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FROM THE CASE GALLERY
Congenital heart disease

Successful hybrid cardiac resynchronization therapy in a patient with failing systemic right ventricle and significant tricuspid regurgitation in transposition of the great arteries after atrial switch procedure according to Mustard

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Background Patients with a systemic right ventricle (sRV) in the context of transposition of the great arteries (TGA) late after atrial switch are prone to heart failure. Complications like tricuspid valve regurgitation (TR) can further aggravate sRV dysfunction. Tricuspid valve regurgitation is usually secondary to annular dilatation and restriction. Criteria for cardiac resynchronization therapy (CRT) in this patient group are not well defined and should be considered on a case-by-case basis.

Case summary We present a case of a 42-year-old male with sRV failure and TR in the context of TGA after atrial switch. Patient had progressive reduction in exercise capacity. Electrocardiogram showed a wide QRS complex (right bundle branch block configuration). Echocardiography showed significant TR and signs of electromechanical dyssynchrony of the failing sRV with severely reduced systolic function. He underwent heart catheterization and invasive haemodynamic evaluation to assess the potential benefit of CRT. During sequential atrial-sRV pacing, 20% increase in *Dp/Dt* was measured, suggesting that he would be a CRT responder. Concomitant angiography showed no baffle leakage nor obstructive coronary artery disease. Hybrid CRT-defibrillator implantation resulted in successful resynchronization and improved sRV function, reduced TR and better exercise capacity.

Discussion Invasive haemodynamic contractility evaluation can help assess the potential benefit of CRT in patients with systemic right ventricular failure in the context of transposition of TGA after atrial switch. Successful CRT can result in improved sRV function, reduced TR and improved exercise capacity.

Keywords Congenital heart disease • Systemic right ventricle • Heart failure • Device therapy • Cardiac resynchronization therapy • Transposition of the great arteries

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Learning points

- Patients with a systemic right ventricle (sRV) in the context of transposition of the great arteries late after atrial switch are prone to heart failure. Complications like tricuspid valve regurgitation (TR) can further aggravate sRV dysfunction. Tricuspid valve regurgitation is usually secondary to annular dilatation and restriction. Criteria for cardiac resynchronization therapy (CRT) in this patient group are not well defined and should be considered on a case-by-case basis. Invasive haemodynamic evaluation prior to device implantation can help assess the potential benefit of CRT in sRV patients. Transvenous approach for CRT is often limited by baffles interfering with access to the atria and the coronary sinus draining into the pulmonary venous atrium. A hybrid approach with a surgically implanted epicardial sRV lead may be required. Successful resynchronization can lead to an improvement of sRV function and reduction in TR.

Timeline

1974	Congenital defects/anatomy: dextro-transposition of the great arteries.
1974	Atrial switch operation according to Mustard; Postoperative atrioventricular (AV) dissociation: pacemaker implantation with epicardial systemic right ventricular (sRV) lead.
1976	Pulse generator pocket infection with *Staphylococcus aureus*: pacemaker lead and device extraction; Recovery of AV conduction: no new pacemaker indication.
2010	Cerebral abscess and baffle leak: surgical baffle revision; Percutaneous closure of residual leakage using an Amplatzer device.
2017	Symptomatic sRV failure: New York Heart Association (NYHA) II and reduced exercise capacity [140 Watt (73% of predicted), VO_2max of 16.1 mL/min/kg (46% of predicted)]; Electrocardiogram: QRS 180 ms (right bundle branch block configuration); Echocardiography/MRI: severely reduced sRV function (ejection fraction 22%) and Grade III+ tricuspid valve regurgitation (TR), sRV electromechanical delay; Invasive haemodynamic evaluation: increase of 16% in *Dp*/*Dt* and QRS narrowing to 120 ms during sequential pacing (atrial-sRV) using intrinsic AV conduction interval (optimal pacing site); Hybrid biventricular implantable cardioverter-defibrillator implantation.
2018	Subjective improvement to NYHA I–II and improved maximal exercise capacity [156 Watt (83% of predicted), VO_2max of 19.1 mL/min/kg (55% of predicted)]; Echocardiography: moderately reduced sRV function and Grade II TR.

