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THE EFFECT OF ELECTRICAL STIMULATION OF VARIOUS ANATOMICAL ZONES ON THE FUNCTIONAL STATE OF THE LEFT HEART CHAMBERS: AN INTRAOPERATIVE STUDY

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Aim. To study the functional state of the left heart chambers during short-term stimulation of the His bundle, the interventricular septum and the apex of the right ventricle (RV) during diagnostic intracardiac electrophysiological study (EPS).

Methods. The study included 5 patients who underwent intracardiac EPS for supraventricular tachyarrhythmias, which included an experimental program of short-term stimulation from various anatomical zones of the RV (His bundle, interventricular septum, apex of the right ventricular) with additional registration of parameters of the left heart chambers's functional state in the sinus rhythm. A comprehensive assessment of hemodynamic parameters was performed: global longitudinal strain (GLS) and postsystolic index (PSI) of the left ventricle (LV), E/e', volume of the left atrium (VLA) and strain of the left atrium (LA) in the reservoir phase. The initial data was processed in Microsoft Excel, and statistical analysis was performed using Statistica 10.0 (StatSoft Inc.) and Python (SciPy, Seaborn, Pandas libraries).

Results. All the parameters under consideration differ significantly between the stimulation modes (in all cases $p<0.01$). The most pronounced changes are observed with apical RV stimulation: patients have worse LV GLS and LA strain values, as well as the highest VLA compared to sinus rhythm and His bundle stimulation. In contrast, with His bundle stimulation, the GLS, VLA, and LA strain values are close to those in sinus rhythm, indicating a more physiological contraction of the heart in this mode. Significant correlations were established between PSI and E/e' ($r=+1.0$), PSI and LA strain ($r=-1.0$), as well as E/e' and VLA ($r=+1.0$) during electrical stimulation of various anatomical zones, which confirms the relationship between dissynchrony, diastolic function and LA overload.

Conclusion. The worst values of LV GLS and LA strain, as well as the highest LAV, were observed with apical stimulation of the RV, while with stimulation of the His bundle, the values of GLS, VLA and LA strain are close to those with sinus rhythm, which indicates a more physiological contraction of the heart in this mode.

Key words: physiological electrocardiostimulation; His bundle pacing; the left branch of the His bundle pacing; right ventricular apical pacing; left ventricular mechanical dyssynchrony; echocardiography; left ventricular global longitudinal deformation; left atrial reservoir strain; atrial fibrillation

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In clinical practice, conventional permanent cardiac pacing is traditionally performed via endocardial lead placement at the right ventricular (RV) apex. However, this pacing site produces a non-physiological pattern of ventricular activation that mimics left bundle branch block, resulting in pronounced intra- and interventricular dyssynchrony [1]. Chronic RV apical pacing has been associated with the development of pacing-induced cardiomyopathy, a specific form of left ventricular (LV) remodelling characterised by progressive systolic dysfunction and clinical manifestations of heart failure. According to meta-analytic data, a reduction in LV ejection fraction is observed in 10-20% of patients with a high burden of ventricular pacing, particularly when the pacing percentage exceeds 40% [1].

Dyssynchronous ventricular activation impairs diastolic filling, increases LV end-diastolic pressure, and elevates left atrial (LA) pressure, contributing to LA dilatation [1]. These pathophysiological changes promote the progression of mitral regurgitation and increase the risk of atrial fibrillation (AF) [2, 3].

Alternatives to conventional RV apical pacing include physiological conduction system pacing (CSP), which targets the His bundle (His bundle pacing, HBP) or the left bundle branch area (left bundle branch pacing, LBBP), as well as interventricular septal pacing. The latter represents a practical compromise between technically simple but non-physiological apical pacing and technically demanding yet highly physiological CSP. Several large studies, including Protect-Pace and SEPTAL CRT, have demonstrated that septal pacing results in narrower QRS duration and improved LV systolic function compared with apical pacing, thereby reducing the risk of pacing-induced cardiomyopathy and left heart chamber dilatation [14, 15]. However, CSP provides the highest degree of electrical and mechanical synchrony, most closely replicating physiological ventricular activation.

