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CASE REPORT

To hit a home run as a heterotopic heart recipient—living with two hearts for over three decades: a case report

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Abstract

Heterotopic heart transplantation (HHT) is an alternative to the orthotopic technique in selected patients with terminal heart failure. We report the case of the longest survival after HHT, with an uneventful follow-up for over three decades after transplantation. At the age of 25 years, endomyocardial fibrosis following myocarditis rendered the patient's native heart unable to maintain the body's needs. An allograft provided a second chance at life. The HHT technique was favoured due to severe pulmonary hypertension. The patient had an uneventful follow-up since then. The scarcity of donors and the revolutionary advances in the mechanical circulatory device field restricted the utilization of the HHT technique, but it has the potential to provide an excellent prognosis with a good quality of life.

Keywords Heterotopic heart transplantation; Survival; Mechanical circulatory support

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Introduction

Since its first introduction in 1974 by Christiaan Barnard, heterotopic heart transplantation (HHT) has been considered a surrogate of the orthotopic technique. It provides a unique opportunity, as the graft is offered the assistance of the native heart. The latter could still maintain the circulation in the case of a primary allograft failure or an acute rejection. Additionally, HHT is more suitable when pulmonary hypertension, size mismatch, or compromised donor hearts render the orthotopic heart transplantation (OHT) unsuccessful.[1] However, the heyday of the ventricular assist devices limited the utilization of the HHT. Mechanical support is a promising alternative to a failing native heart, and the lack of donors is an additional factor shifting the focus of the research in another direction. Thus, data regarding prognosis in HHT are limited.[2] However, to our knowledge, this is a case of the longest survival after HHT with a stable graft function and an uneventful follow-up for more than three decades.[3]

Case report

In November 1990, a 25-year-old male patient with terminal heart failure due to endomyocardial fibrosis following myocarditis underwent transplantation at our institution using the heterotopic transplant technique. The primary indication for this approach was pulmonary hypertension. The post-operative course was uneventful.

The patient's clinical condition has been monitored in 3-month intervals since then. The routinely conducted laboratory investigations comprised complete blood count, coagulation, liver and renal function panels, serological examinations, inflammatory parameters, and N-terminal

prohormone of brain natriuretic peptide (NT-proBNP). Transthoracic echocardiograms were obtained every 6 months or if clinically indicated.

The patient was in stable condition at the most recent presentation and had no relevant impairment according to the New York Heart Association functional classification (NYHA I–II). During the assessment of the aerobic capacity, he was able to achieve a 6-min walk distance of 700 m. An electrocardiogram showed a parasystole with a ventricular rate of the allograft of 85 per minute (*Figure 1*). The most recent non-invasive assessment of the allograft using magnetic resonance imaging was performed 6 months before the current follow-up. The graft showed a normal-sized left and right ventricles with normal systolic function and no late gadolinium enhancement. The native heart, even though severely impaired and minimally perfused during contrast administration (compared with the graft), showed impaired contractility, however, without signs of intracavitary thrombosis. Due to the different heart rates, ECG triggering and subsequent artefact-free CMR images could only be achieved for one of the two hearts (*Figure 2*).

Figure 1 Electrocardiogram. Twelve-lead ECG at routine assessment showing parasystole.

