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CASE REPORT

First Pediatric HeartMate 3 Ventricular Assist Device Implantation in Romania – a Case Report

Iolanda Muntean[1,2*], Diana-Ramona Iurian[1], Dan Octavian Nistor[3], Asmaa Carla Barmou[1,4], Horațiu Suciu[2,5*]

[1] Clinic of Pediatric Cardiology, Emergency Institute for Cardiovascular Diseases and Transplantation, Târgu Mureș, Romania
[2] "George Emil Palade" University of Medicine, Pharmacy, Science and Technology, Târgu Mureș, Romania
[3] IInd Cardiology Clinic, Emergency Institute for Cardiovascular Diseases and Transplantation, Târgu Mureș, Romania
[4] Doctoral School of Medicine and Pharmacy, I.O.S.U.D., "George Emil Palade" University of Medicine, Pharmacy, Science and Technology, Târgu Mureș, Romania
[5] Clinic of Cardiovascular Surgery, Emergency Institute for Cardiovascular Diseases and Transplantation, Târgu Mureș, Romania

[*] These authors contributed equally to the present work.

ABSTRACT

The use of ventricular assist devices as bridge-to-transplantation therapy has a critical role in the management of end-stage heart failure in pediatric patients without available compatible organ donors. The HeartMate 3 is an intracorporeal centrifugal flow pump with a fully magnetically levitated motor currently approved for the management of advanced refractory left ventricular failure in pediatric patients, with positive early outcomes. We report the case of a 17-year-old adolescent girl with end-stage heart failure secondary to dilated cardiomyopathy of idiopathic etiology, with multiple failed attempts of weaning from inotropic support (PEDIMACS 3 profile), who successfully received a HeartMate 3 left ventricular assist device as bridge-to-transplantation therapy with no significant adverse events during the early follow-up period. This paper presents the first case of pediatric ventricular assist device implantation in Romania.

Keywords: HeartMate 3, left ventricular assist device, bridge-to-transplantation therapy, dilated cardiomyopathy, pediatric heart failure

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CORRESPONDENCE

Diana-Ramona Iurian
Str. Gheorghe Marinescu nr. 50
540142 Târgu Mureș, Romania
Email: dianaiurian@yahoo.com

INTRODUCTION

Pediatric heart failure (PHF) represents an immense global burden, yet there are no established guidelines for the management of heart failure in pediatric patients. Most of the cases of PHF are due to congenital heart disease or cardiomyopathies.[1,2]

Although the best choice of treatment for end-stage PHF cases remains heart transplantation, because of limited donor availability, the use of a ventricular assist device has a paramount role in the management of end-stage heart failure in the pediatric population, therefore it is currently being used as either bridge-to-transplantation therapy, bridge-to-recovery, or destination therapy.[1]

The HeartMate 3 (HM3) is an intracorporeal centrifugal flow pump with a fully magnetically levitated motor that is currently successfully used in adult patients, with a survival rate at 2 years after HM3 implantation of about 80% and lower rates of adverse events compared with earlier axial-flow devices.[3–6]

The HM3 is currently approved by the US Food and Drug Administration for the management of advanced refractory left ventricular failure in pediatric patients with

encouraging reported early outcomes and a low incidence of adverse events and mortality.[5,7,8]

CASE PRESENTATION

A 17-year-old female adolescent, with a history of obesity (BMI 33.5, 96.7th percentile), was admitted to a territorial hospital with worsening dyspnea, orthopnea, drowsiness, syncope, and digestive manifestations (vomiting and abdominal pain) with the onset approximately 3 months prior to admission.

Transthoracic echocardiography (TTE) revealed dilated cardiomyopathy with a depressed left ventricular (LV) ejection fraction of 20% and multifocal premature ventricular beats on ECG recordings. Due to low cardiac output, i.v. inotropic treatment with dobutamine 5–7 µg/kg/min and levosimendan 0.1 µg/kg/min were initiated alongside antiarrhythmic therapy with amiodarone 400 mg/day, with a slight improvement in clinical status.

The cardiac magnetic resonance imaging revealed bilateral atrial dilatation, global LV hypokinesia with reduced systolic function (LV ejection fraction 12.6 %), and increased left ventricular volumes (LV end-diastolic volume 114 ml/m2, LV end-systolic volume 100 ml/m^2). No pathologic enhancements suggestive of myocardial edema or scar tissue were identified, although the quality of the examination was reduced due to persistent ventricular bigeminy during the investigation.

