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Bridge to recovery in two cases of dilated cardiomyopathy after long-term mechanical circulatory support

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Abstract

Ventricular assist devices (VADs) have become an established therapeutic option for patients with end-stage heart failure. Achieving the potential for recovery of native heart function using VADs is an established form of treatment in a selected group of patients with HF. We report two cases of VAD patients with different types of pump used for mechanical circulatory support, a continuous flow pump (HeartWare®) and a pulsatile pump (POLVAD MEV®), which allow regeneration of the native heart. Patients were qualified as INTERMACS level 3-4 for elective implantation of an LVAD. Implantations were performed without complications. The postoperative course was uncomplicated. In the HeartWare patient the follow-up was complicated by episodes of epistaxis and recurrent GIB as well as driveline infection. The follow-up of the POLVAD MEV patient was uneventful. Recurrent GIB forced us to withdraw aspirin and warfarin therapy and maintain only clopidogrel in the HeartWare patient. In mid-February 2013 the patient was admitted due to dysfunction of the centrifugal pump with a continuous low-flow alarm and increase power consumption. Under close monitoring of the patient a decision was made to stop the pump immediately and evaluate cardiac function. The serial echocardiography studies showed significant improvement in LVEF up to 45% and no significant valvular pathology. In February 2013 LVAD explant was performed by left thoracotomy without complications. At six-month follow-up the patient was in a good clinical condition, in NYHA class I/II, and on pharmacological treatment.

Key words: heart failure, mechanical circulatory support.

Streszczenie

Mechaniczne wspomaganie serca (VADS) jest uznaną formą terapeutyczną leczenia ciężkiej niewydolności serca. Ta forma terapii przyczynia się w istotny sposób do regeneracji własnego serca w wybranej grupie pacjentów z ciężką niewydolnością serca. W pracy przedstawiono przypadki chorych zakwalifikowanych do transplantacji serca, leczonych pompą o przepływie ciągłym HeartWare® i pompą pulsacyjną POLVAD MEV®, u których możliwa była regeneracja własnego serca. Z powodu pogarszającej się wydolności serca i długiego okresu oczekiwania na dawcę narządu chorych zaliczanych do grupy INTERMACS 3-4 kwalifikowano do leczenia mechanicznym wspomaganiem serca jako pomostu do transplantacji. Zabieg wszczepienia pomp przebiegał bez komplikacji. W trakcie prowadzonego leczenia pacjenci prezentowali okresowo cechy infekcji w okolicy kaniul oraz linii zasilającej. U pacjenta z pompą HeartWare® obserwowano okresowo cechy krwawienia z nosa i przewodu pokarmowego. Stan kliniczny wymagał zredukowania leczenia przeciwzakrzepowego warfaryną oraz leczenia przeciwpłytkowego kwasem acetylosalicylowym. Prowadzono jedynie leczenie przeciwpłytkowe klopidogrelem. Z uwagi na cechy wykrzepiania pompy podjęto decyzję o usunięciu wspomagania w związku z poprawą funkcji serca w badaniu echokardiograficznym do 45%. W lutym 2013 r. pompa została wszczepiona z dostępu przez lewostronną torakotomię bez powikłań. U pacjenta leczonego POLVAD MEV® po ok. 20 miesiącach zaobserwowano poprawę wydolności fizycznej, wzrost frakcji wyrzutowej lewej komory do 45% oraz zmniejszenie wymiarów serca. Taki obraz kliniczny pozwolił na wykonanie z powodzeniem endomiokardialnej ablacji z uwagi na obecność migotania przedsionków. W obserwacji odległej, trwającej ponad 6 miesięcy, nie obserwowano cech niewydolności serca, NYHA I/II z zastosowaniem leczenia farmakologicznego.

Słowa kluczowe: niewydolność serca, mechaniczne wspomaganie serca.

