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Mechanical circulatory support in heart failure

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Abstract

The increasing number of end-stage heart failure patients eligible for heart transplant and the disproportionately low number of donor hearts have led to increased interest in ventricular assist devices (VAD). These devices can be used as a bridge to decision, bridge to recovery, or bridge to candidacy. The main advantage of mechanical circulatory support (MCS) is the improvement of organ perfusion and function, which leads to better quality of life and survival. The MCS can also be used as a destination therapy in end-stage heart failure patients who are not eligible for heart transplant. It should be remembered that, despite the tangible benefits, VAD implantation may also be associated with the risk of serious complications, such as bleeding, infection, arrhythmias, blood clots, right ventricular failure, and cardiovascular events. This study presents an up-to-date overview of the current knowledge on the role of MCS in modern medicine.

Key words: mechanical circulatory support, heart failure.

Streszczenie

Wzrastająca liczba chorych ze schyłkową niewydolnością serca (*heart failure* – HF) zakwalifikowanych do transplantacji tego narządu i jednocześnie nieproporcjonalnie mała liczba dawców serca stanowią przyczynę zwiększonego zainteresowania urządzeniami służącymi do mechanicznego wspomagania krążenia (*ventricular assist device* – VAD). Zadaniem tych urządzeń jest leczenie pomostowe do czasu podjęcia decyzji, poprawy lub też do momentu, kiedy chory stanie się kandydatem do przeszczepienia serca. Zasadniczą korzyścią z zastosowania VAD jest poprawa perfuzji i funkcji wszystkich narządów, czego skutkiem jest poprawa jakości życia i rokowania chorych. Dzięki temu VAD może być również leczeniem docelowym u chorych z krańcową HF, którzy nie kwalifikują się do transplantacji serca. Należy pamiętać, że oprócz wymiernych korzyści, wszczepienie VAD może się wiązać również z ryzykiem wystąpienia poważnych powikłań, takich jak krwawienia, zakażenia, arytmie, zakrzepy, niewydolność prawej komory oraz incydenty sercowo-naczyniowe. W artykule przedstawiono przegląd dotychczasowej wiedzy na temat roli mechanicznego wspomagania krążenia we współczesnej medycynie.

Słowa kluczowe: urządzenia do wspomagania komór, niewydolność serca.

Introduction

Heart failure (HF) is a growing clinical, economic, and social problem due to its increasing incidence and unfavorable prognosis. The prevalence of symptomatic HF in the general population is 2-3% and increases to 20% in patients older than 75 years of age. Within 4 years from the diagnosis, 50% of patients die; in the case of severe HF, mortality reaches 50% within 1 year [1, 2]. The most effective method of treating end-stage HF is organ transplantation; however, due to the disproportion between the number of transplant candidates and the number of donors, alternative methods of treatment must be employed to offer the patients a chance for improving their quality of life and functioning and to prolong their lives until a decision concerning further management can be reached. For the above reasons, the interest in mechanical circulatory support (MCS) devices is on the rise [3-5].

Mechanical circulatory support is used as a bridge to decision, bridge to recovery, or bridge to candidacy for heart transplantation. The primary benefit of using this method is the improvement of the perfusion and functioning of all organs, which improves quality of life and patient prognosis. As a result, MCS can also be used as a destination therapy in patients who are not eligible for a heart transplant [3, 6].

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Types of circulatory support

The role of ventricular assist devices (VADs) is to support or substitute the action of one or both ventricles. VADs can be categorized into rotary pumps, ensuring continuous blood flow with the impeller's movement, and pulsatile pumps, which generate pulsatile blood flow in the vessels. In a continuous flow device, the impeller is placed in a magnetic field, eliminating the presence of spaces not reached by blood, which promote thrombus formation [7]. The most commonly used continuous flow pumps are HeartMate II, HeartMate III, Thoratec, and HeartWare [8, 9]. At present, continuous flow pumps constitute 95% of the cardiac assist devices implanted in adult patients [2].