A cranial computed tomography scan revealed small hypodense cortico-subcortical areas suggestive for chronic ischemic lesions, located in the superficial right temporal and temporo-occipital regions, whereas an abdominal scan was negative.

The first attempt to wean the inotropic support failed due to the recurrence of PHF signs after 2 days, therefore dobutamine 7 µg/kg/min was reinitiated. She was transferred to our clinic, which is the only specialized tertiary care center for advanced pediatric heart failure in Romania, for consideration of inclusion on the heart transplant waiting list.

At the time of admission to our unit, the patient presented clinical signs and symptoms of low cardiac output. TTE revealed an enlarged left ventricle with generalized hypokinesia and severely impaired systolic function (LV ejection fraction of 34%), decreased LV global longitudinal strain (GLS -10%), with moderate secondary mitral valve regurgitation, and a discrete echodense mass in the left ventricular apex suggestive of apical thrombus, for which s.c. anticoagulation therapy with enoxaparine 0.6 ml BID was initiated. Laboratory tests performed at admission showed an elevated NT-proBNP of 2,721.09 pg/ml. Viral serology for viruses with cardiac tropism was also performed, revealing chronic infection with Cytomegalovirus, Epstein-Barr virus and Varicella zoster virus.

In the presence of a gradual slight improvement of the LV function, clinical status and the control of premature

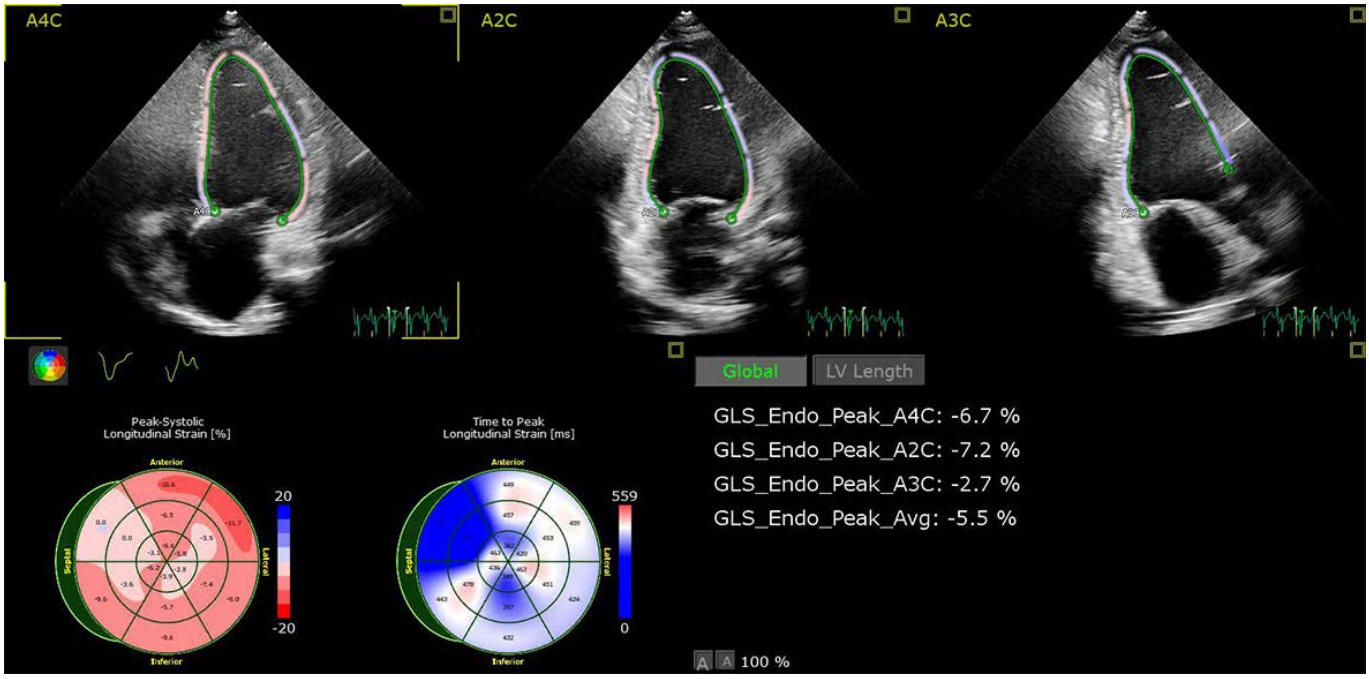

FIGURE 1. Automated 2D assessment of the LV deformation in the longitudinal planes of all the standard views (A4C, A2C, A3C). LV GLS (–5.5%). Bulls eye of the LV for longitudinal strain assessment.

