ORIGINAL ARTICLE

A randomized comparison of His bundle pacing versus right ventricular pacing: Effect on left ventricular function and biomarkers of collagen metabolism

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DOI: 10.33963/KP.a2023.0065

Received:
November 1, 2022

Accepted:
January 2, 2023

Early publication date:
March 9, 2023

ABSTRACT

Background: Right ventricular pacing (RVP) can result in pacing-induced cardiomyopathy (PICM). It is unknown whether specific biomarkers reflect differences between His bundle pacing (HBP) and RVP and predict a decrease in left ventricular function during RVP.

Aims: We aimed to compare the effect of HBP and RVP on the left ventricular ejection fraction (LVEF) and to study how they affect serum markers of collagen metabolism.

Methods: Ninety-two high-risk PICM patients were randomized to HBP or RVP groups. Their clinical characteristics, echocardiography, and serum levels of transforming growth factor β1 (TGF-β1), matrix metalloproteinase 9 (MMP-9), suppression of tumorigenicity 2 interleukin (ST2-IL), tissue inhibitor of metalloproteinase 1 (TIMP-1), and galectin 3 (Gal-3) were studied before pacemaker implantation and six months later.

Results: Fifty-three patients were randomized to the HBP group and 39 patients to the RVP group. HBP failed in 10 patients, who crossed over to the RVP group. Patients with RVP had significantly lower LVEF compared to HBP patients after six months of pacing (−5% and −4% in as-treated and intention-to-treat analysis, respectively). Levels of TGF-β1 after 6 months were lower in HBP than RVP patients (mean difference −6 ng/ml; $P = 0.009$) and preimplant Gal-3 and ST2-IL levels were higher in RVP patients, with a decline in LVEF ≥5% compared to those with a decline of <5% (mean difference 3 ng/ml and 8 ng/ml; $P = 0.02$ for both groups).

Conclusion: In high-risk PICM patients, HBP was superior to RVP in providing more physiological ventricular function, as reflected by higher LVEF and lower levels of TGF-β1. In RVP patients, LVEF declined more in those with higher baseline Gal-3 and ST2-IL levels than in those with lower levels.

Key words: His bundle pacing, markers of collagen metabolism, right ventricular pacing

INTRODUCTION

Myocardial pacing of the right ventricle (RVP) is responsible for declining left ventricular (LV) function and heart failure in some patients. The highest risk of these adverse consequences is seen in older patients with a high burden of RV pacing, decreased left ventricular function, coronary artery disease (CAD), and wider spontaneous or paced QRS complexes [1]. His bundle pacing (HBP) preserves synchronous ventricular activation and represents the most physiological method of ventricular pacing [2, 3]. This pacing method is more complex, with longer procedure times and higher radiation doses, and requires more sophisticated equipment [4]. For these reasons, HBP is best suited for patients who would gain the most from physiological ventricular activation. However, the benefit of HBP in high-risk populations has never been described.

Although RV pacing is non-physiological, most patients tolerate it even for extended

WHAT'S NEW?

In patients at high risk of pacing-induced cardiomyopathy, His bundle pacing does not worsen left ventricular function in contrast to right ventricular pacing, which leads to its decline. Higher galectin 3 and suppression of tumorigenicity 2 interleukin (ST2-IL) levels in patients treated with right ventricular pacing are associated with decline in left ventricular ejection fraction after six months of pacing. Galectin 3 and ST2-IL may improve identification of patients in whom right ventricular pacing will not be associated with decline in left ventricular function.

periods [5]. Currently, we cannot precisely tell (before pacemaker implantation) which patients will experience deterioration in ventricular function after RV pacing. The period after which pacing-induced cardiomyopathy (PICM) starts to develop is estimated to be 2–3 years. However, subtle changes in LV function (i.e., ≥5% decline) can present sooner, and these patients are at the highest risk of further heart failure [6]. Remodeling and altered LV function are present together with changes in the ventricular microstructure. These changes are reflected by perfusion changes in particular ventricular segments, abnormal myocardial metabolism, increased fibrosis, and myocardial disarray [7]. It was already shown that subtle myocardial microstructure changes in patients after myocardial infarction or heart failure could be evaluated using collagen metabolism biomarkers [7]. However, their significance in patients with a permanent pacemaker has not been established yet. Demonstrating their relevance to LV performance in these patients could be an important marker of increased risk of further heart failure.

Our study aimed to assess the effect of RVP and HBP on LV function in patients at high risk of heart failure after cardiac pacing. Another goal was to identify laboratory markers that can predict or detect the adverse effects of RV pacing on LV performance.

METHODS

Patients

This was a prospective open-label randomized study with the anticipated recruitment of 120 patients. The project was approved by the Ethics Committee of the Faculty Hospital Kralovske Vinohrady, Prague, Czech Republic; all subjects signed informed consent before enrollment. Only patients with conduction disease and an indication for permanent cardiac pacing per the 2013 European Society of Cardiology (ESC) guidelines were enrolled. Patients had to have a permanent conduction disease with an anticipated high burden of the RV pacing and life expectancy greater than two years. Also, at least one of the following criteria had to be fulfilled: (1) left ventricular ejection fraction (LVEF) ≤60%; (2) QRS duration >115 ms; (3) presence of ischemic heart disease (defined as previous myocardial infarction or coronary intervention due to significant occlusion of coronary arteries or angina pectoris requiring pharmacological treatment).

