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## HIS BUNDLE PACING IN A PATIENT WITH ATRIOVENTRICULAR CONDUCTION ABNORMALITIES, PERSISTENT ATRIAL FLUTTER AT HIGH THROMBOEMBOLIC AND BLEEDING RISK AFTER HYBRID CORONARY REVASCULARIZATION AND LEFT ATRIAL APPENDAGE CLOSURE – CASE REPORT

M. Szotek<sup>1</sup>, W. Kula<sup>2</sup>, A. Malik<sup>2</sup>, A. Czunko<sup>1</sup>, J. Lelakowski<sup>1, 3</sup>, V. Traykov<sup>4</sup>, P. T. Matusik<sup>1, 3</sup>

<sup>1</sup>Department of Electrophysiology, The John Paul II Hospital, Kraków, Poland

<sup>2</sup>Faculty of Medicine, Jagiellonian University Medical College, Kraków, Poland

<sup>3</sup>Institute of Cardiology, Faculty of Medicine, Jagiellonian University Medical College, Kraków, Poland

<sup>4</sup>Department of Invasive Electrophysiology, Clinic of Cardiology, Acibadem City Clinic University Hospital Tokuda, Sofia, Bulgaria

## СТИМУЛАЦИЯ НА СНОПА НА ХИС ПРИ ПАЦИЕНТ С НАРУШЕНО АТРИОВЕНТРИКУЛАРНО ПРОВЕЖДАНЕ, ПЕРСИСТИРАЩО ПРЕДСЪРДНО ТРЕПТЕНЕ С ВИСОК ТРОМБОЕМБОЛИЧЕН И ХЕМОРАГИЧЕН РИСК СЛЕД ХИБРИДНА КОРОНАРНА РЕВАСКУЛАРИЗАЦИЯ И ЗАТВАРЯНЕ НА ЛЕВОПРЕДСЪРДНОТО УХО.

М. Шотек<sup>1</sup>, В. Кула<sup>2</sup>, А. Малик<sup>2</sup>, А. Чунко<sup>1</sup>, Я. Лелаковски<sup>1, 3</sup>, В. Трайков<sup>4</sup>, П. Т. Матусик<sup>1, 3</sup>

<sup>1</sup>Отделение по електрокардиология, болница Йоан Павел II, Краков, Полша

<sup>2</sup>Факултет по медицина, Медицински колеж на Ягелонския университет, Краков, Полша

<sup>3</sup>Факултет по медицина, Медицински колеж на Ягелонския университет, Краков, Полша

<sup>4</sup>Аджибадем Сити Клиник УМБАЛ Токуда

### Abstract.

We present a case of a 78-year-old patient with persistent atrial flutter, history of atrial fibrillation and atrioventricular conduction disturbances, including first-degree atrioventricular block (AVB) and paroxysmal complete AVB. Echocardiography revealed mildly reduced left ventricular ejection fraction (LVEF, 44%). The patient had high thromboembolic risk, had previous ischemic stroke, suffered from chronic coronary artery disease treated with hybrid coronary revascularization (minimally invasive direct coronary artery bypass grafting and subsequent percutaneous coronary intervention) as well as left atrial appendage closure. Because of high bleeding risk, double antiplatelet therapy (acetylsalicylic acid and clopidogrel) combined with low dose of low-molecular-weight heparin after cardiac surgery were introduced. Due to persistent atrial flutter, complete AVB, lack of intraventricular conduction abnormalities, mildly reduced LVEF and expected high right ventricle pacing burden, the patient was referred for dual-chamber pacemaker implantation using conduction system pacing (CSP), preferentially His bundle pacing (HBP). The procedure was performed with good outcome and CSP was utilized via HBP. After reassessment of thromboembolic and bleeding risk, the patient was discharged home on reduced dose of dabigatran. Short-term follow-up showed stable HBP parameters along with no additional symptoms. Despite good short-term outcomes and no complications in studied patient, large randomized controlled trials are needed to verify long-term safety and efficacy of HBP to optimize clinical care of patients with atrioventricular conduction abnormalities using a personalized approach.