His bundle pacing was first implemented clinically in the early 2000s, although the concept of direct His bundle stimulation had been described earlier [4]. In 1968, Kosowsky et al. demonstrated experimentally that stimulation of the His bundle could reproduce physiological ventricular activation with a narrow QRS complex and preserved mechanical function [4, 16]. Only with the recent development of dedicated delivery systems and specialised pacing leads has this technique become widely applicable in clinical practice. The 2021 European Society of Cardiology guidelines recognise CSP as a preferred strategy for minimising electromechanical dyssynchrony and preserving haemodynamic integrity [4].

Recent clinical and imaging studies have consistently shown that CSP is associated with more favourable parameters of myocardial contractility, diastolic function, and LA morphology compared with conventional pacing [2, 3, 5-7]. However, most available data are derived from comparisons between different patient cohorts. Studies employing intra-individual protocols with acute comparison of pacing sites remain limited. One such example is the study by Xie et al. (2021), which evaluated the acute effects of His bundle, septal, and RV apical pacing in a single patient using speckle-tracking echocardiography [8]. Notably, LA functional parameters were not assessed in that study.

The aim of the present study was to evaluate the functional state of the LA and LV during short-term pacing of the His bundle, interventricular septum, and RV apex in the setting of diagnostic intracardiac electrophysiological study.

MATERIALS AND METHODS

This prospective study was conducted in accordance with Good Clinical Practice standards and the principles of the Declaration of Helsinki and was approved by the local Ethics Committee (protocol No. 8, 21 May 2024). All patients provided written informed consent prior to undergoing invasive electrophysiological study (EPS), including consent for the experimental protocol of short-term intracardiac pacing from different RV anatomical sites (His bundle region, interventricular septum, and RV apex), as well as for the use of collected data for scientific purposes.

Five patients hospitalised for symptomatic supraventricular tachyarrhythmias were included. All patients had preserved atrioventricular conduction and no indication for permanent pacemaker implantation. Exclusion criteria comprised haemodynamically significant valvular heart disease, prior myocardial infarction and/or coronary revascularisation, typical angina symptoms or evidence of transient myocardial ischaemia during preoperative stress testing or ECG monitoring, LV ejection fraction <50%, and/or diastolic dysfunction greater than grade I.

All patients underwent planned intracardiac EPS. As part of the procedure, an experimental protocol of short-term pacing from different RV anatomical sites (His bundle region, interventricular septum, and RV apex) was implemented, with additional assessment of left heart chamber function.

Pacing was performed using a steerable multipolar diagnostic catheter. Catheter positioning was guided fluoroscopically in RAO 30° and LAO 40° projections. His bundle pacing was performed without active fixation, based on anatomical localisation, with non-selective capture confirmed by ECG. Septal pacing was performed in the mid-interventricular septum. RV apical pacing was delivered in the anterolateral region of the RV apex, outside the septal area.

A comprehensive echocardiographic assessment was performed using transthoracic echocardiography with speckle-tracking imaging. The following parameters were evaluated: LV global longitudinal strain (GLS), postsystolic index (PSI), E/e′ ratio as a surrogate of LV filling pressure, left atrial volume (LAV), and LA reservoir strain.

For each patient, all measurements were obtained under identical conditions, allowing direct intra-individual comparison between pacing modes and eliminating inter-patient variability. This design enabled evaluation of the acute haemodynamic effects of intracardiac pacing and assessment of the potential of physiological pacing as a strategy for preventing LA remodelling and atrial fibrillation.

Table 1.

Functional parameters of left heart chambers during intracardiac pacing from the His bundle, interventricular septum, and right ventricular apex

	Sinus rhythm	His bundle pacing	IVS pacing	RVA pacing	p (ANOVA)	p (Friedman)
GLS, %	21.2±1.5	21.7±1.4	20.0±0.8	18.7±1.6	0.00014	0.002851
PSI, %	0.5±0.8	1.2±0.8	4.0±0.6	6.8±1.8	0.0000004	0.002878
E/e′	7.7±1.4	8.2±1.4	10.0±2.0	11.5±2.6	0.00019	0.005047
LA volume, ml	45.4±10.4	47.0±10.2	53.8±12.5	61.2±14.7	0.00007	0.002878
LA strain, %	35.1±8.1	31.0±7.2	24.5±7.8	16.0±5.1	0.00016	0.001817

