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Improved symptoms, exercise capacity and homogeneity of cardiac deformation through conduction system pacing in a patient with symptomatic left bundle branch block

Short Title: His-Bundle-Pacing for symptomatic left bundle branch block

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Left Bundle Branch Block, Symptomatic, Painful, Conduction System Pacing, His-Pacing

Abbreviations
LBB - Left bundle branch block
HBP - His-bundle pacemaker

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Introduction

Painful left bundle branch syndrome is a clinical entity consisting of exertional angina and rate-dependent left bundle branch block (LBBB), affecting patients of all age and sex (1). Because of potentially co-existing other cardiac diseases (i.e. cardiomyopathy, coronary artery disease) that may mimic both LBBB and symptoms, the true prevalence is unknown, but less than 60 cases have been reported so far (1). Diagnostic criteria do not officially exist, but simultaneous onset of LBBB and angina during exercise test support the diagnosis. Pacemaker implantation has been reported to alleviate symptoms; however, high percentages of right ventricular pacing may induce cardiomyopathy, whereas implantation of a cardiac resynchronization therapy device carries an additional short- and long-term complication risk. Conduction-System-Pacing may present a safe and effective alternative pacing method (2), but the effect of this type of pacing in patients with painful LBBB syndrome has not yet been studied. We report a case of painful LBBB with symptom amelioration, increased exercise capacity and improved homogeneity of cardiac deformation after implantation of a His-bundle pacemaker.

Case report

A 45-year-old female patient was referred to our institution for evaluation of progressive exercise intolerance associated with crushing thoracic pain and breathlessness. Symptoms started 9 years prior with occurrence during strong exercise but were progressive for the last years to the extent of restricting everyday exercise capabilities such as grocery shopping. Previous medical work-up revealed no pulmonary cause, while cardiac evaluation documented an intermittent left bundle branch block (LBBB) with normal echocardiographic evaluation. Previous empirical therapy with a calcium channel blocker for suspected vasospastic angina or microcirculatory ischemia and with bronchodilator-inhalation for suspected bronchial asthma was unsuccessful. Also, cardiac rehabilitation with daily exercise sessions had not yielded beneficial results. During normal sinus rhythm (heart rate below 75 bpm), no bundle branch block or repolarization abnormalities were noted. Holter-monitoring, however, revealed rate-dependent left bundle branch block coinciding with the patient’s symptoms starting at a heart rate of 75/min (Figure 1). Exercise stress testing demonstrated reduced exercise capacity (76W = 60% of age and sex adjusted mean, VO2 max 14.4ml/min*kg = 52% of age and sex adjusted mean) with a decreased maximal O2-pulse of 7 ml/beat (= 64% of age and sex adjusted mean), with the LBBB being present throughout the examination (Figure 2). Cardiac MRI was unremarkable without evidence of
ischemia or fibrosis. However, both MRI and echocardiography demonstrated typical dysynchronous motion of the interventricular septum during left bundle branch block. Electrophysiologic study revealed normal intracardiac timing intervals (His ventricle time 48ms) both with and without left bundle branch block, with the latter manifesting below an atrial pacing cycle length of 830ms. Pacing at the area of the His bundle revealed non-selective His capture (stimulation of the His bundle as well as the surrounding myocardium) with a narrow QRS (78ms) without evidence of LBBB. Following the diagnosis of symptomatic left bundle branch syndrome and extensive discussion about the risks and benefits of the available treatment options, the patient underwent successful dual-chamber His-bundle pacemaker (HBP) implantation using a SelectSecure 3830 electrode (Medtronic, Minneapolis, MN, US) through a non-deflectable C315 sheath (Medtronic). Continuous selective His-capture with correction of LBBB was documented with a unipolar threshold of 0.9mV/1.0ms. Rate-dependent atrioventricular delays shortening was programmed, resulting in His-stimulation only at atrial rates above 75/min. After 3 months, the patient reported significant reduction of symptoms and nearly no further limitations during daily activities. Device interrogation revealed 24% of ventricular pacing over time with a unipolar threshold of 2V/1ms for selective His capture with LBBB correction and a unipolar threshold of 0.9V/1ms for selective His capture without LBBB correction (Figure 1).

Repeat exercise test demonstrated improved exercise capacity (95W=79% versus previously 76W=60% of age- and sex-adjusted average) and improved peak oxygen uptake (VO2 max 20.4 ml/min*kg versus previously 14.4ml/min*kg). During echocardiographic evaluation offline strain analysis with three-dimensional rendering of left ventricular deformation was performed using TomTec ImageArena Cardiac Performance Analysis module (v.4.6). Global and segmental strain values were described based on a 16-segment LV model from tracking the LV endocardial border in the apical 2-, 3-, and 4-chamber views according to current recommendations (3). Echocardiographic analysis during LBBB versus His-bundle-pacing (HBP) demonstrated improvement in segmental and global longitudinal strain (-13.2% versus -19.3%, respectively; Figure 3A) as well as improved mechanical dispersion (84 ms versus 51 ms, respectively; Figure 3), indicating increased ventricular deformation and synchronicity of contraction. Similarly, 3D simulation of left ventricular strain map during systole visualized improved ventricular deformation (Figure 3B, supplemental videos 1-4). After 12 months, the patient reported no limitations anymore during daily activities or cardiovascular exercise. She had reduced her BMI from
27 to 24 kg/m² within 1 year due to increased capacity during cardiovascular exercise. Device interrogation demonstrated a stable pacing-percentage of around 25% and a stable unipolar threshold of 2V/1ms for selective His capture with LBBB correction.