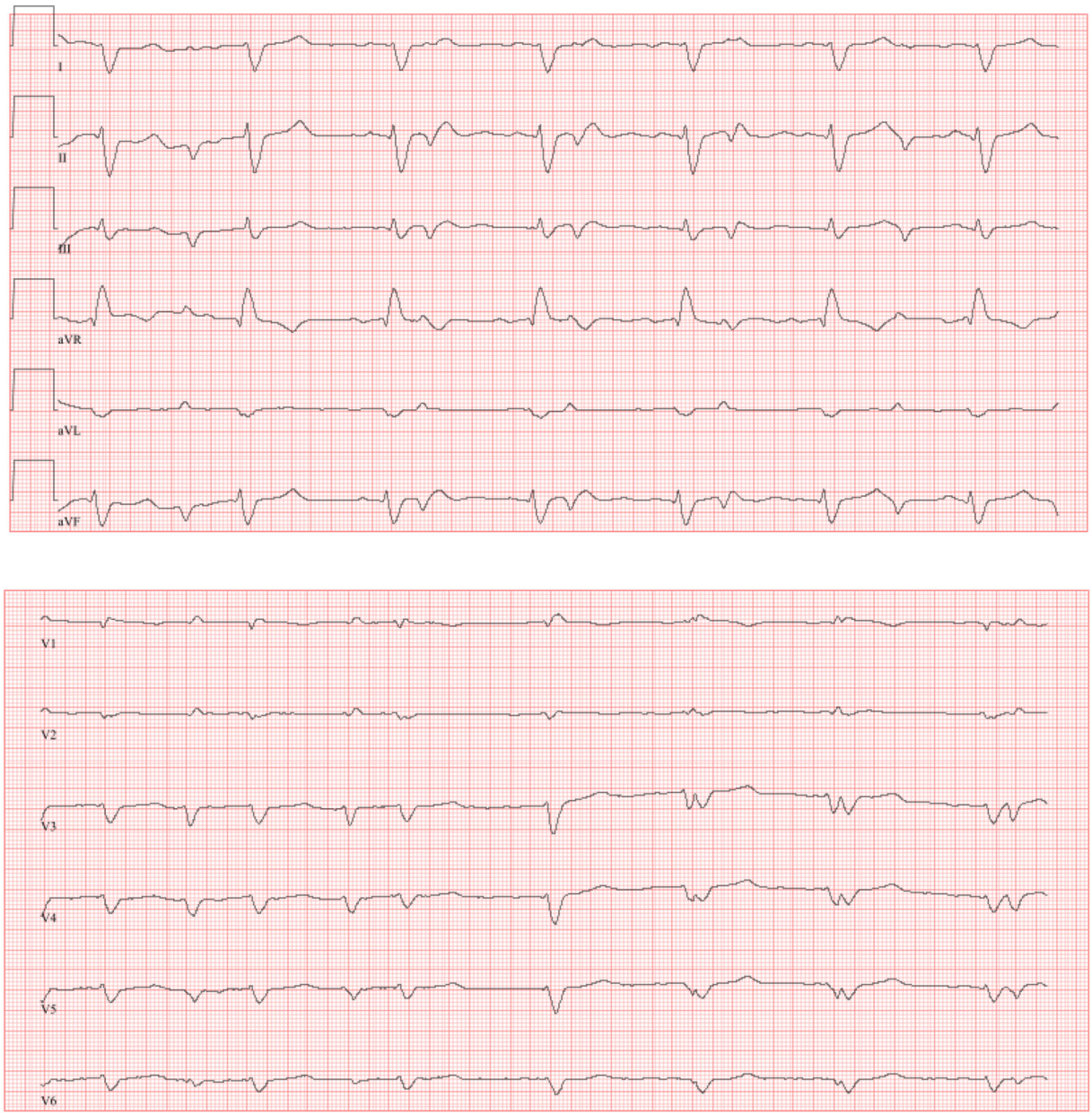

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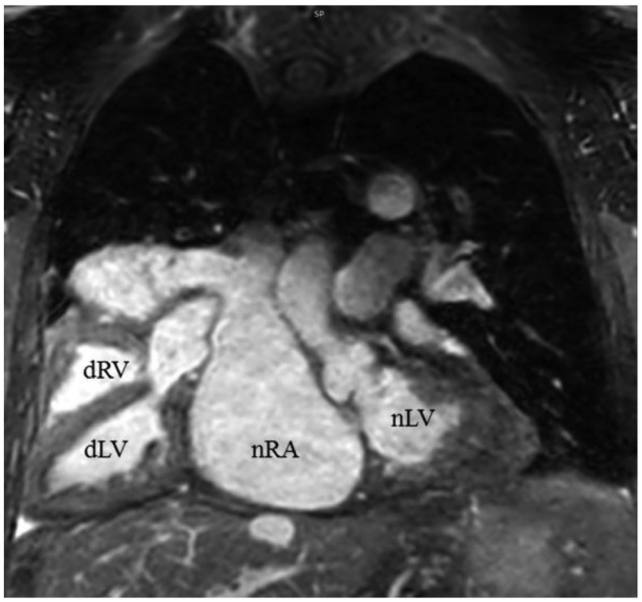
Figure 2 Magnetic resonance image of the two hearts. dLV, donor left ventricle; dRV, donor right ventricle; nLV, native left ventricle; nRA, native right atrium.

