Research Square

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Biventricular Versus His Bundle Pacing After Atrioventricular Node Ablation in Heart Failure Patients With Narrow QRS

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Abstract

Background His bundle pacing (HBP) is a physiological alternative to biventricular (BiV) pacing. Our goal was to compare short-term results of both pacing approaches in ventricular rate refractory atrial fibrillation (AF) patients who underwent atrioventricular node ablation (AVNA).

Methods Consecutive symptomatic AF patients with moderately reduced left ventricular (LV) ejection fraction (EF ≥35% and <50%) and narrow QRS (≤120ms) who received HBP in conjunction with AVNA were compared to historical BiV pacing controls. Electrocardiographic, echocardiographic, and clinical data at baseline and 6 months after the procedure were assessed.

Results Among 24 patients (age 68.8 ± 6.5 years, 50% female, EF 39.6 ± 4%, QRS 95 ± 10ms) who underwent AVNA, 12 received BiV pacing and 12 HBP. Both pacing modalities had similar acute procedure-related success and complication rates. HBP was superior to BiV pacing in terms of post-implant QRS duration, implantation fluoroscopy times, reduction of LV volumes (EDV 127 (86 – 150) ml vs. 146 (121 – 190) ml, P = 0.101; ESV 64 (46 – 81) ml vs. 90 (75 – 123) ml, P = 0.008) and increase in LVEF (46 (41 – 55) % vs. 38 (35 – 42) %, P = 0.005). However, improvement of the New York Heart Association class was similar in both groups.

Conclusions In ventricular rate refractory AF patients with moderately reduced EF and narrow QRS undergoing AVNA, HBP could be a conceivable alternative to BiV pacing. Further prospective studies are warranted to address the outcomes between both “ablate and pace” strategies.

Background

Atrioventricular node ablation (AVNA) with right ventricular (RV) pacemaker implantation is a feasible symptomatic treatment option in patients with atrial fibrillation (AF) and rapid ventricular rate, refractory to optimal medical treatment. However, several studies reported neutral findings regarding heart failure (HF) progression and survival (1–3), implying that beneficial effects of rate control and regularization after AVNA could be hampered by non-physiologic dyssynchronous RV pacing (4, 5). While biventricular (BiV) pacing in conjunction with AVNA derived better results, the benefit was much less distinct in symptomatic AF patients with moderately reduced ejection fraction (EF) and narrow QRS (6–10).

Following AVNA, permanent His bundle pacing (HBP) is a physiological alternative to conventional RV and BiV pacing (11, 12). By capturing the native conduction system, HBP provides normal synchronous activation and preserves left ventricular (LV) function in patients with narrow QRS (13). Recent European Society of Cardiology guidelines for the management of supraventricular tachycardia (SVT) recommend that “ablate and pace” strategy with either BiV pacing or HBP is reasonable when tachycardia-mediated cardiomyopathy cannot be ablated or controlled by pharmacological therapy (Class I, level of evidence C) (14). However, to the best of our knowledge, both pacing modalities in conjunction with AVNA were not previously compared, especially in the subgroups of patients where the benefit of BiV pacing after AVNA was less distinct.

The present study aimed to compare clinical and echocardiographic outcomes between BiV pacing and HBP in symptomatic AF patients with moderately reduced EF and narrow QRS who underwent AVNA.

Methods

Study population

Consecutive AF patients who underwent AVNA and received HBP from May 2018, when the method was adopted in our institution, were compared to consecutive historical BiV device recipients following AVNA before May 2018. HBP was performed by a single experienced operator, BiV device implantations and AVNA procedures were performed by 3 different experienced operators. The inclusion criteria were the following: (i) symptomatic permanent AF / atrial flutter refractory to pharmacological rate or rhythm control where ablation procedure failed or was deemed unwarranted (14); (ii) tachycardiomiopathy with ejection fraction (EF) ≥ 35% and < 50%; (iii) tachycardia with narrow QRS complex (≤ 120 ms) (14); (iv) New York Heart Association (NYHA) class II – III; (v) patients were 18 years or older. The exclusion criteria were the following: (i) end-stage HF (NYHA IV); (ii) severe concomitant non-cardiac disease; (iii) need for surgical intervention; (iv) myocardial infarction less than 6 months before enrolment; (v) previous intracardiac device.

