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CASE REPORT

THE CURRENT MANAGEMENT OF END-STAGE HEART FAILURE: TWO CASE REPORTS

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Abstract

Introduction. Heart failure (HF) is a clinical syndrome caused by structural and/or functional cardiac abnormalities, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress. It is a progressive disease with a high risk of death in the first 6-12 months after the diagnosis of end stage HF.

Cases presentation. We present the successful implantation of a left-ventricular assist device (LVAD) HEART MATE III in a 54-year-old male with ischemic cardiomyopathy and end stage HF, and a heart transplant in a 31-year-old male with non-ischemic dilated cardiomyopathy and end stage HF. Both procedures were guided by experienced surgeons and the overall management was according to the current standardised protocol.

Résumé

L'approche actuelle de l'insuffisance cardiaque en phase terminale: deux rapports de cas

Introduction. L'insuffisance cardiaque est un syndrome clinique causé par des anomalies cardiaques structurelles et/ou fonctionnelles, entraînant un débit cardiaque réduit et/ou des pressions intracardiaques élevées au repos ou pendant le stress. Il s'agit d'une maladie évolutive avec un risque élevé de décès dans les 6 à 12 premiers mois suivant le diagnostic d'insuffisance cardiaque en phase terminale.

Présentation des cas. Nous présentons l'implantation réussie d'un dispositif d'assistance ventriculaire gauche HEART MATE III chez un homme de 54 ans atteint de cardiomyopathie ischémique et d'insuffisance cardiaque en phase terminale, et une transplantation cardiaque chez un homme de 31 ans atteint

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Conclusions. HF is one of the leading causes of death world-wide. The effort to stabilize and effectively treat patients with ventricular assist devices and/or orthotopic heart transplant is increasing. One of the few drawbacks is the complex Heart Team training, a difficult process that involves each member acquiring the necessary skills and knowledge. The end stage HF Team is composed of a large variety of members, such as cardiologists, cardiac surgeons, anaesthetists and intensive care doctors, interventional cardiology doctors, and nurses.

Keywords: cardiac transplant, heart failure, cardiovascular surgery.

List of abbreviations

HF – Heart Failure
LVAD – Left Ventricular Assist Device
NYHA – New York Heart Association
LAD – Left Anterior Coronary Artery
DES – Drug Eluting Stent
NT-proBNP – N-terminal prohormone of Brain Natriuretic Peptide
ECG – Electrocardiogram
PVR – Pulmonary Vascular Resistance
WU – Wood Units
TPR – Total Pulmonary Resistance
TTE – Transthoracic Echocardiography
RA – Right Atrium
RV – Right Ventricle
TEE – Transoesophageal Echocardiography
MRI – Magnetic Resonance Imaging
LV-EDV – Left Ventricle End-Diastolic Volume
RV-EDV – Right Ventricle End-Diastolic Volume
CT – Computed Tomography
INTERMACS – Interagency Registry for Mechanically Assisted Circulatory Support
CRT-D – Cardiac Resynchronization Therapy Defibrillator
SVR – Systemic Vascular Resistance
pHM – predicted total Heart Mass

Conclusions. L'insuffisance cardiaque est l'une des principales causes de décès dans le monde. Les efforts pour stabiliser et traiter efficacement les patients avec des dispositifs d'assistance ventriculaire et/ou une transplantation cardiaque orthotopique augmentent. L'un des rares inconvénients est la formation complexe de l'équipe cardiaque, un processus difficile qui implique que chaque membre acquiert les compétences et les connaissances nécessaires. L'équipe d'insuffisance cardiaque en phase terminale est composée d'une grande variété de membres, tels que des cardiologues, des chirurgiens cardiaques, des anesthésistes et des médecins de soins intensifs, des médecins en cardiologie interventionnelle et des infirmières.

Mots-clés: transplantation cardiaque, insuffisance cardiaque, chirurgie cardiovasculaire.

Introduction

Heart failure (HF) is a complex clinical syndrome and a leading cause of death worldwide[1,2,3]. From the first heart surgery, involving the wound of the ventricular wall, to the cutting-edge technology of stem-cell cardiac regeneration, cardiac surgeons have been developing new techniques and devices to improve or replace cardiac function[4,5].