Exclusion criteria were as follows: a severe valvular disease with a planned intervention, cardiac surgery due to valvular disease or CAD in the previous three months, permanent or persistent atrial fibrillation, dilated or hypertrophic cardiomyopathy, active myocarditis and an indication for cardioverter-defibrillator implantation or cardiac resynchronization therepy. Patients were randomized to the HBP or RVP arms with a 4:3 ratio; the anticipated His bundle pacing success rate was 80%–90%. After randomization, patients were informed which arm of the study they were enrolled in. After pacemaker implantation, outpatient clinic follow-ups were at six weeks and six months. During these visits, the pacemaker was checked (with data collection), patient clinical status was assessed, and a physical examination was performed. Blood sampling and echocardiography were performed before pacemaker implantation and at the six-month follow-up visit.

Pacemaker implantation

His bundle pacing was performed using Select Secure leads (model 3830, 69 cm, Medtronic Inc., Minneapolis, MN, US) delivered through a fixed-curve sheath (C315 HIS, Medtronic, Minneapolis, MN, US) preferentially from the left subclavian approach. The end of the sheath was delivered to the tricuspid annulus over the guidewire, and then the pacing lead was advanced through the sheath 1–2 mm beyond the tip of the catheter. The His bundle area was mapped in unipolar settings using an electrophysiology system (Lab system Pro, Boston Scientific, Marlborough, MA, US) at a sweep speed of 200 mm/s. After the His bundle signal was identified, the lead was fixed by 3–5 clockwise rotations, and pacing from the lead tip was initiated. For the implant procedure to be considered successful, selective, or nonselective, His bundle capture had to be present during the pacing with a pacing output below 2.5 V at 1 ms.

RV septal pacing was performed using Tendril® (Abbott, Little Canada, MN, US) or Ingevity® (Boston Scientific, Marlborough, MA, US) pacing leads, preferably from the left subclavian approach. Once the lead was placed in the RV outflow tract/pulmonary artery, the stylet was pre-shaped, and the lead was fixed in the RV septum using the RAO projection and counter-clockwise torque on the leads' stylet. The lead tip septal position was verified in the RAO 30° and LAO 30° projections.

Echocardiography

Echocardiography assessments were performed one day before and six months after pacemaker implantation by three cardiac sonographers using a GE Vivid E95 Cardiovascular Ultrasound (Boston, MA, US). Two evaluators blinded to the studied groups measured and calculated end-diastolic and end-systolic volumes from the apical 4- and 2-chamber views, and LVEF was calculated using the formula: EF = ([LVEDV – LVESV] ÷ LVEDV) (modified Simpson's method) (definitions: EF, ejection fraction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume). The mean value of LVEF calculated by each evaluator was used for statistical analyses.

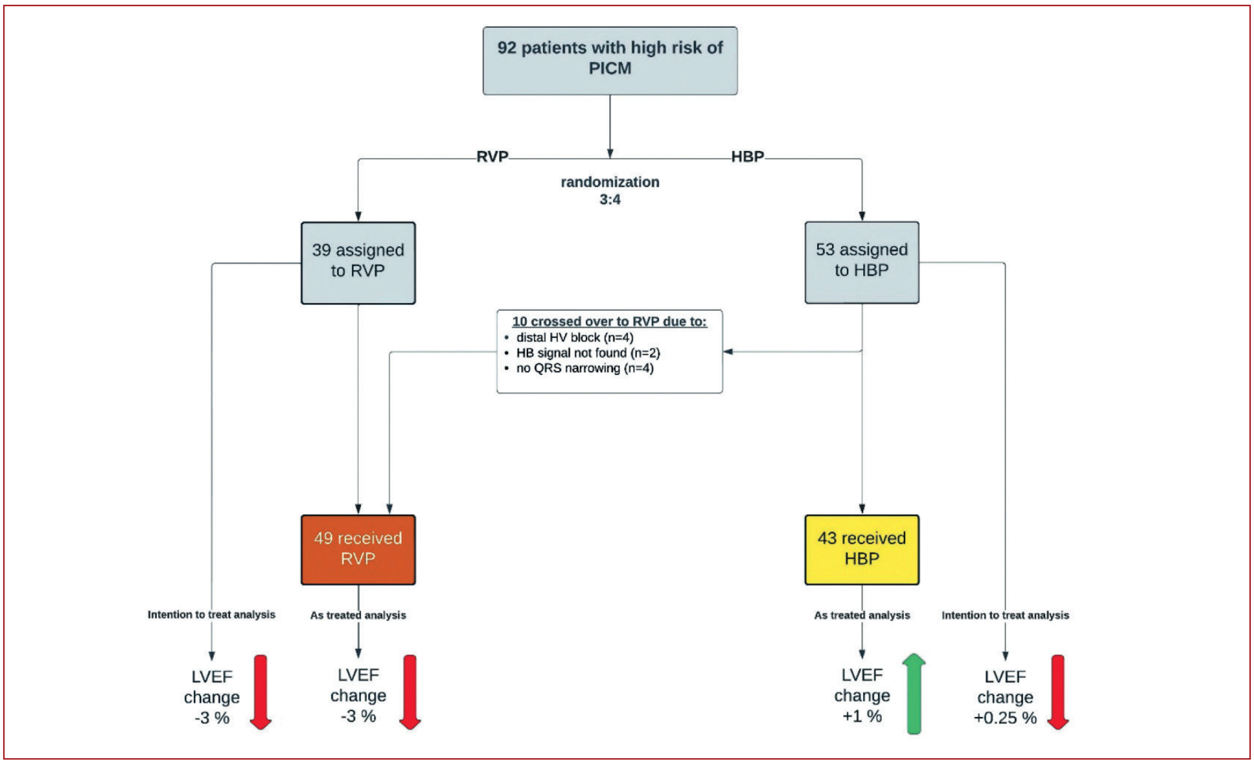
Blood sample collections and quantification of cytokines