Procedures

Device implantation was always performed first, followed by AVNA. Lower rate of the pacing device was initially set to 80 bpm (Fig. 1) and programmed to 70 bpm at 1-month follow-up.

His bundle pacing

The procedure was performed as previously described (11, 12). In short, a 4.1 Fr bipolar active fixation lead (SelectSecure 3830, Medtronic, Minneapolis, MN, USA) and dedicated delivery sheath (C315His or C304, Medtronic, Minneapolis, MN, USA) were used for His bundle area mapping. His bundle potential mapping was performed in a unipolar setting with the use of the electrophysiological system (LAB system Pro, BARD / Boston Scientific, Lowell, MA, USA) at a sweep speed of 100 mm/s and under fluoroscopy. Additional visualization of the tricuspid valve annulus via contrast injection through delivery sheath was usually performed before mapping to delineate the anatomical landmark of His bundle area. Distal HB potential with large ventricular signal and small atrial signal (ventricular to atrial electrogram ratio > 3:1) was targeted before pacing lead was screwed into position. Acute HBP threshold ≤ 2.5V at 1 ms was considered acceptable. HBP was categorized as selective or non-selective according to the recently proposed definitions (13). Additional backup lead was implanted in all patients and HBP lead was connected to the atrial port of the dual-chamber device.

Biventricular pacing

Implantation of BiV device was performed using standard techniques. The RV lead was positioned in the RV apex or septum. Non-apical, free lateral wall LV lead placement was preferred if permitted by the

venous anatomy. Commercially available devices and leads were used. ECG-based VV delay optimization to ensure left ventricular capture (Q wave in lead I, R wave in lead V_1) and optimal QRS duration was performed after AVNA.

Atrioventricular node ablation

AVNA was performed following device implantation which was temporarily set to 40 bpm for the duration of the procedure. After femoral vein access was obtained, a 4- or 3.5-mm irrigated tip ablation catheter (Flexability™, Abbott, Abbott Park, IL, USA or Celsius® Thermocool®, Biosense Webster, Irvine, CA, USA) was advanced through a long sheath (SR0; Fast-Cath™, Abbott, Abbott Park, IL, USA) into the right atrium. Right anterior oblique or anteroposterior view was used for positioning the catheter tip to the presumed area of the AV node in the mid-septum. Additional positioning was done according to the intracardiac electrograms (targeting atrial to ventricular ratio for proximal AV node site). In case of HBP, ablation in the close vicinity of the HBP lead tip was avoided by maintaining the ablation catheter tip at or below the level of the ring electrode (Fig. 1A). Ablation was performed in a temperature-controlled mode (40 W, up to 60 seconds). If ablation was performed close to the HBP tip-electrode, as soon as AV block was achieved, pacing started from HBP lead at 0.5–1 V above capture threshold to monitor for any loss of capture. Successful AVNA was recognized with an abrupt drop of heart rate to 40 bpm and was continued for 60 seconds thereafter. A waiting period of 20 minutes was typically implemented. Any acute change of device lead position or pacing threshold following AVNA was documented.

Follow-up

All electrocardiographic measurements were performed with the use of digital callipers at 400% magnification calibrated for paper speed 25 mm/s. Device interrogations, clinical and laboratory evaluations were performed at our device outpatient clinic at 1 month and 6 months post-implantation. Adverse events and device-related complications were closely monitored. Transthoracic two-dimensional echocardiography was performed at baseline and 6 months after device implantation. Left ventricular volumes and EF were calculated with the biplane Simpson method.

Statistical analysis

For baseline and clinical characteristics, continuous variables were expressed as means and standard deviations or medians with interquartile ranges and compared with either paired or independent t-tests, or Mann-Whitney U tests, as appropriate. Categorical variables were expressed as relative counts and percentages and compared with χ^2 tests of association. For all tests, a two-tailed P value ≤ 0.05 was considered statistically significant. All statistical analyses were conducted using IBM SPSS Statistics (Version 25.0., Armonk, NY, USA).