We present the successful implantation of a left-ventricular assist device (LVAD) HeartMate III in a 54-year-old male with ischemic cardiomyopathy and class IV New York Heart Association (NYHA) HF, and a heart transplant in a 31-year-old male with non-ischemic dilated cardiomyopathy and class IV NYHA HF.

Presentation of the first case

We report the case of a 54-year-old patient, with cardiovascular risk factors such as hypertension, dyslipidaemia, diabetes and a long-time smoking habit. The patient presented with HF symptoms that started two weeks prior to admission; he developed dyspnoea

at light exertion, polypnea, orthopnoea, coughing, nausea and vomiting that impeded the administration of normal medication prescribed for HF. This was the third episode of cardiac decompensation after a previous (6 months prior to current admission) anterior myocardial infarction treated with left anterior coronary artery (LAD) primary drug eluting stent (DES) angioplasty.

At admission the patient was haemodynamically unstable, in need of both inotropic and vasopressor support, with a blood pressure of 80-90/50 mmHg and heart rate 75 bpm. The laboratory tests revealed mild anaemia, N-terminal prohormone of brain natriuretic peptide (NT-proBNP) of 97000 pg/mL, hyponatremia (127 mmol/L), mild hypercholesterolemia, creatinine 1.5 mg/dL and mildly increased inflammatory markers. Bacteriological and viral screenings were negative.

At admission, the electrocardiogram (ECG) showed a narrow QRS complex with a Q wave in all precordial leads, consistent with a large anterior myocardial infarction, with biphasic T waves in the entire anterior territory. Chest X-ray described a small right pleural effusion, both free and loculated, and a discreetly opaque left costal-diaphragmatic sinus. The lining of the bronchi was accentuated bilaterally. The diameter of the heart was increased due to right atrium enlargement.

At a previous admission, the right heart catheterization revealed no pulmonary hypertension, with a pulmonary vascular resistance (PVR) of 3.25 Wood Units (WU) and total pulmonary resistance (TPR) of 12.1 WU.

At the current admission, transthoracic echocardiography (TTE) showed a dilated left ventricle with severe systolic dysfunction, with apex, anterior wall, antero-septal and inferior posterior wall akinesis and a 30% left ventricle ejection fraction, severe dilated left, and right atrium (RA), a mildly dilatated right ventricle (RV) with preserved systolic ejection fraction. The valvular assessment revealed mild aortic regurgitation – grade I, severe ischemic mitral regurgitation, severe tricuspid regurgitation and severe secondary pulmonary hypertension (110 mmHg). Other pathological findings were a mild pericardial effusion and bilateral moderate pleural effusion. The transoesophageal echocardiography (TEE) revealed persistent patent foramen ovalis, with right to left atrial shunt.

The coronarography showed the left main trunk with diffused atherosclerosis, without significant lesions, a left anterior descending artery with diffused atherosclerosis and a patent stent in the proximal segment, a circumflex artery with diffused atherosclerosis and 50% distal stenosis, a marginal branch with a distal recanalized occlusion and the dominant right coronary artery with diffused atherosclerosis, without any significant lesion.

The cardiac magnetic resonance imaging (MRI) (Fig. 1) showed ischemic dilated cardiomyopathy with severely reduced ejection fraction (37%) secondary to a recent myocardial infarction in the left coronary artery territory and with non-recent small myocardial infarction of the inferolateral wall (two segments). In the infarction areas there was no myocardial viability. There was no intraventricular thrombosis. Other findings of the MRI were severe ischemic mitral valve regurgitation. The left ventricle end-diastolic volume (LV-EDV) was 254 ml, the indexed LV-EDV was 125 ml/m^2, the LV end-systolic volume was 160 mL and systolic volume was 94 mL. The right ventricle end-diastolic volume (RV-EDV) was 130 mL, the indexed RV-EDV was 64 ml/m^2, the RV end-systolic volume was 40 mL, and the right ejection fraction was 69%.

