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Continuous cardiac monitoring in a patient with terminal pulmonary hypertension and eventual bilateral lung transplantation

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SUMMARY

As pulmonary arterial hypertension (PAH) progress, arrhythmias are becoming an increasingly prominent phenomenon. Supraventricular tachycardias have been shown to have an incidence of up to 35% in pulmonary hypertension.

Continuous cardiac monitoring was deployed in a patient with severe PAH 100 days before bilateral lung transplantation (BLTX). Despite being graded as WHO functional class IV, no arrhythmias were observed before BLTX. Furthermore, the case describes clinical improvement, along with a significant increase in heart rate variability (HRV) and decrease in night-time heart rate in the post-transplantation period.

No arrhythmias were observed preoperatively during continuous monitoring in a 100-day period despite the patient's intrinsically high risk for arrhythmias. Increasing HRV and lower resting heart rate were observed after BLTX. Since these parameters correlate with the clinical condition, they might be valuable in risk assessment in patients with pulmonary hypertension.

symptoms progressed from WHO functional class (WHO FC) III to IV, with the observation of increasing shortness of breath, fatigue, dizziness and palpitations. Four years ago, the patient was listed for bilateral lung transplantation (BLTX). An ECG showed sinus rhythm and right bundle branch block. At the same time, the patient was included in a study with continuous cardiac monitoring with the placement of an implantable loop recorder due to symptoms of palpitations; in order to assess arrhythmias, heart rate variability (HRV) and heart rate.

INVESTIGATIONS

From the primary diagnosis 8 years ago and until the listing for BLTX 4 years after, the tricuspid regurgitation gradient had increased from 55 mm Hg to 104 mm Hg, and the right atrium and ventricle had become increasingly dilated with reduced right ventricular ejection fraction (figure 1). At the time of listing for BLTX, the tricuspid annular plane systolic excursion was reduced to 15 mm. The left ventricle was D-shaped and with reduced left ventricular ejection fraction. Additional echocardiographic and cardiovascular MR (CMR) data are presented in tables 1 and 2, these findings likewise supported the diagnosis. Lung function test with forced expiratory volume in the first second (FEV1) of 2.3 L (96% of expected) and forced vital capacity (FVC) of 3.1 L (109% of expected), while diffusing capacity for carbon monoxide (DLCO) was reduced to 58.1%. An N-terminal prohormone of brain natriuretic peptide (NT-proBNP) level of 670 pmol/L was observed. Furthermore, at the time of the listing for BLTX a 6 min walking test was performed with oxygen supplementation of 2 L/min; walking distance was 380 m, and pretest/post-test levels of blood oxygen saturation, heart rate and baseline dyspnoea index were 92%/79%, 87/132 beats per minute and 2/10, respectively.

BACKGROUND

Pulmonary hypertension (PH) is a progressive disease affecting both the pulmonary vasculature and the heart. PH is defined by a resting mean pulmonary artery pressure (mPAP) of ≥ 20 mm Hg. In addition, pulmonary arterial hypertension (PAH) is defined by a pulmonary arterial wedge pressure of ≤ 15 mm Hg and pulmonary vascular resistance (PVR) ≥ 3 wood units (WU), as assessed by right heart catheterisation (RHC).¹ Previous studies have shown an incidence of supraventricular tachycardia (SVT) between 8% and 35% in PH, increasing as the disease becomes more advanced.^{2–8} In this case report, continuous cardiac monitoring was applied in an end stage PAH patient.