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Introduction

Heart transplantation remains the definitive therapy for patients with end-stage heart failure (HF). Unfortunately the number of transplants, estimated at less than 3500 yearly worldwide, is inadequate for the treatment in this rapidly growing heart failure population. Ventricular assist devices (VADs) have become an established therapeutic option for patients with HF. Mechanical circulatory support (MCS) with either left ventricle (LVAD) or bi-ventricle (BiVAD) support is a treatment option for several indications:

- as a bridge to transplantation (BTT) – where a heart transplant candidate is provided temporary support with either an LVAD or a BiVAD until a suitable donor organ can be found,
- as destination therapy (DT) for terminally ill heart failure patients who are not candidates for transplant where VAD support is permanent,
- as a bridge to recovery where MCS therapy aims to support circulation for long enough to allow the native heart to recover from an acute or chronic insult.

Realizing the potential for recovery of native heart function using MCS is an established form of treatment for HF patients. We present two cases of patients with dilated cardiomyopathy (DCM) with two types, centrifugal HeartWare® International, Inc, Framingham, MA, USA and pulsatile, POLVAD MEV® Intracordis, Zabrze, Poland MCS support, who recovered native heart function and underwent successful explant of their MCS.

Case report

Patient 1. Centrifugal mechanical circulatory support – HeartWare® LVAD

A 66-year-old man with DCM, LVEF 25% and NYHA III symptoms for over a year underwent in June 2008 an evaluation for cardiac transplantation. Pulmonary artery catheterization showed a cardiac index (CI) of 1.5 l/min/m^2, PAP 47/18/31 mmHg, PCWP 28 mmHg, TPG 13 mmHg and PVR 4.8 Woods units. The potential for reversibility of his pulmonary hypertension was assessed with nitroprusside (NPS) at a dose of 2 µg/kg/min and decreased to 2.2 Woods units; he was accepted for heart transplantation. In August 2008 the patient suffered a cardiac arrest due to ventricular arrhythmia and received an implantable cardioverter-defibrillator (ICD) as secondary prevention of sudden cardiac death. Due to worsening in functional capacity, persistent symptoms of heart failure and frequent hospitalizations, the patient was qualified at INTERMACS level 3 for elective implantation of a mechanical circulatory support with a HeartWare® type of LVAD.

Left ventricular assist device implantation was performed without complications in September 2009, the patient's postoperative course was uncomplicated and he quickly recovered to NYHA class I/II symptoms.

Further follow-up was complicated by episodes of epistaxis, requiring periodic laryngological instrumental methods to control the bleeding as well as a single episode of major gastrointestinal bleeding (GIB) with a significant reduction in blood counts. The patient's episodes of minor and major bleeding were usually associated with too aggressive anticoagulant therapy; however, they were also observed with INR levels of no more than 2.0. After postoperative rehabilitation the patient was discharged home with stable hematocrit and hemoglobin levels. His surgical wounds healed by first intention without evidence of drive line infections.

His long-term course was significant for 2-3 hospitalizations for standard treatment of healing at the drive line due to local infections. From June 2012 the patient required daily ambulatory care for dressing changes at home because of a superficial infection in the area of the drive line. Bacteriological tests showed pathogenic flora including *Staphylococcus aureus* MSSA and *Klebsiella pneumoniae* ESBL. Targeted antibiotics treatment with daily dressing changes and surgical debridement allowed for proper but prolonged wound healing.

The patient was evaluated for 3 months in our heart failure/mechanical support outpatient clinic.

In the third year of LVAD support the patient presented with a significant GIB and recurrence of drive line healing problems. The episode of GIB required modification of his anticoagulation therapy; warfarin therapy was withdrawn and dual antiplatelet therapy was started with aspirin and clopidogrel. Recurrent GIB forced us to withdraw aspirin and warfarin therapy and maintain only clopidogrel. This clinically driven decision resulted in a mid-February 2013 admission due to dysfunction of the centrifugal pump with a continuous low-flow alarm and increased power consumption. This event was accompanied by a transient ischemic attack (TIA) of the central nervous system and thus we suspected a pump clot. Under close monitoring of the patient a decision was made to stop the pump immediately and evaluate cardiac function. We saw no immediate cardiac decompensation and serial echocardiography studies showed significant improvement in LVEF to 45% and no significant valvular pathology. In February 2013, after multidisciplinary consultation, a decision was made to explant the centrifugal pump.

