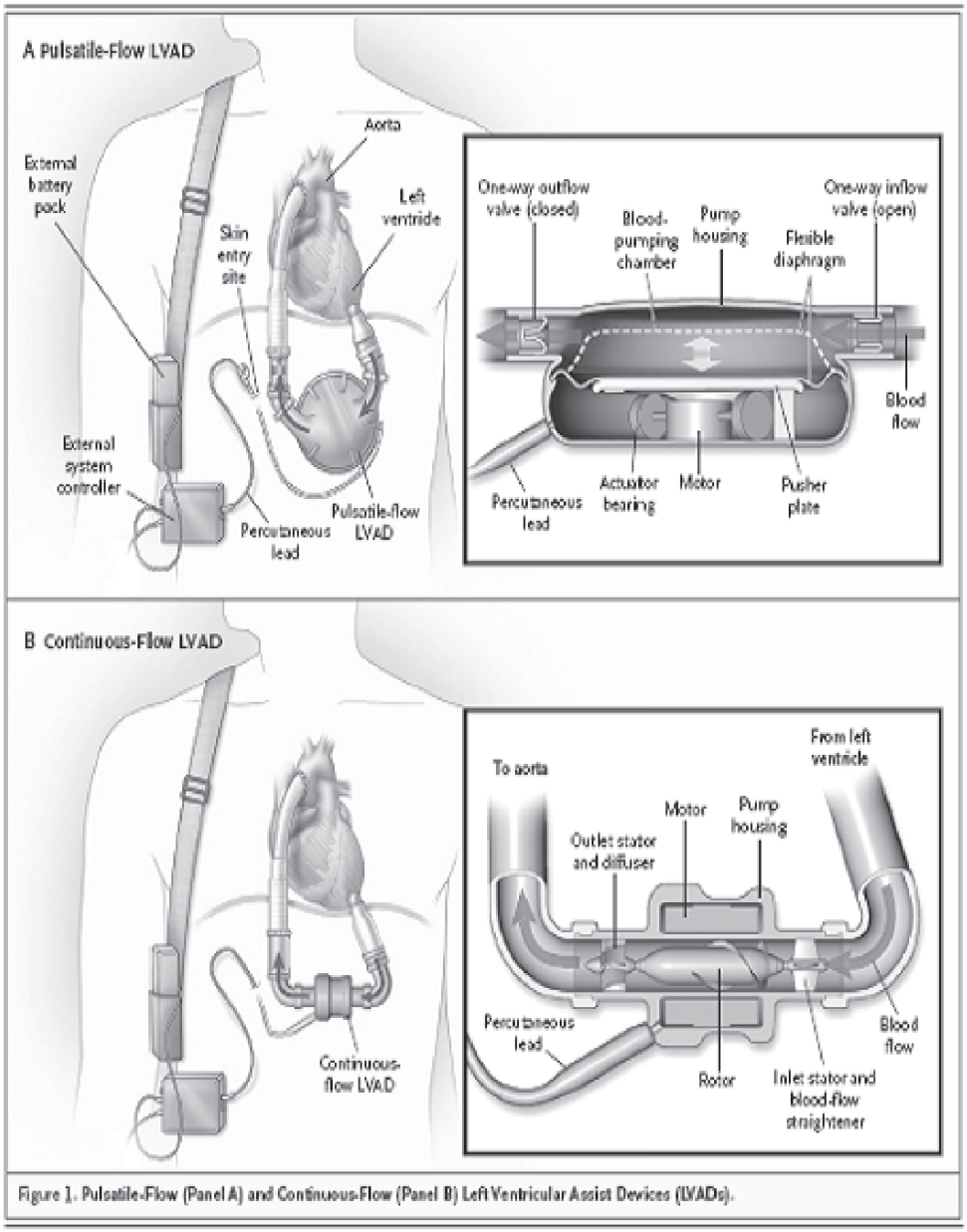


Fig. 1. Pulsatile and continuous-flow Left Ventricular Assist Devices (LVADs)