Discussion

The “Painful LBBB syndrome” consists of anginal symptoms and rate dependent LBBB during exertion, first published more than 70 years ago (4). In the largest published series of 50 patients, there seems to be no sex- or age preponderance, a characteristic electrocardiographic LBBB pattern with a low S/T wave ratio and – most importantly - a good long-term prognosis (1). Substantial interpatient variability is observed, with reported symptoms from “heart throbbing” to “debilitating pain limiting everyday physical activity” (1). Our patient reported a progressive nature of her symptoms over several years, experiencing symptoms even during simple daily activities at the time of referral to our clinic (5, 6).

LBBB and associated symptoms appear to be easily reproducible in such patients by physical activity, atrial pacing or pharmacological challenge (i.e. application of isoproterenol, atropine), and symptoms usually vanish with resolution of LBBB below a certain heart rate. It is fundamental to exclude a relevant underlying structural or functional heart disease as other cardiac conditions may present with similar symptoms and ECG patterns. Mechanistically, previous reports have excluded ischemia as the causative mechanism of painful LBBB (1), while current pathophysiologic theories favour dyssynchronous cardiac ventricular contraction and increased interoceptive sensitivity (1, 7).

While no specific treatment protocols for symptomatic LBBB exist, therapeutic options include a physical exercise regimen to increase the rate-threshold of LBBB onset, Betablockers to limit heart rate or pacemaker implantation (1, 8). In our patient, physical training had no effect and betablocker therapy was not tolerated, therefore we jointly decided for a pacemaker implantation. Even though right- and biventricular pacing have both been reported to be successful in alleviating symptoms in patients with painful LBBB (9), chronic RV pacing is known to be a risk factor for pacing-induced cardiomyopathy (10), while CRT implantation carries an increased risk of short- and long-term complications. His bundle pacing presents a valid alternative to restore cardiac electrical synchronicity through physiological stimulation (11). Because of the longitudinal electrical dissociation within the His bundle, left bundle branch block with proximal or intrahisian origin may be overcome with direct His bundle pacing (12, 13).
To estimate the level of electrical block in patients with painful LBBB syndrome, an electrophysiological study is warranted, where non-selective His capture with successful correction of bundle branch block was documented in our patient. Hence, His-bundle pacing with correction of LBBB was deemed feasible and a His-bundle-pacemaker was successfully implanted. Similarly, His bundle pacing has been reported as a successful therapy in painful LBBB syndrome in at least four other case reports (6, 14, 15).

However, the effect of His-bundle pacing on objective parameters including exercise capacity and echocardiographic parameters of ventricular electrical synchrony in this type of patients has, to the best of our knowledge, not yet been reported. A higher exercise capacity (110W=89% versus previously 76W=60% of age and sex adjusted mean) and peak oxygen uptake (VO2 max 18.4 ml/min*kg versus previously 14.4ml/min*kg) after HBP implantation was documented in our patient, corresponding well to her significantly improved symptoms. Echocardiographic evaluation demonstrated improved global left ventricular strain, improved electrical dispersion and improved homogeneity of cardiac contraction (Figure 3, Videos 1-4) underscoring the hypothesis of dyssynchronous ventricular contraction being corrected by HBP in this population.

Conclusions

The painful LBBB syndrome is a potentially underestimated and underreported disease with potentially debilitating symptoms. In patients with anginal symptoms, LBBB and absence of other causative diseases, painful LBBB should be considered. His-bundle-pacing may ameliorate symptoms, increase exercise capacity and improve homogeneity of cardiac deformation.
Figure 1: ECG during Sinus rhythm and His-lead pacing. A: Sinus rhythm without LBBB, QRS 84ms. B: Sinus rhythm with LBBB starting at a heart rate of 75/min, QRS 153ms. C: His-lead pacing resulting in selective His capture with correction of bundle branch block at a unipolar threshold of 2V/1ms, QRS
92ms. D: His-lead pacing resulting in selective His capture without correction of bundle branch block at a unipolar threshold of 0.9V/1ms, QRS 149ms.

Figure 3:

A: Left ventricular longitudinal strain without (left panel, pacemaker programmed to AAI 100/min) and with (right panel, pacemaker programmed to DDD 100/min with LBBB correction) his-pacing demonstrating improved global and segmental strain and mechanical dispersion. LV GLS: Left Ventricular Global Longitudinal Strain. Mech. Disp.: Mechanical Dispersion.

B: 3D simulation of left ventricular strain map during systole showing improved regional strain as observed from the apical view. A4C: four chamber view. A2C: Two chamber view. A3C: Three chamber view. Pre: Without His-bundle-pacing, pacemaker programmed to AAI 100/min. Post: With His-bundle-pacing, pacemaker programmed to DDD 100/min with LBBB correction.
References


A

I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6
At rest  Maximal  Recovery
85/min  177/min  125/min

B

C

D

Max Watt  95W (79%)
VO2max  20.4 l/(min*kg) (81%)
RER  1.17
O2-Puls  8.63 ml/beat (95%)

Max Watt  76W (60%)
VO2max  14.4 l/(min*kg) (52%)
RER  1.18
O2-Puls  7.06 ml/beat (64%)
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Key Teaching Points

• The painful left-bundle-branch-block-syndrome is a potentially underestimated and underreported disease with potentially debilitating symptoms
• In patients with anginal symptoms, LBBB and absence of other causative diseases, painful LBBB should be considered.
• His-bundle-pacing may ameliorate symptoms, increase exercise capacity and improve homogeneity of cardiac deformation.