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CLASSICAL CASE REPORT
Heart failure

Sudden cardiac death after implantation of a cardiac resynchronization therapy pacemaker: a case report illustrating that not always *less is more*

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Background Cardiac resynchronization therapy (CRT) improves symptoms and survival in selected patients with systolic heart failure and ventricular conduction delay. In subjects without prior life-threatening ventricular arrhythmia, clinicians have to select between implanting a CRT pacemaker (CRT-P) or a more complex device with additional defibrillator capability (CRT-D). This individual decision can be challenging in light of the available evidence and the potential risks and benefits.

Case summary A 76-year-old male with non-ischaemic cardiomyopathy, heart failure New York Heart Association Class III, left bundle branch block (QRS duration 185 ms) and a left ventricular ejection fraction of 30% despite optimal medical therapy was indicated for CRT. In light of the patient characteristics and clinical condition, a CRT-P device was implanted. No complication occurred, and the patient was discharged after an appropriate device function was confirmed. Despite the clinical improvement, he died suddenly without prior symptoms approximately 2 months thereafter. Post-mortem device interrogation provided no evidence for device malfunction and confirmed sudden cardiac death (SCD) due to spontaneous ventricular fibrillation.

Discussion Patients indicated for CRT often have overlapping internal cardioverter defibrillator indication for the primary prevention of SCD. By weighing individual risks and potential benefits, clinicians have to decide whether to implant a CRT-P (*less is more*) or a more complex and costly CRT-D device. Despite careful consideration of patient characteristics and clinical conditions, however, SCD can occur in subjects categorized as *low risk* and implanted with a CRT-P. More data from randomized clinical trials are needed to better support physicians in the often challenging process of selecting the most appropriate device for CRT.

Keywords Heart failure • Cardiac reynchronization therapy • Pacemaker • Sudden cardiac death • Cardiac implantable electronic device • Case report

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Learning points

- Patients indicated for cardiac resynchronization therapy (CRT) often have an overlapping internal cardioverter defibrillator (ICD) indication for the primary prevention of sudden cardiac death (SCD). It is uncertain, however, if subjects with CRT indication and no prior life-threatening ventricular arrhythmia benefit from the implantation of a more complex and costly device with additional defibrillator capability (CRT-D).
- According to current ESC guidelines, clinicians should consider individual patient characteristics and clinical conditions to decide between CRT-P or CRT-D implantation. However, SCD due to ventricular fibrillation may still occur as a tragic adverse event in subjects categorized as 'low risk' and implanted with a CRT-P.
- More evidence from randomized clinical trials is therefore needed to better guide and support clinicians in the often challenging process of device selection in patients indicated for CRT.

Introduction

Cardiac resynchronization therapy (CRT) improves symptoms and survival in selected patients suffering from heart failure with reduced left ventricular ejection fraction (HFrEF) and ventricular conduction delay.[1,2] Cardiac resynchronization therapy can be delivered with a biventricular pacemaker (CRT-P) or with a more complex device that also incorporates an implantable defibrillator (CRT-D). It is still uncertain if patients without prior life-threatening ventricular arrhythmia should rather receive a CRT-P or a CRT-D device.[1,3] The latter may provide additional protection against sudden cardiac death (SCD), but this potential benefit could be outweighed by the higher risk for device-related complications (e.g. infection, inappropriate shocks),[4,5] shorter battery longevity, and higher device costs for CRT-D vs. CRT-P. Thus, the selection of the appropriate CRT device is an individual and often challenging decision for the treating clinician.

In this report, we present the case of an elderly patient with a non-ischaemic cardiomyopathy (NICM) that received a CRT-P device in line with current ESC guidelines and after careful evaluation of patient characteristics and clinical conditions. Despite clinical improvement with CRT, the patient unfortunately died suddenly 2 months after the procedure. Post-mortem device interrogations confirmed SCD due to ventricular fibrillation. Current scientific evidence and future perspectives for CRT-P vs. CRT-D device selection are discussed in light of this tragic case.

