His Bundle pacing for congenital complete AV block: an attempt to fix a broken heart ?

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Abstract

Introduction. The treatment of congenital complete AV block (CCAVB) is burdened by RV-associated ventricular dysfunction at long-term in a subgroup of patients. Methods and Results. Two CCAVB adolescents with mild systolic dysfunction associated to VVIR pacing reached elective pacemaker replacement after 10±1 years. They were upgraded to physiologic stimulation by restoring AV synchrony and ventricular activation via His bundle pacing (HBP). At 9-months follow-up both had reverse left ventricular (LV) remodeling: LV end-diastolic volume index decreased from 89±4 to 70±7 ml/m2, LV end-systolic volume index decreased from 49±1 to 32 ml/m2, LVEF increased from 43±1% to 53±4%. Conclusions. HBP can improve LV function in CCAVB adolescents. It should be considered in the setting of LV dysfunction associated to RV pacing, and should be explored as first-choice treatment from late childhood onward.

Background

The incidence of congenital complete atrioventricular block in a normal heart (CCAVB) is 0.5-1/15.000 births (1) and is due to failure of atrio-ventricular (AV) nodal conduction with preservation of the His Purkinje system.

The implantation of a pacemaker is recommended for symptomatic patients and for asymptomatic patients with ventricular dysfunction or at risk of syncope and sudden death; nonetheless, right ventricular (RV) pacing can have detrimental effects on cardiac function (2-4). Left ventricular (LV) remodeling can occur, and be associated to exercise intolerance/heart failure in up to 20% of adult patients (5), congestive heart failure being observed in 7-10% of patients paced because of CCAVB (3, 4).

While RV pacing- associated cardiomyopathy benefits from CRT, its indication is less clear in pediatric than in older patients, owing to the low prevalence of dilated cardiomyopathy (4). Since the His-Purkinje system is preserved in CCAVB patients, it can be expected that His bundle pacing (HBP) would be a suitable treatment for CCAVB patients with RV pacing–associated LV dysfunction, and could become the gold standard for CCAVB in the future.

Case 1. An 18-years old girl with a history of CCAVB had a VVIR pacemaker implanted at 9. Elective replacement was indicated after 9 years of 90% VVIR pacing; echocardiographic evaluation showed slightly increased LV volume (LVEDVi=86 ml/m^2 and LVESVi=50 ml/m^2) with a mildly depressed LVEF (42%) and moderate mitral and tricuspid regurgitation. The 12-lead ECG showed sinus rhythm with complete atrioventricular block and a ventricular-paced QRS (duration 164 ms, Fig. 1, panel A). While in need to open the pocket for device replacement, we planned an upgrade to triple-chamber pacemaker with HBP to

improve cardiac function by restoring the physiologic atrioventricular, interventricular and intraventricular synchronicity. An active-fixation atrial lead was advanced in the right atrium and a SelectSecure 3830 pacing lead was delivered by a Medtronic C315His catheter (Medtronic Inc, Minneapolis MN) (Fig.1). Selective HBP was achieved at 1.5 V@1.0 ms pacing threshold. The 3 leads were connected to a Serena CRT-P (Medtronic Inc, Minneapolis MN); SelectSecure was connected into the LV port. Atrioventricular physiologic pacing (DDD, lower rate 40 bpm and upper rate 170 bpm) with selective HBP was programmed in LV-only mode, with a QRS duration and morphology identical to the native QRS at a sensed AV interval of 100 ms (Fig. 1, panel C). At 9-month follow-up the HBP threshold was stable (1.5 V@1.0 ms), with 100% of pacing in DDD mode. Echocardiography showed reverse remodeling: LVEDVi=65 ml/m^2, LVESVi=32 ml/m^2, LVEF= 50%, mitral and tricuspid regurgitation decreased to mild (Table).