Note: IVS - interventricular septum; RVA - right ventricular apex; GLS - global longitudinal strain; PSI - postsystolic index; E/e′ - ratio of early transmitral inflow velocity (E) to early diastolic mitral annular velocity (e′); LA - left atrium

The study protocol included sequential single-chamber RV pacing in VOO mode at a rate of 90 bpm from three anatomical sites: His bundle region, mid-septal region, and RV apex. Native sinus rhythm served as the control condition. The pacing rate of 90 bpm was selected to suppress intrinsic rhythm (typically 60-80 bpm) and ensure stable, continuous pacing without pauses or artefacts.

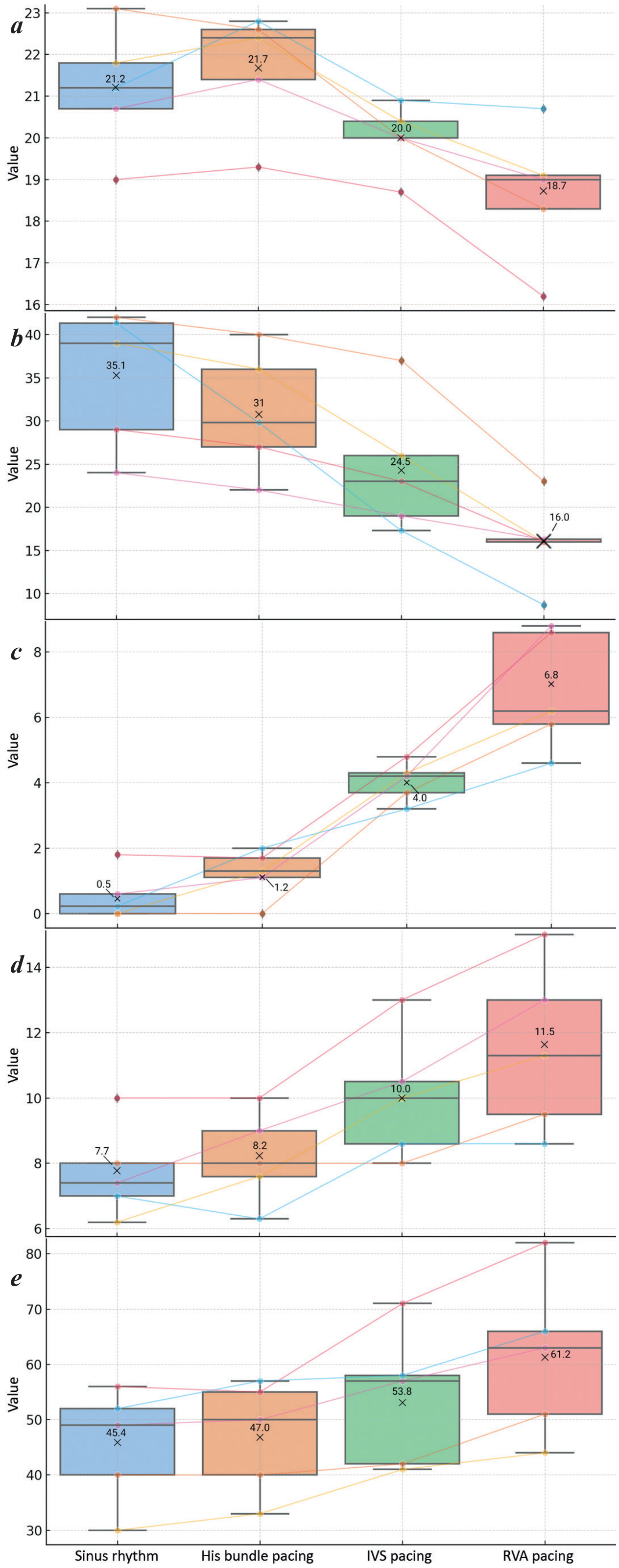

Figure 1. Box plots with superimposed individual trajectories (n=5): (a) left ventricular (LV) global longitudinal strain (GLS), (b) left atrial (LA) reservoir strain, (c) postsystolic index (PSI), (d) E/e′ ratio, and (e) left atrial volume (LAV) across different pacing modes. Each line represents the individual trajectory of a given parameter in a single patient. The dashed line within each box plot indicates the median value.