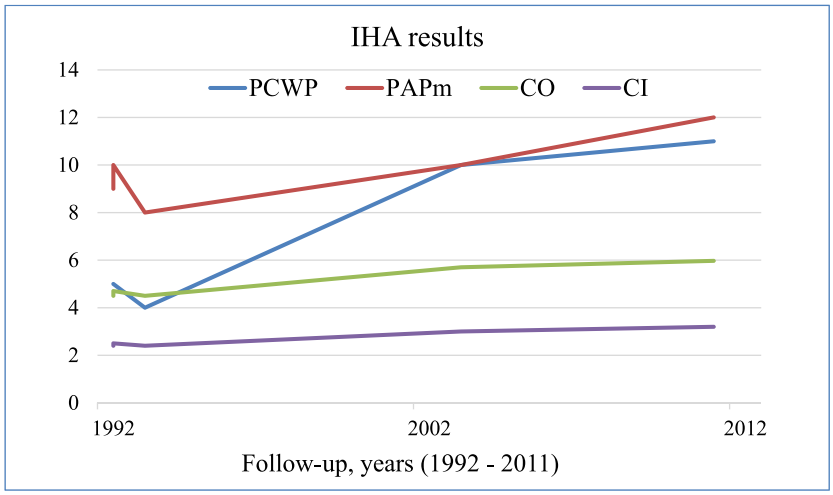


The clinical evaluation of the patient delivered no evidence of pulmonary obstruction or restriction. The last radiographic assessment of the lungs showed no signs of congestion or other pathological pulmonary findings.

Laboratory assessment revealed normal serum pseudocholinesterase level, thus precluding relevant impairment of the liver's synthetic function. The renal function was slightly reduced (estimated glomerular filtration rate 67 mL/min/m^2) according to the NKF classification of chronic kidney disease but stable over the last years.[4] To maintain a well-compensated volume status, he was taking low-dose torasemide (5 mg/day).

The maintenance immunosuppressive medication was based on cyclosporine A (CsA) with a lower target level due to the prolonged follow-up and prednisone with a daily dose of 5 mg. Additionally, diltiazem was prescribed as a CsA-sparing agent (120 mg/day).[5] The mean maintenance trough level of CsA was 107.1 ± 14.5 ng/ml (an average of the last 10 measures). The remaining medication included vitamin D and a vitamin K antagonist. The virological examina-

Figure 3 Right heart catheterization results (1992–2011). CI, cardiac index (L/min/m^2); CO, cardiac output (L/min); IHA, invasive haemodynamic assessment; PAPm, mean pulmonary artery pressure (mmHg); PCWP, pulmonary capillary wedge pressure (mmHg).



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tion revealed negative results concerning the CMV-DNA, EBV-DNA, HSV-1-DNA, HSV-2-DNA, and VZV-DNA. The percentage of panel reactive antibodies was 7% in the first year and 0% in the following years after HHT.

The patient's history since HHT included a knee hematoma while being on heparin, a cholecystectomy, and a partial amputation of a small finger due to trauma.

In the years following HHT, the patient underwent at least 30 invasive examinations of the graft's coronary circulation and/or haemodynamic (at least 14 coronary angiographies and 24 right heart catheterizations with/without biopsy sampling). Neither of the angiographies showed signs of coronary artery disease of the native heart or vasculopathy of the allograft.