Case presentation

A 76-year-old white male was referred for cardiac evaluation because of progressive shortness of breath and chest tightness upon physical exercise. Symptoms had been experienced for more than 2 years, had slowly increased over time, and occurred now upon mild physical exertion. The patient took a statin against hypercholesteraemia and stopped cigarette smoking 2 decades ago. Physical examination revealed a body mass index 27.1 kg/m^2 (overweight category), a regular heart rate of 79/min, a blood pressure of 140/80 mmHg, no ankle oedema, no jugular vein distension, and no heart murmur or pulmonary rales upon auscultation. The electrocardiogram (ECG) showed normal sinus rhythm and AV-conduction but a 'typical' left bundle branch block (LBBB) with a QRS width of 185 ms (*Figure 1A*). Echocardiography revealed mild left ventricular (LV) dilatation (LV end-diastolic diameter 58 mm) with visual LV asynchrony and depressed systolic function [estimated left ventricular ejection fraction (LVEF) 30%]. Upon blood testing, haemoglobin and kidney function were normal, and LDL cholesterol was elevated (190 mg/dL). We initiated heart failure medication (Bisoprolol 1.25 mg/day, Ramipril 1.25 mg/day) and recommended coronary angiography.

A week later, invasive testing excluded coronary artery disease (*Figure 2*, top). Heart failure medication was escalated (Bisoprolol 2.5 mg/day, Ramipril 2.5 mg/day, Spironolacton 25 mg/day), and additional dose adjustment was recommended. In addition, cardiac magnetic resonance imaging (CMR) was scheduled. Cardiac magnetic resonance imaging confirmed a severely impaired systolic LV function

Timeline

01/20	Progressive shortness of breath and angina upon exertion in the last years	
02/20	Heart failure (HFrEF)	New York Heart Association (NYHA) Class III
	Left bundle branch block	QRS 185 ms
	Reduced left ventricular systolic function	left ventricular ejection fraction (LVEF) ~30%
	Heart failure medication initiated	ACE inhibitor + beta-blocker
02/20	Coronary angiography	no coronary artery disease
	Heart failure medication intensified	ACE inhibitor ↑ + betablocker ↑ + MR antagonist
02/20	Cardiac magnetic resonance imaging	LVEF 25% Marked mechanical dyssynchrony No relevant LV fibrosis
04/20	Heart failure (HFrEF)	NYHA class III (↔)
	Left bundle branch block	QRS 185 ms
	Reduced left ventricular systolic function	LVEF ~30%
04/20	CRT-P implantation	QRS 142 ms
05/20	Heart failure (HFrEF)	NYHA Class II (↓)
06/20	Sudden death CRT device interrogation (post-mortem)	No evidence for device malfunction stored episode of ventricular fibrillation

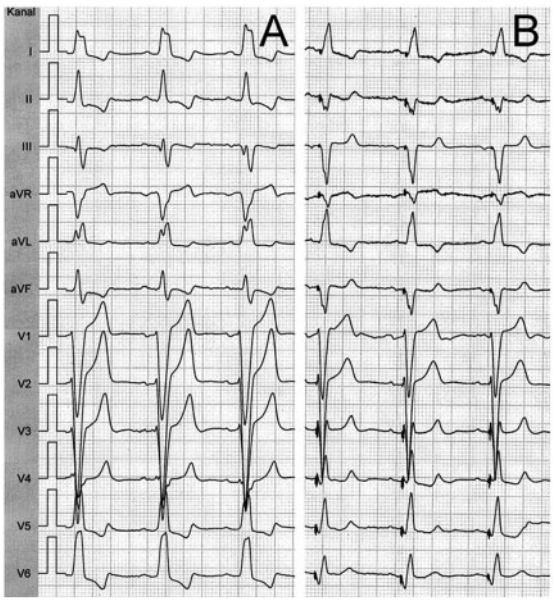
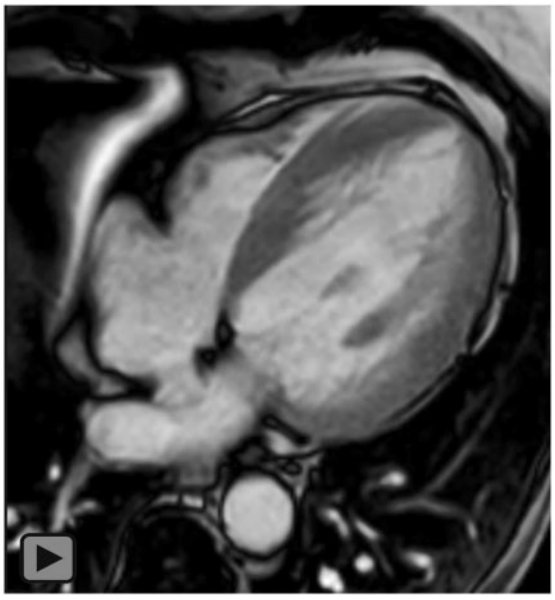
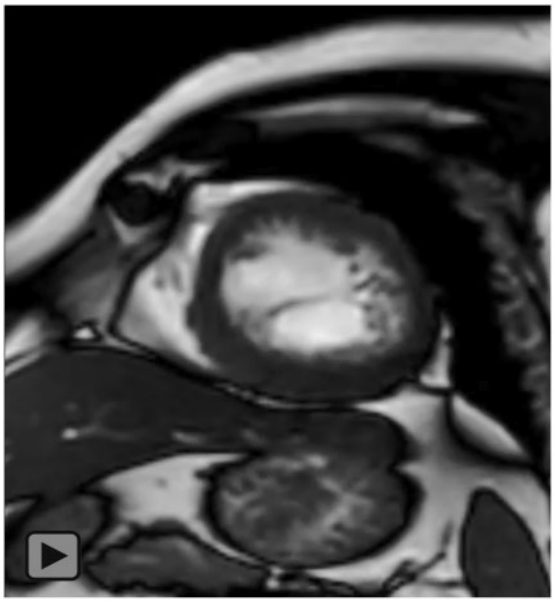