Approximately four mL of peripheral venous blood were collected from each patient. Blood samples were centrifugated at 950 g for 20 minutes. Serum samples were aliquoted and stored at –80 °C. Samples were thawed before quantifying transforming growth factor β1 (TGF-β1), matrix metalloproteinase 9 (MMP-9), suppression of tumorigenicity 2 interleukin (ST2-IL), tissue inhibitor of metalloproteinase 1 (TIMP-1), and galectin 3 (Gal-3) levels. Per the manufacturer's instructions, the measurements of the selected biomarkers were performed using specific Quantikine ELISA kits (R&D Systems, Minneapolis, MN, US).

Statistical analysis

Statistical analysis was performed using Software: R version 4.0.5 (March 31, 2021). Exploratory data analysis was performed for all variables. Categorical data were presented as count with frequency and continuous data as mean with standard deviation (SD) or median with interquartile ranges (IQR) for nonparametric data. Kolmogorov and Smirnov tests were used for normality testing, and further statistical analysis included a linear mixed effect model with random intercept, Student's t-test, Fisher's exact test, and χ^2 test.

For the linear mixed effect model, the fixed part of the model is represented by the interaction between two binary parameters: stimulation site (His vs. septum) and visitation (Day 0 vs. Day 180). The random part of the model is represented by the random intercept, which is the patient identification number. A maximum likelihood estimator was used to fit models (function lmer of package lme4) [8]. Post-hoc analysis was performed using the emmeans package. Intention-to-treat and as-treated analyses were performed. For nonparametric data, the Wilcoxon test and Mann-Whitney U test were used. A P <0.05 was considered statistically significant. The area under the curve (AUC) of the receiver operating characteristic (ROC) curve was calculated for ST2-IL and Gal-3 to assess their predictive value for LVEF deterioration. The optimal cut points of both markers were calculated using maximization of the Youden index (sensitivity + [specificity – 1]). This was a pilot feasibility



Central illustration. Study flow-chart and the effect of right ventricular pacing and His bundle pacing on LVEF after six months of pacing in intention-to-treat and as-treated analyses

Abbreviations: HBP, His bundle pacing; LVEF, left ventricular ejection fraction; PICM, pacing-induced cardiomyopathy; RVP, right ventricular myocardial pacing

Table 1. Baseline clinical characteristics of the study population

	Intention-to-treat			As-treated		
	RVP (n = 39)	HBP (n = 53)	*P*-value	RVP (n = 49)	HBP (n = 43)	*P*-value
Age, years, mean (SD)	78 (7)	78 (8)	0.99	79 (7)	77 (8)	0.33
Male sex, n (%)	39 (80)	38 (88)	0.26	33 (85)	44 (83)	0.84
LVEF, %, mean (SD)	58 (7)	60 (5)	0.27	59 (6)	59 (4)	0.54
Arterial hypertension, n (%)	38 (97)	51 (96)	0.75	48 (98)	41 (95)	0.49
Diabetes mellitus, n (%)	16 (41)	20 (38)	0.75	18 (37)	18 (42)	0.62
CAD, n (%)	15 (38)	23 (43)	0.64	18 (37)	20 (47)	0.34
Myocardial infarction in history, n (%)	5 (14)	14 (27)	0.15	8 (17)	11 (26)	0.32
Spontaneous QRSd, ms,mean (SD)	126 (27)	125 (25)	0.80	126 (26)	126 (27)	0.98
Spontaneous QRS morphology, n (%)						
BBB	16 (41)	20 (38)	0.78	19 (39)	17 (40)	0.66
Narrow (<115 ms)	12 (31)	20 (38)		16 (33)	17 (40)	
NIVCD	11 (28)	13 (24)		14 (28)	9 (20)	
Pacing indication, n (%)						
AV block I. degree	5 (13)	7 (13)	0.95	6 (12)	6 (14)	0.94
AV block II. degree	16 (41)	25 (47)		21 (43)	20 (47)	
AV block III. degree	16 (41)	19 (36)		20 (41)	15 (35)	
BBB + syncope	2 (5)	2 (4)		2 (4)	2 (4)	

Abbreviations: AV block, atrioventricular block; BBB, bundle branch block; CAD, coronary artery disease; NIVCD, non-specific intraventricular conduction delay; other — see Central illustration

trial, and no power calculation was performed before the initiation of the study.

RESULTS

Ninety-two patients were enrolled in the study. The mean age was 78 years, and all had atrioventricular conduction disease as the pacing indication. Planned patient recruitment was not reached, and randomization was stopped due to challenges during the COVID-19 pandemic. Fifty-three patients were randomized to the His bundle pacing (HBP) group, and 39 were randomized to the right ventricular pacing (RVP) group. Lead placement in the HB region failed in 10 of 53 patients (19%) randomized to the HBP group. The lead was then successfully placed in the RV with myocardial capture in all patients. However, two of these patients (20%) required ventricular lead revision due to pacing threshold rise. The reasons for lead implant failure in the HB region were as follows: (1) in two patients, the HB signal was not found; (2) in four patients, the distal HV block could not be corrected by HB pacing; and (3) in four patients, pacing the HB region did not lead to conductive tissue capture with QRS narrowing. As a result, 49 patients had RVP (47 septal and two apical lead positions), and 43 had HBP. No difference in clinical characteristics was observed between groups relative to intention-to-treat and as-treated analyses (Table 1).

