

# His bundle pacing is still relevant for patients with atrial fibrillation and bradycardia without prior atrioventricular nodal ablation: Data from mid-term follow-up

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## ABSTRACT

**Background:** In patients with atrial fibrillation (AF) and symptomatic bradycardia, His bundle pacing (HBP) is used to achieve an appropriate heart rate and physiological depolarization of the left ventricle (LV).

**Aims:** We aimed to evaluate the impact of HBP on LV function in two different populations: with normal LV ejection fraction (LVEF) and low LVEF (<50%).

**Methods:** Patients who received HBP as *de novo* therapy or as an upgrade were divided into two groups based on initial LVEF, followed by echocardiographic and device monitoring.

**Results:** One hundred and twenty-three patients (aged 76.0 [69.2–79.8] years, 74.0% men) with AF and bradycardia received HBP and completed follow-up with a median of 6.2 months (6.0–8.0). LV function remained unchanged in patients with initially normal LV function (65 participants, LVEF 59.0% [55.0–62.0] vs. 58.0% [55.0–63.0]). In patients with low LVEF (58 participants), there was an increase in LVEF (37.5% [30.0–43.0] vs. 44.0% [35.0–50.0];  $P < 0.0001$ ), a reduction in indexed LV end-systolic volume (62.4 [20.7] ml vs. 51.5 [21.5] ml;  $P = 0.001$ ) and indexed LV end-diastolic volume (97.5 [26.2] ml vs. 88.1 [25.1] ml;  $P = 0.009$ ), and an improvement in the New York Heart Association class (2.3 [0.71] to 1.6 [0.9];  $P < 0.0001$ ).

**Conclusion:** With permanent HBP, patients with AF and bradycardia and without prior atrioventricular nodal ablation did not experience deterioration in LV systolic function. Those with reduced baseline LVEF experienced improvements in LV function and its reverse remodeling at the mid-term follow-up.

**Key words:** atrial fibrillation, bradycardia, conduction system pacing, heart failure, LV reverse remodeling

## INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia, with severe consequences and an ever-increasing number of cases [1]. The arrhythmia's irregular heart rhythm causes a condition called arrhythmia-induced cardiomyopathy regardless of concomitant tachycardia or bradycardia [2]. While left ventricle (LV) function deterioration can be alleviated with a pacemaker and rate-controlling drugs, this solution is not free of downsides.

A phenomenon called pacing-induced cardiomyopathy (PICM) is widely known and occurs in patients with right ventricular (RV)

myocardial pacing in about 12% of cases, with a range between 6% and 25% depending on definition, clinical and pacing conditions, and observed population [3]. In this study, we defined PICM as a pacing burden  $\geq 40\%$  with a decrease in LV ejection fraction (LVEF)  $\geq 10\%$ , final absolute LVEF value below 50%, and worsening of heart failure symptoms [4]. Unfortunately, cardiac resynchronization therapy (CRT), which is used to resolve such problems, has limitations [5, 6].

Conduction system pacing (CSP), consisting of both His bundle pacing (HBP) and left bundle branch area pacing (LBBAP), has

## WHAT'S NEW?

His bundle pacing (HBP) is a recently emerged pacing technique that can be used in patients with atrial fibrillation and symptomatic bradycardia. With HBP, it is possible to achieve both an appropriate heart rate and physiological depolarization of the left ventricle (LV). Our study shows that patients with atrial fibrillation and preserved LV ejection fraction at baseline did not experience LV function worsening. On the other hand, in patients with reduced LV ejection fraction, HBP was associated with an improvement in LV contractility and reverse remodeling marked by a reduction in LV dimensions.

been shown to provide a reliable way of maintaining an appropriate rhythm rate and synchronous propagation of depolarization [7, 8]. This solution represents a promising prospect of improving, or at least maintaining, ventricular function and can become the standard approach for patients with atrial fibrillation when a pacemaker is required.

Most clinical evidence in this field relates to patients receiving CSP following atrioventricular nodal ablation (AVNA). In turn, follow-up data are lacking for patients with pacemakers implanted due to bradyarrhythmia and without prior AVNA [9]. Available data remain insufficient to form explicit recommendations. Therefore, our study aimed to analyze mid-term HBP outcomes in two different patient populations with AF and bradycardia, with normal and low LVEF.