CASE PRESENTATION

Eight years ago, a woman in her 50s was diagnosed with idiopathic PAH. The mPAP was 48 mm Hg, PVR 10 WU (823 dynes/s/cm⁵), cardiac index 2.3 L/min/m² and pulmonary capillary wedge pressure 9 mm Hg. Specific PAH therapy was sequentially increased to include tadalafil, macitentan and treprostinil IV (Chrono five infusion pump device), supplemented with warfarin, spironolactone and long-term oxygen therapy (2 L O₂/min). Despite intensified triple therapy including treprostinil up to 34 ng/kg/min, PAH

DIFFERENTIAL DIAGNOSIS

The patient had a quick onset of dyspnoea 8 years ago and was admitted to the hospital after 3 weeks of deterioration with chest pain on suspected pulmonary embolism or pneumothorax. Echocardiography revealed a highly dilated right ventricle and a tricuspid regurgitation gradient of 60 mm Hg but no other pathology. CT angiography showed no signs of pulmonary embolism. Coronary enzymes were only discreetly elevated, and ECG showed no



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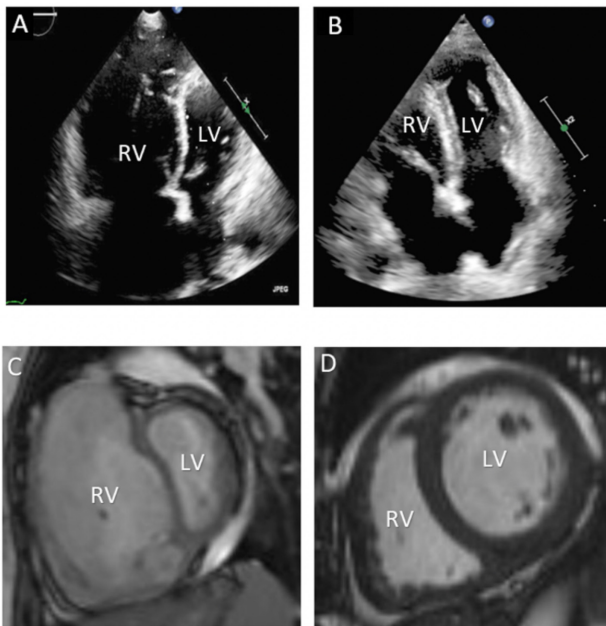


Figure 1 Anatomical normalisation in the size of the right atrium and ventricle within 2.5 months. (A) Echocardiography at the time of loop-recorder implantation (100 days prior to BLTX). (B) Echocardiography 1 month after BLTX. (C) CMR image at the time of loop-recorder implantation (100 days prior to BLTX), right ventricle EDV: 430.8 mL. (D) CMR image 2.5 months post-BLTX, right ventricle EDV: 103 mL. CMR, cardiovascular MR; BLTX, bilateral lung transplantation; EDV, end diastolic volume; RV, right ventricle; LV, left ventricle.

ST-deviations. The patient was admitted to the PH clinic, and RHC confirmed the diagnosis of PAH with mPAP of 48 mm Hg, PVR of 10 WU and a cardiac index of 2.31 L/min.

TREATMENT

BLTX management

The patient deteriorated with increasing dyspnoea despite triple PAH-specific therapy. Due to donor status, the first BLTX had to be aborted after sternotomy. After an additional 6 days, the patient underwent successful transplantation after being listed for urgent transplantation. Extracorporeal membrane oxygenation treatment was initiated 1 day post-transplantation and continued 4 days due to biventricular heart failure.

Table 1 Echocardiography characteristics

Echocardiography results	Approximately 100 days prior to BLTX	30 days after BLTX	Difference
Right atrium			
Length (cm)	6.2	5.9	-0.3
Diameter (cm)	8.4	3.9	-4.5
Area (cm ²)	37	19	-18
Right ventricle			
Diameter (cm)	6.11	4.2	-1.91
Longitudinal length (cm)	9.4	7.3	-2.1
Ventricle area (cm ²)	49	26	-23
TR (mm Hg)	104	77	-27
RVEF (%)	18	46	+28

BLTX, bilateral lung transplantation; RVEF, right ventricle ejection fraction; TR, tricuspid regurgitation.