### Key words

conduction system pacing; heart failure; His bundle pacing; pacemaker; thromboembolic risk; bleeding risk

### Address

### for correspondence:

Paweł T. Matusik, MD, PhD, Department of Electrophysiology, Institute of Cardiology, Jagiellonian University Medical College, 80 Prądnicka Str., 31-202 Kraków, Poland. Phone: +48 12 614 22 77; Fax: +48 12 614 22 26; e-mail: pawel.matusik@wp.eu

### Резюме.

Представяме случай на 78-годишен пациент с персистиращо предсърдно трептене, анамнеза за предсърдно мъждене и нарушено атриовентрикулярно провеждане, вкл. атриовентрикуларен блок (AVB) първа степен и пароксизмален пълен AVB. Ехокардиографията обективизира леко намалена левокамерна фракция на изтласкване (LVEF) от 44%. Пациентът беше с висок тромбоемболичен риск поради преживян мозъчен инсулт и хроничен коронарен синдром, лекуван с хибридна коронарна реvascularизация (минимално инвазивен аорто-коронарен байпас и последваща перкутанна коронарна интервенция) и беше третиран със затваряне на левопредсърдното ухо. Поради висок хеморагичен риск, след кардио-

<b>Резюме.</b>	хирургичната интервенция беше стартирана двойна антиагрегантна терапия (ацетилсалицилова киселина и клопидогрел) в комбинация с ниска доза нискомолекулярен хепарин. Пациентът беше насочен за имплантация на двукухинелектрокардиостимулатор със стимулация на проводната система (CSP) с предпочитания към стимулация на снопа на Хис (HBP) поради персистиращ епизод на предсърдно трептене, пълен AVB, липсата на нарушения във вътрекамерната проводимост и очаквания висок дял на деснокамерна стимулация при леко намалена LVEF. Постигна се успешна имплантация като CSP се осъществи чрез HBP. След преоценка на тромбоемболичния и хеморагичния риск пациентът беше дехоспитализиран на терапия с ниска доза дабигатран. Краткосрочното проследяване демонстрира стабилни параметри на стимулация и липса на симптоматика. Въпреки добрия резултат и липсата на усложнения при описания случай, са необходими големи рандомизирани проучвания, които да потвърдят дългосрочната безопасност и ефикасност на HBP и ролята на метода за оптимизацията на грижата за пациентите с нарушения в атриовентрикулното провеждане чрез използване на персонализиран подход.
<b>Ключови думи:</b>	стимулация на проводната система, сърдечна недостатъчност, стимулация на снопа на Хис, електрокардиостимулатор, тромбоемболичен риск, хеморагичен риск
<b>Адрес за кореспонденция:</b>	д-р Павел Т. Матусик, дм, Институт по кардиология, Факултет по медицина, Медицински колеж на Ягелонския университет, ул. „Прудничка“ 80, 31-202 Краков, Полша Phone: +48 12 614 22 77; Fax: +48 12 614 22 26; e-mail: pawel.matusik@wp.eu

## INTRODUCTION

Conduction system pacing (CSP), including His bundle pacing (HBP) and left bundle branch area pacing (LB-BAP) has emerged as an alternative approach to traditional right ventricular pacing (RVP) [1]. These methods aim to predominantly capture conduction system, compared to dominant myocardial pacing with traditional RVP. There is growing evidence that CSP provides more physiological cardiac pacing, preserving ventricular synchrony (or reducing ventricular dyssynchrony) as well as preventing decrease in left ventricular ejection fraction (LVEF) and development of pacing induced cardiomyopathy (PICM), which may be observed in about 12% of patients with atrioventricular block (AVB) after a mean period of about 4 years [1, 2]. Considering the above, current European Society of Cardiology (ESC) guidelines state that HBP may be considered, among others, as a viable method in patients with AVB, expected high RVP percentage and preserved or mildly reduced LVEF [3].

## CASE PRESENTATION

We present a case of the 78-year-old patient with persistent atrial flutter, a history of atrial fibrillation, atrioventricular conduction disturbances, including first degree and paroxysmal complete AVB as well as heart failure with mildly reduced LVEF (HFmrEF) who was admitted to the hospital for cardiac implantable electronic device placement.