## METHODS

### Patient selection

The study was based on a single-center prospective registry of patients implanted using HBP in the Department of Electrocardiology at Professor Leszek Giec Upper-Silesian Medical Centre of the Medical University of Silesia in Katowice, Poland. Appropriate approval from the local Ethics Committee was obtained.

Study participants were recruited from patients with permanent or long-lasting persistent AF with either permanent bradycardia or frequent episodes of symptomatic bradycardia referred for cardiac device implantation or its upgrade. Selection of a pacemaker, implantable dual-chamber cardioverter-defibrillator (ICD), or CRT device depended on clinical data and current ESC guidelines. All participants were required to be at least 18 years old, with a predicted survival of 12 months in the case of ICD. Finally, during follow-up, we excluded from the study participants with conditions significantly affecting cardiac function post-implantation, such as myocardial infarction or cardiac surgery that led to a loss of such pacing, as the purpose of the study was to assess HBP in AF patients.

All patients consented to their treatment and underwent an HBP attempt, which was the preferred pacing method, or right ventricular pacing (RVP) or biventricular pacing if the first method failed. An echocardiographic follow-up examination was scheduled six to nine months after the procedure. As bradyarrhythmia was the main clinical problem, atrioventricular junction ablation was

not considered part of the treatment strategy, and no participant underwent this procedure.

### Implantation procedure

All patients underwent the same procedure using a 3830 SelectSecure lead and a C304 or C315 sheath (Medtronic, Inc., Minneapolis, MN, US), according to the operator's preference. Standard subclavian or axillary access with a guidewire and a dilator was used. His bundle location was identified using unipolar mapping, or if no His bundle signal was visible, the pace mapping technique was used. Since our study predates the release of the European Heart Rhythm Association clinical consensus statement for CSP [10], we based our criteria for successful HBP on the reports and recommendations available at that time [11, 12]: pacing threshold  $\leq 3.0$  V @ 1.0 ms in the case of resynchronization and  $\leq 2.0$  V @ 1.0 ms otherwise, RV wave amplitude  $\geq 2.0$  mV in cases without RV back-up lead, preserved His-ventricle conduction at a rate of at least 120 beats per minute, and confirmed His bundle capture on the surface ECG with output-dependent transitions in QRS morphology. If the HBP approach was unsuccessful, an RV or biventricular lead was implanted according to the primary indication. If the operator decided it was needed for safety reasons, an additional backup lead was implanted. In the ICD case, His bundle lead was connected to the atrial port, and the defibrillation lead was in the RV port. The stability of threshold, signal amplitude, and impedance were confirmed before the procedure's final stage, and correct lead placement was ensured with a chest X-ray before suturing. The device was programmed to the final settings before discharge according to the patient's requirements and medical history.

### Clinical assessment and follow-up

The echocardiographic measurements were performed at baseline and during the follow-up assessment using transthoracic 2-dimensional Doppler and color Doppler echocardiography (iE33 or EPIQ 7 ultrasound system, Philips, Amsterdam, Netherlands). LVEF using Simpson's 4-chamber method and measurements of LV volumes indexed to the body surface area were taken to evaluate the hemodynamic response. The severity of mitral and tricuspid regurgitation was graded on a four-point scale (none = 0, mild = 1, moderate = 2, severe = 3) with a comprehensive assessment using the regurgitation area to the atrial area

ratio and the Proximal Isovelocity Surface Area (PISA) method. The area of the atria and tricuspid annular plane systolic excursion were obtained from 4-chamber views while LV dimensions from the parasternal long-axis view.

The location of the HBP lead was often visible during the echocardiographic study, so blinding echocardiographers to the pacing modality was impossible. Lead measurements were performed during the implant procedure, and the follow-up assessment was performed on the same day as echocardiographic measurements in most cases or up to 7 days earlier. Twelve-lead ECG recordings were obtained at baseline, discharge, and follow-up. A single investigator evaluated the pacing modality and duration of QRS complexes. Patients were divided into groups with normal LVEF and low LVEF based on baseline LVEF ( $\geq 50\%$  and  $< 50\%$ , respectively).