Results

Patient characteristics

A total of 24 consecutive patients who underwent HBP or BiV device implantation and AVNA met the inclusion criteria; 12 patents received HBP and 12 a BiV device. The mean age of the study population was 68.8 ± 6.5 years, 50% were female, mean NYHA class was 3, mean EF was 39.6 ± 4%, and mean QRS width was 95 ± 10 ms. Permanent atrial flutter was present in 21% of the patients. All patients were receiving antiarrhythmic and anticoagulation therapy. No significant differences in baseline characteristics were observed between the groups (Table 1).

Table 1
Baseline demographic and clinical characteristics of patients by pacing modality after atrioventricular node ablation.

Characteristics	HBP (n = 12)	BiV (n = 12)	P value
Male	5 (41.7%)	7 (58.3%)	0.414
Age (years)	68.5 (6.8)	69.3 (6.6)	0.799
Heart rate (bpm)	127 (10.7)	127 (13.6)	0.999
QRS (ms)	91 (12)	98 (7)	0.101
Atrial flutter	3 (25.0%)	2 (16.7%)	0.615
LVEF	40 (37–45)	39 (35–40)	0.266
Medication			
BB	12 (100%)	12 (100%)	
ACE/ARB/ARNI	9 (75.0%)	9 (75.0%)	0.999
MRA	4 (33.3%)	6 (50.0%)	0.408
Loop diuretic	7 (58.3%)	6 (50.0%)	0.682
Digoxin	3 (25.0%)	5 (41.7%)	0.386
Amiodarone	2 (16.7%)	2 (16.7%)	0.999
Anticoagulation	12 (100%)	12 (100%)	
Comorbidities			
AH	8 (66.6%)	9 (75.0%)	0.615
CAD	3 (25.0%)	6 (50.0%)	0.205
Diabetes	5 (41.7%)	2 (16.7%)	0.178

LVEF – left ventricular ejection fraction; BB – beta-blocker; ACE – angiotensin-converting enzyme inhibitor; ARB – angiotensin II receptor blocker; ARNI – angiotensin receptor neprilysin inhibitor; MRA – mineralocorticoid receptor antagonist; AH – arterial hypertension; CAD – coronary artery disease; BiV – biventricular pacing; HBP – His bundle pacing.

Procedural outcomes

Device implantation and AVNA were acutely successful and performed simultaneously in all HBP patients. Initially, C315 sheath was used and switched to C304 in only 2 patients. Ventricular backup lead was implanted in all HBP patients. Selective HBP was achieved in 5 patients (41.7%). Acute increase of HBP lead threshold after AVNA was registered in 1 patient (from 1.8 V to 3.2 V at 1 ms). As capture of conduction system was still present, lead revision was not performed. There were no other procedure-related adverse events. No significant change was found in HBP lead threshold at baseline compared to 6-month follow-up (1.55 (1.07–2.00) V vs. 1.75 (0.75–2.88) V, P = 0.230).

All BiV devices were successfully implanted. LV lead was positioned in the LV lateral free wall in all patients (postero-lateral vein in 9 patients). In 3 patients, AVNA was successfully performed within 21 days after BiV device implantation and in 9 during the same hospitalization. Left ventricular capture during BiV pacing was confirmed with ECG in all patients following AVNA. In one patient slight quadripolar LV lead dislodgement was documented after AVNA, however, BiV pacing (R wave present in lead V_1) with previous ECG morphology was restored after additional pacing vector programming. Thus, LV lead revision was not needed. There were no other procedure-related adverse events. No significant change in LV lead threshold (1.35 (1.05–1.72) V vs. 1.45 (1.00–1.69V) V, P = 0.475) was noted at follow-up.

Three patients had a defibrillator device for primary prevention in the BiV group and none in the HBP group (P = 0.064). No ventricular tachyarrhythmias were registered during at 6-month follow-up. Device implantation fluoroscopy time was significantly shorter in HBP group compared to BiV group (P < 0.0001). Baseline QRS duration was similar in both treatment groups. Post-implant QRS duration did not change significantly in the HBP group (91 ± 12 ms vs. 95 ± 15 ms, P = 0.281) and prolonged in the BiV group (from 98 ± 7 ms to 172 ± 13 ms, P < 0.0001). Comparisons of both pacing modalities are presented in Table 2.