LVAD explant was performed by left thoracotomy without complications. After a period of postoperative rehabilitation and thorough assessment of cardiac function the patient was discharged home. At six-month follow-up the patient was in a good clinical condition with NYHA class I/II heart failure symptoms. The patient continues on optimal heart failure medical therapy with: AT II inhibitor (prestarium 10 mg per day), β-blocker (vivacor 6.25 mg twice daily), digitalis (0.25 mg per day), hydrochlorothiazide (50 mg per day), controloc (40 mg per day), zotral (100 mg per day) as well as treatment with inhaled drugs due to obstructive pulmonary disease.

Patient 2. Pulsatile mechanical circulatory support – POLVAD MEV®

A 40-year-old man with a history of DCM since 2008, LVEF 13%, NYHA class II/IV symptoms with associated permanent

atrial fibrillation, s/p ICD implantation as a prevention of sudden cardiac death from 2009 and with anomaly of the superior vena cava was admitted because of decompensation heart failure. The patient failed conservative pharmacological therapy with infusion of furosemide, dopamine, dobutamine and even implantation of an intra-aortic balloon pump (IABP). Echocardiography revealed RV 39 mm, LV 70/68 mm, LA 52 mm, LVEF 13%, moderate to severe type I + IIIb according to Carpentier mitral regurgitation, moderate tricuspid regurgitation, an RVSP estimated at 55 mmHg and TAPSE 13 mm. Invasive hemodynamics revealed no pulmonary hypertension with PAP 28/12 and mean PAP 18 mmHg. PCWP was 5 mmHg with a TPG 13 mmHg and pulmonary vascular resistance of 1.85 Woods units. The patient was accepted for urgent heart transplantation and because of the quickly deteriorating clinical course he was offered rescue implantation of MCS with the pulsatile POLVAD MEV® system. The patient underwent the implant procedure in October 2011 without complications. The patient underwent standard post-operative rehabilitation and begun on full heart failure medical management. The anticoagulation protocol was composed of aspirin and warfarin (INR within 2.5-3.5). Low molecular heparin (LMWH) was administered in the case of low INR (≤ 2.5). The patient underwent three exchanges of the LVAD – twice because of a clot in the LVAD membrane and once according to the protocol. We observed gradual improvement in exercise capacity and in May 2013 – almost two years after the implant procedure – the patient underwent a controlled stress test in stop mode of the LVAD. Echocardiography showed a significant improvement in cardiac function with LV dimensions 52/46 mm, EDV 119 mL, ESV 79 mL, LVEF 35% and FS 23%. VO_2 max improved to 24.6 mL/kg/min at 7.0 METs. Despite pharmacological control of the ventricular rate because of AF the patient underwent cryoablation of atrial fibrillation with restoration to sinus rhythm. At the same time an atrial electrode was implanted and the patient had his ICD unit exchanged. After restoration of sinus rhythm the control stress test on a treadmill proved the regeneration of the heart in echocardiographic evaluation: LV 49 mm/30 mm, LVEF 40% and FS 19%. The decision was made to remove the device system POLVAD MEV after 21 months of left ventricle support. The patient underwent explant of the POLVAD MEV system in July 2013 without complications. The patient was extubated on the second postoperative day and rehabilitated appropriately. Post-explant oxygen consumption was VO_2 max – 20 mL/kg/min at 5.7 METs.

The patient was discharge home in a good condition without signs of HF symptoms. Pre-discharge echocardiography revealed LV dimensions 57/46, EDV 112 mL, ESV 69 mL, LVEF 38% without valvular pathology. The patient continues on optimal heart failure medical therapy with: AT II inhibitor (losartan 25 mg per day), β-blocker (carvedilol 25 mg twice), digitalis (0.25 mg per day), amiloride (5 mg)/hydrochlorothiazide (50 mg) per day, eplerenone (25 mg per day), atorvastatin (20 mg per day), warfarin (according to INR, therapeutic level 2.0-3.0).