All pacing was performed within a single procedure without changes in pacing output or pulse duration. The sequence of pacing sites was identical for all patients. A single steerable multipolar catheter connected to a standard electrophysiological system was used, without atrial synchronisation. Each pacing episode lasted 1-2 minutes, during which transthoracic echocardiography was performed. Retrograde atrioventricular conduction was not assessed, and AV intervals were not analysed due to the absence of atrial synchronisation and their limited relevance to the study objectives.

Echocardiographic imaging was performed using a Vivid S7 system (GE Healthcare, USA). For each pacing mode and during sinus rhythm, the following parameters were recorded: LV GLS (speckle-tracking), PSI, E/e′ ratio, LAV, and LA reservoir strain.

Two-dimensional echocardiography with speckle-tracking analysis was performed using ultrasound images acquired at a frame rate of 56 frames per second. LV GLS was assessed from apical two-chamber, four-chamber, and apical long-axis views by tracking the LV endocardial border at end-systole. Global LV GLS was calculated as the average strain value across these three views. Absolute (non-negative) strain values were used for statistical analysis, as they reflect longitudinal LV contractility; higher values correspond to better systolic function [9, 10].

The PSI was calculated as the ratio of the difference between peak postsystolic longitudinal strain and longitudinal strain at aortic valve closure (i.e., end of LV ejection) to the peak postsystolic longitudinal strain in a given segment, expressed as a percentage [11]. PSI reflects the degree of intrasegmental dyssynchrony and postsystolic shortening, a marker of mechanical inefficiency. The mean PSI across all LV segments was used for analysis.

The E/e′ ratio was calculated as the ratio of peak early transmitral inflow velocity (E) to early diastolic mitral annular velocity (e′). This parameter serves as a non-invasive surrogate of LV filling pressure, with higher values indicating impaired diastolic function.

LA assessment included measurement of LAV and LA reservoir strain. LAV was calculated using the Simpson’s biplane method based on apical four- and two-chamber views. Increased LA volume is a marker of chronic pressure overload and progressive diastolic dysfunction.

LA reservoir strain was defined as the peak longitudinal deformation of the LA myocardium during ventricular systole. It reflects atrial compliance and reservoir function. Strain curves were generated following manual tracing of the LA endocardial border in the apical four-chamber view, with R-wave gating used to define the zero-strain reference point [12].

Data were analysed using a within-subject (intra-individual) design, in which each patient underwent all pacing conditions. This approach controlled for inter-individual variability and enabled direct comparison between pacing modes.

Statistical analysis was performed using Statistica 10.0 (StatSoft Inc.) and Python (SciPy, Seaborn, Pandas libraries). Differences between four conditions (sinus rhythm, His bundle pacing, septal pacing, and RV apical pacing) were assessed using repeated-measures analysis of variance (ANOVA).

Given the small sample size and potential deviations from normality, the Friedman test was additionally applied as a non-parametric method to confirm the robustness of the findings. Spearman correlation analysis was used to assess relationships between parameters of mechanical dyssynchrony, diastolic function, and LA function.

Data visualisation included box plots illustrating individual patient trajectories and scatter plots with stratification by pacing modality. A p-value <0.05 was considered statistically significant.

RESULTS

The study included five patients aged 54 to 75 years, with a mean age of 64.4±8.7 years. Three patients (60%) were male. Four patients (80%) were overweight or obese (body mass index >25 kg/m²; mean BMI 27.7±4.5 kg/m²), and three patients (60%) had a diagnosis of arterial hypertension. The mean intrinsic QRS duration was 82±3.6 ms, indicating preserved intraventricular conduction in all included patients.

Echocardiographic analysis demonstrated that, during sinus rhythm, all patients exhibited normal left heart chamber function. Both His bundle pacing and interventricular septal pacing showed more favourable parameters of systolic and diastolic function compared with RV apical pacing (Table 1).