Depending on the planned duration of circulatory support, the following can be distinguished:

– short-term circulatory support (up to 7 days) provided by rotary pumps supporting the functioning of the right or left ventricle and extracorporeal membrane oxygenation (ECMO) systems [10];
– medium-term circulatory support (from 7 days to 3 months) provided by pulsatile pumps (POLCAS, ABIOMED) and some centrifugal pumps [4];
– long-term circulatory support (several months or years) provided by left ventricular or biventricular assist devices (LVAD, BiVAD) using continuous flow (HeartMate II, Thoratec, and HeartWare) or pulsatile flow (Novacor LVAD).

Currently in Poland, the POLCAS and Berlin Heart systems are used as bridge-to-transplantation therapy along with the continuous flow pumps HeartMate II and HeartWare [5–7].

Indications for VAD implantation

In accordance with the guidelines of the European Society of Cardiology from 2012 pertaining to the management of acute and chronic heart failure, the use of VAD is a class I recommendation as a bridge to cardiac transplantation and a class IIa recommendation as a destination therapy [1]. In practice, due to the cost of this therapy and the complications associated with its long-term use, MCS is primarily used as a bridge therapy in individuals who are active waiting list candidates for heart transplantation.

Patients are eligible for VAD implantation when, despite optimal pharmacotherapy and electrotherapy, symptoms of HF exacerbation persist for at least two months and are accompanied by at least two of the following:

1) at least three episodes of HF exacerbation requiring hospitalization within the past 12 months,
2) necessity of using intravenous positive inotropes,
3) significant impairment of left ventricular systolic function (LVEF < 25%) and reduction of maximal oxygen consumption demonstrated by spiroergometry (VO_2max < 12 ml/kg b.w./min),
4) impairment of kidney and/or liver function caused by perfusion disturbances resulting from low cardiac output,
5) progressing impairments of right ventricular function [1, 2, 11].

The following hemodynamic parameters also constitute important eligibility criteria for VAD implantation:

1) systolic arterial blood pressure < 80 mm Hg,
2) cardiac index < 2 l/min/m^2,
3) central venous pressure > 20 mm Hg,
4) pulmonary wedge pressure > 20 mm Hg [6].

Absolute contraindications for VAD implantation include irreversible injury of the central nervous system and generalized neoplastic disease. Relative contraindications include severe organ lesions and infections refractory to treatment [11].

The choice of an appropriate device is key in achieving improvement in the prognosis of patients qualified for MCS. The first thing to consider is whether the VAD is to serve the role of a bridge to transplantation, bridge to recovery, or long-term destination therapy. After establishing the preliminary management plan, the patient's age and body surface area should be taken into account, and, in the presence of indications for left ventricular assist device (LVAD) implantation, the risk of developing right ventricular HF should be assessed.

Prognosis of patients treated with VADs

One-year survival of patients undergoing VAD implantation exceeds 75%, but it decreases successively as the duration of support is extended. The benefits from this form of therapy depend on the indication for which the device was implanted. In 1-year follow-up, decidedly better results are achieved by patients with VADs implanted as a bridge to transplantation in comparison with patients deemed ineligible for heart transplantation in whom the circulatory support is a destination therapy. One-year survival in these patient groups is 86% and 78%, respectively, while two-year survival is similar in both groups, being approximately 50%. Patients with VADs implanted as a bridge to transplantation present with a worse initial clinical condition than patients undergoing transplantation without preceding VAD treatment. Notwithstanding, during the adjunctive treatment, the function of the heart, the perfusion of organs, and, subsequently, their function improve considerably; as a result, there is no significant difference between the two patient groups in terms of survival after transplantation [2, 12, 13]. Mechanical circulatory support significantly improves the hemodynamic parameters of the heart. In patients in whom VADs were used as a bridge to transplantation or destination therapy, significant improvements were observed with regard to the cardiac output along with increases of the cardiac index and decreases in mean pulmonary artery pressure. In some cases, circulatory support allows the heart to regenerate, allowing the device to be removed and enabling the patient to return to pharmacological therapy [12]. Substituting heart function with a VAD ensures the improvement of liver and kidney function, which is impaired in the course of HF [14]. Improving kidney function after VAD implantation is associated with a number of systemic benefits, including the reduction of sympathetic system hyperreactivity as well as a positive influence on regulation of the renin-angiotensin-aldosterone system and nitric oxide secretion [15].