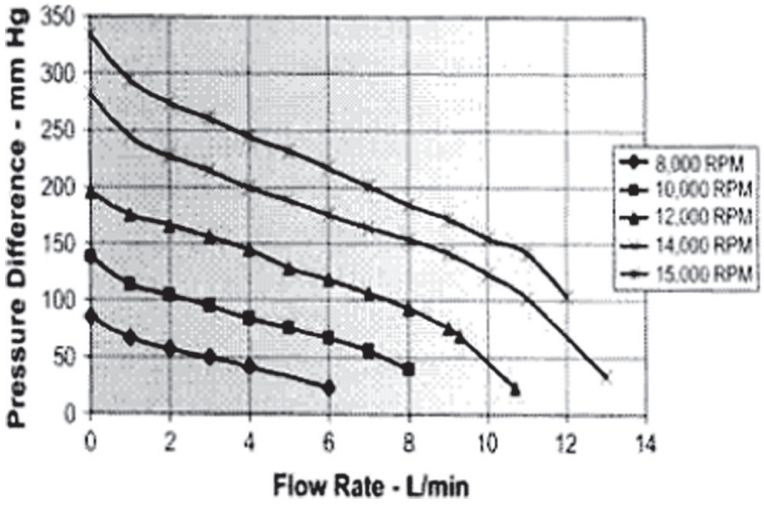


Fig. 2. The H–Q curve demonstrates the relationship between the pump speed (RPM) and the pressure difference across the inlet and outlet orifices of an axial-flow pump

Paracorporal positive displacement ventricular assist device (PVAD) (Figure 3) has been implanted in over 3,000 patients. It produces a beat rate range of 40–110 beats per minute, and a flow rate of 1.3 to 7.2 L/min. It is suitable for use in smaller patients (BSA>0.73m2) due to its external position. Chronic warfarin anticoagulation (International normalized ratio INR 2.5–3.5 units) is required with the Thoratec pump. The PVAD is actuated pneumatically by the dual drive console for in-hospital use and portable TLC-II pneumatic driver for ambulatory use, either inside or outside the hospital. In 2003, the TLC-II was approved by the FDA for home discharge.

Out of 1,941 patients who had received PVAD, BVADs were used in 54 %, isolated LVADs in 34 %, and RVADs in 3 % of patients. For all patients who were receiving PVAD assistance, the mean

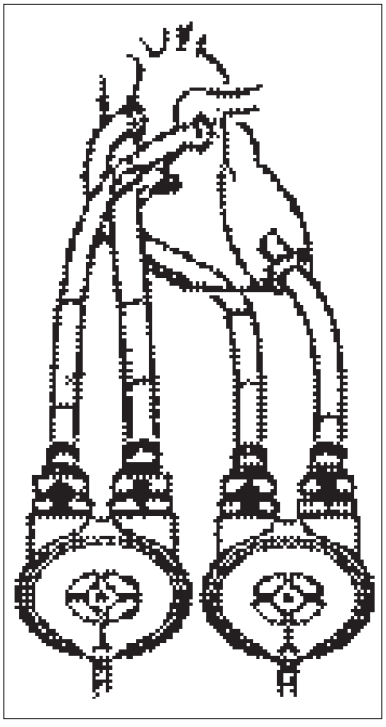


Fig. 3. Paracorporal positive displacement ventricular assist device (PVAD)