All evaluated parameters differed significantly between pacing modes (p<0.01 for all comparisons). The most pronounced adverse changes were observed during RV apical pacing, characterised by reduced LV GLS (Fig. 1A) and LA strain (Fig. 1B), increased postsystolic index (PSI) (Fig. 1C), impaired LV diastolic function (Fig. 1D), and the highest LAV (Fig. 1E) compared with sinus rhythm and His bundle pacing.

In contrast, during His bundle pacing, LAV and LA strain values were comparable to those observed during sinus rhythm. Notably, LV GLS demonstrated a statistically significant improvement during His bundle pacing compared with sinus rhythm.

Overall, these findings indicate significant differences between pacing modes, supporting the superiority of more physiological pacing strategies (His bundle and septal pacing) over RV apical pacing in preserving LV systolic function and LA reservoir function.

Significant correlations were identified between PSI and E/e′ (ρ=+1.0), PSI and LA strain (ρ=-1.0), and E/e′ and LAV (ρ=+1.0), confirming the close relationship between ventricular mechanical activation, diastolic function, and LA overload (Fig. 2).

DISCUSSION

This acute physiological study in a cohort of five patients enabled an intra-individual comparison of four cardiac activation modes: intrinsic sinus rhythm, His bundle pacing, mid-septal pacing, and RV apical pacing. Despite the small sample size, the within-subject design and simultaneous comparison of all pacing modes in each patient substantially increase the robustness of the findings and the reliability of the observed differences.

The results confirm that His bundle pacing provides the most physiological pattern of ventricular activation, characterised by minimal mechanical dyssynchrony. This was reflected in both narrower QRS complexes and lower PSI values (Fig. 3). Septal pacing demonstrated intermediate values of QRS duration and PSI, indicating less pronounced dyssynchrony compared with RV apical pacing. These findings are consistent with data from larger studies such as PROTECT-PACE and SEPTAL CRT [14, 15]. In contrast, RV apical pacing was associated with the widest QRS complexes and the highest PSI values, reflecting marked electrical and mechanical dyssynchrony.

LV GLS, assessed using speckle-tracking echocardiography, was most favourable during His bundle pacing, with values close to physiological levels. Septal pacing resulted in a modest reduction in GLS, likely reflecting partial dyssynchrony. RV apical pacing led to a more pronounced decrease in GLS despite preserved ejection fraction, which may represent an early marker of impaired longitudinal contractility and a predictor of adverse LV remodelling. These observations are consistent with findings by Michalik et al., who demonstrated preservation of longitudinal systolic function during His bundle pacing and its deterioration during RV apical pacing, as well as with the results of Xie et al., who reported significant differences in LV contractility depending on pacing site [5,8].

The most pronounced differences between pacing modes were observed in parameters of diastolic function, including the E/e′ ratio, LAV, and LA reservoir strain (Fig.

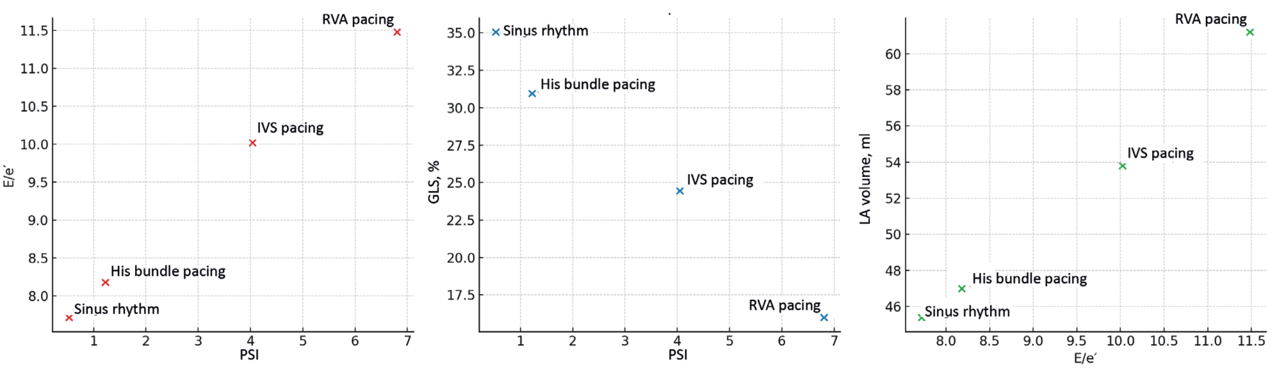

Figure 2. Scatter plots illustrating correlations between mean group values: (a) PSI and E/e′, (b) PSI and LA reservoir strain, and (c) E/e′ and LAV.