### Ethics

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Local Bioethics Committee of the Medical University of Silesia (KNW/0022/KB/17/18). Following the opinion of the Local Bioethics Committee, patient consent to participate in the study was waived because the collected data were derived from clinically indicated standard procedures for which informed consent was taken. Patient identification was impossible.

### Statistical analysis

Continuous variables were expressed as means (standard deviations). The Shapiro–Wilk test was used to check and confirm normal data distribution. For nonparametric data, the Mann–Whitney test and Wilcoxon test were used for independent and paired samples, respectively. The independent two-sample t-test was used to compare data between groups with correction for unequal variance (Welch test), and the paired t-test was used to compare data within the same group. Categorical data were presented as numbers and percentages and compared using the  $\chi^2$  test for independent samples or the McNemar test otherwise. A *P*-value of 0.05 or less was considered statistically significant in 2-sided statistical tests. Analyses were performed using MedCalc Statistical Software version 22.006 (MedCalc Software Ltd., Ostend, Belgium; <https://www.medcalc.org>).

## RESULTS

### Study population

One hundred and thirty-five patients with successful HBP performed between December 2015 and June 2021 were included in the study. Two patients died before follow-up; the cause of death was unknown. One hundred and thirty-three completed a full follow-up consisting of device interrogation and clinical and echocardiographic assessment. However, three of them experienced other cardiac conditions significantly affecting LV function (myocardial

infarction, cardiac surgery). Seven patients experienced lead-related complications – a significant rise in His-bundle capture threshold and subsequent myocardial capture from His bundle or backup lead (5 patients), lead dislodgement (1 patient), and reprogramming to ventricular pacing from the backup lead due to unspecified symptoms (1 patient). Three patients with the rise in threshold were managed conservatively due to low and stable myocardial capture threshold. The remaining two underwent lead replacement. One of them, after an upgrade from ICD-VVI, developed PICM once again after myocardial pacing prevailed, and the His bundle lead was finally replaced with the left bundle branch lead. The other patient with a single-lead device and the one with lead dislodgement received an RV lead instead.

### General statistics

The study group included 123 patients who completed follow-up after a median of 6.2 months (interquartile range [IQR] 6.0–8.0 months). The observation period of patients with initially preserved LVEF was slightly longer (median of 202 and IQR 185.5–270.5 days vs. median of 187 and IQR 182–193 days; *P* = 0.001). Baseline clinical and demographic characteristics and echocardiographic measurements are shown in [Tables 1](#) and [2](#), respectively.

### Indications and implanted devices

There were 82 *de novo* implantations. In patients with normal LVEF at baseline, indications for device implantation involved either bradycardia alone (93.8%; *n* = 61) or bradycardia with prevention of sudden cardiac death (6.2%; *n* = 4). Patients with LVEF  $< 50\%$  had composite indications: bradycardia (20.7%; *n* = 12), prevention of sudden cardiac death (37.9%; *n* = 22), and cardiac resynchronization therapy (77.6%; *n* = 45). There were 37 (63.8%) upgrades in this group; all due to previously diagnosed PICM or when it was deemed necessary to replace an existing device due to a very high ventricular pacing burden. There were several possible mechanisms of LV dysfunction in the patients with LVEF  $< 50\%$  at baseline. Arrhythmia-induced cardiomyopathy and suboptimal rate control due to bradycardia were regarded as the main causes in patients receiving a device for the first time (36.2%; *n* = 21). In the normal LVEF group, most of the patients had narrow QRS  $< 120$  ms (78.4%) while all of those with reduced EF at baseline had widened QRS  $\geq 120$  ms resulting from either interventricular conduction disorder (nonspecific or bundle branch block) or RVP. Baseline clinical conditions, including PICM, intraventricular conduction disturbances, and past ischemic events, are presented in [Table 1](#).