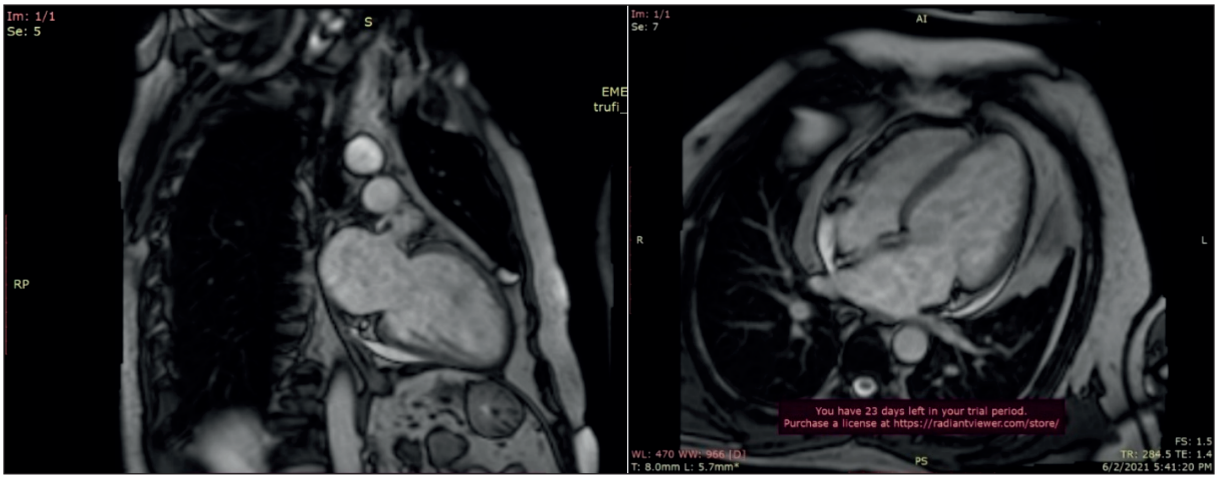


Figure 1 A (left) and 1 B (right). MRI findings of ischemic cardiomyopathy.

Thoraco-abdominal-pelvic computed-tomography (CT) scan described a diffusely reduced pulmonary transparency with ground-glass opacities, symmetric distribution around the hilum, alterations consistent with cardiogenic pulmonary oedema. The bilateral pleural effusion was 4.8 cm on the right side and 5.2 cm on the left side, with passive collapse of the adjacent pulmonary parenchyma. The pulmonary tree had free lumen, with bilateral apical subpleural bubbles of emphysema. There were bilateral apical fibro-micronodular sequelae and small atheromatous parietal calcification of the aortic arch. The liver was slightly enlarged, both kidneys were normal. There was no intraperitoneal accumulation, and no other pathological findings.

The diabetology check-up, the upper gastrointestinal endoscopy, and psychiatric evaluation showed no pathological findings.

The bacteriological screening revealed a contaminated urine sample, positive for coagulase-negative staphylococcus, therefore Vancomycin treatment was initiated, after which urine samples cleared.

During the investigations, the patient status worsened, his dyspnoea and orthopnoea deeming him fit for admission in the intensive care unit, with continuous oxygen and inotropic support, a high-risk patient class 2 Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS)[6], class IV NYHA HF and 15% LV ejection fraction. The rapid decay of the patient made him suitable for an emergent implant of a LV mechanical circulatory assist device, in our case, HEART MATE III.

Due to the rapid progression of the HF, the patient was operated (Fig. 2). This was the first experience with the LVAD- HEART MATE III of our centre and the Heart Team was led by a proctor from an experienced centre. Discussions about the eligibility of the patient were started a few weeks prior to the intervention, when the end-stage HF diagnosis was made and, according to the European current guidelines[2], there was no other solution than the LVAD. The proctor aided in our initiative concerning assisting device implantation, giving the whole team (surgeons, cardiologists, anaesthetists, all auxiliary personnel involved) a briefing on the day before the procedure and helpful advice and careful guiding over the preoperative investigation period.