Case content

Patient presentation

A 42-year-old male with a systemic right ventricle (sRV) in the context of dextro-transposition of the great arteries (TGA) after atrial switch according to Mustard was evaluated in the outpatient clinic. He had a history of atrioventricular (AV) dissociation and slow nodal escape rhythm and subsequent pacemaker implantation with an epicardial lead on the sRV apex at the age of 2. Two years later, he developed a complicated pulse generator pocket infection with *Staphylococcus aureus* that persisted despite antibiotic treatment and led to the extraction of the pacemaker leads and device. The intrinsic conduction restored, consequently, there was no indication for a new pacemaker. At the age of 35 years, the patient was admitted with a cerebral abscess and a baffle leakage was diagnosed during the work-up. He underwent a surgical baffle revision with repair of the leakage and several months later, a percutaneous closure of the residual leakage was performed using an Amplatzer device.

The patient was presented to our congenital heart disease centre for re-evaluation due to symptomatic sRV failure. He was euvolaemic, functioned in New York Heart Association (NYHA) Class II and was treated with the highest tolerated dose of valsartan. Chest X-ray showed cardiomegaly and the electrocardiogram (ECG) showed a wide QRS of 180 ms with a right bundle branch block morphology (RBTB, Figure 1). The patient had an elevated N-terminal pro-brain natriuretic peptide (NT-pro-BNP) of 700 pg/mL and preserved renal function.He had an exercise capacity of 140 Watt (73% of predicted), VO_2max of 16.1 mL/min/kg (46% of predicted) at cardiopulmonary exercise testing. Transthoracic echocardiography and magnetic resonance imaging showed a severely reduced function [ejection fraction (EF) 22%] of the dilated sRV with at least moderate (Grade III) tricuspid valve regurgitation (TR) (*Videos 1*–*3*, Figure 2). Given the poor systolic sRV function, this TR was thought to have moderate to severe haemodynamic consequences for this patient.

Work up

Additional evaluation using transthoracic echocardiography showed sRV electromechanical dyssynchrony with a mechanical delay (septal to free wall of sRV) of 150 ms and the peak sRV free wall contraction

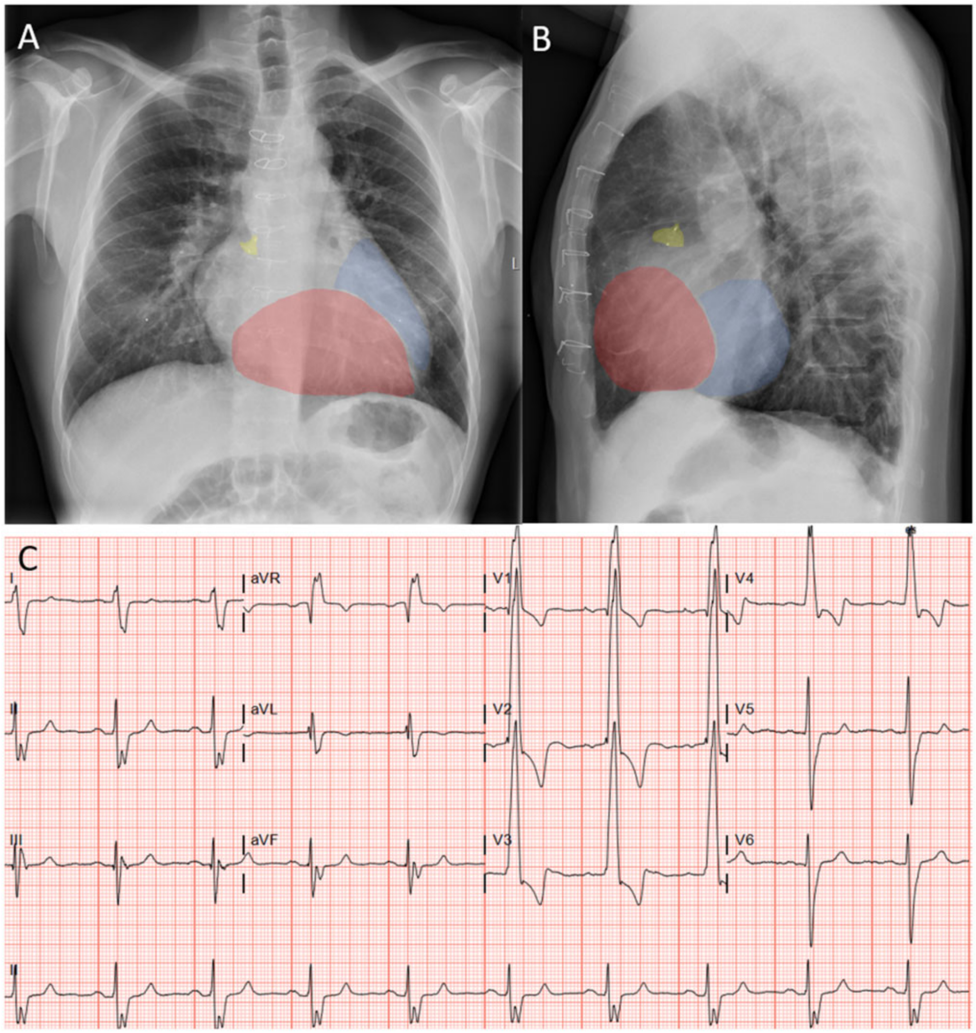
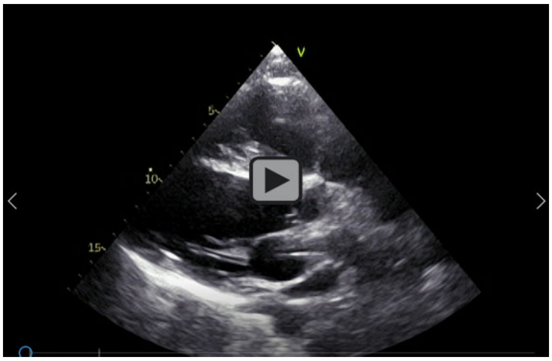