Table 2 CMR characteristics

CMR results for right ventricle (sex and age reference interval)	Approximately 100 days prior to BLTX	75 days after BLTX	Difference
EDV (mL)	431 (81; 166)	103	-328
ESV (mL)	330 (15; 68)	46	-284
SV (mL)	101 (56; 108)	57	-44
EF (%)	24 (55; 79)	56	+32
EDV/BSA (mL/m ²)	254 (53; 90)	62	-192
ESV/BSA (mL/m ²)	194 (11; 37)	27	-167
Cardiac output (L)	2.8	5.3	+2.5
Cardiac index (L)	1.6	3.1	+1.5

BLTX, bilateral lung transplantation; BSA, body surface area; CMR, cardiovascular MR; EDV, end diastolic volume; EF, ejection fraction; ESV, end-systolic volume; SV, stroke volume.

OUTCOME AND FOLLOW-UP

Heart rhythm and HRV

During continuous cardiac monitoring for 100 days preceding BLTX, unexpectedly no arrhythmias were observed. However, in the first 3 weeks after BLTX, a total of 23 episodes of self-limiting atrial fibrillation (AF) occurred lasting from 6 min to 10 hours (figure 2). Short-term amiodarone was given until the seventh-day post-BLTX. Apart from 22 min of self-limiting AF, sinus rhythm was stable from week 4 to 36 after BLTX (figure 2). Two and a half months after BLTX, CMRI showed complete normalisation of cardiac index, end diastolic volume (EDV), stroke volume (SV) and RVEF, left ventricle ejection fraction (LVEF) (figure 1).

Pre-BLTX/post-BLTX mean values of night-time heart rate and HRV were 83/73 beats per minute (p=0.012) and 61/77 ms (p≤0.0001), respectively (figure 3).

The patient was discharged from the hospital after a month with improved clinical condition and a simultaneous increase in HRV (figure 3).

DISCUSSION

To our knowledge, this is the first case with continuous cardiac monitoring in a patient with PAH pre-BLTX and post-BLTX. In the present patient with end-stage PAH, interestingly no arrhythmias were observed before sternotomy despite disease progression. The patient did experience palpitations and once activated a symptom activator, which revealed sinus tachycardia (120 beats per minute). Additionally, this patient average HRV increased significantly by a mean 17 ms post-BLTX.

Previous studies have shown an incidence of SVT between 8% and 35% in PH, increasing as the disease becomes more advanced.³⁻⁸ Arrhythmias lead to progression in symptoms of right heart failure and more frequent hospitalisations and restoration of sinus rhythm have shown to be prognostically advantageous.⁵ Several parameters have previously been associated with the development of arrhythmias in PAH, including (1) enlarged right-sided atrial and ventricular volume, (2) increased right atrial pressure, (3) increased PVR, (4) decreased cardiac index, (5) increased NT-proBNP level and (6) left atrial diameter.^{3,4} In this case, the left atrial diameter was normal, while all the other parameters were severely affected.

As this patient's risk for arrhythmias was intrinsically high, it is noteworthy that no arrhythmias were observed preoperatively despite the use of continuous monitoring.

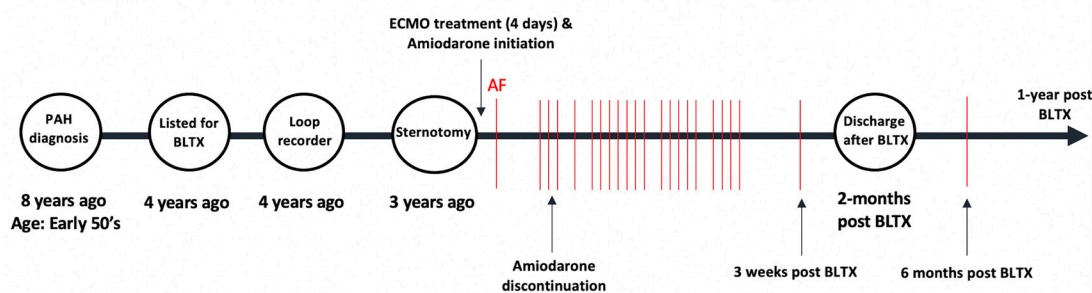


Figure 2 Representation of events before and after BLTX. Apart from 22 min of self-limiting AF, sinus rhythm was stable from week 4 to 98 after BLTX. AF, atrial fibrillation; CMR, cardiac MR; BLTX, bilateral lung transplantation.