Overall, 57 patients received single-lead devices, which were predominantly used in patients with LVEF  $\geq 50\%$  at baseline (70.8 vs. 19.0%; *P*  $< 0.001$ ; *n* = 46 and *n* = 11, respectively). Dual-lead devices were implanted in 29.3% (*n* = 36) of the patients where the system had to be upgraded in the presence of indications for ICD, when

**Table 1.** Baseline clinical and demographic characteristics

	Total (n = 123)	LVEF ≥50% (n = 65)	LVEF <50% (n = 58)	P-value
Age, year	76.0 (69.2–79.8)	76.2 (70.4–82.3)	75.1 (68.0–79.1)	0.17
Males	91 (74.0%)	41 (63.1%)	50 (86.2%)	0.004
BMI, kg/m <sup>2</sup>	29.8 (5.0)	29.8 (4.6)	29.9 (5.5)	0.97
Medical history				
CAD	63 (51.2%)	23 (35.4%)	40 (69.0%)	<0.001
PCI in the past	44 (36.1%)	14 (21.9%)	30 (51.7%)	<0.001
MI in the past	30 (24.4%)	8 (12.3%)	22 (37.9%)	0.001
Stroke in the past	18 (14.6%)	9 (13.8%)	9 (15.5%)	0.79
Hypertension	108 (87.8%)	58 (89.2%)	50 (86.2%)	0.61
Diabetes mellitus	47 (38.2%)	20 (30.8%)	27 (46.6%)	0.07
Renal dysfunction	26 (21.1%)	7 (10.8%)	19 (32.8%)	0.003
Intraventricular conduction disturbances				
LBBB	5 (4.1%)	2 (3.1%)	3 (5.2%)	0.56
RBBB	18 (14.6%)	5 (7.7%)	13 (22.4%)	0.02
IVCD	14 (11.4%)	7 (10.8%)	7 (12.1%)	0.82
Baseline medical regimen				
Diuretic (loop)	69 (56.1%)	28 (43.1%)	41 (70.7%)	0.002
Diuretic (other)	14 (11.4%)	9 (13.8%)	5 (8.6%)	0.36
β-Blocker	71 (57.7%)	24 (36.9%)	47 (81.0%)	<0.001
ACEI/ARB	91 (74.0%)	48 (73.8%)	43 (74.1%)	0.97
MRA	59 (48.0%)	25 (38.5%)	34 (58.6%)	0.03
Digoxin	22 (17.9%)	7 (10.8%)	15 (25.9%)	0.03
Calcium blocker	31 (25.2%)	23 (35.4%)	8 (13.8%)	0.006
QRS duration (ms)	120.0 (90.0–170.0)	100.0 (85.0–120.0)	170.0 (120.0–200.0)	<0.001

Values are n (%), median (IQR) for nonparametric variables, and mean (SD) otherwise

Renal dysfunction was defined as <50 ml/min

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CAD, coronary artery disease; IVCD, intraventricular conduction delay; LBBB, left bundle branch block; MI, myocardial infarction; MRA, mineralocorticoid receptor antagonist; PCI, percutaneous coronary intervention; RBBB, right bundle branch block

**Table 2.** Echocardiographic morphology and hemodynamics at baseline

	Total (n = 123)	LVEF ≥50% (n = 65)	LVEF <50% (n = 58)	P-value
LVEDD, mm	55.1 (8.0)	50.6 (5.7)	60.1 (7.2)	<0.001
LVESD, mm	39.8 (10.22)	33.6 (6.2)	46.6 (9.4)	<0.001
LVESVi (ml)	42.6 (24.0)	25.5 (8.4)	62.4 (20.7)	<0.001
LVEDVi (ml)	78.8 (28.0)	62.5 (17.3)	97.5 (26.2)	<0.001
LVSVi	36.1 (10.0)	37.0 (10.4)	35.1 (9.5)	0.32
LVEF, %	51.0 (38.0–59.0)	59.0 (55.0–62.0)	37.5 (30.0–43.0)	<0.001
LAA, cm <sup>2</sup>	32.0 (28.0–37.0)	30.0 (27.5–35.0)	34.0 (29.8–38.0)	0.01
RAA, cm <sup>2</sup>	28.7 (7.5)	26.0 (7.5)	30.7 (7.0)	0.005
TAPSE	18.9 (4.9)	20.4 (4.5)	17.1 (4.7)	<0.001
MR ≥2, n (%)	45 (39.8%)	19 (31.1%)	26 (50.0%)	0.04
TR ≥2 n (%)	58 (47.2%)	31 (47.7%)	27 (46.6%)	0.90