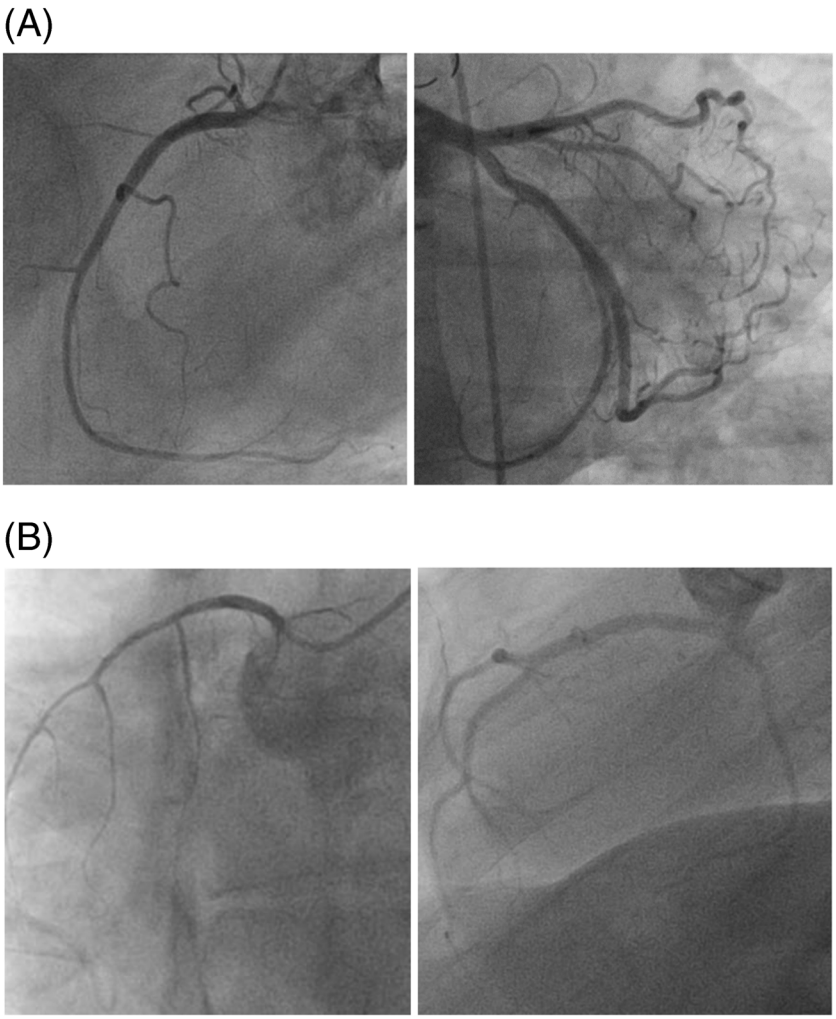
Furthermore, the obtained biopsies delivered no evidence of rejection requiring therapy (≥2R) according to the revised classification of the ISHLT from 2004.[6] One year following HHT, narrowing the pulmonary artery anastomosis was described. However, no further progression of the obstruction or deterioration of the right ventricular function in the following 30 years was observed, and the haemodynamic measures were stable (*Figure 3*).

Discussion

To the best of our knowledge, we describe the case of the longest survival after HHT with an outstanding quality of life.

Despite the long-term immunosuppressive therapy with CsA, no relevant side effects were observed. Due to the uneventful follow-up, the targeted maintenance level of CsA was lower than in the immediate post-transplant period.[7] As an alternative of CsA, tacrolimus was introduced in 1989 and was successfully utilized in the following years due to the beneficial side-effect profile. Nevertheless, as TAC was

Figure 4 Angiographic images. (A) Native right coronary artery (RCA) (LAO 60°) and left coronary artery (LCA) (PA/caudal 38°). (B) RCA (RAO 30°) and LCA (LAO 90°) of the allograft. LAO, left anterior oblique; PA/caudal, posteroanterior/caudal; RAO, right anterior oblique.



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emerging as an alternative, our patient was already on treatment with CsA. Due to the stable clinical course, no evidence of rejection, or any relevant CsA-related side effects, the treatment regimen was maintained. This strategy proved to be successful.

The occasional blood pressure measurements delivered normal findings and no evidence of hypertension, which could be linked to the immunosuppression, although HHT recipients are previously reported to have a lower blood pressure than the OHT recipients.[8]

The left ventricular ejection fraction of the native heart remained highly reduced in contrast to reports on the recovery of the systolic function after HHT.[9] A drawback of the HHT is the potential for thrombi formation in the native heart, particularly if the ventricles are enlarged. Thus, lifelong maintenance oral anticoagulation is indicated, increasing the bleeding risk compared with the orthotopic technique. However, only minor bleeding following knee trauma was observed, and the patient had no history of thromboembolic complications.