Figure 1 Electrocardiogram (ECG) before and after cardiac resynchronization therapy implantation. Twelve-lead ECG (25 mm/s) showing sinus rhythm and complete 'typical' left bundle branch block with a QRS duration of 185 ms prior to cardiac resynchronization therapy (*A*) and marked narrowing of the QRS (142 ms) upon implantation of a cardiac resynchronization therapy pacemaker (*B*). Note ventricular fusion with biventricular pacing due to nominal activation of the SyncAV™ algorithm (delta cardiac resynchronization therapy -50 ms).



Video 1 Cardiac magnetic resonance imaging (steady-state free precession cine imaging in horizontal long axis) showing marked dyssynchrony and severly depressed left ventricular ejection fraction.



Video 2 Cardiac magnetic resonance imaging (steady-state free precession cine imaging in contiguous short axes) with marked dyssynchrony and severly depressed left ventricular ejection fraction.

(EF 25%) due to global hypokinesia and asynchrony (*Videos 1* and *2*). The LV was found to be markedly dilated (LVEDVI 152 mL/m^2, normal ≤97 mL/m^2) with hypertrabeculation and hypertrophy (LVMMI 112 g/m^2, normal ≤78 g/m^2). Late gadolinium enhancement imaging 15 min after gadolinium administration did not reveal significant mid-myocardial fibrosis, infarction scar, or post-myocarditis remnants (*Figure 2*, bottom). Some subepicardial fibrosis was found at the inferior right ventricular insertion in the interventricular septum (*Figure 3*).

Almost 3 months later, the patient presented for a follow-up. The medication was unchanged (heart failure medication was not up-titrated due to low blood pressure), and symptoms had not improved significantly. Electrocardiogram showed sinus rhythm with a rate of 64/min and the pre-existing LBBB. Echocardiography revealed no significant change in LV dilatation and systolic dysfunction.

In light of the above findings, CRT was indicated. In consideration of the available evidence and after weighing the pros and cons for and against primary-prophylactic internal cardioverter defibrillator (ICD) therapy (as summarized in the current ESC guidelines[1]) we scheduled the patient for implantation of a CRT-P device.

A week later, a Quadra Allure MP™ 3562 CRT-P (St. Jude Medical/Abbott) was implanted. Chest X-ray on the day thereafter confirmed stable lead position with the quadripolar LV electrode in a lateral position and excluded a pneumothorax (*Figure 3*). On ECG, a reduction in QRS duration from the initial 185 ms to 142 ms was observed with biventricular pacing (*Figure 1B*). Two days after CRT-P implantation the patient was discharged without complications. Lead