Only in the postoperative period did the patient have transiently occurring arrhythmias, which are a known and common complication to BLTX.^{9 10}

As HRV is correlated with the autonomic system, with a low HRV representing high sympathetic tone and low cardiac adaptability,^{11 12} the significant increase (28%) from pretransplantation to post-transplantation could be seen as a sign of increased autonomic balance with less sympathetic activity after the afterload reduction subsequent to BLTX. The same phenomenon seems to be reflected in the decrease in heart rate at night-time. The fact that the onset of change in HRV and heart rate at night-time first occurred after the recovery period from the BLTX emphasise the value of long-term cardiac monitoring and the potential of HRV as a clinical marker of risk. Larger studies are ongoing to assess the prognostic significance of HRV in relation to PAH.

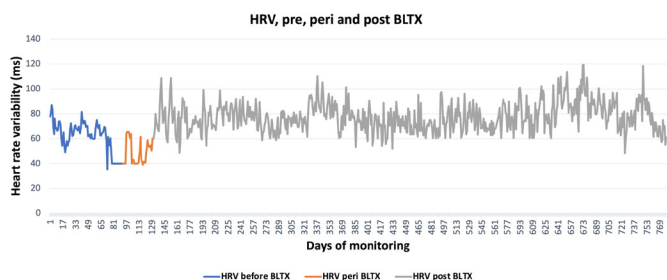


Figure 3 HRV measured by loop recorder. One value for each 24 hours of HRV plotted as a line chart. Average value of HRV before BLTX: 61, peri: 50 and post: 78. The average in HRV increased by a mean 17 ms post-BLTX ($p < 0.0001$). HRV, heart rate variability; BLTX, bilateral lung transplantation.

Learning points

- ▶ Implantation of a loop recorder offers a unique opportunity to long-term monitoring of heart rhythm. Interestingly, no arrhythmias were observed before bilateral lung transplantation in this patient with terminal pulmonary arterial hypertension.
- ▶ Increasing heart rate variability (HRV) and lower resting heart rate were observed after bilateral lung transplantation.
- ▶ Since HRV and heart rate at night-time correlate with this patient's clinical condition, they might be of value in risk assessment and guidance of therapy in patients with pulmonary arterial hypertension.

CONCLUSIONS

This is the first presentation of long-term continuous cardiac monitoring in pulmonary arterial hypertension pre-BLTX and post-BLTX. Notably in a patient with terminal PAH, WHO FC IV, no arrhythmias were observed in a 100-day period pretransplantation. Post-BLTX, the patient experienced clinical improvement and CMR showed complete normalisation of cardiac index, EDV, SV, left and right ejection fraction. Interestingly, HRV increased and heart rate at night-time decreased significantly in the post-BLTX period. Especially, the HRV was correlated to this patient's clinical condition. Continuous cardiac monitoring in PAH not only provides the assessment of arrhythmias but also HRV and heart rate that could be a significant parameter in risk assessment in patients with pulmonary arterial hypertension.

Correction notice The article has been corrected since it is published. The author names Søren Zøga Diederichsen and Jesper Hastrup Svendsen have been corrected.

Contributors All authors have approved the final version of the manuscript. MØA: Implanted the loop recorders, analysed and interpreted data, and drafted and wrote the paper. SD: Implanted the loop recorders and analysed and interpreted data, and wrote the paper. JHS: Analysed and interpreted data and wrote the paper. JC: Conceived and designed the study, analysed and interpreted data, and wrote the paper.

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Competing interests SD is a part-time employee of Vital Beats, not related to this work. JHS is a member of an advisory board for Medtronic, has received research grant and speaker fee from Medtronic unrelated to this study and has received research grant from Gilead unrelated to this research project. JC is a member of an advisory board for Janssen, and the institution has received research grants and speaker fees. In the same way for United Therapeutics for clinical trials and Astra Zeneca and Ferrer for speaker fees.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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