Table 2
Procedural characteristics and device parameters by pacing modality after atrioventricular node ablation at baseline and follow-up

Characteristics	HBP (n = 12)	BiV (n = 12)	P value
Fluoroscopy time (min)	7.0 (3.8)	16.8 (7.6)	< 0.0001
Electrocardiographic characteristics			
QRS (ms)	91 (12)	98 (7)	0.101
post-implantation	95 (15)	172 (13)	< 0.0001
Lead measurements			
HBP (V @ 1 ms) or LV (V @ 1 ms) threshold	1.55 (1.07–2.00)	1.35 (1.05–1.72)	0.378
at follow-up	1.75 (0.75–2.88)	1.45 (1.00–1.69)	0.630
HBP or LV impedance (ohms)	548 (490–598)	739 (573–953)	0.010
at follow-up	437 (404–531)	667 (567–838)	< 0.0001

BiV – biventricular pacing; HBP - His bundle pacing; ICD – implantable cardioverter defibrillator; LV - left ventricular.

Echocardiography and clinical outcomes

Nine (75%) patients in HBP group and 6 (50%) in BiV group improved ≥ 1 NYHA class. Two patients (16.7%) declined by 1 functional class, both in BiV group (P = 0.162). Median baseline NT-proBNP was 1771 (1010–2752) pg/ml and was similar between groups. In the HBP group, there was a significant reduction of NT-proBNP at follow-up (905 (479–1911) pg/ml) compared to baseline (1616 (1010–2792) pg/ml); P = 0.010. No significant decrease was observed in the BiV group at follow-up (1656 (1190–2396) pg/ml) compared to baseline (1904 (1098–2559) pg/ml); P = 0.625.

There were no significant baseline differences in LV volumes and LVEF in patient groups based on treatment. At follow-up, LVEF improved significantly in HBP (40 (37–45) % to 46 (41–55) %, P = 0.010). No significant change was observed in the BiV group (39 (35–40) % vs 38 (35–42) %, P = 0.579). LV volumes decreased in HBV group (LVEDV 145 (93–179) ml to 127 (86–150) ml, P = 0.012) and LVESV 88 (55–102) ml to 64 (46–81) ml, P = 0.114). No significant change in LV volumes was observed in BiV group: LVEDV from 139 (126–167) ml to 146 (121–190) ml, P = 0.246) and LVESV from 84 (76–102) ml to 90 (75–123) ml, P = 0.290). Comparison of mean changes in echocardiographic parameters are shown in Fig. 2 and clinical and echocardiographic outcomes between the groups are presented in Table 3.

Table 3
Clinical and echocardiographic characteristics of patients by pacing modality after atrioventricular node ablation at baseline and follow-up.

Characteristics	HBP (n = 12)	BiV (n = 12)	P value
NYHA class	3	3	0.307
2		1 (8.3%)	
3	12 (100%)	11 (91.7%)	
at follow-up	2 (1.25–2.75)	2.5 (2–3)	0.212
1	3 (25.0%)		
2	6 (50.0%)	6 (50.0%)	
3	3 (25.0%)	5 (41.7%)	
4		1 (8.3%)	
NT-proBNP	1616 (1010–2792)	1904 (1098–2559)	0.999
at follow-up	905 (479–1911)	1656 (1190–2396)	0.068
Echocardiographic characteristics			
LVEDV	145 (93–179)	139 (126–167)	0.799
at follow-up	127 (86–150)	146 (121–190)	0.101
LVESV	88 (55–102)	84 (76–102)	0.630
at follow-up	64 (46–81)	90 (75–123)	0.008
LVEF	40 (37–45)	39 (35–40)	0.266
at follow-up	46 (41–55)	38 (35–42)	0.005

NYHA – New York Heart Association, NT-proBNP – N-terminal pro-B-type natriuretic peptide; LVEDV – left ventricular end-diastolic volume; LVESV – left ventricular end-systolic volume; LVEF – left ventricular ejection fraction; BiV – biventricular pacing; HBP – His bundle pacing.