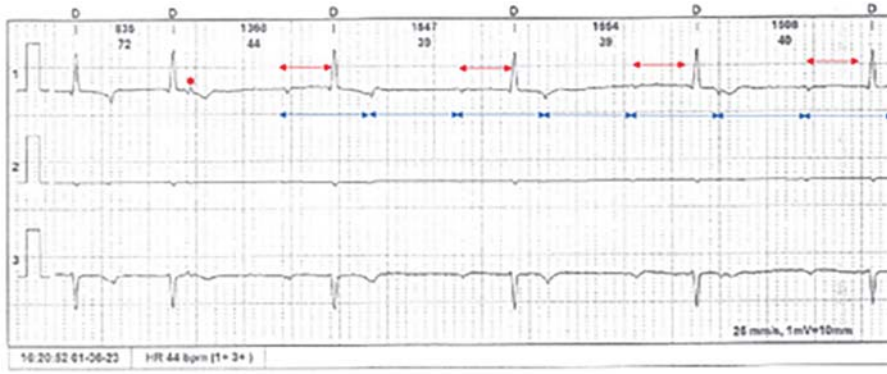
Previous electrocardiogram (ECG) recordings revealed first-degree AVB and paroxysmal complete AVB (Figure 1) with concomitant pauses over 2 seconds.

Evaluation of the medical history revealed multiple comorbidities. The patient had a history of ischemic stroke (signs of Wallenberg's syndrome), chronic coronary syndrome with multivessel disease, which was treated using hybrid coronary revascularization, due to high surgical risk

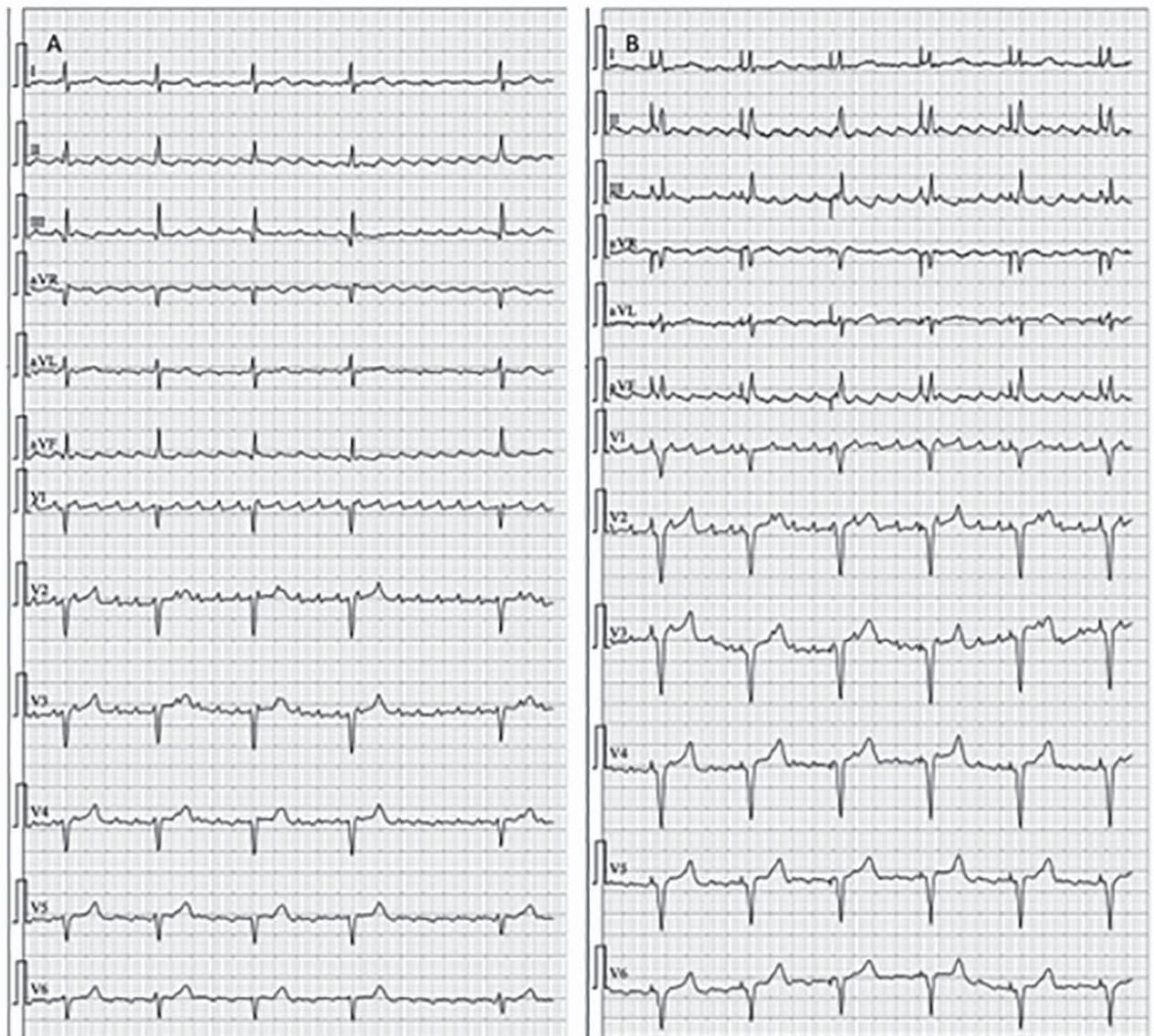
when performing standard coronary artery bypass grafting. The patient underwent minimally invasive direct coronary artery bypass grafting through left minithoracotomy with left internal mammal artery to left anterior descending coronary artery (MIDCAB, LIMA-LAD) with concomitant left atrial appendage (LAA) closure using epicardial clip (AtriClip) and percutaneous coronary angioplasty (PCI) of right coronary artery with the use of drug eluting stent implantation 3 weeks after MIDCAB. Additionally, the patient presented with several additional conditions: hypertension, type 2 diabetes mellitus, obesity, cholelithiasis, cysts of the left kidney, incidentaloma of left adrenal gland and discopathy. The patient had been hospitalized due to severe anemia with red blood cells transfusion, then additional endoscopic examination had revealed sigmoid diverticuli and esophageal varices. However, no signs of active bleeding had been observed during previous hospitalization.