Even though LVAD placement is already standardized and proven to be the best through left thoracotomy approach (due to its protective role for the heart in prospect of further cardiac surgical procedures, such as heart transplant, and RV dysfunction), we opted for a median sternotomy. This approach was preferred because of our limited experience and the patient's need of patent foramen ovalis closure. A partial upper pericardiotomy was performed before starting extracorporeal circulation, to protect RV function (as some studies have shown, making the minimal invasive approach the preferred one), therefore leading to a reduced rate of postoperative RV dysfunction. After draining out the heart on extracorporeal circulation, full pericardiotomy was performed with inferior vena cava cannulation. Snares are passed around the cava veins to open right atrium and close the patent foramen ovalis, after which the right atrium is closed and the right heart deaired. Meanwhile LVAD is prepared for implantation on beating heart with extracorporeal circulation. The implant site was marked with echo-finger-guiding, after which 12 3-0 polypropylene pledged stitches were passed through the thickness of the myocardium and the textile cuff of the device. During the procedure, TEE monitoring was used to verify the orientation of the pump, towards the mitral valve and parallel to septum (Fig. 3). Bio-Glue was used for better sealing. Then the graft was measured and sutured with 5-0 polypropylene running suture to the antero-lateral ascending aorta. For deairing the graft, we repeatedly declamped the ascending aorta and prosthesis. The drive line externalisation was through a subcutaneous tunnel in the abdomen. The driveline and the external battery were connected and LVAD worked properly. The patient was progressively weaned off the heart-lung machine, as the LVAD output increased, in a standard fashion (heart-lung machine output decreased with 1 litre and LVAD increased with 200 rpm). The RV had proper contractility, the patient required medium doses of vasopressors and inotropes. The pleural cavities were drained (around 2 litres from each of them). Before chest closure, a large bovine pericardial patch was set in place on the anterior part of the heart, also covering the side graft and the pump. This was to ensure a faster and safer access if necessary – heart transplant (HTX) or LVAD complications.

The LVAD HEART MATE III was set in place using cardio-pulmonary by-pass.

The surgical intervention had no complications, the postoperative course was favourable, with the rapid decrease in the need for inotropic support and oxygen support. He was then admitted back on the ward, haemodynamically and respiratory stable.

The overall status of the patient significantly improved, his dyspnoea disappeared, exertion capacity was significantly increased, and he was discharged 3 weeks later.

Second case presentation

A 31-year-old male, with a family history of cardiac diseases (father with sudden cardiac death at around 40 years of age), who was previously known with

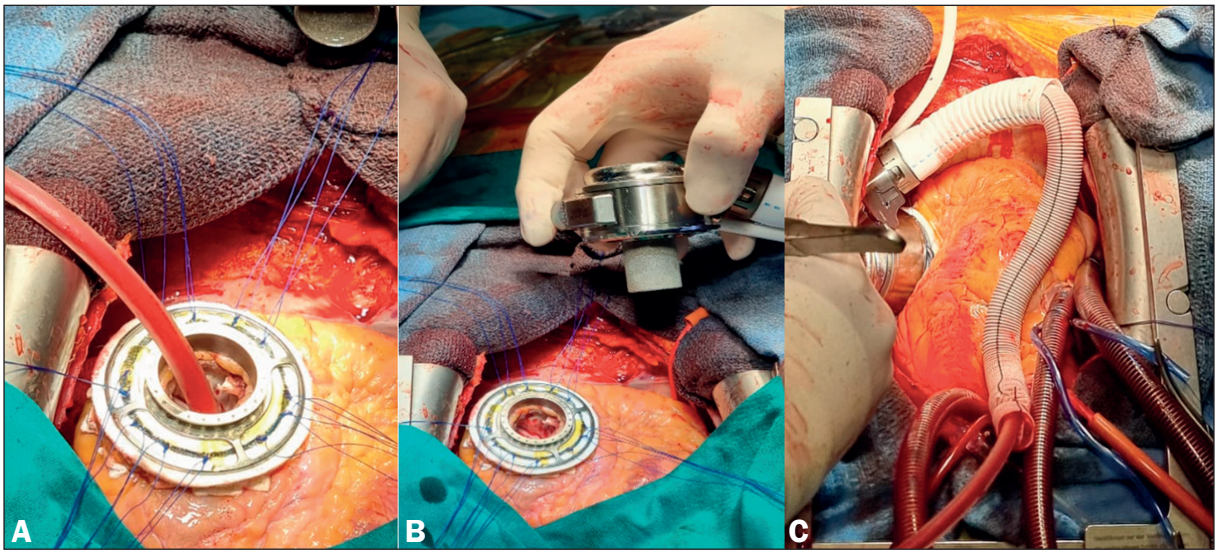


Figure 2 A, B, C (left to right). Intraoperative images of LVAD implantation.