4). RV apical pacing was associated with elevated LV filling pressures, increased LAV, and reduced LA reservoir strain (down to 16.0%), indicating impaired diastolic function and atrial compliance. These findings are in line with the known adverse effects of dyssynchronous activation associated with RV apical pacing on myocardial relaxation [3, 13]. In contrast, His bundle and septal pacing preserved more favourable diastolic parameters, comparable to those observed during sinus rhythm, suggesting maintenance of near-physiological diastolic function.

The observed relationships between PSI, E/e′, and LA strain highlight the central role of LV mechanical dyssynchrony as a determinant of atrial overload and a potential driver of atrial remodelling. These findings provide mechanistic support for the hypothesis that pacing-induced dyssynchrony contributes to the development of atrial dysfunction and may increase the risk of atrial fibrillation.

Our results are consistent with the study by Zhao et al., which demonstrated that conduction system pacing (in that study, left bundle branch pacing) improves LA morphofunctional parameters compared with conventional RV pacing [2]. Importantly, in our study, similar differences between physiological and apical pacing were demonstrated under acute intraoperative conditions, emphasising the clinical relevance of pacing site selection even in patients without baseline LA dysfunction.

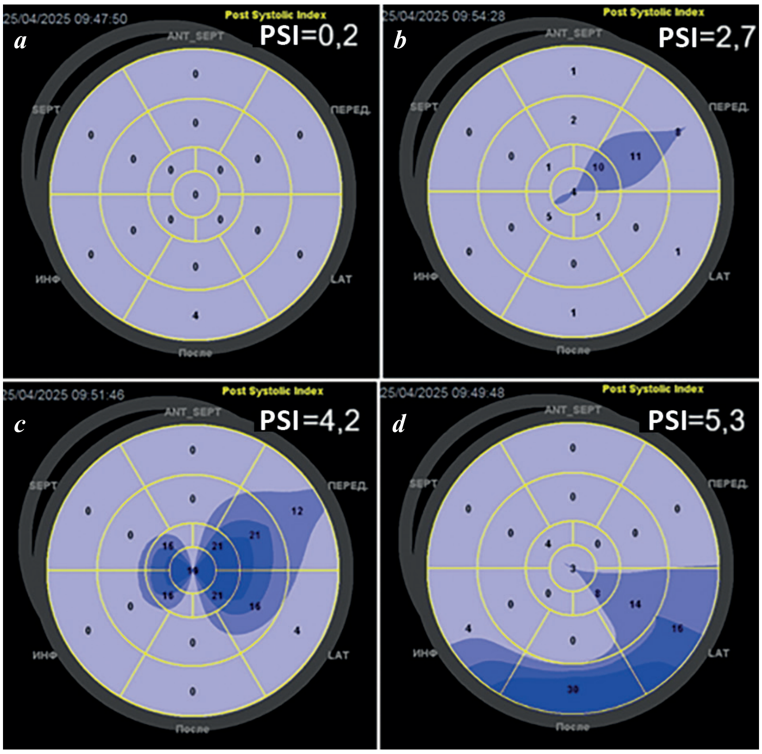

Figure 3. Effect of ventricular activation sequence on postsystolic shortening (PSS) and postsystolic index (PSI) during pacing from different anatomical sites: (a) sinus rhythm (no PSS observed), (b) His bundle pacing (minimal PSS), (c) mid-interventricular septal pacing (PSS observed in lateral segments), and (d) right ventricular apical pacing (PSS observed in lateral and posterolateral segments).

To our knowledge, there are currently no published studies evaluating LA morphofunctional parameters during acute pacing from different cardiac sites within the setting of intraoperative electrophysiological testing, which underscores the novelty of the present work.