Complications after VAD implantation

Early and late postoperative complications may occur after VAD implantation [16]. The main early complications include severe bleeding, local infections, arrhythmias, right ventricular insufficiency, and cardiovascular incidents; in the long term, generalized infections as well as device-related infections and thrombi are dominant [16-18]. The risk of complications after VAD implantation depends primarily on the type of the device, the duration of the support, and the patient's clinical condition. The incidence of complications is much higher when pulsatile pumps are used than in the case of continuous flow VADs. The significant differences regarding complications pertain mainly to the more frequent occurrence of generalized infections and device damage in the case of pulsatile pumps [2, 8].

Bleeding

Perioperative bleeding is one of the most common complications after VAD implantation [19, 20]. Massive bleeding occurs in 15-30% of patients implanted with VADs; it is most often caused by impairment of the liver's synthetic function regarding adequate production of coagulation factors. A relatively common phenomenon in this patient group is iatrogenic bleeding associated with the use of antiplatelet agents and vitamin K antagonists [20, 21]. A study by Bunte *et al.* demonstrated that serious bleeding complications during the early postoperative period after VAD implantations may occur in as many as 58% of patients, while repeated bleeding is observed in 44% of patients. The risk of bleeding is highest in the 2 weeks following the implantation; it is during this period that bleeding causes the largest percentage of deaths [19]. Furthermore, the necessity of blood transfusion as a result of massive bleeding in VAD patients is a significant factor for increased 30-day and 1-year mortality [20]. It should also be stressed that the presence of thrombocytopenia or anemia in patients qualified for VAD implantation increases the incidence of complications regardless of the employed method [20, 21].

Thromboembolic complications

Another factor that significantly limits the survival of VAD patients is the occurrence of thromboembolic complications. The general incidence of these complications in patients implanted with VADs does not exceed 5%. Among factors that promote blood coagulation, inadequate antithrombotic and/or antiplatelet therapy during long-term use of the pump is of particular significance. Other procoagulant factors include concomitant infection and hypovolemia [22, 23]. If a thrombus forms on the VAD, the treatment of choice is thrombolysis; its efficacy is estimated at 91-96%. If pharmacotherapy fails, the pump needs to be replaced, which is associated with a decrease of the 1-year survival rate to 65%; if another replacement is required, the survival rate is reduced to 50%. Bleeding from the gastrointestinal tract associated with perfusion disturbances in this area and with anticoagulation treatment has a particularly negative influence on the prognosis [2, 24]. It has been suggested that the incidence of thrombotic complications can be reduced significantly by adhering to guidelines on pharmacotherapy provided to VAD patients [22].