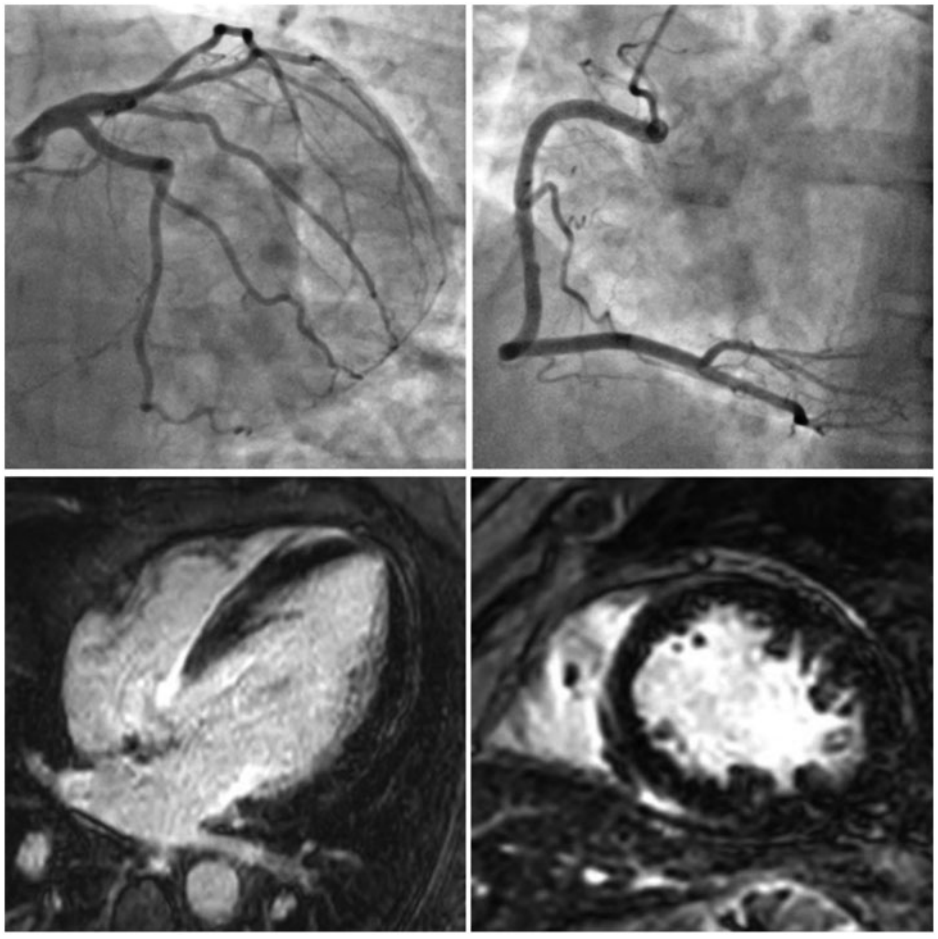


Figure 2 Exclusion of coronary artery disease and relevant left ventricular fibrosis. *Top:* Angiogram of the left (left) and right (*right*) coronary artery with no evidence for relevant atherosclerosis and exclusion of significant stenosis. *Bottom:* Cardiac magnetic resonance imaging with late gadolinium enhancement providing no evidence for relevant mid-myocardial left ventricular fibrosis, infarction scar, or typical post-myocarditis remnants.

values and device programming at the time of discharge are summarized in *Table 1*.

Approximately 6 weeks later, shortly before regular follow-up, the patient was unfortunately found dead on the sofa, where he had been watching TV the same night. His wife reported that his symptoms had improved with the device, that he had no acute complaints shortly before, and that his medication had not changed within the previous weeks. Sudden cardiac death was suspected, and we decided to interrogate the implanted device. Automatically measured lead values had been stable over time and provided no evidence for device dysfunction. However, corresponding with the SCD, a ventricular high rate episode had been stored (*Figure 4*). Electrogram analysis confirmed that ventricular fibrillation had occurred spontaneously, without preceding sinus tachycardia or inappropriate pacing impulse delivery.

Discussion

A significant overlap in the indication for CRT and primary-prophylactic ICD therapy exists in patients with HFrEF and ventricular conduction delay.[1] Cardiac resynchronization therapy alone,

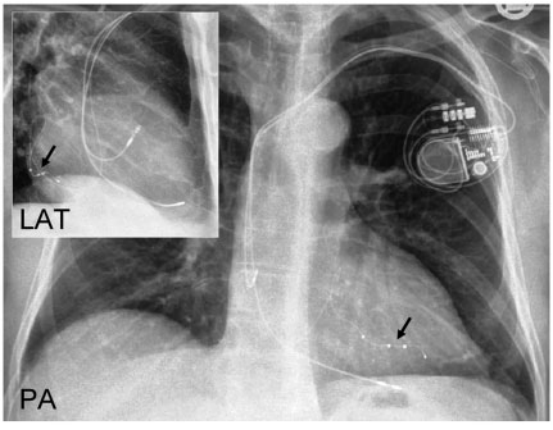


Figure 3 Chest X-ray after CRT-P implantation. Stable lead position in the right atrium, the right ventricular apex and a lateral vein of the coronary sinus. No evidence for pneumothorax. LAT, lateral view; PA, posterior-anterior view.