Cardiac allograft vasculopathy (CAV) is a major comorbidity limiting the prognosis of heart transplant recipients. According to recent reports, almost 50% of the HTx recipients develop CAV in 10-year follow-up.[10] However, our patient had no angiographic signs of coronary involvement at the most recent assessment, and a magnetic resonance imaging with vasodilator stress also delivered no evidence of myocardial ischaemia (*Figure 4*). According to the recent guidelines, annual or biannual invasive assessment is indicated in the first years following transplantation.[7] As the patient was free from CAV, neither of the biopsies showed rejection, and the haemodynamic measures were stable over the years, so no further invasive assessment was performed.

The obtained electrocardiograms showed non-synchronous electrical activity of both hearts, which is previously reported to be associated with a reduced exercise capacity due to the counter-pulsation.[11] Nevertheless, the patient had no subjective functional impairment, and the last assessment revealed no relevant reduction of his exercise capacity.

The heterotopic approach was fundamental in investigating the immunological phenomena in the early era of allogenic transplantation. The revolutionary advances in the developing field of xenotransplantation are also achieved using a heterotopic technique with an intra-abdominal positioning of the donor hearts. The clinical course of our patient demonstrates that the utility of the HHT exceeds by far the experimental field (*Table 1*). However, the scarcity of donors and the need for immunosuppression and surveillance biopsies leave an open door for the development in the field of MCS.[12]

Due to the limited experience with HHT, there are limited data concerning the long-term outcomes. According to the United Network for Organ Sharing (UNOS) database reports, the 1-year, 5-year, and 10-year survival in HHT are 83.8%, 59%, and 35.1%, respectively.[13] To our knowledge, the longest surviving HHT recipient to date had to be relisted 22 years after transplantation. The patient's native heart was replaced with a total artificial heart, and he underwent OHT 24 years following the HHT.[3] Thus, our patient's ongoing journey following HHT exceeds by 10 years

Table 1 Comparison of the HHT with OHT, Xeno-Tx, and LVAD

	HHT	OHT	Xeno-HTx	LVAD
1. Pre-operative factors				
- Waitlist and donor dependency	+	+	+/–	–
- Possible in pulmonary hypertension	+	–	–	+/–
- Requirement for size-matched organs	–	+	+	-
- Risk for transmission of infections	+	+	+[a]	–
- Minimally invasive procedure	–	–	–	+/–
2. Post-operative considerations				
- Remaining native heart	+	–	–	+
- Possible angina of the native heart	+	–	–	+
- Immunosuppressive therapy with consequent side effects	+	+	+	–
- Anticoagulation and bleeding risk	+	–	–	+
- Acquired infections/infectious complications	+	+	+	+
- Need for recurrent invasive procedures (monitoring for cardiac allograft vasculopathy, surveillance biopsies, rejection risk)	+	+	+	–
- Limitation of the QoL (extracorporeal components—driveline, controller, power source)	–	–	–	+
- Re-do procedures (device implantation/Tx)	+	+	+	+
- Implantation as a bridge to HTx	–	–	–	+
- Explantation in case of recovery	–	–	–	+

HHT, heterotopic heart transplantation; HTx, heart transplantation; LVAD, left ventricular assist device; N/A, not applicable; OHT, orthotopic heart transplantation; QoL, quality of life; Tx, transplantation; Xeno-Htx, xenoheart transplantation.
[a]Particularly zoonotic infections.

the longest survival reported to date. It is to be mentioned that four out of the 16 adult HHT recipients transplanted in our centre displayed long-term survival of more than 10 years.[14] This 10-year survival is very close to the above-mentioned data.

Our patient's treatment course reveals the utility of the HHT, despite being largely overlooked in the last years. The close monitoring and personalized approach, combined with good compliance, allowed to adjust the immunosuppressive therapy. We were able to use lower target ranges to reduce the side effects of the lifelong medication over the years. Additionally, the success of the clinical course is also attributable to the beneficial cardiovascular profile prior to and following the HHT. In selected cases, HHT can provide adequate support and survival benefit combined with a good quality of life.

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Conflict of interests

None in relation to this article.

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