Discussion

The results of our study indicate that in rate control refractory AF patients with moderately reduced EF (EF ≥ 35% and < 50%) and narrow QRS (≤ 120 ms), HBP after AVNA provides superior ventricular activation and improvement of cardiac function compared to BiV pacing. However, both pacing modalities yielded similar symptomatic benefit.

Electrocardiographic and Echocardiographic outcomes

Biventricular pacing could be detrimental in HF patients without significant electrical dyssynchrony as non-physiological ventricular resynchronization does not return LV activation times to those seen in individuals with intrinsically narrow QRS (16, 17). Patients in our study who received BiV pacing and AVNA for symptomatic AF exhibited significant prolongation of QRS duration and no improvement in echocardiographic parameters. Although post-BiV QRS measurements in AVNA studies (8–10) were not specifically addressed, similar increase in QRS duration (40.2 ms) after BiV pacing could be observed in The Evaluation of Resynchronization Therapy for Heart Failure (LESSER-EARTH) trial which enrolled HF patients with narrow QRS (18). Furthermore, Post AV-Nodal Ablation (PAVE) study showed that BiV pacing superiority was the consequence of functional deterioration in the RV pacing group rather than improvement in the BiV group where LVEF remained unchanged (7). In the study by Khan et al. (19), which compared pulmonary-vein isolation and “ablate and pace” strategy, slight deterioration of LVEF (mean absolute change of -1 ± 4%) was noticed in BiV group after AVNA. In contrast, the Ablate and Pace in Atrial Fibrillation (APAF) trial reported significant improvement of echocardiographic parameters in the BiV group alone and compared to RV pacing (8). Heterogenous study population could explain the discrepancy, as it is conceivable that treatment effect of BiV pacing was more pronounced in patients with EF ≤ 35% (47% of patients) and QRS ≥ 120 ms (50% of patients) which were not included in our study (8). The same observation could be made in Ablate and Pace in Atrial Fibrillation plus Cardiac Resynchronization Therapy (APAF-CRT) trial where, although echocardiographic parameters were not presented, no clear benefit of BiV pacing and AVNA compared to pharmacological treatment was observed in AF patients with narrow QRS and LVEF 36–50% (10). Focusing on these patients, the results of our study showed that HBP plus AVNA is associated with significant improvement of cardiac function compared to BiV pacing. Structural improvements observed in our HBP group resemble those in previous studies (11, 12). Therefore, it is reasonable to assume that HBP in conjunction with AVNA could be a better alternative to BiV pacing in rate control refractory AF patients with moderately reduced EF and narrow QRS.

Clinical outcomes

Alleviation of symptoms in HF patients with permanent AF is an interplay of adequate rate control and improvement of LV function (15). Symptomatic benefit after AVNA in our study was equal in both pacing modalities, but natriuretic peptides reduction was more pronounced in the HBP group. Similar conclusions were made in the APAF-CRT trial, where patients with LVEF > 35% exhibited significant symptomatic benefit after AVNA and BiV pacing, yet no clear benefit regarding mortality or HF progression (10). Thus, with our findings of greater LV volumes and natriuretic peptide levels reduction in HBP compared to BiV patients, we might speculate that regularization of ventricular rate after AVNA is the primary driver of symptom improvement in patients with moderately reduced EF, but physiological ventricular activation with HBP could enable additional LV reverse remodelling.

Procedural outcomes and clinical implications

Recent development of dedicated tools and encouraging data from the literature made HBP a logical physiologic pacing option for patients undergoing “ablate and pace” strategy (11–14). The results of the

present study further support wider adoption of this technique in routine clinical practice. Our study showed similar success and adverse event rates of HBP compared to BiV pacing with significantly lower device implantation fluoroscopy times. Lower HBP fluoroscopy times in our study compared to previous reports (20) may be attributed to the implantation technique which primarily relies on intracardiac signals. Compared to BiV device, AVNA procedure could prove more challenging in HBP due to the vicinity of HBP lead. However, with implanting the HBP lead more distally (no visible atrial electrograms) and by maintaining the ablation catheter tip at or below the level of the ring electrode we were able to avoid ablation-related complications. Of note, only one acute increase in His capture threshold was registered after AVNA. In line with previous reports, no significant increase in short-term HBP lead threshold was observed (11, 12).