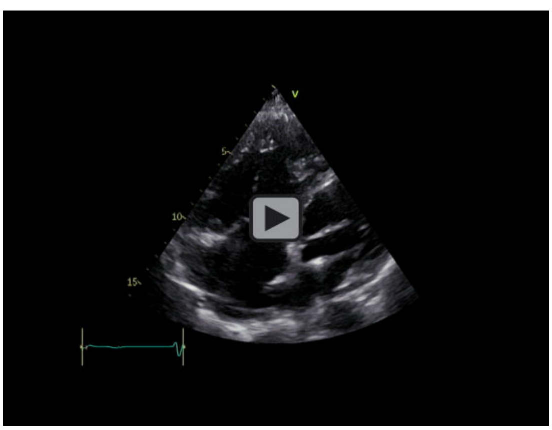
Figure 1 (*A*) Postero-anterior and (*B*) lateral chest X-ray image of the patient illustrating the cardiomegaly. (*C*) A 12-lead electrocardiogram with a broad QRS (180 ms) complex in a right bundle branch block configuration. Red: systemic right ventricle; blue: subpulmonic left ventricle; yellow: Amplatzer occluder device.

Video 5 Transthoracic echocardiography parasternal long-axis view before cardiac resynchronization therapy-defibrillator implantation showing the dilated systemic right ventricle and the overall severely reduced systolic function.

exceeded aortic valve closure by 60 ms, suggesting part of the sRV contraction was not contributing to the ejection phase of the cardiac cycle. These findings, combined with the broad QRS complex, suggested that sRV resynchronization could address the electromechanical delay and potentially improve the mechanical contraction efficiency. The patient underwent a heart catheterization for further evaluation. Angiography revealed no significant baffle leakage and there was no obstructive coronary artery disease. With a quadripolar catheter in the left ventricle (LV) and an ablation catheter in the sRV, the sRV was mapped. This confirmed that the septum was the site of earliest activation and the sRV basal free/lateral wall was the site of the latest activation (delay of 138 ms). An invasive haemodynamic evaluation of the intraventricular pressure gradient (*Dp*/*Dt*) was performed to assess the haemodynamic consequences of different pacing modalities (Figure 3). Various intervals and pacing modes were tested (including a.o. intrinsic activation, various AV intervals, LV and



Video 6 Transthoracic echocardiography apical view before cardiac resynchronization therapy-defibrillator implantation showing the dilated systemic right ventricle and the overall severely reduced systolic function.



Video 7 Transthoracic echocardiography apical view showing at least moderate (Grade III) tricuspid regurgitation before cardiac resynchronization therapy-defibrillator implantation.

sRV only and biventricular pacing modalities with various LV-sRV delay intervals). The optimal pacing site during sequential pacing (atrial-sRV) using intrinsic AV conduction (with 260 ms PR interval) resulted in QRS narrowing from >180 to 120–130 ms and an increase of the baseline *Dp/Dt* 1033 mmHg/s to 1196 mmHg/s (Figure 3). The increase of *Dp/Dt* of 16% suggested that CRT could lead to a significant hemodynamic improvement in this patient.[1] Due to the limited acoustic windows, the effects of the alternative pacing modalities on the functional TR could not be evaluated. Given the anatomy with the coronary sinus (CS) draining into de pulmonary venous atrium, a transvenous sRV lead placement into the CS tributary was not possible (Figure 2) and a hybrid approach was proposed.