Table 1 Device programming and lead values and prior to hospital discharge

Pacing parameter	Lead value	Atrium	RV	LV
DDD 50–130/min	Signal amplitude	2.6 mV	>12 mV	–
SAV 100 ms	Pacing threshold	0.5V	0.4 V	0.9 V
PAV 140 ms	Pacing impedance	480 Ω	600 Ω	730 Ω
LV→RV 30 ms				
Impulse amplitude		1.5V (Auto)	2.0V (Auto)	2.0V (Auto)
Impulse width		0.5 ms	0.5 ms	0.5 ms
Sensitivity		0.3 mV (Auto)	0.5 mV (Auto)	–

LV→RV, Interval between left ventricular and right ventricular pacing; PAV, paced AV interval; SAV, sensed AV interval.

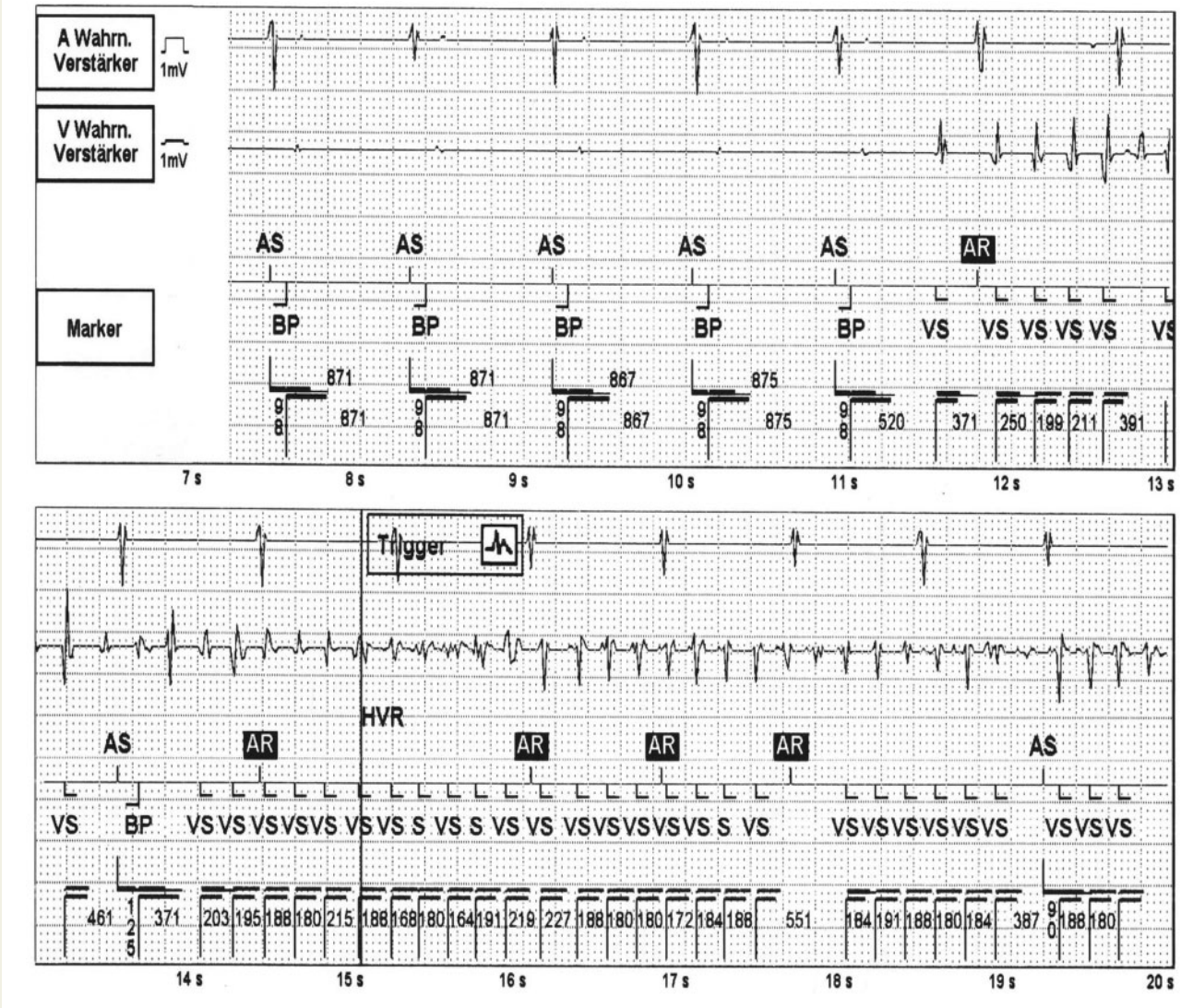


Figure 4 Stored electrograms showing ventricular fibrillation. Post-mortem device interrogation showing an episode of ventricular fibrillation, correlating with the time of sudden death. Atrial signals on top, ventricular signals below, marker channels at the bottom. Note normal sinus rhythm (AS) with adequate biventricular pacing (BP) prior to spontaneous initiation of rapid polymorphic ventricular tachycardia (VS/HVR).

however, does already lead to a significant reduction in mortality and risk of sudden death,[6] and no randomized trial has yet proven an incremental survival benefit of CRT-D over CRT-P.[3] The ESC guidelines on cardiac pacing and CRT[1] do therefore identify patient characteristics and clinical conditions that physicians should consider for individual device selection. Listed factors in favour of CRT-D are ischaemic heart disease, stable heart failure NYHA II, lack of co-morbidity, and higher life expectancy. Accordingly, several recent studies found no evidence for a significant benefit of CRT-D over CRT-P implantation in subjects with NICM,[7–9] particularly within the subgroup aged ≥ 75 years[10,11] or if relevant LV mid-wall fibrosis had been excluded by CMR imaging.[12]

The patient in our case had a Class I (Level A) indication for CRT (symptomatic heart failure, QRS duration >150 ms with left LBBB morphology, and LVEF ≤35% despite optimal medical therapy) according to current ESC guidelines.[1,2] The decision to implant a CRT-P device (and no CRT-D) was based on the following individual factors: (i) age >75 years, (ii) NICM, (iii) heart failure NYHA Class III, and (iv) no relevant LV fibrosis on CMR. Despite thorough device selection, the patient unfortunately suffered SCD 2 months after CRT-P implantation.