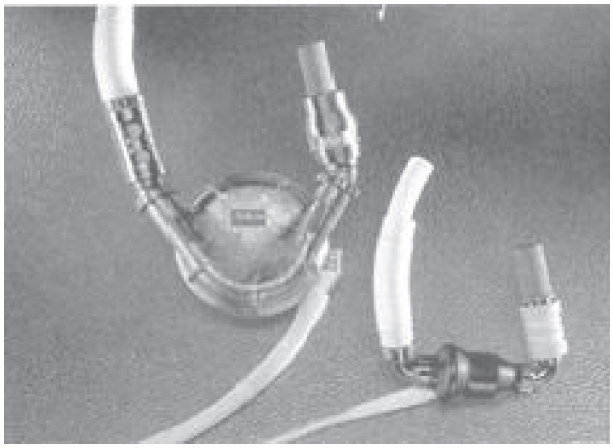


Fig. 4. HeartMate XVE

period of support was 51.8 days, and the longest time that BVAD had been implanted was 3.3 years. Worldwide, survival from implant to transplantation or recovery was 64.8 % for patients who had BVAD, 56.6 % for patients with LVAD, and 31.2 % for patients with RVADs (Table 9). Five hundred patients had undergone cardiotomy and were supported with PVADs (BVAD 31.2 %; LVAD 42.8 %; RVAD 13.4 %; in combination with other pumps 12.6 %). Mean PVAD support duration was 21.9 days (the longest duration 340 days). The survival was 44.7 %.

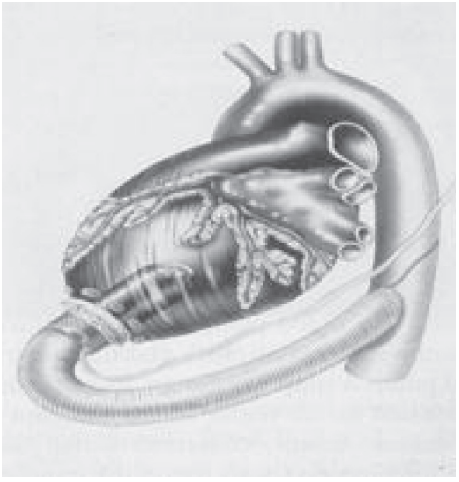
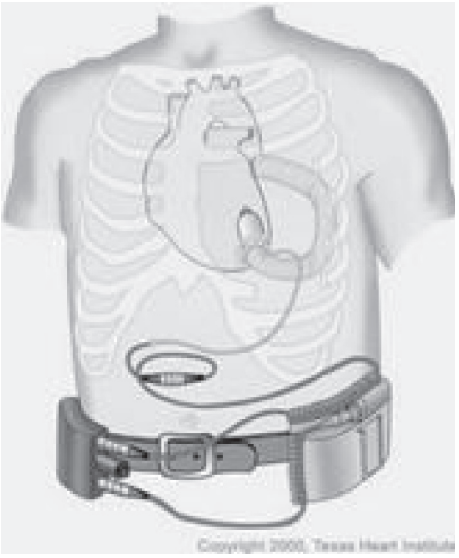


Fig. 5. Jarvik 2000 Left Ventricular Assist Device



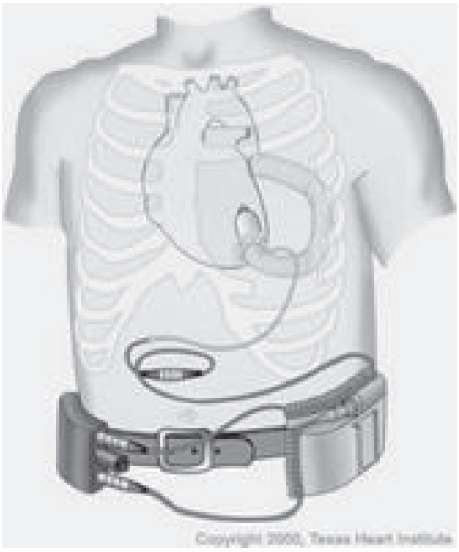


Fig. 6. Micromed – DeBakey Left Ventricular Assist Device assembly

In the period between its first application in 1986 and 2001, nearly 5,000 patients had been supported with **HeartMate XVE** (Figure 4); the survival of patients until transplantation or recovery was 65 %. The HeartMate LVAD is a positive displacement pulsatile pump, which – unlike all the other such LVADs available – is unique, as its textured inner surface allows for circulatory assistance without anticoagulation other than antiplatelet agents [5,6].

The Jarvik 2000 Left Ventricular Assist Device is a miniature electrically powered axial-flow pump that provides continues flow from the left ventricle to the descending thoracic aorta (Figure 5). It is placed within the left ventricle. The pump's operating range is between 8,000 and 12,000 rpm, and it can generate a flow of up to 8 L/min. It can be implanted through a left thoracotomy, median sternotomy, or extrathoracically. It requires the application of anticoagulation dicumarol therapy. In the period 2000–2005, the device has been implanted in 110 patients. The median period support with Jarvik 2000 was 148±204 until BTT, and 477±544 until DT. The technology is associated with minimal infections and other complications, and it offers an optimistic option for terminal and heart failure patients [7].