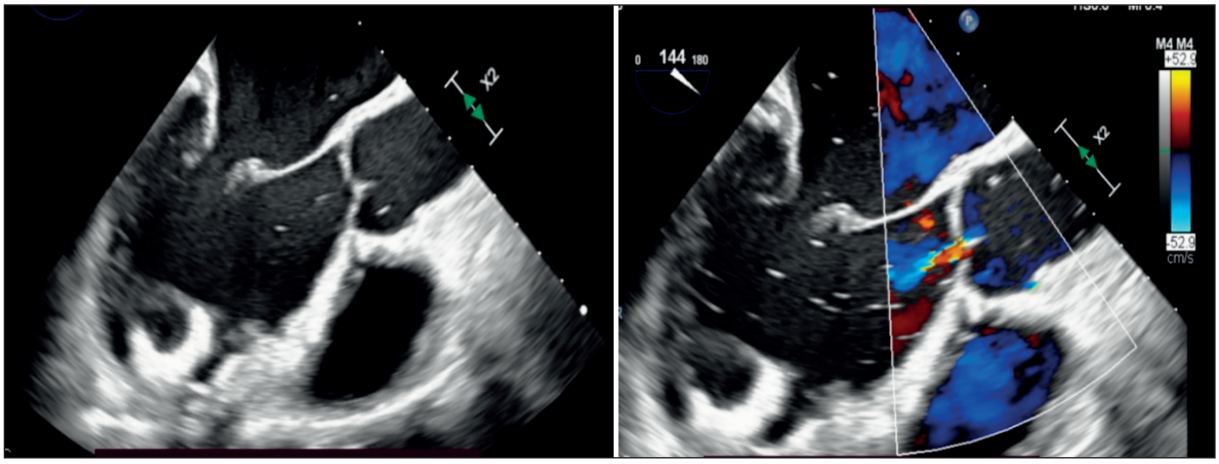


Figure 3. Intraoperative TEE captures after the placement of the LVAD without Doppler colour flow – A(left), and with Doppler colour flow – B (right).

non-ischemic dilated cardiomyopathy, class IV NYHA HF with severe LV systolic dysfunction (LV ejection fraction of 20-25%) and severe mitral valve regurgitation, with maximum treatment and a cardiac resynchronization therapy defibrillator (CRT-D) set in place one year before, with severe shortness of breath and systolic mitral murmur irradiated in the axillar region, was admitted when a matching organ became available (same blood type and Rh factor). At admission, the patient had a blood pressure of 135/80 mmHg, heart rate of 78 bpm and no peripheral oedema. The ECG showed sinus rhythm under cardiac stimulation.

Bacteriological and viral screenings revealed the presence of Staphylococcus aureus in the nasal exudate and a coagulase-negative Staphylococcus on the skin, both adequately treated in accordance with the antibiogram. Blood tests revealed no significant findings. The admission X-ray showed the presence of the CRT-D properly placed, no acute pleural or pulmonary alterations and a severely enlarged heart, mainly due to the dilated RV.

The previous cardiac catheterisation (three months prior to the intervention) showed PVR = 3.2 WU, TPR = 6.5 WU, systemic vascular resistance (SVR)= 29 WU, total systemic resistance (TSR)=30 WU. The previous TTE (two months prior) revealed a severely dilated LV with diffuse hypokinesia, severe systolic dysfunction LV ejection fraction 20%, elevated LV filling pressures, a slightly dilated right atrium, a severe functional mitral valve regurgitation, a normal RV with mild systolic dysfunction and a low probability of pulmonary hypertension. The cervical-cerebral Doppler evaluation and the complete body CT scan revealed no significant findings.

When a donor heart became available, the patient was operated (Fig. 4, 5) and an orthotopic