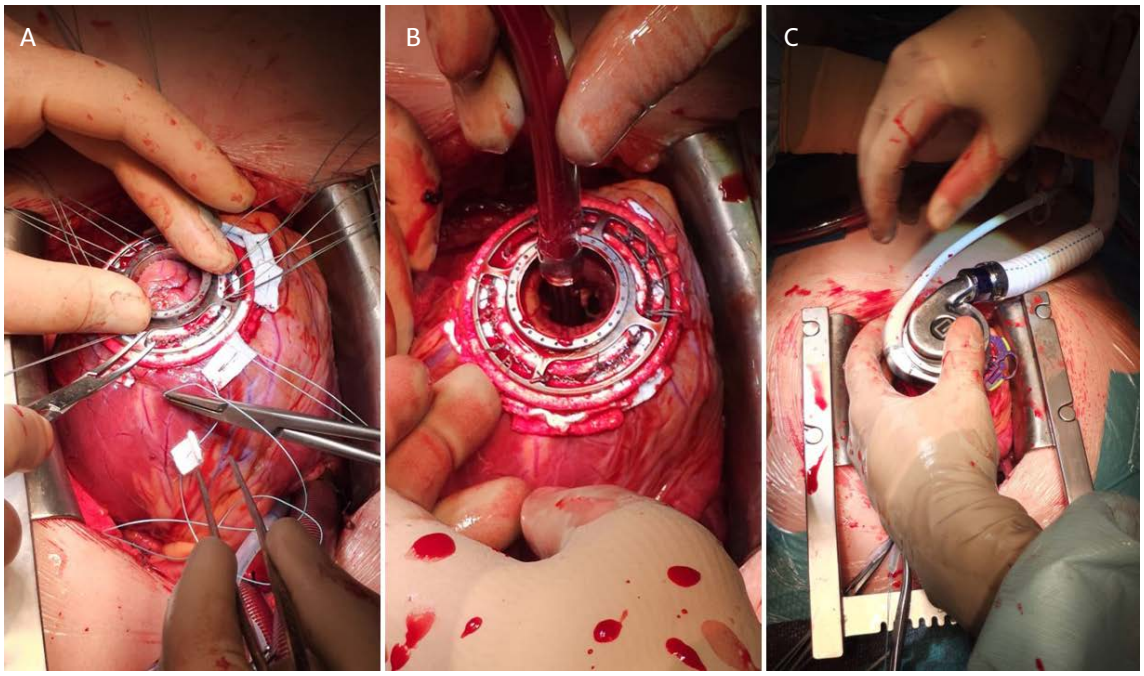

FIGURE 2. Apical cannulation using the 'first sew then core' method. **A**. Attachment of the Apical Cuff to the myocardium by sutures. **B**. After removing core, inspection of the ventricular cavity. **C**. Establishing the pump orientation in the desired position.

ventricular dysrhythmia, inotropic therapy with dobutamine was ceased for the second time, and the dose of antiarrhythmic therapy was reduced to 200 mg/day.

During hospitalization, after an infectious process with positive blood culture for Pseudomonas fluorescens/putida, for which an association of antibiotic therapy was commenced, the patient experienced recurrent signs of low cardiac output: drowsiness, profuse sweating, cold extremities, discrete swelling of the inferior limbs, and an increased rate of premature ventricular beats on ECG telemetry. TTE evaluation showed an even greater impairment of LV systolic function with an LV ejection fraction of 16–20% and LV GLS of -5.5% (Figure 1).

As a result, inotropic therapy with dobutamine was reinitiated at a dose of 7 µg/kg/min but was considered insufficient and subsequently milrinone 0.5 µg/kg/min and levosimendan 0.1 µg/kg/min were associated, with an additional increase of the amiodarone dose to 400 mg/day.

Due to the multiple subsequent failed attempts to wean the patient from inotropic support (PEDIMACS 3 profile), the implantation of a LV assist device (LVAD) was taken into consideration as bridge-to-transplantation therapy.

A preoperative cardiac catheterization was performed to assess cardiopulmonary filling pressures, with results within normal range.