Discussion

Long-term mechanical circulatory support (MCS) is a form of treatment for end-stage heart failure patients. To help with decision making and in order to have uniform classification of MCS, the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) scale was developed. INTERMACS levels are clinical stages and each level defines the patient's clinical status: level 1 – critical cardiogenic shock; 2 – progressive decline; 3 – stable but inotrope dependent; 4 – recurrent advanced HF; 5 – exertion tolerance; 6 – exertion limited; and 7 – advanced NYHA III [1].

In this paper we presented a patient with INTERMACS level 4 for the HeartWare LVAD and level 2 for the POLVAD MEV. Both patients were eligible candidates for heart transplantation.

The number of transplantations is limited and not all patients are lucky enough to undergo cardiac transplantation.

Patients suffering from advanced heart failure secondary to myocardial infarction, myocarditis, intoxication, graft failure immediately after transplantation as well as females with peripartum cardiomyopathy may qualify for a "bridge to recovery" indication. Chronic non-ischemic cardiomyopathy patients are less feasible for removal of VADs due to recovery. However, parameters of pre-explant cardiac function such as LV size and geometry, their stability during final off-pump trials and HF duration allowed detection of those patients with a potential to remain stable for more than 5 years following explantation of the device [2].

The molecular, cellular, biochemical, and structural changes occurring in the myocardium often referred to as remodeling have been studied extensively in patients with heart failure [3-5]. One intriguing feature of remodeling is that at least some of its manifestations can occasionally be reversed. There is now compelling evidence that prolonged, near-complete unloading of the left ventricle using a left ventricular assist device (a mechanical pump) is associated with structural reverse remodeling that can be accompanied by functional improvement [6, 7]. However, recovery that is sufficient to permit explantation of the device has been observed in only 5 to 24% of patients in various series, with a relatively high incidence of early recurrence of HF. There is no general consensus on which biomarkers may be reliable to predict the recovery process. Krabatsch from the Berlin Heart Center Group investigated whether the bridge to recovery was more likely to happen with pulsatile or non-pulsatile devices: in 34 patients, LVAD removal due to myocardial recovery was performed with long-term stable cardiac function (weaning rate, 8.8%). Younger patients had significantly higher recovery rates than older patients. We published our experience with recovery of the heart in young patients with HF in 2008 [8]. Up to now the patient is without heart failure symptoms. Patients with a pulsatile-flow LVAD had an almost threefold higher chance for myocardial recovery than patients who received continuous-flow devices [9]. He concluded that

further studies should investigate whether pulsatility in itself or the different degrees of left ventricular unloading by the two types of systems played the major role in myocardial recovery.

In our patient on a pulsatile pump the mechanical support of the left ventricle allows increase of the pharmacological management to high doses of HF medication. Treatment with four drugs (AT II inhibitor, β blockers, diuretics) was initiated immediately after the patient had been weaned from inotropic therapy with adequate end-organ recovery. During the mechanical support the patient underwent an extensive rehabilitation program. Daily exercise can have a large impact on the improvement of heart failure. However, the most important fact was a significant reduction in the size of the heart and the left ventricle and atrium. By achieving such parameters the ablation procedure could be performed successfully due to atrial fibrillation restoring sinus rhythm.

When a constant left ventricular size had been maintained for a week, according to echocardiographic assessment with the pump in synchronized mode the final stress test was performed. The result proved stable conditions of the heart, so the removal of the pulsatile device supporting the left ventricle was reasonable.

In the patient with an implanted centrifugal, continuous-flow HeartWare® pump, regeneration of native heart was a surprise, an accidental discovery in connection with a dysfunction of the device. In view of the clinical problems in the third year of left ventricular support in the form of recurrent GIB, periodic problems with a wound within the supply lines and the lack of donors for this patient, explantation of the pump was the only option for this patient. Replacing the pump with a new device in our opinion could exacerbate life-threatening side effects which may be bleeding from the gastrointestinal tract due to anticoagulation treatment.

The patient remains in the observation group. In the past six months, there have been no signs of bleeding from the gastrointestinal tract. The wound after the removal of the pump is properly healed.

In conclusion, based on our experience with mechanical circulatory support in patients with HF, the possibility of regeneration of native heart function through the applied pharmacotherapy and mechanical unloading of the left ventricle should always be taken into consideration.

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