Patients with tachycardiomyopathy are often very symptomatic and have greater mortality (15). The “ablate and pace” strategy is a feasible therapeutic option when rhythm control interventions are no longer pursued (14). With long-term consequences of irreversible AVNA in mind, appropriate patient and therapy selection should be thoroughly considered. The results of our study indicate that compared to BiV pacing, HBP could provide additional hemodynamic advantage in symptomatic AF patients with moderate HF and narrow QRS undergoing AVNA. Thus, larger prospective studies are warranted to address clinical and structural outcomes between both “ablate and pace” strategies in different subgroups of rate control refractory AF patients.

Limitations

Retrospective design of the study and low number of patients limits the strength of our findings. As only short-term procedural, clinical, and echocardiographic outcomes at 6-months were assessed, longer follow-up might have produced different results. Comparison of two pacing modalities implanted at different time periods may have led to treatment bias. However, all device implantations and AVNA procedures were performed in the same electrophysiological laboratory and by the same operators. Relatively high post-implant QRS duration (172 ± 13 ms) in the BiV paced group might have impacted on the lack of echocardiographic improvement. Addition intra-operative measures (activation times, identification of scars) and device optimization could have yielded shorter BiV paced QRS intervals. However, ECG-based VV delay optimization to ensure left ventricular capture was performed in all patients. Finally, as only rate control refractory AF patients with moderately reduced EF (EF ≥ 35% and < 50%) and narrow QRS (≤ 120 ms) were specifically assessed, the results cannot be extrapolated to other subgroup of patients undergoing AVNA. While we can assume similar effect in patients with reduced EF (12), superiority of HBP in patients with wide QRS may be controversial since only proximal conduction abnormalities are amenable by recruitment of latent Purkinje fibres distal to the site of block (21).

Conclusions

In symptomatic AF patients with moderately reduced EF and narrow QRS, His bundle pacing in conjunction with AVNA showed superior ventricular activation and improvement of cardiac function compared to BiV pacing. Short-term symptomatic benefit in both pacing modalities was similar. Larger

prospective studies are warranted to address clinical and structural outcomes between both “ablate and pace” strategies in different subgroups of rate control refractory AF patients.

Abbreviations

AVNA
Atrioventricular node ablation; RV:Right ventricle; AF:Atrial fibrillation; HF:Heart failure; BiV:Biventricular; EF:Ejection fraction; HBP:His bundle pacing; LV:Left ventricle; SVT:Supraventricular tachycardia; NYHA class:New York Heart Association class; EDV:End-diastolic volume; ESV:End-systolic volume

Declarations

Ethics approval and consent to participate

The study complies with the Declaration of Helsinki and was approved by The Republic of Slovenia National Medical Ethics Committee (Komisija za medicinsko etiko Republike Slovenije) and institutional review board. All patients gave a written informed consent before the procedures were performed.

Consent of publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

David Žižek received consulting / advisory board support from Medtronic and Boston Scientific. Bor Antolič and Matevž Jan received proctorship fees from Biosense Webster. Andrej Pernat received consulting / advisory board honoraria from Biosense Webster. All other authors have no relationships relevant to the contents of this paper to disclose.

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Author contributions

DŽ – drafting of the manuscript, interpretation of data, study conception; BA – interpretation of data, critical revision of the manuscript; AZM – data analysis, critical revision of the manuscript; DZD – data analysis and statistics; JŠ – data analysis and interpretation; MJ and AP – study design, final approval of the manuscript. All authors reviewed the manuscript.