Case 2. A 16-years old male with CCAVB was implanted at 5 with a VVIR pacemaker; in 2019 the device reached replacement indication. Echocardiography showed mildly reduced LVEF (44%), LVEDVi=92 ml/m^{2}and LVESVi=48 ml/m^2, mild aortic regurgitation. Paced QRS was 147 ms (Fig 2, panel A) while the intrinsic junctional rhythm at 33 bpm had a QRS duration of 104 ms. Upgrading with an active fixation right atrial lead and a SelectSecure 3830 pacing lead (Medtronic Inc, Minneapolis MN) was achieved, with a selective HBP threshold as 0.75 V@0.6 ms (fig. 2, panel D. Physiologic HBP was delivered by a Serena CRT-P programmed as in the former patient. At 9-month follow-up a significant improvement of ventricular function was observed: LVEDVi=76 ml/m^2; LVESVi=32 ml/m^2; LVEF=57% (Table). HBP threshold increased at 1.5V@0.6ms, showing minimal para-Hisian capture at 3V@0.6ms (Fig.2, panel B).

Discussion

Our adolescent patients had an upgrade at their first pacemaker replacement after 9 to 11 years of RV pacing, exhibiting improvement of LV function and exercise tolerance following restoration of AV synchrony and of ventricular activation via the His-Purkinje network. CCAVB in patients with a normal heart disrupts 2 of the 3 electrophysiological determinants of cardiac performance: atrioventricular synchrony and chronotropic response. Though CCAVB patients can have a normal physical development and, occasionally, a normal life expectancy, the majority have signs of LV dysfunction, atrial arrhythmias, or symptomatic heart failure at long term follow-up. When a pacing indication ensues, chronotropic response is restored at the expense of the loss of inter-/intraventricular synchrony, with or without restoration of AV synchrony depending on pacing mode (DDD vs VVIR).

In this perspective, key questions in CCAVB are yet unanswered owing to the impossibility to run methodologically correct studies in this pediatric population. The timing to consider pacing is individually based. The choice of the pacing site and mode has been mostly debated in literature (2, 6, 7): despite convincing evidence of superior cardiac performance and exercise tolerance with AV-synchronous pacing, VVIR mode seems a reasonable choice as the initial pacing strategy in small children to minimize intravascular hardware (risk of vein thrombosis) and lead malfunction, given the modest difference in clinical endpoints and quality of life in pre-adolescence (8, 9).

A first pacemaker implant or replacement in adolescence is a different setting, because key decisions are taken for long-term cardiac pacing in a view to restore - possibly - all the 3 electrophysiologic determinants of cardiac function. A mild LV systolic dysfunction, especially when associated to functional mitral or tricuspid regurgitation and initial left atrial enlargement, is a clinical hint of the RV pacing detrimental effect, and may promote upgrading the system to restore cardiac synchronicity. CRT is well known to improve cardiac function in RV pacing-induced heart failure/LV dysfunction (10); recent evidence, however, points toward a similar effect of HBP and CRT in this setting, both in terms of LV function and clinical status improvement (11). These results are not surprising, given the comparable efficacy reported for HBP and CRT in heart failure patients, with a possible beneficial effect of HBP also in non-responders to conventional CRT (12-14).

A single case of cardiac resynchronization via direct HBP in a CCAVB patient with RV pacing-associated cardiomyopathy has been reported to date (15), highlighting the concept of reversible LV dysfunction that can be corrected by restoration of the normal activation pathway via the His-Purkinje network. Our experience

with milder degrees of LV dysfunction suggests a role for the preservation of LV mechanics at long term in CCAVB with persistent His-to-ventricle conduction, when the first replacement in adolescence offers the opportunity to upgrade the pacing system.

The ongoing development of dedicated tools and the improved skillfulness in HBP implantation have now set the ground for the expansion of this pacing modality also to CCAVB patients (14).

Limitations . The observations about these two patients need to be confirmed in a large series of CCAVB patients. Moreover, some caveats are to be considered, such as: persistence of conduction in the His-Purkinje network at long term; minimization of intravascular leads that dwell lifelong in young patients; device longevity when a moderate-to-high HBP threshold dictates a high current drain, as the number of replacements is a main predisposing factor to infection (16). Technical aspects like the amount of lead slack needed to accommodate for patients' growth are better addressed in late rather than in early childhood.

Conclusions . Taken the abovementioned points as a cautious habit at innovation, we believe that HBP should be explored as the first-choice strategy in CCAVB undergoing pacemaker implantation in late childhood, and in CCAVB candidates to upgrading because of RV pacing-associated LV dysfunction.