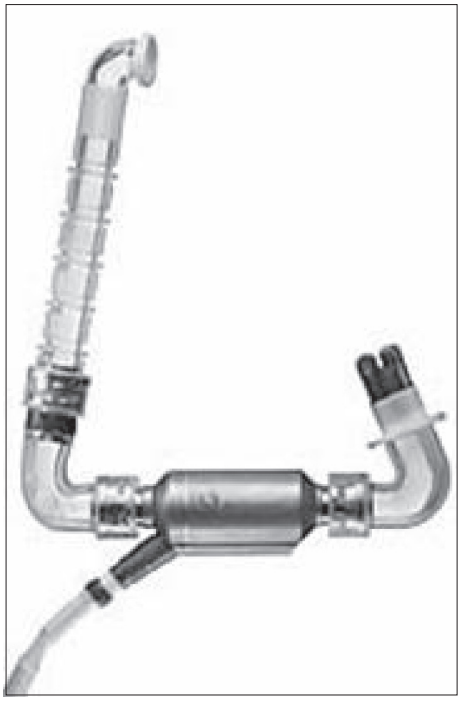


Fig. 7. Incor (Berlin Heart)

The Micromed – DeBakey Left Ventricular Assist Device (Figure 6) is a rotary pump of axial-flow design, which has

been developed in a collaborative effort of engineers from National Aeronautics and Space Administration (NASA), Dr. DeBakey and Dr. George Noon, MicroMed Technology in 1996. The support was first implanted clinically in Europe in 1998, and it received CE Mark approval.