HBP required a longer fluoroscopy time (in intention-to-treat analysis), higher acute and chronic pacing thresholds, and presented with lower acute and chronic ventricular sensing than RVP. However, there was no difference in rates of lead repositions due to higher pacing thresholds between HBP and RVP groups (Table 2).

There was no difference between HBP and RVP groups in the preimplant LVEF in both intention-to-treat and as-treated comparisons. However, LVEF significantly decreased after six months of RVP but remained the same in the HBP group. Also, LVEF was significantly lower in the RVP group than in the HBP group after six months of follow-up in both as-treated (P <0.001) and intention-to-treat analysis (P = 0.008) (Figure 1).

A decline in LVEF ≥5% after six months of pacing was observed in 13 of 46 patients (28%) in the RVP group but in none in the HBP group. Among patients with RVP, a decline in LVEF ≥10% was observed in nine patients (20%); and in eight patients (17%), the resultant LVEF was ≤ 45% after six months of pacing.

There was no difference in baseline serum levels of TGF-β1, MMP-9, ST2-IL, TIMP-1, and Gal-3 between patients with HBP vs. patients with RVP (both as-treated and intention-to-treat comparison). In the RVP group, in an as-treated comparison, a significant decline in the levels of ST2-IL and TIMP-1 was observed after six months of pacing, but no difference in the serum levels of TGF-β1, MMP-9, and Gal-3 was detected. In the HBP group, a significant decline in the serum level of ST2-IL, MMP-9, and TGF-β1 was seen after six months of pacing; the levels of Gal-3 and TIMP-1 remained statistically the same. When comparing differences in serum levels of studied biomarkers between HBP and RVP patients six months after pacemaker implantation, the only difference was observed in the levels of TGF-β1, which were significantly lower in the HBP group than in the RVP group (Figure 2).

To determine whether cytokine levels before pacemaker implantation could predict an LVEF decline of ≥5%, we compared cytokine levels in patients with RVP and an LVEF decline of ≥5% (13 patients) vs. cytokine levels in patients with RVP and an LVEF decline < 5% (36 patients). Patients in both groups did not differ with respect to age, sex, pre-

Table 2. Procedural and follow-up pacing characteristics

		Intention-to-treat			As-treated		
		RVP	HBP	*P*-value	RVP	HBP	*P*-value
Pacing thresholds, V, at 0.4 ms, mean (SD)	D1	0.7 (0.3)	1.4 (0.6)	<0.001	0.8 (0.4)	1.5 (0.6)	<0.001
	D180	0.9 (0.6)	1.7 (1.1)	0.004	1.1 (0.7)	1.7 (1.1)	0.005
	D1 vs. D180 *P*-value	0.35	0.11		0.40	0.21	
Ventricular sensing, mV, mean (SD)	D1	9.4 (3.5)	4.5 (3.3)	<0.001	9.3 (3.7)	3.5 (2.0)	<0.001
	D180	9.5 (2.9)	4.3 (3.2)	<0.001	9.3 (3.1)	3.2 (2.0)	<0.001
	D1 vs. D180 *P*-value	0.91	0.75		0.98	0.54	
Fluoroscopy time, sec, median (IQR)		242 (171–413)	505 (270–835)	<0.001	329 (190–553)	399 (249–679)	0.34
Burden of ventricular pacing after 180 days, mean (SD)		92 (18)	98 (4)	0.02	95 (17)	98 (4)	0.09
Threshold rise requiring lead revision, n (%)		2 (5)	4 (8)	0.64	4 (8)	2 (5)	0.50