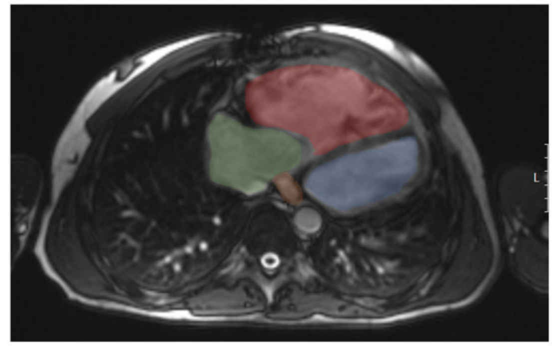


Figure 2 Transverse plane of the cardiac magnetic resonance imaging illustrating the anatomy and coronary sinus draining into the pulmonary venous return atrium (systemic circulation). Red: systemic right ventricle; blue: subpulmonic left ventricle; orange: coronary sinus; green: pulmonary venous return atrium.

Diagnosis and management

Although the criteria for CRT in sRV patients are not well defined, QRS duration alone is not a robust predictor.[2,3] Cardiac resynchronization therapy in sRV failure should therefore be considered on a case-by-case basis. Invasive haemodynamic evaluation with a *Dp/Dt* increase ≥15% is correlated with a clinical response to CRT.[1,3] Our patient had an increase of 16%, which was suggestive that he would be a responder. Current guidelines recommend that a primary prevention implantable cardioverter-defibrillator (ICD) may be considered (Level IIb) in patients with advanced sRV dysfunction (EF < 35%) who are in NYHA class II/III and have a wide QRS complex (>140 ms).[2] Our patient met these criteria, and after evaluation by a specialized team he was enlisted for a CRT-defibrillator (CRT-D) implantation with an epicardial sRV lead. In patients requiring a pacemaker/ICD, closure of any baffle leaks prior to transvenous lead placement is recommended.[2] Our patient had no significant baffle defect as assessed by heart catheterization. Current guidelines also recommend that patients with severe tricuspid regurgitation without significant sRV dysfunction (EF > 40%) should be considered (Level IIa) for tricuspid valve surgery.[2] However, given the poor sRV function in our patient with an EF of 22%, associated perioperative risks and the potential of adequate CRT to reduce TR severity, a multidisciplinary team advised to defer tricuspid valve surgery. The patient underwent an uncomplicated epicardial bipolar sRV lead implantation via an anterior thoracotomy. The lead was implanted on the basal sRV lateral/free wall and had an adequate sense (21 mV) and pacing threshold (1.2 mV/0.4 ms). This lead was tunnelled subpectorally towards the left subclavicular region to the pocket. An atrial pacing and a ventricular ICD leads were implanted through the subclavian vein into the systemic venous atrium and subpulmonary LV, respectively. The sense and pacing thresholds were acceptable and the leads were connected to a CRT-D pulse generator that was programmed accordingly.