Values are n (%), median (IQR) for nonparametric variables, and mean (SD) otherwise

Abbreviations: LAA, left atrial area; LVEDD, left ventricular end-diastolic diameter; LVEDVi, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVESVi, left ventricular end-systolic volume index; LVSVi, left ventricular stroke volume index; MR, mitral regurgitation; RAA, right atrial area; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation

a backup lead was needed, or when the return to healthy sinus rhythm was not certain. CRT devices with a CSP lead in the LV port were used when there was an upgrade from an existing dual-lead device. Except for dual-chamber pacemakers, more advanced devices were more common in the low LVEF group ( $P = 0.0001$  overall;  $P = 0.07$  for CRT-P systems and  $P = 0.001$  for defibrillation-capable systems). There was unusual use of CRT devices in three patients with normal LVEF, as it was necessary to replace the ex-

isting devices for other reasons, with the probability of developing PICM deemed very high due to the degree of atrioventricular block.

### Procedure and echocardiographic outcomes

The procedure details and electrophysiologic outcomes at both implantation and follow-up are presented in **Table 3**. There were several differences between the analyzed groups, with QRS duration being the most significant.

**Table 3.** Procedure characteristics and electrophysiological outcomes

	LVEF $\geq$ 50% (n = 65)	LVEF <50% (n = 58)	P-value
Procedure duration, min	60.0 (50.0–65.0)	70.0 (60.0–75.0)	0.11
Fluoroscopy duration, min	7.9 (3.5–16.1)	8.8 (4.6–12.5)	0.94
Fluoroscopy dose, mGy	68.8 (109.6)	80.2 (98.8)	0.55
His-ventricular delay, ms	50.0 (42.0–53.0)	54.5 (50.0–60.0)	0.006
Implant			
Paced QRS duration, ms	125.0 (120.0–140.0)	130.0 (110.0–160.0)	0.12
Capture threshold, V @ ms	1.2 (1.0–1.8)	1.2 (1.0–1.7)	0.27
Pacing impulse time, ms	1.0 (0.5–1.0)	1.0 (0.5–1.0)	0.62
R wave amplitude, mV	3.8 (2.2)	2.6 (2.0)	0.002
Lead impedance, ohm	540.0 (477.5–623.8)	534.0 (483.0–603.0)	0.81
Follow-up			
Paced QRS duration, ms	125.0 (110.0–135.0)	125.0 (120.0–160.0)	0.22
Capture Threshold, V @ ms	1.0 (0.8–1.5)	1.0 (0.8–1.5)	0.68
Pacing impulse time, ms	0.4 (0.4–1.0)	1.0 (0.4–1.0)	0.01
R wave amplitude, mV	3.4 (2.7)	2.4 (1.8)	0.08
Lead impedance, ohm	438.0 (410.5–482.5)	432.2 (98.2)	0.49
Ventricular pacing, %	90.7 (68.4–97.8)	96.8 (85.0–99.2)	0.03

Values are n (%), median (IQR) for nonparametric variables, and mean (SD) otherwise

Between measurements at implant and follow-up, there was a significant decrease in impedance for both groups, as presented in Table 3. Changes in other electrical parameters were insignificant.

Compared to baseline measurements, there were no echocardiographic differences in the normal LVEF group at the follow-up assessment. The low LVEF group experienced an increase in LVEF from 37.5% (30.0–43.0) to 44.0% (35.0–50.0) ( $P < 0.0001$ ), which correlated with a decrease in both LV end-systolic and LV end-diastolic volumes (LVESV and LVEDV, respectively) indexed to the body surface area (Figure 1). No significant changes in valve function were observed. Analysis of the subgroup that underwent an upgrade from an existing device with RVP showed an increase in LVEF from 34.0% (31.0–39.5) to 45.0% (36.0–50.0) ( $P < 0.0001$ ). The New York Heart Association (NYHA) class improved from 1.9 (0.6) to 1.2 (0.6) in patients with baseline LVEF  $\geq$ 50% and from 2.3 (0.7) to 1.6 (0.9) in the other group ( $P < 0.0001$  in both groups). Other relevant measurements are presented in Table 4.