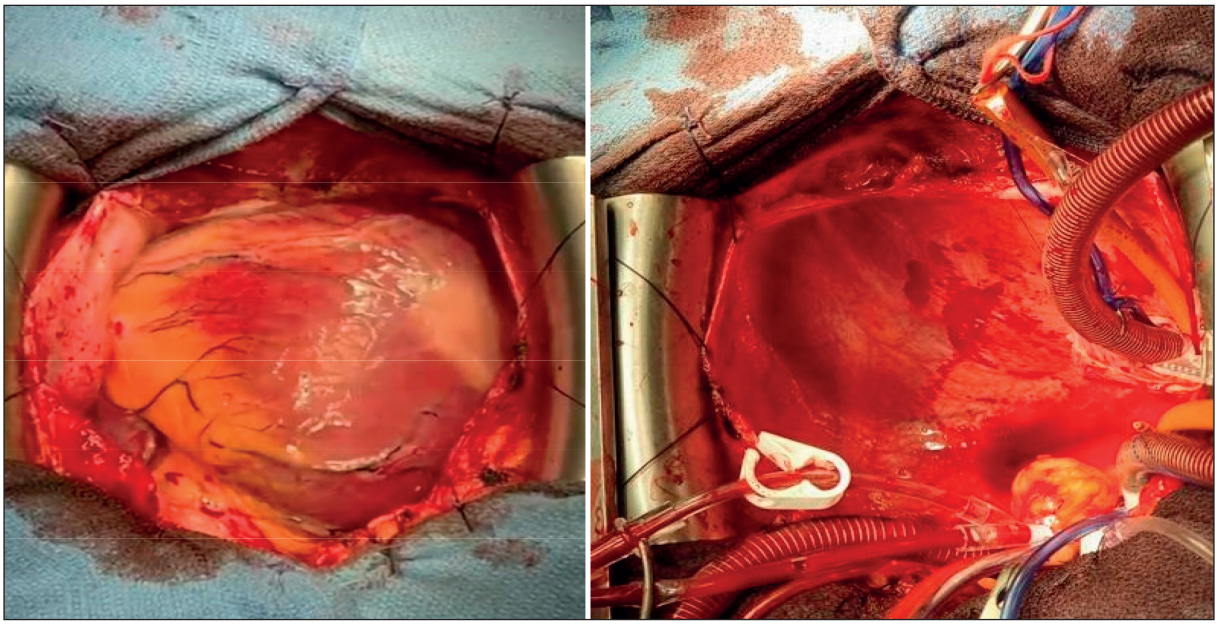


Figure 4. Intraoperative aspect of: **A)** receptor heart (left); **B)** free pericardial cavity after the removal of the heart (right)

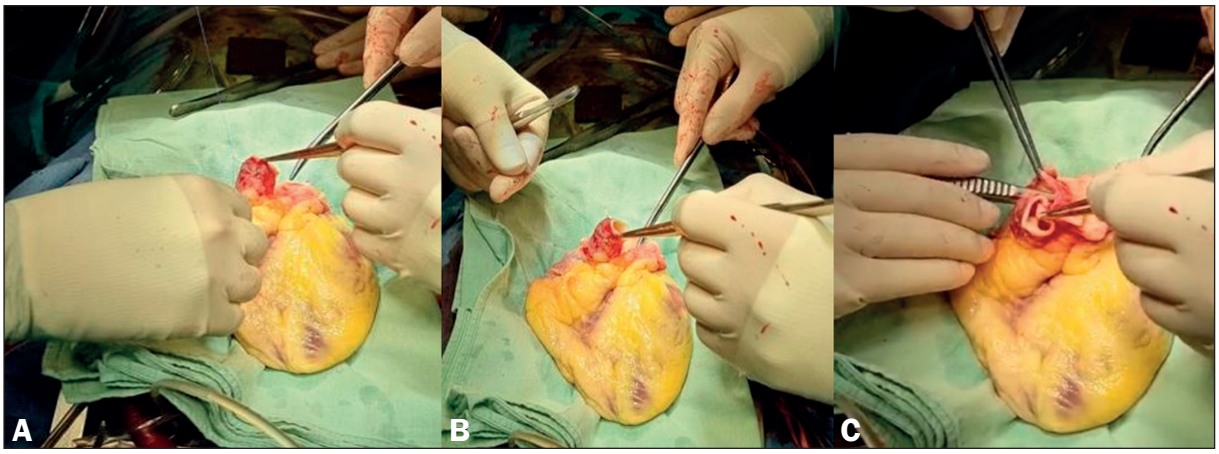


Figure 5 A, B, C (left to right): Intraoperative preparing of the donor heart during the implantation

cardiac transplant was performed in accordance with the international standards, with the careful guiding of an experienced professor, both for the harvesting and the implantation of the heart.

The donor was a 20-year-old female, 168 cm height and 73 kg weight. The recipient was 170cm height and 70kg weight. Regarding weight, there was no mismatch, but an organ size mismatch was observable. We use predictive models to calculate the predicted total heart mass (pHM) for recipient and donor pairing. Organ size mismatch can be found by calculating the percentage difference between the donor and recipient pHM as [(pHMrecipient – pHMdonor)/(pHMrecipient)]*100.