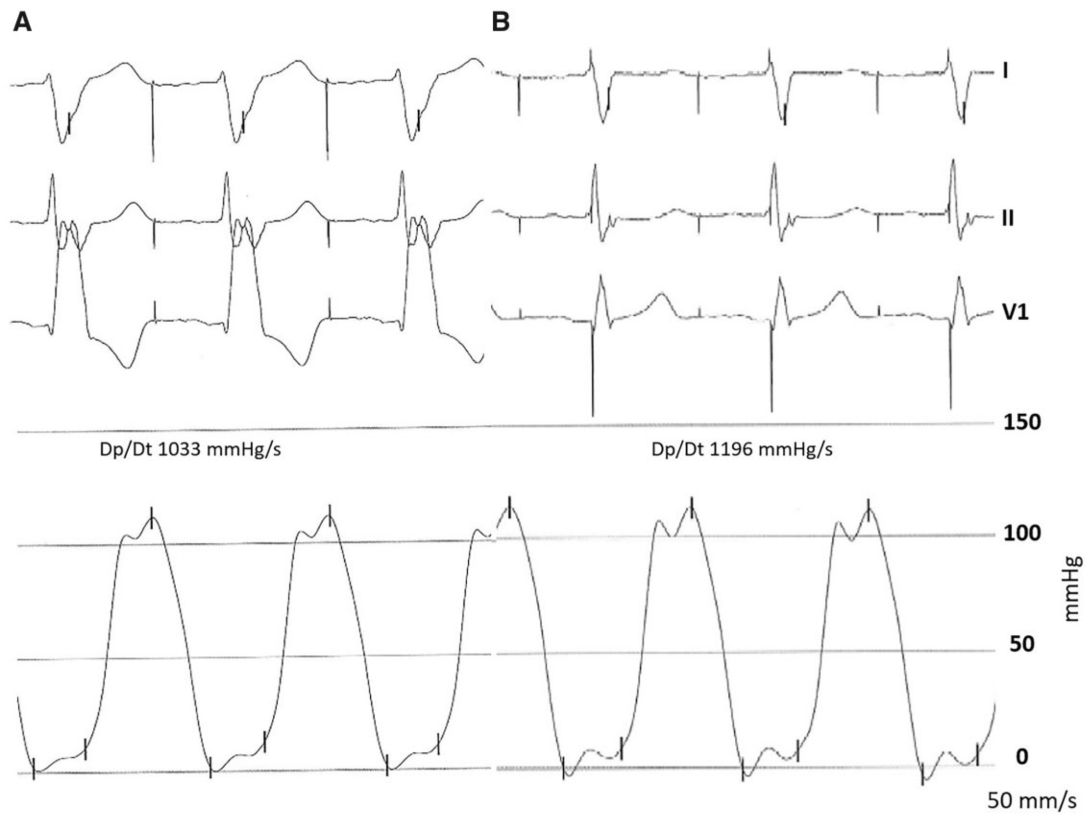


Figure 3 The intraventricular pressure curves registered during the invasive haemodynamic evaluation of the different pacing modalities. (*A*) During atrial pacing 90/min with intrinsic atrioventricular conduction and (*B*) during sequential pacing 90/min (atrial-systemic right ventricle pacing) with an atrioventricular delay of 260 ms.

Follow-up

Post-procedural ECG showed sinus rhythm with biventricular pacing with QRS duration of 130 ms. Chest X-ray confirmed adequate lead position and no signs of complications (Figure 4). Patient was discharged the day after the procedure.

The patient underwent periodic follow-up at the outpatient clinic. One year after, the procedure, he was in NYHA functional class I–II and no heart failure related admissions occurred. Device interrogation showed adequate biventricular pacing and no tachyarrhythmia episodes. The patient showed improved exercise capacity at cardiopulmonary exercise testing [156 Watt (83% of predicted), VO_2max of 19.1 mL/min/kg (55% of predicted)]. Echocardiography showed a dilated sRV with an improved, moderately reduced sRV function and mild TR (reduction from Grade III+ to Grade II; Supplementary material online, *Videos S1–S3*).

Conclusion(s)

In conclusion, one should be aware of the systolic dysfunction prone sRV in TGA patients after atrial switch. Secondary TR, usually due to annular dilatation and restriction, can aggravate the course of sRV failure. Criteria for CRT in this patient group are not well defined and CRT should be considered on a case-by-case basis. Extensive echocardiographic and invasive haemodynamic evaluation prior to device implantation can help assess the potential benefit of CRT in sRV patients. Transvenous approach for CRT can be limited by baffles and the CS draining into de pulmonary venous atrium. Baffle patency and function should be evaluated prior to transvenous lead implantation. A hybrid (transvenous and epicardial approach) for effective CRT can be considered. Resynchronization may lead to improvement of sRV function, reduction in TR and improvement in the functional capacity of the patient.

Patient perspective

Born with a transposition of the great vessels and having undergone the atrial switch procedure in the 1970s, I am trained as a general practitioner, married and father of two daughters. Until the age of 40, I had a reduced, but stable endurance. However, from that age on my condition gradually declined. I was not able to cycle with a non-