## DISCUSSION

### Study findings

The study presents the beneficial mid-term effect of HBP in patients with AF and bradycardia who did not previously undergo AVNA. In the group of patients with low LVEF, we observed an increase in both LVEF and reverse remodeling, which was indicated by a decrease in both LVESV and LVEDV indexed to the body surface area. At the same time, we found no deterioration in LV hemodynamic parameters in the group with normal LVEF receiving HBP.

An improvement in the NYHA class was present in both groups. The percentage of ventricular pacing differed between the analyzed populations. Nonetheless, its

high value, significantly exceeding 40%, was sufficient to demonstrate relevant effects in both of them [13].

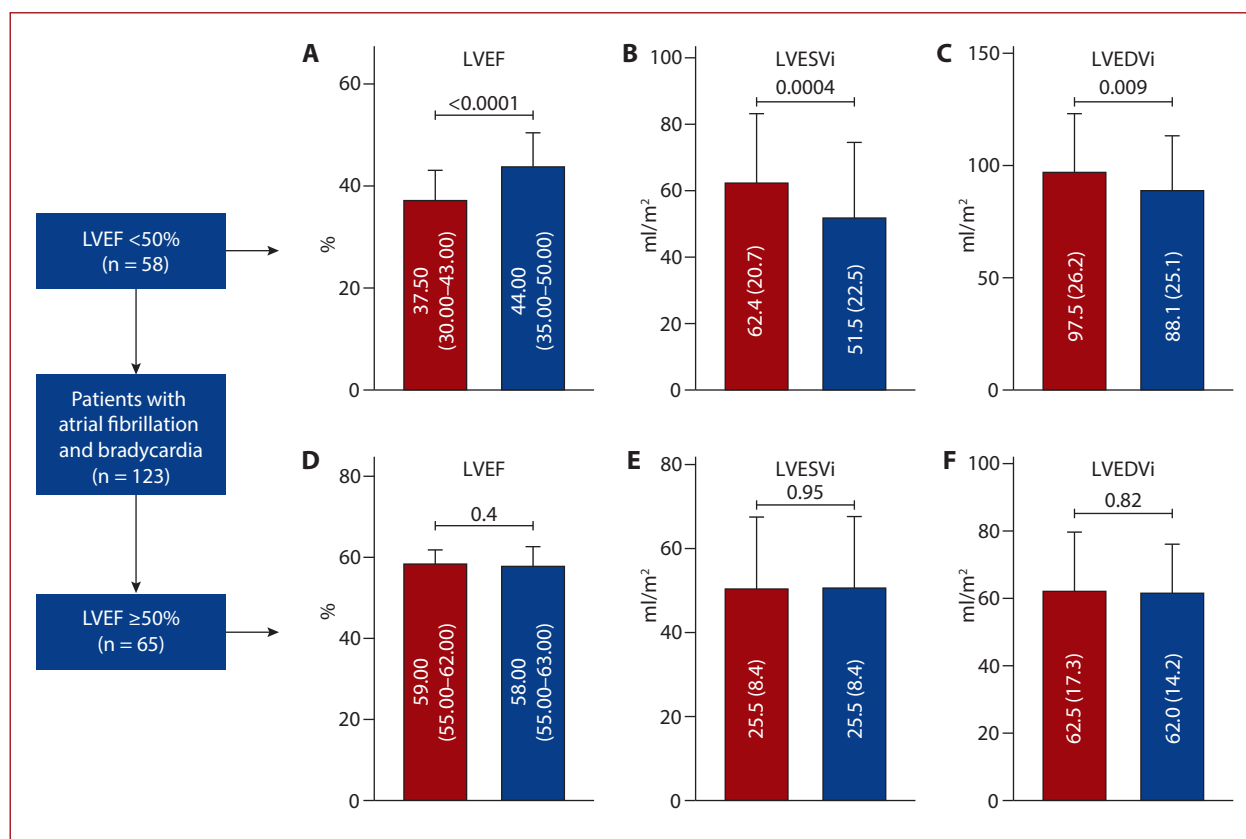
### Background

With the number of yearly implantations of cardiac implantable electronic devices approaching 1000 per million inhabitants and an increasing frequency of both AF and bradyarrhythmia due to the aging population, the coexistence of these problems remains a significant issue [14–16]. The primary goal in treating bradycardia is restoring the normal heart rate, which is an essential function of a pacemaker. AF, however, can affect cardiac function in several ways. Loss of atrial contraction and slow heart rate in bradyarrhythmia patients result in reduced cardiac output. Nonetheless, a rhythm irregularity leads to arrhythmia-induced cardiomyopathy [2], with a decrease in cardiac output observed by Clark et al. [17]. Permanent pacing, with any pacing modality, may improve cardiac function in patients with AF and low ventricular rate by ensuring an adequate and regular heart rate [18].

Non-physiological electromechanical activation caused by RVP may, however, diminish the positive effect of permanent pacing on cardiac function. Conversely, CSP maintains more physiological activation, especially regarding LV. By using CSP, which provides better electromechanical synchrony, we achieve more optimal LV function than with RVP. The effect was observed in a relevant subgroup of our patients, and, according to other studies, it seems to be at least not worse than the effect of biventricular pacing [7, 19–23].