Earlier reports noted that initiation of CRT may precipitate sustained ventricular tachyarrhythmias in some rare instances.[13] This uncommon ventricular pro-arrhythmia, however, always occurred within the first week after CRT device implantation, and is thus unlikely the cause of SCD in our case. In a subgroup of patients with NICM, Leyva *et al.*[7] observed a total mortality of 38% during a median follow-up of 4.7 years after CRT-P implantation. SCD was infrequent and occurred in 7% of the subjects during the same period of time. Gras *et al.*[11] did not specifically analyse rates of SCD but found no significant difference in total mortality between CRT-P and CRT-D in 2962 patients with NICM and age >75 years.

In our patient, post-mortem device interrogation confirmed SCD by revealing spontaneous and sustained ventricular fibrillation. Tseng *et al.*[14] previously outlined the value of post-mortem device interrogation to exclude device malfunction or non-cardiac causes of sudden death in patients with cardiac implanted electronic devices. No evidence for device malfunction was found when all stored data were reviewed in our patient.

To solve (or at least attenuate) the clinical dilemma of decision making for clinicians in the future, a randomized clinical trial (RESET-CRT)[3] is currently comparing the impact of CRT-P vs. CRT-D on total mortality. Until the results of this study become available, it is up to the treating physician to estimate whether *less is more*.

Lead author biography

Dirk Vollmann is a cardiologist with a clinical focus on interventional electrophysiology. He graduated from medical school and finished his doctoral thesis in Gießen and completed his training in internal medicine and cardiology at the University Clinic Göttingen. After scientific work at the Cardiovascular Research Institute in Maastricht (CARIM) and the Brigham and Women's Hospital in Boston, Dr Vollmann specialized in clinical electrophysiology and became a Professor of Medicine at the University of Göttingen. Since 2014, he works at the Herz- & Gefäßzentrum (HGZ) Göttingen / Agaplesion Krankenhaus Neu Bethlehem.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as Supplementary data.

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's relative in line with COPE guidance.

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