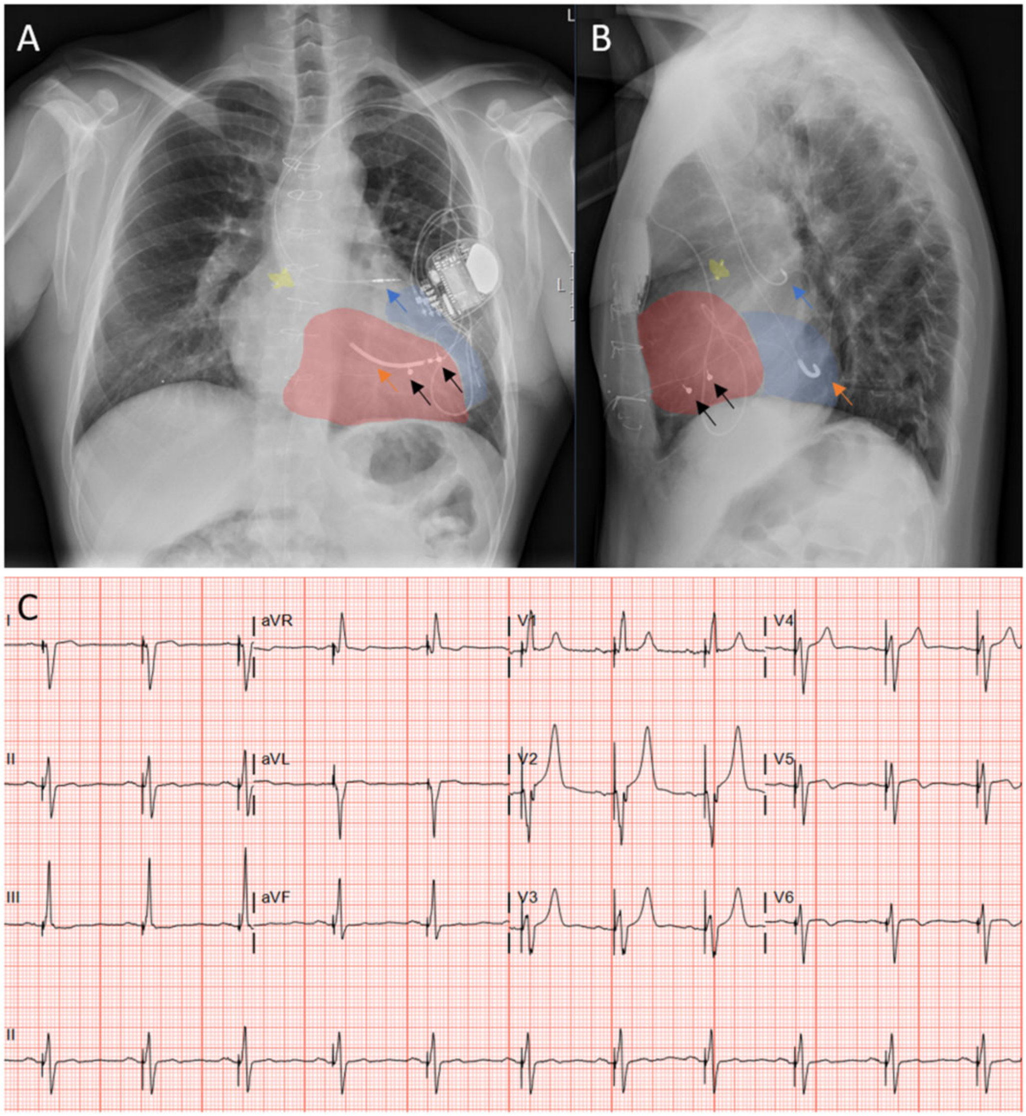


Figure 4 (*A*) Postero-anterior and (*B*) lateral chest X-ray image of the patient with the hybrid cardiac resynchronization therapy-defibrillator *in situ*. (*C*) A 12-lead electrocardiogram during biventricular pacing showing significant QRS narrowing. Red: systemic right ventricle; blue: subpulmonic left ventricle; yellow: Amplatzer occluder device. Black arrow: epicardial leads on systemic right ventricle; blue arrow: atrial lead in the systemic venous return atrium; orange arrow: implantable cardioverter-defibrillator shock lead in the subpulmonic left ventricle.

electric bike anymore, and at the end of a working week I felt exhausted.

When I was almost 43 years old, a CRT-D was implanted. Immediately after implantation, I noticed that my heartrate was lower, and my chest felt calmer and less 'bumpy'. After implantation, my cardiologist advised a cardiac rehabilitation programme. Since then, I consistently walk at least 6500 steps every day (measured by smartwatch). Although the improvement in endurance in the first years after implantation was slow, the feeling of being exhausted at the end of a week improved quickly. Now, I am able to do more activities in a single day and week, and to date my endurance is still improving.

Lead author biography

Marieke Nederend (1993) is currently a PhD candidate at the Leiden University Medical Center, the Netherlands. Her thesis is focusing a clinical outcomes in (the ageing) congenital heart disease, centralizing on Fontan circulation and systemic right ventricular failure. During her time in the clinic, the work described in this case report was performed.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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