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Table . Main characteristics of the two patients.

Patient Age (years)		18	16
VVIR pacing duration (years)		9	11
LV EDVi (ml/m^2)	Baseline	86	92
	Follow up	65	76
LV ESVi (ml/m^2)	Baseline	50	48
	Follow up	32	32
LV EF (%)	Baseline	42	44
	Follow up	50	57
AV valves	Baseline	moderate	mild
Regurgitation	Follow up	mild	mild
6 MWHT (meters)	Baseline	570	740
	Follow up	790	990
His Pacing	Implantation	1.5V@1ms	0.75V@0.6
Threshold	Follow up	1.5V@1ms	1.5V@0.6

AV=Atrio-ventricular; EDVi= end-diastolic volume index; EF= ejection fraction; ESVi=end-systolic volume index; LV= left ventricular; 6 MHWT= 6-minutes hall walking test; VVIR= single chamber right ventricular pacing.

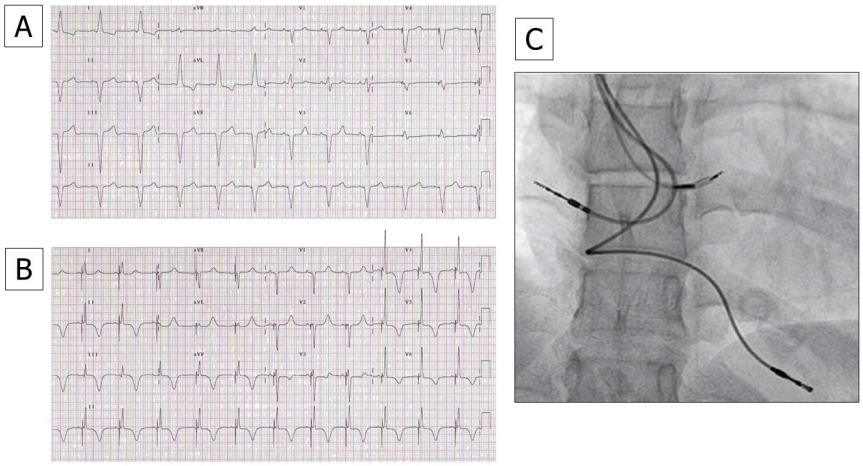

Fig 1. Panel A. *12-lead ECG showing RV pacing in DDD mode.* **Panel B.** *12-lead ECG showing selective HBP.***Panel C.** *Fluoroscopic view of HBP lead during implantation.*

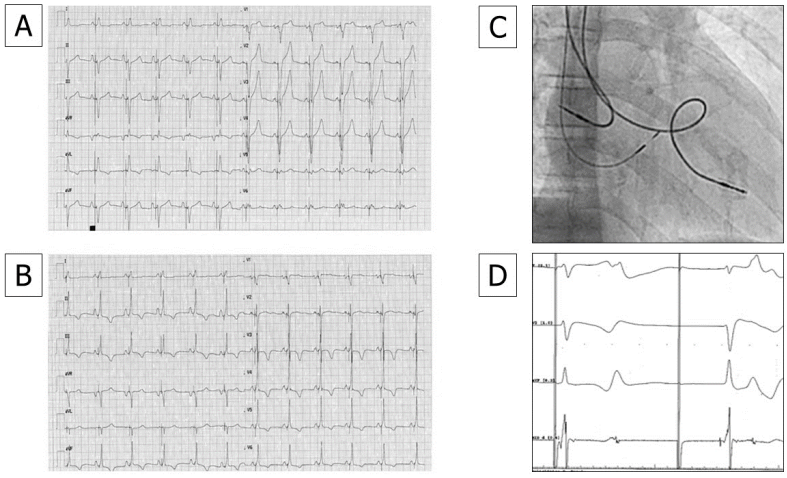

Fig 2. Panel A. *12-lead ECG showing RV pacing in DDD mode.* **Panel B.** *12-lead ECG showing para-Hisian pacing.***Panel C.** *Fluoroscopic view of HBP leads during implantation.* **Panel D.** Selective *His bundle capture threshold during the implant: loss of capture is followed by a junctional escape beat.*