Abbreviations: see Central Illustration

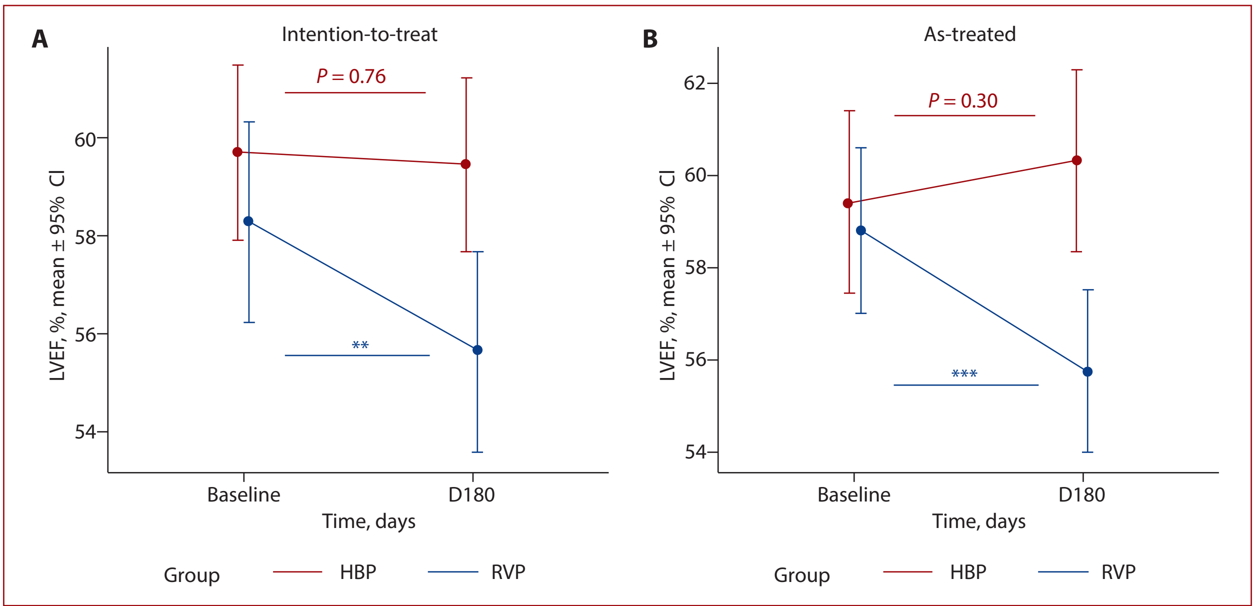


Figure 1. Comparison of LVEF in the HBP and RVP groups using per intention-to-treat (**A**) and as-treated (**B**) analyses
**P <0.01. ***P <0.001

Abbreviations: see Central illustration

implant LVEF, QRS duration during spontaneous rhythm, the prevalence of CAD, myocardial infarction, hypertension, or diabetes mellitus.

Patients with an LVEF decline of ≥ 5% after six months of RVP had higher baseline levels of Gal-3 and ST2-IL. After six months, the elevations of both markers persisted and were higher than in patients with an LVEF decline of < 5% in the primary analysis and also after adjustment to the baseline levels of both molecules (Figure 3 and Supplementary material, *Figure S1*). During RVP, a decline in TIMP-1 was observed in patients without deterioration of LVEF (P = 0.04). No difference in serum levels of the other studied biomarkers was found before and after six months of RVP (Figure 3). The ROC analysis showed an AUC of 0.79 for Gal-3 and 0.71 for ST2-IL relative to the prediction of a decline in LVEF ≥5% (Figure 4). Gal-3 serum concentrations ≥8.88 ng/ml were 100% sensitive and 61% specific, with a positive predictive value of 45%, a negative predictive value of 100%, and an accuracy of 72%; ST2-IL concentrations ≥19 ng/ml showed 90% specificity and 52% specificity, with a positive predictive value of 38%, a negative predictive value of 94%, and an accuracy of 71% for detection of patients with a decline in LVEF ≥5% after six months of RV pacing.

In the HBP group, patients with higher baseline Gal-3 (>8.88 ng/ml) and ST2-IL (>19 ng/ml) levels did not differ in LVEF change after 6 months of follow-up in comparison to patients with lower baseline Gal-3 and ST2-IL levels (LVEF change 1 vs. 1% and 1 vs. 1%; P = 0.66 and P = 0.72, respectively).

DISCUSSION

This study compared the effect of His bundle pacing and RV myocardial pacing on LVEF in patients at high risk of pacing-induced cardiomyopathy. Also, this is the first trial studying fibrosis biomarkers in patients with pacemak-