On admission, during medical interview, the patient reported reduced exercise tolerance, vertigo and presyncope that had been present for two months.

The 12-lead ECG revealed atrial flutter with unknown onset, no intraventricular conduction disturbances with QRS duration of about 90 ms (Figure 2, Panel A). Atrial flutter persisted throughout the whole hospital stay. Transthoracic echocardiography (TTE) revealed: mildly reduced LVEF (44%), hypokinesis of inferior-lateral wall, inferior wall, apex and anterior part of intraventricular septum, increased left atrium area (23 cm<sup>2</sup>) and right atrium area (20 cm<sup>2</sup>), mild regurgitation of mitral valve and restrictive left ventricular filling pattern. Following discussion with the patient and shared decision making rhythm control strategy was undertaken. After careful evaluation of patients' overall health status including expected high RVP percentage, the patient was qualified for permanent dual-chamber pacemaker implantation with CSP, preferentially HBP. After obtaining patients informed consent, pacemaker implantation procedure was performed.



**Fig. 1.** 24-hour Holter electrocardiogram monitoring revealing paroxysmal complete atrioventricular block. PP cycles are indicated by blue arrows, while additional premature atrial ectopic beat is marked by asterisk, variability of PR intervals is indicated by red arrows



**Fig. 2.** Twelve-lead ECG during endogenous rhythm (atrial flutter with variable atrioventricular conduction, Panel A) and during His bundle pacing (Panel B)

The lead (Medtronic, SelectSecure™ lead, model 3830) was introduced through the cephalic vein using preshaped catheter (Medtronic, model C315HIS). The lead was introduced and placed in the His bundle re-