Prior to LVAD implantation, in the operating room, a comprehensive transesophageal echocardiographic (TEE) examination was performed, which ruled out the presence of LV apical thrombus, intracardiac shunts, or aortic insufficiency. Also, right ventricular function was assessed, with no signs of severe dysfunction identified.

Implantation of a HM3 via median sternotomy was successfully performed in cardiopulmonary by-pass, on-pump, with no periprocedural events (Figure 2).

During surgery, repeated TEE evaluations were performed. The position of the inflow cannula was established with the 'finger sign'. After the device implantation, the inflow cannula (with a flow velocity of 0.5–0.6 m/s) was found to be parallel to the interventricular septum, correctly oriented towards the mitral valve opening. The initial interventricular septum position was intermediate, with no shift between the ventricles.

The aortic valve opening was assessed by 2D and M-mode echocardiography. There was no aortic valve regurgitation, and some improvement of the mitral regurgitation was observed. In the outflow graft the flow was continuous, with a velocity of 0.8–1.2 m/s at the site of anastomosis with the ascending aorta (Figure 3). In the operating room, the HM3 pump speed was initially set at 4,500 rpm.

The patient was hemodynamically stable after LVAD implantation and was subsequently transferred from the intensive care unit to the general ward after 4 days. The inotropic support was ceased gradually, with no support

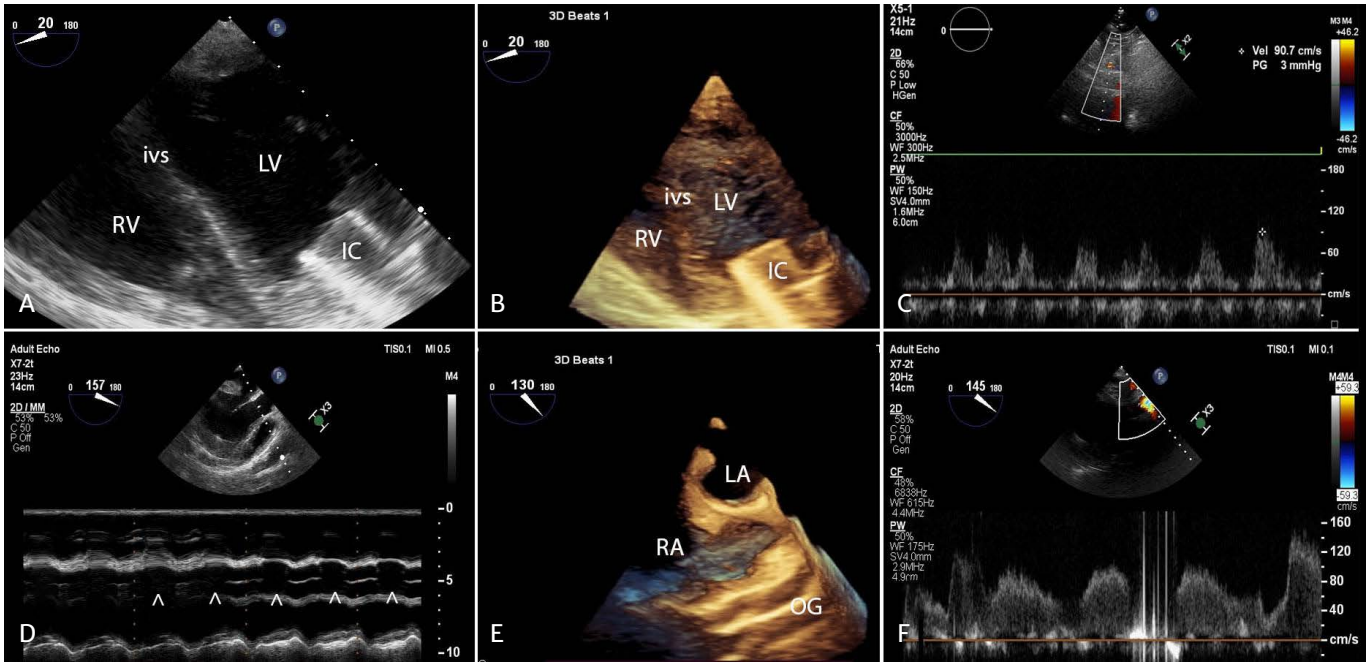

FIGURE 3. Perioperative TEE, after LVAD implantation. **A**. Mid-esophageal LV view. The inflow cannula (IC) lies within the LV apex, almost parallel to the interventricular septum and is directed toward the mitral valve. The interventricular septum is in medium position. **B**. Real-time 3D imaging of the inflow cannula (IC). **C**. PW spectral Doppler interrogation of the inflow cannula reveals a low velocity (0.9 m/s), laminar, unidirectional flow from the LV towards the inflow cannula. **D**. M-mode imaging of the aortic valve shows too frequent aortic valve opening at every cardiac cycle (^). **E**. 3D imaging of the outflow graft in the modified bicaval view. F, PW Doppler interrogation of the outflow graft reveal a low velocity flow (1–1.4 m/s)

needed after 12 days, and the post-implant duration of hospitalization was 16 days in all.