The complete equation:

1) Predicted left ventricular mass(g)
= a · Height$^{0.54}$ (m) · Weight$^{0.61}$ (kg),
where *a* = 6.82 for women and 8.25 for men; and

2) Predicted right ventricular mass(g)
= a · Age$^{-0.32}$ (years) · Height$^{1.135}$ (m) · Weight$^{0.315}$ (kg),
where *a* = 10.59 for women and 11.25 for men.

Several studies have shown that pHM is more accurate in determining the donor-recipient heart size mismatch with an increased risk of associated complications and decreased survival rates[7].

After surgery, the patient had a slow recovery in the ICU, with one episode of fever and leucocytosis and requirement for vasopressor and inotropic support for the first two days. The immunosuppressive, prophylactic antiviral, antifungal and antibiotic treatment was given according to current European guidelines. The ICU TTE showed normal LV, RV and a LV ejection fraction of 60%, with minimal tricuspid and mitral regurgitation and a 20 mm free echo space

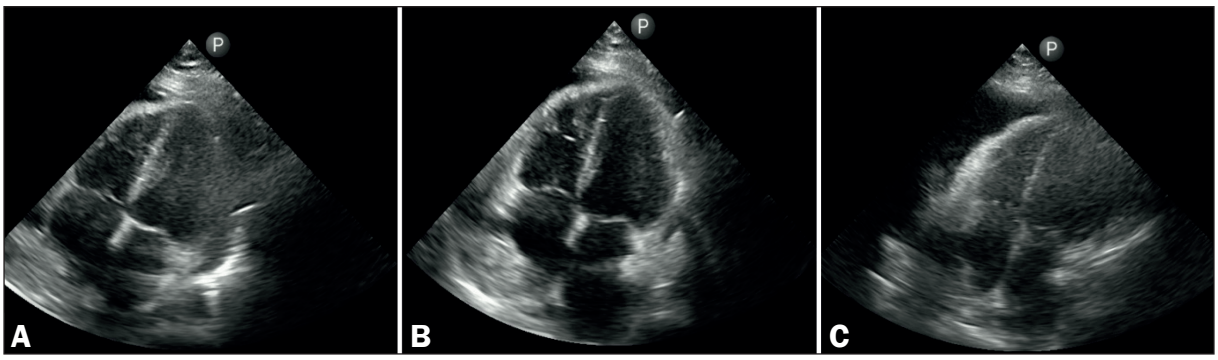


Figure 6 A, B, C (left to right). Postoperative TTE four-chamber view.

in the pericardium (donor-receptor cavity mismatch) (Fig. 6). After an uneventful stay in the ICU, the patient was transferred to the ward. The transfer cardiopulmonary X-Ray revealed no significant findings.

Bacteriological and viral screenings were made according to the established protocol and the results were negative. The patient was daily monitored (heart rate, blood pressure, saturation) and TTE screenings were performed. One month after surgery, a myocardial biopsy was harvested, and the histopathological evaluation found heart minor multifocal cellular rejection with unique associated myocyte lesion. Discharge TTE was similar to the ICU one. The ECG revealed sinus rhythm with heart rate of 90 bpm, slow progression of R wave in the precordial derivations, Q wave in DIII, T wave negative in DI and aVL and a Shumway index of 22.

The patient was discharged after one month, haemodynamically and respiratory stable and clean surgical wounds adequately healed.

Discussion

Heart assisting devices have been developing from the late 1960s and still have many issues to deal with[8]: infectious potential, anticoagulation/antiplatelet therapy, immunosuppressive protocol, renal and neurological impact, the best implantation technique and the best device appropriate for the patient[3,6,9-11]. These technological achievements were first thought as bridge-therapy for transplant, but now they are end-therapy for some end-stage HF patients or support for candidates of myocardial recovery[12-17].

The orthotopic heart transplant worldwide was first performed by the South African surgeon Doctor Christian Barnard, in December 1967[18]. The first heart transplant in Romania was performed in our centre 23 years ago by Dr. Serban Bradisteanu.

The bi-atrial approach of orthotopic cardiac transplantation, which comprises anastomoses of donor and recipient atrial cuffs, has been the gold standard for more than 35 years. Bicaval and total procedures have lately been developed in an attempt to improve cardiac anatomy, physiology, and postoperative outcome. The donor atria are preserved with a bicaval method, which combines a normal left atrial anastomosis with a distinct bicaval anastomosis. Complete excision of the recipient atria, as well as bicaval end-to-end anastomoses and pulmonary venous anastomoses, are required for total orthotopic heart transplantation[18-24]. Our method of choice was the bicaval one. The bicaval approach has proven to be the method that improved post-transplant mortality, atrial geometry, and hemodynamic, as well as lowered valvular insufficiency, arrhythmias, pacing requirements, vasopressor requirements, and hospital stay. For a variety of outcome variables, the bicaval technique outperformed both biatrial and total techniques, making it the current preferred method[18,21,23-25].