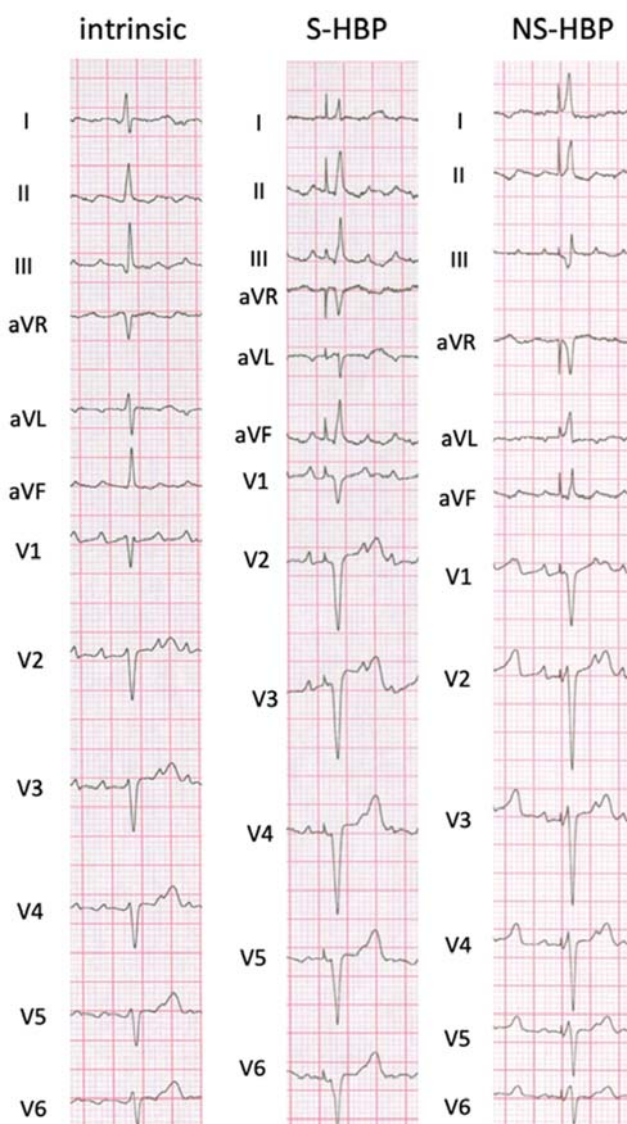
gion. Electrophysiologic measurements revealed His bundle potential sensing of 1.875 mV (according to SelectSecure™ 3830 lead technical manual minimal acute sensing amplitude at His bundle should be 1.35 mV)

and successful selective His bundle capture at pacing output of 1.3–1.8 V @ 0.5 ms, while non-selective His bundle capture > 1.875 V @ 0.4 ms and loss of capture below 1.3V @ 0.4 ms. Impedance of the lead was 418 Ohms. Due to His-ventricle (HV) interval of 58 ms and HV 1:1 conduction at 160/min pacing rate there was a decision on not to put back up pacing lead. After deployment of the HBP lead, the atrial Medtronic 5076 lead was inserted via subclavian vein access and placed in the region of right atrial appendage. Good parameters of pacing system were achieved during bipolar configuration (impedance of 551 Ohms and sensing of 2.25 mV). Atrial flutter was present during the whole procedure, thus atrial pacing threshold was not measured. Transitions from non-selective to selective HBP as well as V6 R-wave peak time (RWPT) < 100 ms are shown on Figure 3. Stable HBP was achieved (Figure 2, Panel B). Control transthoracic echocardiography revealed no pathologic fluid in the pericardial sac, device check revealed satisfactory electrical parameters of the pacing system, while chest X-ray (Figure 4, Panel A and B) has shown no post-procedural complications and stable positions of the leads.

In the past, during periprocedural period regarding MIDCAB with LAA closure and subsequent PCI, the patient had been treated with dual antiplatelet therapy (75 mg of acetylsalicylic acid and 75 mg of clopidogrel) and reduced dose of low molecular weight heparin (40 mg twice daily). The patient had a high thromboembolic and bleeding risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc score and HAS-BLED scores of 5 and 6, respectively) and later acetylsalicylic acid had been withdrawn, because of high bleeding risk concerns outweighing risk of stent thrombosis. Short-duration triple antithrombotic therapy is in line with the 2019 ESC guidelines on chronic coronary syndromes [4].

During the hospitalization antiplatelet and anticoagulation therapy were reassessed. Based on overall clinical status the patient was discharged home with reduced dose of dabigatran (110 mg) twice daily with planned assessment in the ambulatory after at least 3 weeks of non-interrupted anticoagulation with strategy of performing pharmacological and/or electrical cardioversion, according to patient preferences, and potential referral for catheter ablation.