As per the manufacturer's recommendations, post-implantation anticoagulation was initiated, first with unfractionated heparin adjusted by aPTT, then with oral vitamin K antagonist (acenocoumarin) and a target INR of 2.0–3.0, alongside antiplatelet therapy with aspirin 75 mg QD. Additionally, heart failure medications were initiated with an ACEI (ramipril 2.5 mg QD) for maintaining a mean blood pressure of 70–80 mmHg, a beta blocker (bisoprolol 5 mg QD) and ivabradine 5 mg BID for a target heart rate of <70 bpm.

During early in-hospital follow-up, there were no significant adverse events or signs of driveline infections recorded. Laboratory tests indicated a preserved hepatic and renal function, and regarding neurological status, there were no episodes of stroke or seizures.

In terms of pump functionality, in the first 2 days after HM3 implantation there were several low-flow alarms as a consequence of hypovolemia, which were managed with volume supplementation (Figure 4). There were no episodes of pump thrombosis, or any pump malfunction, bleeding, or modified laboratory tests suggesting of intravascular hemolysis (LDH, plasma hemoglobin, and bilirubin in normal range) recorded.

The HM3 LVAD speed was initially set at 4,500 rpm and subsequently increased to 5,100 rpm, under echocardiographic monitoring.

Repeated TTE evaluation performed in the follow-up revealed an adequate unloading of the LV, a constant improvement of the mitral regurgitation to a mild severity, and persistence of the interventricular and interatrial septa in a midline position, with intermittent aortic valve opening at an average of one in every four–five cardiac cycles. This allowed for a gradual increase in the HM3 pump speed from 4,500 rpm to 5,100 rpm, which equivalated to an estimated pump flow of 4.9 L/min. The assessment of right heart function revealed inspiratory collapse of the inferior vena cava greater than 50%, with a diameter of 15 mm, a mild tricuspid regurgitation with peak systolic tricuspid regurgitation gradient of 20–25 mmHg in end expiration, and a tricuspid annular plane systolic excursion of 15 mm.

Because the patient was close to young adulthood age, she was treated by a collaborative team of both pediatric and adult cardiologists to provide an in-hospital children-to-adult healthcare transition. Significant attention was placed on both patient and caregiver education in managing the device and possible complications, which allowed a safe discharge at home of the patient in stable condition.