Even if the 1-year survival rate for heart transplant is about 85% and median survival period is 11 to 14 years, only about 10% of the needed heart transplants are performed worldwide because of the lack of donor hearts[26-28].

For patients with rapid progression of HF, an urgent solution is needed, so assisting devices are more accessible. Assisting devices first started as a bridge therapy to heart transplant, but with the current improved characteristics (HEART MATE III, third generation of assist device) such devices have been more and more used as a destination therapy. Also, with LVAD support, patients benefit from improved quality of life, reduced HF, improved clinical condition and are no longer on top of the transplant list. Although a life rescueing option for end-stage HF patients, LVAD implantation can have multiple complications, such as periprocedural or postoperative ones. The most frequent periprocedural complications are: bleeding, stroke, immediate RV dysfunction, thrombosis and sepsis. To avoid all these, standardized techniques of implantations are recommended, as well as

complete guidelines on how to manage patients with recent LVAD implant. One of the most severe complications is acute RV failure. Its ethology is variable and does not always respond to maximal treatment. There are some reports that suggest calculating scores to set the risk of evolving to RV failure after LVAD implantation. This complication can appear immediately after surgery or in the next days. Despite the best efforts, mortality rates reach up to 29%[29-32].

The challenges of heart transplantations are vast, such as the immunosuppressive protocol, antibiotic and antiviral protocols, antiplatelet/anticoagulation protocol, multi-organ impact and eligibility criterion. Standardized protocols have been recently renewed (2018) in order to decrease the risk of acute reject, infection, renal failure, neurological damage, liver failure and other complications that can emerge from such a procedure[8,9,32-36].

Other heavily debated subjects are whether the bridging therapy prior to transplant is useful or not (general consensus reveals higher survival rate for patients on the transplant waiting list with LVAD implants) and whether the bridging therapy should be accompanied or not with valve replacement or repair (no consensus was reached)[8,15,26,37]. The patient who received the LVAD had a patent foramen ovalis and required the repair, but also a coronary lesion of debatable indication, which proved to be the adequate course in this case.

The field of cardiac surgery is continuously developing by cardiac stem cell therapy, valvular and pericardial tissue stem cell harvesting, but also machine-learning LVADs for patients who are eligible for myocardial regeneration. Furthermore, there is another category of patients still in need of more than one transplant centre in our country, that is the paediatric population. The eligibility criterion of such patients and the low availability of donor organs give these patients the solution of LVADs or biventricular assist devices, and in the future the development of stem-cell technology[4,38-43].

Conclusions

HF is one of the leading causes of death and therefore it has always been a focus of constant development. Assisting devices, replacements or cell-stem developing for end-stage HF need standardized protocols, which are already proven to be effective (eligibility, implantation technique, preoperative and postoperative management of the patient and other organs impact). The current report is the evidence of our centre's first heart transplant and LVAD implantation, a start that came as an answer to the increasing incidence of end-stage HF.

Author Contributions

„H.M., O.F., C.N., M.C., C.V., S.P., M.B., A.S., R.T., S.S., L.C., O.Z., L.M., C.C.D. were responsible for the consultations and procedures of patient. H.M., O.F., C.N., M.C., C.V., S.P., M.B., A.S., R.T., S.S., L.C., O.Z., L.M., C.C.D., H.S. analyzed and interpreted the patient data. H.M., O.F., C.N., M.C., C.V., S.P., M.B., A.S., R.T., S.S., L.C., O.Z., L.M., C.C.D., H.S. performed the literature review. H.M., O.F., C.N., M.C., C.V., S.P., M.B., A.S., R.T., S.S., L.C., O.Z., L.M., C.C.D., H.S. were the contributors for writing the manuscript. All authors read and approved the final manuscript. All the authors have an equal contribution to this manuscript"

Compliance with Ethics Requirements:

„The authors declare no conflict of interest regarding this article"

„The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from the patients included in the study"

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