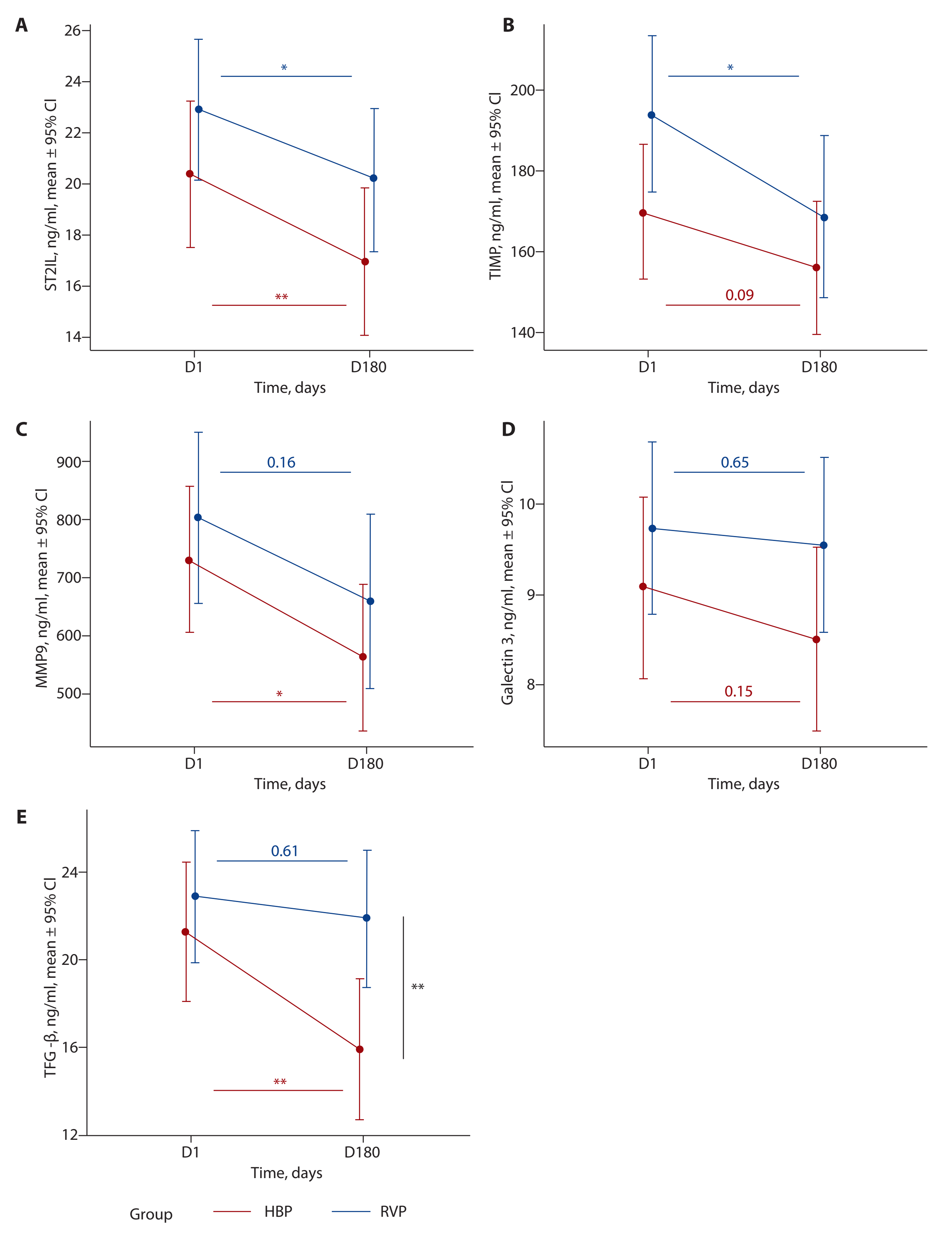


Figure 2. Comparison of serum levels of ST2-IL, TIMP-1, MMP-9, galectin 3, and TGF-β1 at baseline and after six months of pacing in the HBP vs. RVP groups per as-treated analysis

*P <0.05. **P <0.01

Abbreviations: MMP-9, matrix metalloproteinase-9; ST2-IL, suppression of tumorigenicity 2 interleukin; TGF-β1, transforming growth factor β1; TIMP-1, tissue inhibitor of metalloproteinase-1; other — see Central illustration

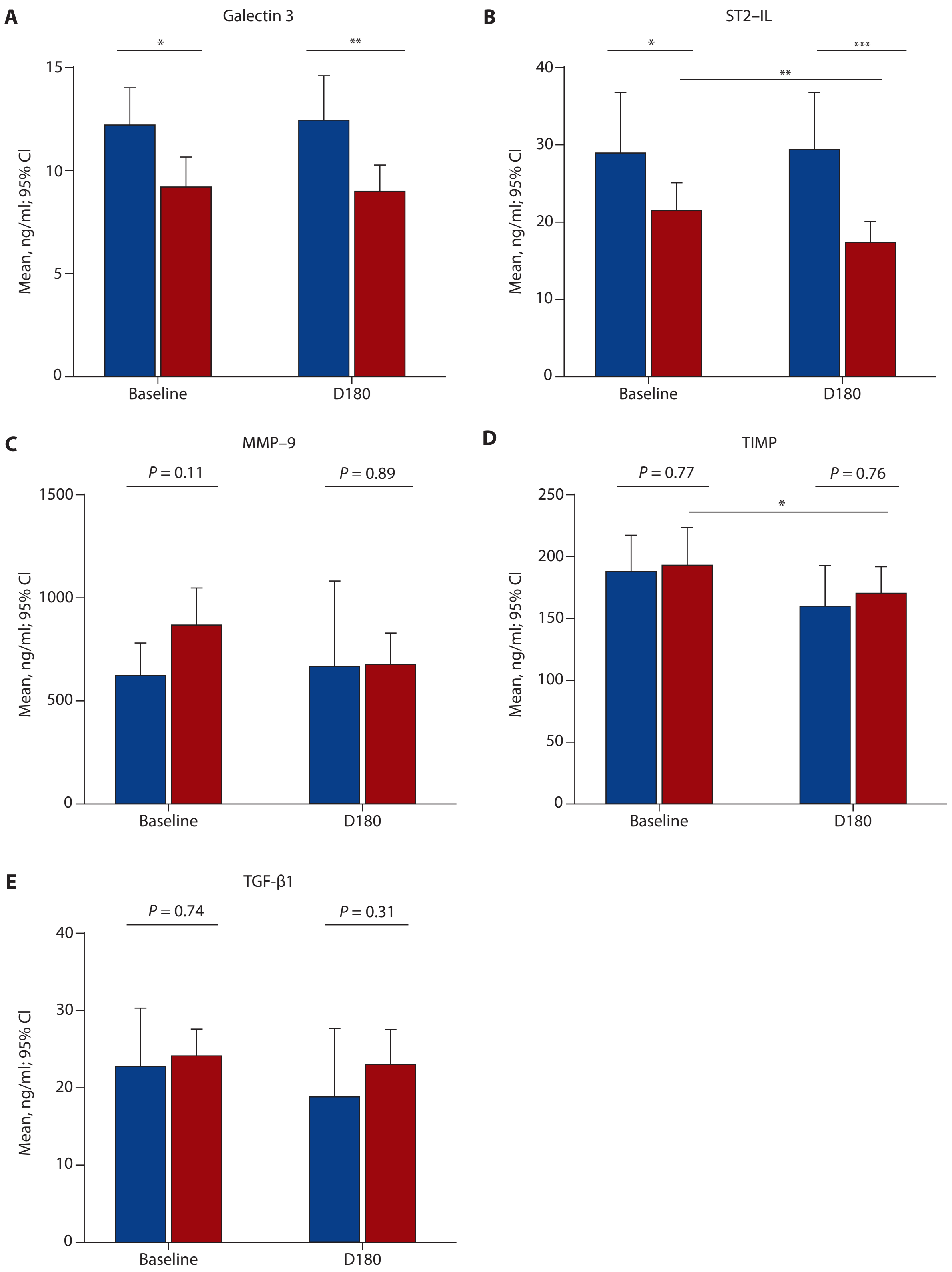


Figure 3. Comparison of serum levels of galectin 3, ST2-IL, MMP-9, TIMP-1, and TFG-β1 before implant and after six months of pacing in patients with RVP and preserved LVEF vs. patients with reduced LVEF by ≥5%