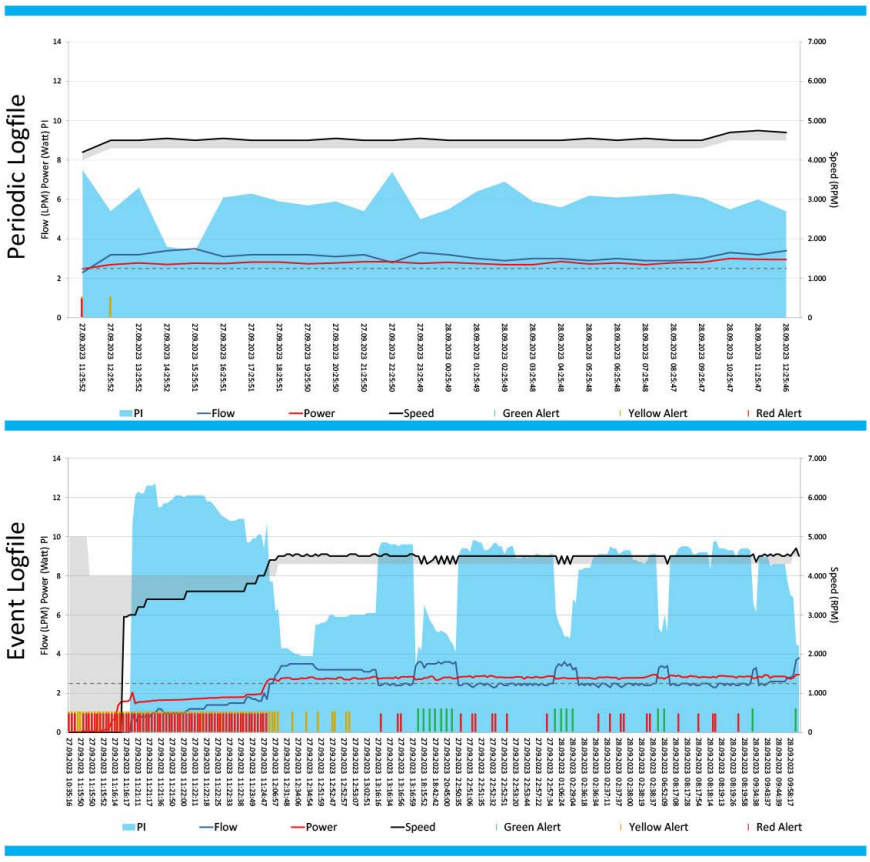

FIGURE 4. In the event log-file, in the first 2 days after HM3 implantation there were several low-flow alarms because of hypovolemia, which were managed with volume supplementation.

The publication of the case was approved by the ethics committee of the medical institution, and all the procedures required for the retrospective publication of the case were done in accordance with the Declaration of Helsinki.

DISCUSSION

The management of end-stage PHF secondary to dilated cardiomyopathy is challenging and implies a collaborative and multidisciplinary team. Herein both the impossibility to wean the patient from inotropic support and the absence of an available compatible organ donor directed our team's decision of LVAD implantation as a bridge-to-transplantation.

Echocardiography (both TTE and TEE) has a paramount role in the pre-, intra-, and postoperative management of both the patient and the implanted device.

Prior to LVAD implantation we assessed the eligibility of the patient. A comprehensive echocardiographic assessment was made in order to rule out the four paramount factors that command a later unsuccessful LVAD support, concisely presented by the mnemonic 'STAR': the presence of intracardiac Shunts, the presence of Thrombi, Aortic insufficiency and Right ventricular severe dysfunction.[9,10]

During LVAD implantation, intraprocedural continuous TEE assessment must be performed with the aim of confirming the coring location ('finger test'), a proper de-airing of the LV and the pump, avoiding subsequent air embolism, and ensuring an adequate position of both the inflow and outflow cannulae, with unidirectional, laminar blood flow, and normal velocities.[9–11]

Additionally, possible previous undetected intracardiac shunts must be ruled out. Aortic root, ascending, transverse, and descending thoracic aorta must be assessed to exclude any iatrogenic dissection. Aortic valve opening and function were meticulously evaluated. Also, a screening for pericardial effusion, and assessment of tricuspid and mitral valve function is mandatory.[9–11]

Following LVAD implantation, continuous assessments were made to establish an adequate LV unloading. Both inadequate unloading and excessive unloading with subsequently adverse events of 'suction cascade' could have led to hemodynamic instability and RV failure.[9,11] In our

case, an adequate unloading of the LV, with the interventricular septum maintained in midline position was finally obtained at a HM3 pump speed of 5,100 rpm.

In terms of post-LVAD implantation adverse events, in our case there were no episodes of pump malfunction, thrombosis, driveline infection, stroke, or bleeding requiring any device exchanges. In the ACTION cohort of 35 pediatric and young adult patients with a median age of 15.7 (range 8.8–47.3) years, during a median follow-up period of 78 days after HM3 implantation, there were no episodes of pump thrombosis, stroke, or pump dysfunction, whereas reoperation for bleeding was required in one patient, and driveline infection was reported in 11% (n = 4) of patients.[5] The absence of pump thrombosis, stroke, and driveline infection was also reported in a single-center cohort of pediatric patients with a median follow-up of 138 days post implantation.[8]

Regarding length of hospitalization after LVAD implantation, in our case the patient spent 4 days in the intensive care unit and was discharged home after 16 days, with comparable results to those obtained in the ACTION cohort in which the median hospital length of stay to the time of discharge or heart transplantation after HM3 implantation was 29.5 (range 2–170) days, while the median number of days spent in intensive care unit was 14 (range 2–48) days.[5]

CONCLUSION

In conclusion, this report presents the pioneering case of VAD implantation in the Romanian pediatric population with encouraging early outcomes. It emphasizes the critical role of VAD as a bridge-to-transplantation therapy in end-stage PHF cases without available compatible organ donors.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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