Interrogation of pacemaker during early follow-up revealed: impedances of 377 ohms and 345 ohms in atrial and HBP lead, respectively, atrial flutter waves amplitudes of 1.40-2.00 mV, His bundle potential of 2.00-2.80 mV. Selective HBP was achieved at 0.25-0.5V @ 0.4 ms, nonselective HBP above 0.5 V @ 0.4 ms, while loss of capture below 0.25 V @ 0.4 ms, with decreasing output, transition from non-selective to selective HBP was observed (Figure 3 and 5).



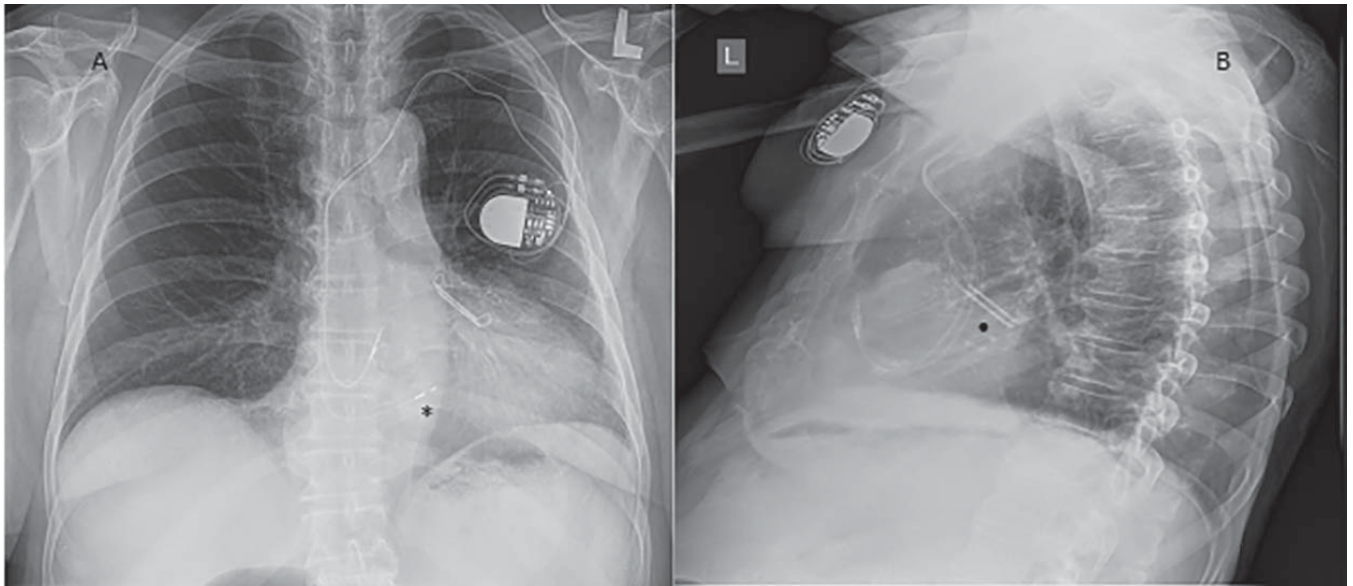
NS-HBP – non-selective His bundle pacing, S-HBP – selective His bundle pacing. In S-HBP an isoelectric line between stimulus and QRS complex can be seen in all 12 leads, while in NS-HBP a pseudo-delta wave is present which prolongs QRS complex (measured from pacing stimulus, as in myocardial capture only, to the latest part of QRS in any lead from 12 leads [8])

**Fig. 3.** Twelve-lead electrocardiogram after dual chamber pacemaker implantation with conduction system pacing presenting patients' intrinsic rhythm and paced QRS complexes with selective and non-selective His Bundle pacing