Infections

Another important complication after VAD implantation is infection; its frequency is estimated at 18-59% depending on device type, patient group, and support duration [25]. Infections associated with VADs are most often situated at the implantation site or in the vicinity of the location where the cannulas pass through the patient's skin. An important group of infections in VAD patients comprises systemic infections, which are most often caused by strains of hospital microorganisms. A substantial majority of these infections are caused by gram-positive bacteria, primarily *Staphylococcus aureus* and *Staphylococcus epidermidis*. Knowledge about the most commonly isolated bacteria enables physicians to take swift action when symptoms of infection are observed by administering empirical antibiotic therapy until the antibiogram is obtained. The risk of infection increases markedly with the duration of support [18]. The results of studies concerning the influence of infections on the survival of VAD patients are ambiguous [18, 26-28]. An analysis conducted by Rosenfeldt *et al.* demonstrated that the occurrence of bacteremia soon after implantation of the device does not influence the patient's prognosis before or after the heart transplant [18]. Tong *et al.* presented similar results [6]. The above-mentioned authors did not observe a relation between the frequency of infection and the survival of patients during the waiting period for the heart transplant or during short- or long-term follow-up after the procedure [20]. However, other researchers have found that, among individuals implanted with VADs, mortality is significantly increased by infections [27], while lack of bacteremia has a positive influence on patient survival [24]. Moreover, frequent recurrent infections may pave the way for the development of generalized infections, shortening the survival time significantly [27]. It appears that these discrepancies may result from the experiences of the VAD implantation centers and differences in the populations of patients qualified for the procedure. The prognosis of patients in whom VAD is used as destination therapy due to contraindications for transplantation is worse than that of patients in whom VAD serves the role of a bridge to transplantation.

Right ventricular insufficiency in patients with left ventricular assist devices (LVAD)

The manifestation of right ventricular (RV) insufficiency or its aggravation is an especially unfavorable prognostic factor in VAD patients. The incidence of RV insufficiency after LVAD implantation ranges from 6 to 44% and depends on the device type and the adopted definition of right ventricular insufficiency [29]. Insufficiency of the right ventricle is associated with a significant increase in mortality during the early postoperative period and has a negative influence on the survival of patients both before and after the proce-

dure [30]. Therefore, special attention should be devoted to the evaluation of RV function when patients are qualified for LVAD implantation [30, 31]. Severe tricuspid valve insufficiency, abnormalities in right ventricular geometry, and increased pressure in the right atrium or the pulmonary artery constitute factors indicating increased risk of RV insufficiency after LVAD implantation. Another risk factor for RV insufficiency is the ratio between the end-diastolic dimension of the right ventricle and the end-diastolic dimension of the left ventricle. If the ratio exceeds 0.72, the probability that severe HF will develop after LVAD implantation is increased significantly [21, 29]. In such cases, implanting a device which supports the function of both ventricles may be considered.

Immunization during VAD therapy

A significant factor limiting the survival of patients after a heart transplant in whom VAD implantation had been used as a bridge to transplantation is the presence of lymphocytotoxic antibodies in the blood circulation. Patient immunization is caused by numerous blood transfusions, which lead to the formation of antibodies against antigens present in the transfused preparation. Another factor promoting sensitization is the occurrence of infections during MCS [13, 32]. Immunization may also result from the interactions between the surface of the implanted device and the patient's immune system [32]. The necessity of numerous blood transfusions and the frequent infections associated with VAD promote patient immunization to transplantation and increase the risk and frequency of humoral rejection, which often results in worse post-transplant prognosis [13, 33]. Although labeling the titer of anti-HLA antibodies is not routinely performed in patients qualified for heart transplantation, there is evidence indicating that monitoring the level of lymphocytotoxic antibodies in patients undergoing VAD therapy as a bridge to transplantation may be helpful in evaluating the risk of transplant rejection [32, 33].

Conclusions

The growing population of severe HF patients treated with MCS necessitates the introduction of comprehensive changes to the healthcare system. The pulsatile pumps requiring long-term hospitalization, which have been used until now, are increasingly being replaced with continuous flow pumps, which are much smaller and easier to operate, and which enable the patients to continue their treatment at home. Notwithstanding, the patients should be monitored carefully by teams of specialists and trained nurses. Apart from out-patient supervision, planned periodic hospitalizations are required to evaluate the patient's subjective and objective condition as well as the functioning of the VAD. This is primarily a logistical challenge, but the economic aspect of comprehensive care provided to VAD patients is equally important. The prevention of complications, provision of psychological and psychiatric care, as well as technical, microbiological, and hematological supervision, are but a few aspects of managing patients treated with MCS.

Disclosure

Authors report no conflict of interest.

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