Abbreviations: see Central illustration and Figure 2

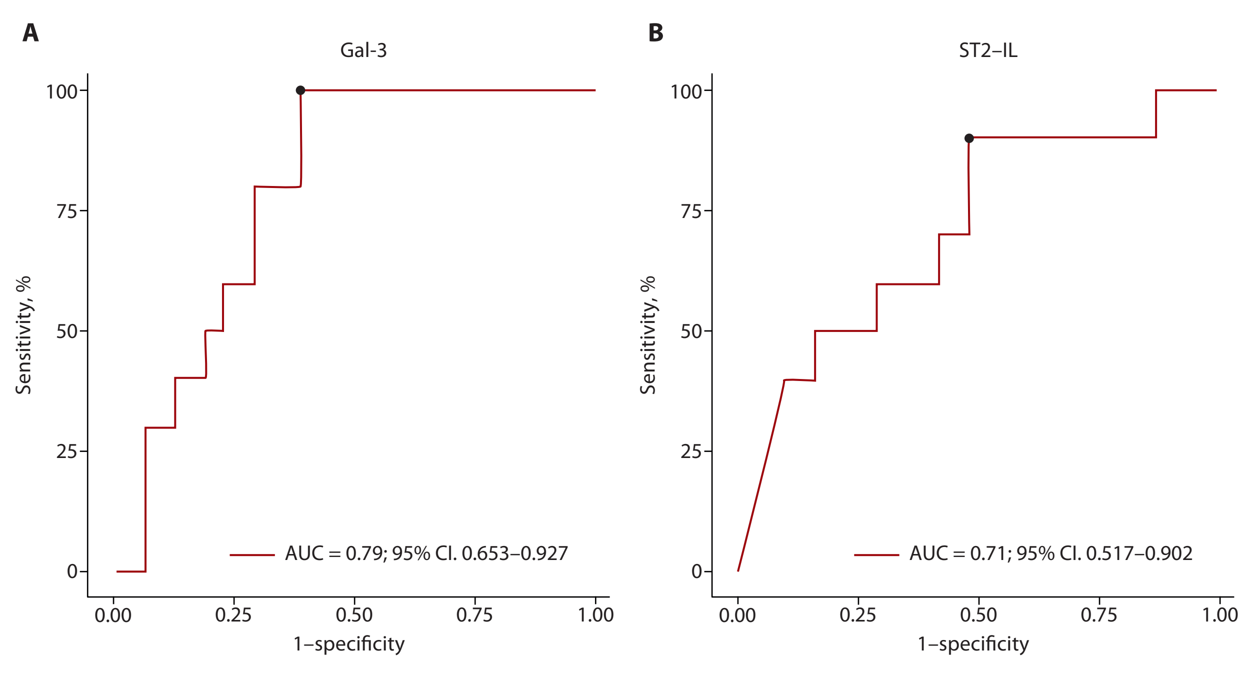


Figure 4. Receiver operating characteristic (ROC) curves of galectin 3 (**A**) and ST2-IL (**B**) in patients with and without decrease in LVEF of ≥5% after six months of RVP

Abbreviations: see Central illustration and Figure 2

ers. We showed that the adverse effect on LV function with a LVEF decline of ≥5% after pacing was not uncommon and affected almost one-third of patients with RV pacing, with LVEF falling below 45% in 17% of patients in that group. On the other hand, HBP preserved LV function in all patients. We also showed that initiation of permanent cardiac pacing resulted in changes in the serum levels of some of the studied biomarkers, with serum TGF-β1 levels reflecting different ventricular activation during HBP and RVP. Lastly, patients with a decline in LVEF of ≥5% due to non-physiological RV pacing had significantly higher serum levels of Gal-3 and ST2-IL than patients with a <5% decline in LVEF, both at the baseline and after six months of RV pacing.

HBP vs. RVP

His bundle pacing is well established, and guidelines support the treatment option in selected patients with bradycardia [9]. However, data from randomized trials supporting its use in a wider spectrum of patients are missing. So far, only one randomized trial comparing His bundle pacing to right ventricular septal pacing in patients with conduction disease has been published [10]. It used a crossover design, with HBP and RV pacing being utilized in the same patients for 12 months, and the number of randomized patients was small. Moreover, the studied population differed from our group, e.g., it only had patients with narrow QRS complexes (the average was 93 ms), and most were without coronary artery disease. The study showed that HBP preserved LVEF and ventricular synchrony better than right ventricular septal pacing, which resulted in a significant decline in LVEF (mean decline of 4 ± 1%). A similar level of LVEF deterioration during RVP occurred in a shorter period in our study; possibly reflecting the higher risk profile of our patients. Coronary artery disease was present in one-third of our patients, and the average QRS duration was 126 ms; both have been associated with higher risk of adverse LV remodeling during pacing [1]. Considering the relationship between the severity of the LVEF decline and the duration of non-physiological RV pacing, it is possible that the difference in LVEF between HBP and RVP patients would be even greater with a longer follow-up. In our study, a ≥5% decrease in LVEF was seen only in patients with RV pacing. Although a 5% decline in LVEF could be considered clinically negligible, it was previously shown that patients who demonstrate a slight decrease in LVEF soon after the pacemaker implantation were at the highest risk of further PICM [11]. PICM is often defined as a decline in LVEF of more than 10% and/or LVEF <50% [1]. Using this definition, 20 % of patients in our high-risk population developed PICM after six months of pacing. This agrees with the numbers reported by other investigators; however, PICM occurred later after pacemaker implantation than in our study [1].