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Figures

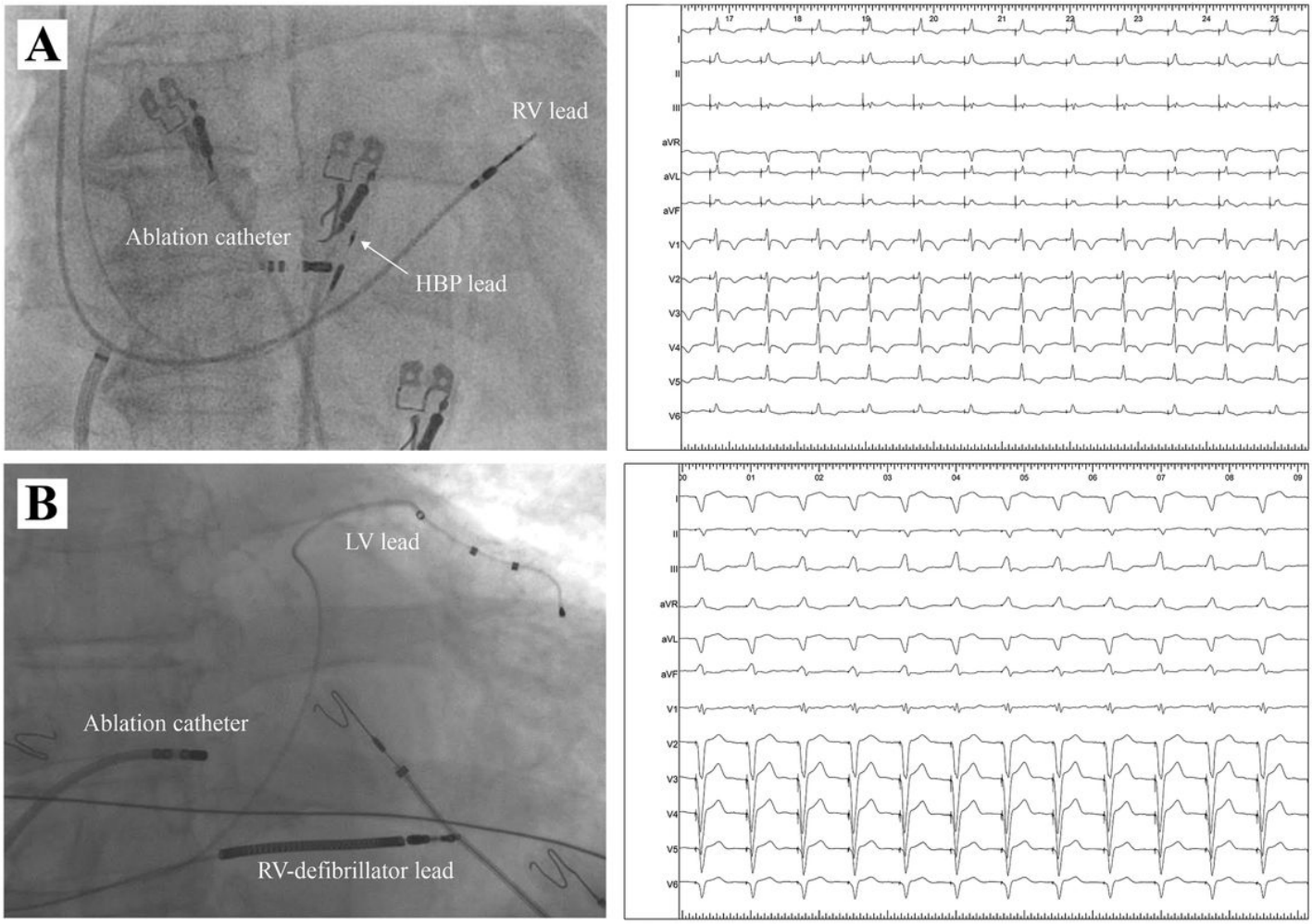

Figure 1

Fluoroscopic view of the ablation catheter in relation to His bundle pacing (Panel A) or biventricular pacing (Panel B) leads and 12-lead ECG after atrioventricular node ablation during both pacing modalities. RV – right ventricular; LV – left ventricular.