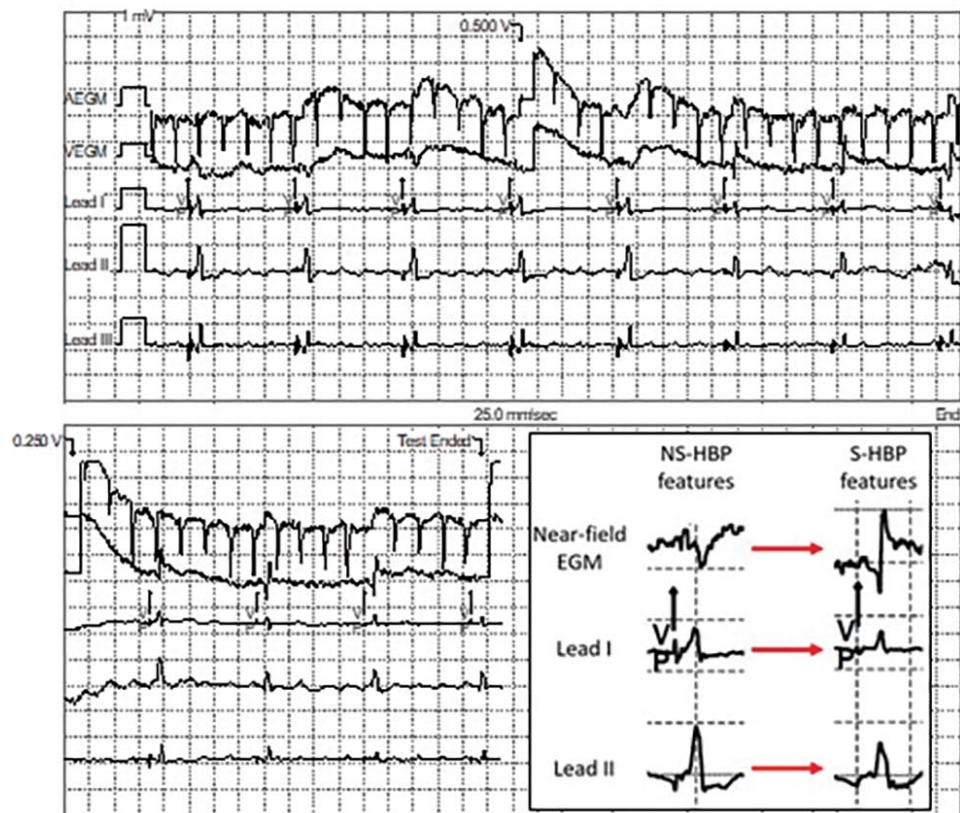
The patient reported no additional symptoms and there were no signs of bleeding during short follow-up of treatment with dabigatran.

## DISCUSSION

Our case shows successful HBP in lieu of RVP. The most recent guidelines on pacing and cardiac resynchronization therapy suggest HBP potentially beneficial compared to RVP in patients with preserved or mildly reduced LVEF and expected high RVP percentage [3].



**Figure 4.** Anterior-posterior (panel A) and lateral (panel B) X-ray of the patient after dual-chamber pacemaker implantation with conduction system pacing. His bundle pacing lead is indicated by asterisk, AtriClip system is indicated by dot.



EGM – electrogram, AEGM – atrial EGM, NS-HBP – non-selective His bundle pacing, S-HBP – selective His bundle pacing, VEGM – ventricular EGM, VP – ventricular pacing (lead located in the His bundle region).

NS-HBP features in ECG include pseudo-delta wave, QRS prolongation and usually higher QRS amplitudes (in leads I and II), while in electrogram pacing stimulus is fused with local potential, near-field electrogram (bipolar sense polarity) is negative and reflects shorter time to peak. S-HBP features in ECG include isoelectric line between stimulus and QRS, narrower QRS (measured from QRS onset), while in electrogram discrete potential may be observed after pacing stimulus. Moreover, there is no instantaneous negative deflection in near-field electrogram and time to peak is longer. Based on [5, 8, 9].

**Figure 5.** Electrocardiogram and intracardiac electrocardiogram during interrogation of pacemaker presenting pacing threshold measurement with features of selective and nonselective His bundle pacing features.