### Other relevant studies

Numerous studies examine HBP, and our results align with other observations regarding preserving or improving LVEF [24]. However, other studies include mostly patients



**Figure 1.**

Abbreviations: LV, left ventricle; Vp, ventricular pacing; other — see Table 2

**Table 4.** Comparison of echocardiographic measurements in the normal and low LVEF groups at baseline and during follow-up

	LVEF ≥50% at baseline (n = 65)			LVEF <50% at baseline (n = 58)		
	Baseline	Follow-up	P-value	Baseline	Follow-up	P-value
LVEDD, mm	50.6 (5.7)	51.0 (6.3)	0.45	60.1 (7.2)	57.9 (7.0)	0.006
LVESD, mm	33.5 (6.2)	33.9 (7.0)	0.57	46.8 (9.4)	44.7 (9.0)	0.04
LVSVi, ml	37.0 (10.4)	36.5 (7.8)	0.66	35.1 (9.5)	36.6 (9.4)	0.24
LVEF, %	59.0 (55.0–62.0)	58.0 (55.0–63.0)	0.4	37.5 (30.0–43.0)	44.0 (35.0–50.0)	<0.001
TAPSE, mm	20.4 (4.6)	19.7 (4.3)	0.26	17.1 (4.8)	17.9 (4.3)	0.30
MR ≥2, n(%)	19 (31.1%)	19 (31.1%)	1.00	26 (51.0%)	18 (35.3%)	0.10
MR area, cm <sup>2</sup>	6.7 (3.0)	6.5 (2.9)	0.8	9.7 (3.6)	7.2 (3.2)	0.007
TR ≥2, n(%)	31 (47.7%)	38 (58.5%)	0.14	27 (46.6%)	28 (48.3%)	1.00
TR area, cm <sup>2</sup>	8.8 (3.8)	9.7 (4.4)	0.48	11.2 (5.2)	11.6 (4.5)	0.79

Values are n (%), median (IQR) for nonparametric variables, and mean (SD) otherwise

Abbreviations: see Table 2

with preserved sinus rhythm, and data on patients with AF only are scarce.

Huang et al. also showed a promising reduction in the NYHA class and an improvement in LV function, especially in patients with baseline LVEF <40% [25]. While the results are better than in our trial, their team used more strict inclusion and exclusion criteria and targeted different kinds of patients. The population was smaller (n = 42 with HBP) and had an average heart rate of 83.9 (14.1) beats/min. At baseline and subsequently, AVNA was performed in all cases.