Numerous studies have demonstrated the advantages of conduction system pacing over both septal and apical pacing. In contrast to RV apical pacing, which leads to QRS widening and disruption of intraventricular coordination, His bundle pacing is associated with QRS narrowing and improved mechanical synchrony of myocardial contraction [5]. GLS is increasingly recognised as a sensitive marker of systolic function. Available evidence indicates that GLS remains comparable to physiological values during His bundle pacing, whereas a decline is observed with RV apical pacing [2, 8]. In a 6-month follow-up study, Michalik et al. showed that LV GLS was preserved during His bundle pacing but deteriorated during RV apical pacing, suggesting the development of dyssynchrony-related contractile dysfunction [5].

Physiological pacing not only preserves systolic function but also exerts favourable effects on diastolic function. In the present study, both His bundle and septal pacing were associated with lower E/e′ values, smaller LAV, and higher LA reservoir strain compared with RV apical pacing, indicating improved diastolic filling and reduced LA pressure. These findings are consistent with the results of Xie et al. and Zhao et al., who demonstrated the benefits of physiological myocardial activation on diastolic function and LA remodelling [2, 8].

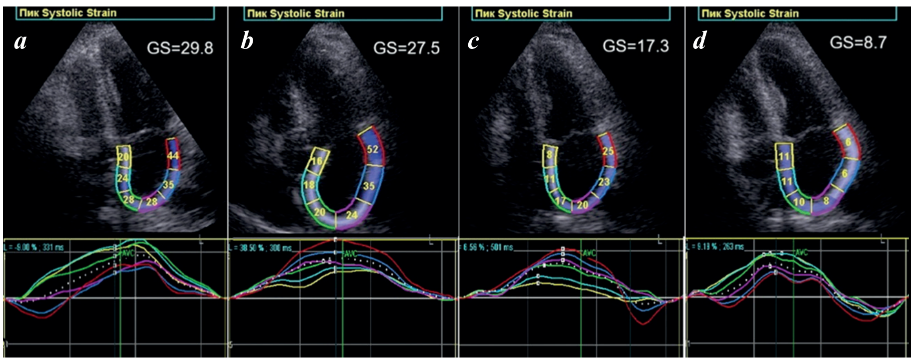

Figure 4. Effect of pacing from different anatomical sites on left atrial (LA) reservoir strain: (a) sinus rhythm (LA strain 29.8%; peak LA deformation occurs synchronously across all segments), (b) His bundle pacing (LA strain 27.5%; near-synchronous deformation), (c) mid-septal pacing (LA strain 17.3%; reduced synchrony), and (d) right ventricular apical pacing (LA strain 8.7%; marked dyssynchrony of LA deformation).

An additional important aspect is the functional state of the left atrium, which reflects chronic diastolic loading conditions. In a randomised study by Zhao et al., physiological pacing of the left bundle branch area in patients with atrioventricular block resulted in significant improvements in LA parameters compared with RV septal pacing, including reduction in anteroposterior LA dimension and improvement in LA strain and pump function [2]. Furthermore, Ravi et al. demonstrated that conduction system pacing (specifically left bundle branch pacing) was associated with a lower incidence of new-onset atrial fibrillation compared with RV apical pacing [3].

These findings support the concept that the choice of pacing site influences not only ventricular mechanics but also atrial haemodynamics, potentially modulating the risk of atrial remodelling and arrhythmogenesis.

CONCLUSION

Our findings demonstrate that even in the acute setting, pacing from different anatomical sites exerts distinct effects on LA function. This suggests that the choice of pacing site may contribute to the formation of conditions that either promote or mitigate the development of atrial fibrillation.

The observed differences in LA morphofunctional parameters highlight the potential clinical importance of pacing strategy selection. In particular, these results support the early implementation of physiological conduction system pacing at the time of initial device implantation, especially in younger patients and in those with an anticipated high burden of ventricular pacing.

The main limitation of this study is the small sample size (n=5), which reflects the technical complexity of intraoperative imaging and the restricted clinical indications for such protocols. However, the within-subject design and controlled pacing conditions reduced inter-individual variability and allowed for the identification of consistent and reproducible trends.

In addition, the assessment was limited to the acute phase, which precludes conclusions regarding long-term adaptive changes and clinical outcomes associated with different pacing strategies.

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