There is evidence showing that chronic RVP may lead to PICM which manifests itself as decreased LVEF as well as potential heart failure symptoms, especially when RVP percentage is above 20% [6, 7]. HBP can be selective and non-selective. It is selective, when depolarization of the heart goes precisely through His-Purkinje fibers without concomitant additional depolarization of myocardial tissue around the bundle of His, which creates isoelectric line between pacing stimulus and QRS complex (also reflected by an isoelectric interval on the filtered electrogram which is similar to the HV interval) [8]. An increase in QRS amplitudes in I, II and V6 may help to indicate a transition from S-HBP to NS-HBP (summation of myocardial activation and capture through the bundle of His) [8]. NS-HBP leads to capture of working myocardium in proximity to His bundle region, easily recognized on ECG as a pseudo-delta wave. Lead V6 RWPT < 100 ms and lack of notching, slurring and/or plateaus in I, V1 and V4-6 may help to differentiate NS-HBP from myocardial capture [9]. Clinical data suggests that selective and non-selective HBP may be associated with similar clinical outcomes (including death or heart failure related hospitalization in the mean follow-up of about 2.8 years) [1, 9, 10]. The 2021 ESC guidelines on cardiac pacing state that patients with HBP should be examined at least every 6 months, taking into account the possibility of increasing HBP thresholds [3]. Importantly, non-selective HBP is associated with better sensing amplitudes and potential of ventricular myocardium backup capture [9].

Growing number of research evidence suggests that CSP may be a very useful method to prevent development of PICM because it is associated with more physiological ventricular depolarization. There is also data suggesting that CSP can be used as a method of cardiac resynchronization in patients with heart failure, and may be considered when classical cardiac resynchronization therapy (CRT), using combination of RVP and left ventricular pacing via coronary sinus can not be successfully utilized [1].

2021 ESC guidelines state that CRT is recommended in symptomatic patients with heart failure and reduced LVEF ( $\leq 35\%$ ) and QRS of left bundle branch block morphology ( $\geq 150$  ms) [3]. It lowers mortality in long term follow-up and reduces hospitalizations due to heart failure, but about 30% of patients may not benefit from this form of treatment [1, 3]. CRT has its pitfalls, including difficulties in coronary sinus cannulation, optimal placement of left ventricular pacing lead into coronary vein over viable myocardium and/or increased left ventricular pacing thresholds. Recent data, based pre-

dominantly on small studies, suggests that CSP, compared to CRT, may lead to higher LVEF improvement and may shorten QRS duration [1].

On the other hand, long-term clinical outcomes after CSP should be provided and current high-quality data on the use of CSP still seems to be outnumbered by evidence regarding CRT. Importantly, HBP and LB-BAP have their downsides. Concerns regarding HBP are: suboptimal sensing of His bundle potential, oversensing of atrial signal and high pacing thresholds, increasing over time in over 10% of patients, which may lead to premature battery depletion or necessity of lead revision [1]. LBBAP often solves these difficulties, by presenting better sensing values and lower pacing thresholds, however it may be associated with acute coronary syndrome, possible perforation into the left ventricular cavity during too deep pacing lead placement and its utilization similarly to HBP is sometimes very difficult or impossible to introduce [1].

Another interesting issue related to our case is that in presented patient with multivessel coronary artery disease both hybrid coronary revascularization (MID-CAB + PCI) and LAA closure were performed. Available data shows that abovementioned treatment may combine benefits arising from LIMA-LAD coronary bypass and minimizing invasiveness which results in fewer complications and shorter duration of hospital stay [11]. Another subject is the potential benefit from concomitant LAA closure during cardiac surgery. It seems very viable option to be performed concomitantly during another invasive surgical procedure to reduce the risk of thromboembolic events in patients with atrial fibrillation, however data on its efficacy is still lacking. After at least 3 weeks of optimal anticoagulation, we consider our patient a suitable one for pharmacological and/or electrical cardioversion and according to patients preference in the case of lack of success or unacceptable recurrence to undergo potential atrial flutter ablation. This approach may lead to not only intraventricular, but also atrioventricular synchrony.

## CONCLUSIONS

Careful patient evaluation is crucial in qualification for permanent cardiac pacemaker, especially in light of potential benefits from new pacing techniques, such as CSP. CSP with the use of HBP has its limitations and is more time-consuming compared to traditional RVP. However, when performed successfully it seems to have long-term benefits resulting in left ventricular reverse remodelling or preserved LVEF, especially when

high RVP burden is expected. Despite good short-term outcomes and safety in the studied patient, along with promising current evidence, large randomized controlled trials are needed to verify long-term safety and efficacy of HBP, in various populations, to optimize clinical care of patients with atrioventricular conduction abnormalities in personalized medicine.

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