Occhetta et al. [26] conducted a study focusing on patients with permanent AF but who had earlier received

AVNA. In that randomized trial, HBP was better than both baseline and RVP in terms of the NYHA, 6-minute walk test, and mitral regurgitation, while tricuspid regurgitation was lower in the HBP group than in the RVP group. There were no significant differences in LVEF, LVEDV, and LVESV; however, the sample size was small (n = 16), device upgrades were not considered, and only patients with narrow QRS and tachycardia were included.

Another study involving a group of 65 patients who received HBP was presented by Jastrzębski et al. [27], who stated that HBP can be used as an alternative standard method of pacing in patients with AF and symptomatic

bradycardia. While showing promising and stable electrical parameters, Jastrzębski and colleagues did not focus on clinical follow-up. Similar procedure times were reported for another CSP method, namely LBBAP. The inequality in fluoroscopy time was related to differences in electrocardiographic methods while other reported numbers were more pacing-method specific [28].

A group of patients similar to ours who received CSP without prior AVNA was presented by Sheng et al. They reported no significant difference in LV and RV synchrony between HBP and LBBAP, along with better interventricular synchrony provided by HBP [29]; however, they did not address potential clinical effects. Also, this crossover study included only 20 patients with AF and bradycardia and presented only three months of short-term follow-up limited to electrophysiological data.

Interestingly, conclusions similar to ours were drawn by Bednarek et al. [30] in a group of 151 patients with bradycardia who received CSP in the form of LBBAP. They found that in long-term follow-up, LBBAP improves LV systolic function in subjects with decreased EF, and preserves it in patients with initially normal EF. In the that study, 16.8% of subjects had persistent AF while in our case, only patients with permanent or long-lasting persistent AF were included. Moreover, 30% of our patients underwent an upgrade from the existing device with RVP.

### Other observations and perspectives

The synchrony maintained or restored by HBP results in QRS identical to or strongly resembling the native one, potentially with correction of bundle branch block. It correlates with improved cardiac contractility and reverse remodeling observed by us and other researchers, which translates to clinical improvements [7, 8]. Therefore, HBP may be a promising pacing method to treat heart failure or prevent its development in patients with a high anticipated pacing burden, possibly better than RVP. The additional advantage is that it enables more aggressive treatment of tachycardia-bradycardia syndrome without the risk of developing PICM. Improved rate control may have played a role in our population since, to minimize the risk of developing PICM, it was initially moderate (70.4% [33.4] of RVP in patients undergoing an upgrade).

Moreover, the effects of physiological pacing may involve more than ventricular reverse remodeling. In two of our patients, AF disappeared spontaneously before the follow-up visit. Based on all available data from our registry, five patients experienced a spontaneous return to sinus rhythm between two and forty-nine months after the HBP procedure. While this observation was unexpected, other reports suggest that physiological pacing reduces the risk of developing AF or reduces its burden [31–33]. These findings suggest a need for more cautious decisions during the implantation phase and careful analysis during the follow-up phase, even if AF is considered permanent.

In our study, 24.4% of the population was over 80 years old, and we did not observe any age-related differences in outcomes or complications. The feasibility and safety of HBP and LBBAP in elderly populations was previously demonstrated [34, 35].

### Study limitations

The research was a single-center, non-randomized study. Although the follow-up period was sufficient to show the effects of pacing, it might not have been long enough to show its full extent [36]. Clinical outcomes like mortality and hospitalization for heart failure were not assessed. It should be noted that all patients from the presented cohort received HBP. Currently, CSP is most often performed using LBBAP; however, HBP is considered the most physiological pacing approach and a recognized CSP method.

## CONCLUSION

The findings of this prospective observational study suggest that HBP is a promising technique in patients with AF without prior AVNA who require a pacemaker due to bradycardia. This pacing method was associated with positive results by providing almost physiological activation and synchrony. With HBP, we observed LV function maintained in patients with normal LVEF at baseline despite a high pacing burden. In patients with impaired LV function, however, not only did LVEF improve, but LV dimensions were also reduced as a marker of reverse remodeling. With these effects, such pacing seems a current alternative to RVP and classical biventricular pacing.

### Article information

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