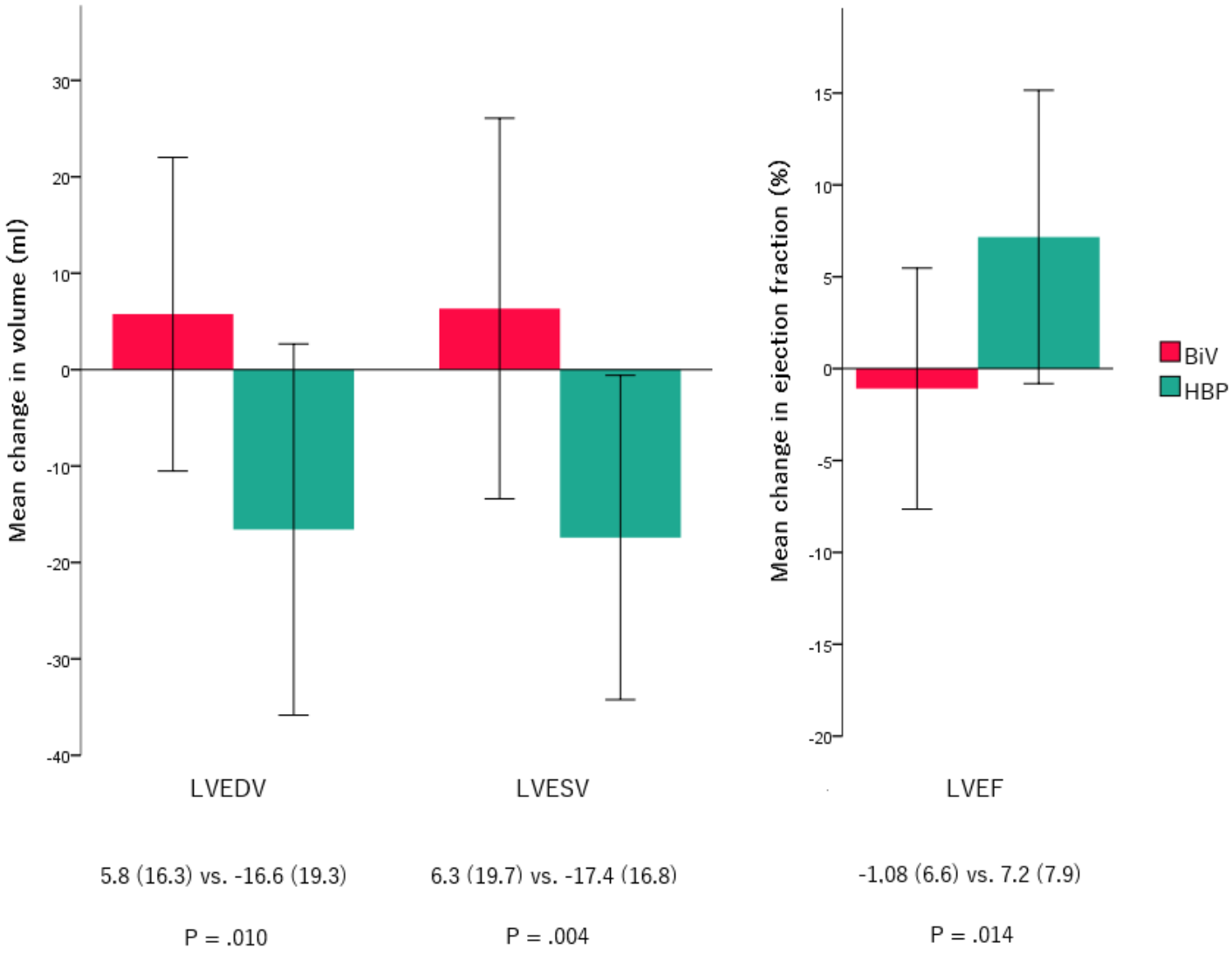

Figure 2

Comparison of mean changes in echocardiographic left ventricular volumes and ejection fraction between biventricular and His bundle pacing after atrioventricular node ablation at baseline and short-term follow-up. LVEDV – left ventricular end-diastolic volume; LVESV – left ventricular end-systolic volume; LVEF – left ventricular ejection fraction; BiV – biventricular pacing; HBP – His bundle pacing.