The difference in serum levels of studied cytokines between HBP and RVP

In patients with bradycardia and pacemaker implantation, we studied serum levels of collagen metabolism and fibrosis biomarkers, which were already shown to play a role in adverse ventricular remodeling in different clinical scenarios [12–15]. Right ventricular myocardial pacing leads to non-physiological ventricular activation with adverse remodeling and LVEF deterioration in some patients [7]. These changes should be reflected in serum levels of biomarkers of fibrosis although they have yet to be studied in patients with pacemakers. We showed that cardiac pacing (HBP or RVP) led to a decline in the serum levels of some of the studied cytokines; however, after six months of pacing, the groups differed only in the levels of TGF-β1. TGF-β1 is a pleiotropic cytokine critically involved in cardiac injury, repair, remodeling, and fibrogenesis. It also exerts potent matrix-preserving actions by suppressing the activity of MMPs and by inducing the synthesis of protease inhibitors, such as TIMP-1. Elevated TGF-β1 levels in experimental vivo models of heart failure were associated with increased myocardial stiffness, fibrosis, and LV diastolic dysfunction [16]. We found that TGF-β1 declined after the institution of HBP but remained the same in RVP patients. This may reflect normalization of atrioventricular synchrony with truly physiological ventricular activation in HBP patients [17]. In RVP patients, AV synchrony was also normalized, but at the cost of non-physiological ventricular activation due to RV pacing, which is associated with worsening LV diastolic function [18].

New pacing strategies, such as His bundle pacing and left bundle branch area pacing, reduce the risk of adverse LV remodeling and heart failure in bradycardia patients [3, 19]. However, because they are more complex, the techniques may be best suited for those with the highest risk of LVEF deterioration after RVP. This remains a challenge because we still cannot accurately predict which patients will have a decline in LVEF due to RVP. Our theory was that the detrimental effect of RVP would be seen mostly in patients susceptible to the harmful effect of RV pacing, i.e., with pre-existing conditions, such as increased myocardial fibrosis, which could be reflected in serum levels of studied biomarkers. Therefore, we compared these biomarkers in patients with an LVEF decline of ≥5% vs. those with preserved LVEF during RVP (i.e., <5%). The only cytokines that showed different preimplant levels were Gal-3 and ST2-IL, both known as prognostic biomarkers in heart failure patients and involved in collagen metabolism and ventricular remodeling [14, 15]. Data on their significance in patients with pacemakers are scarce. However, it was already shown that higher preimplant Gal-3 levels were negatively associated with response to cardiac resynchronization therapy and higher levels of myocardial fibrosis in ventricular myocardium, as seen on preimplant cardiac magnetic resonance [20]. It is possible that increased levels of Gal-3 and ST2-IL in our patients with a more significant decline in LVEF during RVP reflected a higher degree of pre-implant myocardial fibrosis, which led to a more deleterious effect of RV pacing on LV performance. On the other hand, patients without significant myocardial fibrosis have a greater ability to compensate for dyssynchronous ventricular activation during RVP while maintaining LVEF.

Limitations

This was a single-center study with echocardiographic follow-up restricted to six months, which prohibited tracking LVEF changes and clinical outcomes over a more extended period. Potential bias could have been present during the evaluation of echocardiographic measurements. Although the evaluator was blinded to the randomization of patients to the studied groups, the position of the pacing lead in the His bundle or RV septal region could be seen during the evaluation. An LVEF decline of 5%, which was used to compare groups, is relatively small and difficult to measure precisely, especially in patients with LV dyssynchrony due to pacing. The burden of ventricular pacing was taken from the programmer's printouts, and we did not study the incidence of fused pacing beats during Holter-ECG monitoring, which could lead to a higher burden of ventricular pacing as was, in fact, present. Finally, the number of patients in the RVP group and, more specifically, those with a decline in LVEF after pacing was small, preventing more robust conclusions about the PICM prediction based on specific levels of studied molecules.

CONCLUSIONS

In patients at high risk of PICM, right ventricular pacing led to a decline in LVEF compared to His bundle pacing, which preserved LV function after six months of pacing. Gal-3 and ST2-IL have the potential to better identify patients in whom right ventricular pacing does not pose a significant risk. Further studies with more patients, longer follow-up, and clinical endpoints are needed to verify their predictive value relative to pacing-induced cardiomyopathy.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

Article information

Conflict of interest: None declared.

Funding: This paper was supported by the Charles University Research Center program Cooperatio–Cardiovascular Science, National Institute for Research of Metabolic and Cardiovascular Diseases (Programme EXCELES, ID Project No. LX22NPO5104) – funded by the European Union – Next Generation EU and Ministry of Health of the Czech Republic, grant number NU21-02-00584 [to KC].

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