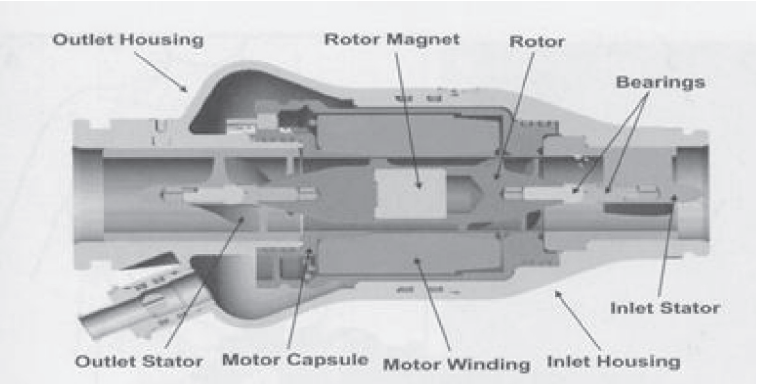


Fig. 8. Diagram of an internal view of the Heart Mate II pump

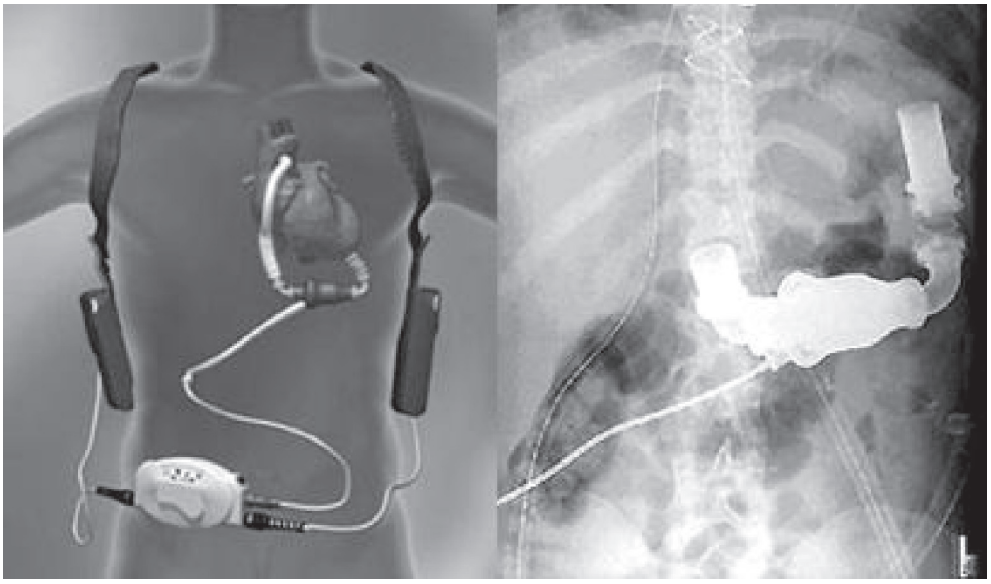


Fig. 9. (A) HeartMate II Schematic representation of the anatomic position and placement of Heart Mate II LVAS; (B) Chest radiograph demonstrating anatomic positioning of the Heart Mate II LVAS

The implantation of the device requires classical surgical techniques, and anticoagulation therapy with dicumarol and asprine/dicumarol is required. Monitoring with thromboelastography is recommended. Not many postoperative complications, like bleeding and thromboemboly, have been noted. Until 2005, the device had been implanted in 326 patients. The Micromed – DeBakey LVAD is specially recommended with pediatric patients [8].

The Incor (Berlin Heart) LVAD is a small axial-flow pump (Figure 7). The pump weighs 200g and generates flows up to 7L/min. It can be used with children (Excor Pediatric), and clinical BTT and DT trials have reported good initial results.

The HeartMate II left ventricular assist system (LVAS) is a rotary blood pump with axial-flow design, and it represents the second generation of implantable assist devices designed to be small, more reliable devices, suitable for long-term circulatory support. The major advantage of this device is its axial flow, which reduces its size by excluding the existence of a reservoir necessary for pulsatile flow.

HeartMate II blood pump has inlet and outlet cannula and percutaneous driveline, the HeartMate II system driver (computer controller) and power source (batteries). The power base unit has an alternative power source and battery charging system.

The internal parts of the Heartmate II pump are the titanium tube; the pump rotor; the rotor magnet; inlet and outlet stators with bearings and motor windings (Figure 8). The pump is designed for surgical implantation at the left costal margin below the heart and in the left pleural space (Figure 9). The inflow cannula exits in the left ventricle and is attached to the pump. The pump lays parallel to the diaphragm. The outflow cannula is tunneled back under the sternum to the ascending aorta. The percutaneous driveline is connected to an external system driver and a power source.

The anticoagulation regime is based on antiplatelet therapy (aspirin) and warfarin therapy (INR 2.0–3.0) at expected therapeutical range.

HeartMate II provides excellent support in the outpatient setting as well, with significant improvement in functional activity, ease of use and comfort due to the small size of the driveline. Excellent device reliability has also been noted.

It is at the moment used as both a device for patients awaiting heart transplantation and a device for patients meeting criteria for destination therapy.

Conclusion

Axial-flow implantable devices for mechanical circulatory support had shown a certain advantage as a bridge-to-transplantation and, for some patients, as destina-

tion therapy. Specialized centers with heart transplantation programs should develop a ventricular assist device program. Multidisciplinary teams participate in the evaluation and treatment of patients with the "end-stage" heart disease. Collecting all the relevant medical data, and monitoring the patients' health and – particularly – quality of life should represent the major part of the program.

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Sažetak

Pregled novijih uređaja za asistirano srce i asistiranu cirkulaciju

Uređaji za asisitirano srce i asistiranu cirkulaciju postali su standard u liječenju pacijenata s kroničnim zatajenjem srca, kojima je neophodna dugoročna mehanička potpora srcu i cirkulaciji. U ovom članku ukratko su opisane povijest razvoja različitih starijih (pulsatilnih) i novijih (kontinuirani tok) uređaja te važnost kliničke primjene ovih modernih uređaja.

Ključne riječi: asistirano srce; transplantacija srca

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Aco Zrnić

Naklada
700 primjeraka

Tisak
Intergrafika TTŽ d.o.o.

Zagreb, ožujak 2011.