


# Evaluation of electrophysiological characteristics and ventricular synchrony: An inpatient-controlled study during His-Purkinje conduction system pacing versus right ventricular pacing

Xueying Chen MD, PhD<sup>1</sup> | Xiaolan Zhou MD<sup>2</sup> | Yanan Wang MD<sup>3</sup> |  
Qinchun Jin MD<sup>1</sup> | Yufei Chen MD<sup>3</sup> | Jingfeng Wang MD, PhD<sup>1</sup> |  
Shengmei Qin MD, PhD<sup>1</sup> | Jin Bai MD, PhD<sup>1</sup> | Wei Wang MD, PhD<sup>1</sup> |  
Yixiu Liang MD, PhD<sup>1</sup> | Haiyan Chen MD, PhD<sup>3</sup> | Yangang Su MD, PhD<sup>1</sup> |  
Junbo Ge MD, PhD<sup>1</sup> 

<sup>1</sup>Department of Cardiology, National Clinical Research Center for Interventional Medicine, Shanghai Clinical Research Center for Interventional Medicine, Shanghai Institute of Cardiovascular Diseases, Zhongshan Hospital of Fudan University, Shanghai, China

<sup>2</sup>Huashan Worldwide Medical Center, Huashan Hospital, Fudan University, Shanghai, China

<sup>3</sup>Department of Echocardiology, Zhongshan Hospital, Fudan University, Shanghai, China

## Correspondence

Haiyan Chen, MD, PhD, Department of Echocardiology, Zhongshan Hospital, Fudan University, 180 Fenglin Rd, Shanghai 200032, China.  
Email: [chen.haiyan@zs-hospital.sh.cn](mailto:chen.haiyan@zs-hospital.sh.cn)

Yangang Su, MD, PhD, Department of Cardiology, National Clinical Research Center for Interventional Medicine, Shanghai Clinical Research Center for Interventional Medicine, Shanghai Institute of Cardiovascular Diseases, Zhongshan Hospital of Fudan University,

## Abstract

**Objectives to Background:** To compare electromechanical ventricular synchrony when pacing from different sites, including right ventricular apex pacing (RVAP), right ventricular septum pacing (RVSP), His bundle pacing (HBP), left bundle branch pacing (LBBP), and RVSP during unipolar pacing from the ring electrode of LBBP lead (RVSP<sub>ring</sub>) in each patient and evaluate the correlations between electrophysiological characteristics and ventricular synchrony.

**Methods:** Twenty patients with complete atrioventricular block indicated for dual-chamber pacemaker implantation were included in the study. Unipolar pacing at different sites, including RVAP, RVSP, HBP, LBBP, and RVSP<sub>ring</sub>, was successively performed in each patient. The pacing characteristics and echocardiogram parameters were collected and compared among intrinsic rhythm and pacing at different sites.

**Results:** Similar to HBP (114.84 ± 18.67 ms), narrower paced QRSD was found in LBBP (116.15 ± 11.60 ms) as compared to RVSP<sub>ring</sub> (135.11 ± 13.68 ms), RVSP (141.65 ± 14.26 ms), and RVAP (160.15 ± 19.35 ms) ( $p < .001$ ). LBBP showed comparable pacing parameters to RVAP or RVSP and was significantly better than HBP, with maintained cardiac function. TS-12-SD was significantly improved in LBBP (41.80 ± 20.97 ms) than RVAP (69.70 ± 32.42 ms,  $p = .003$ ) and RVSP

**Abbreviations:** AVB, atrioventricular block; EP, electrophysiology; HBP, His bundle pacing; HPCSP, His-Purkinje conduction system pacing; IVCD, intraventricular conduction defect; IVMD, interventricular mechanical delay; LBBP, left bundle branch pacing; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; RBBB, right bundle branch block; RVAP, right ventricular apex pacing; RVP, right ventricular pacing; RVSP, right ventricular septum pacing; RVSP<sub>ring</sub>, RVSP during unipolar pacing from the ring electrode of LBBP lead; Sti-LVAT, the stimulus to left ventricular activation time; TAPSE, tricuspid annular plane systolic excursion; TS-12-SD, standard deviation of the time-to-peak myocardial sustained velocity of 12 left ventricular segments.

Xueying Chen, Xiaolan Zhou, Yanan Wang, and Qinchun Jin contributed equally to the work.

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2022 The Authors. *Clinical Cardiology* published by Wiley Periodicals, LLC.

Shanghai, China.

Email: [yangangsu@yeah.net](mailto:yangangsu@yeah.net) and  
[su.yangang@zs-hospital.sh.cn](mailto:su.yangang@zs-hospital.sh.cn)

#### Funding information

Clinical Research Plan of Shanghai Hospital Development Center (SHDC), Grant/Award Number: SHDC2020CR4003; National Natural Science Foundation of China, Grant/Award Number: 82170387; Shanghai Clinical Research Center for Interventional Medicine, Grant/Award Number: 19MC1910300; The Clinical Research Special Fund of Zhongshan Hospital, Fudan University, Grant/Award Number: 2020ZSLC08

( $63.30.56 \pm 32.53$  ms,  $p = .018$ ) but similar to HBP ( $51.50 \pm 25.67$  ms,  $p = .283$ ) or RVSP<sub>ring</sub> ( $57.80 \pm 25.65$  ms,  $p = .198$ ). Among these pacing strategies, negative values of interventricular mechanical delay (IVMD) were only identified in LBBP ( $-19.25 \pm 18.43$  ms), significantly different from RVAP ( $35.00 \pm 30.72$  ms), RVSP ( $22.85 \pm 22.05$  ms), HBP ( $5.20 \pm 18.64$  ms), and RVSP<sub>ring</sub> ( $16.00 \pm 26.76$  ms) (all  $p < .05$ ). Using Pearson's analysis, Sti-LVAT was positively correlated with QRS duration, IVMD, TS-12-SD, LVEDV, and LVESV, while a negative relationship could be observed for left ventricular ejection fraction.

**Conclusions:** His-Purkinje conduction system pacing (HPCSP) achieved better electrical and mechanical synchrony than conventional RV pacing. For interventricular synchrony, only LBBP initiated earlier LV activation than RV, in accordance with the right bundle branch block (RBBB) pattern of paced QRS during LBBP. Sti-LVAT might be a good parameter correlating with LV systolic function and mechanical synchrony.

#### KEYWORDS

atrioventricular block, electromechanical synchronization, His bundle pacing, His-Purkinje conduction system pacing, left bundle branch pacing

## 1 | BACKGROUND

For decades, right ventricular pacing (RVP) has been established as a conventional pacing technique indicated for symptomatic bradycardia for its pacing efficacy and safety. However, RVP is obviously not a physiological pacing strategy and it could lead to interventricular and intraventricular electrical desynchrony, which might result in atrial fibrillation and heart failure,<sup>1-3</sup> especially in ventricular pacing dependent patients.

His-Purkinje conduction system pacing (HPCSP), His bundle pacing (HBP), and left bundle branch pacing (LBBP), have emerged as two physiological conduction system pacing strategies and have been demonstrated to achieve narrower QRS duration and better mechanical synchrony than RVP.<sup>4</sup> Nowadays, HPCSP has been widely adopted from inside and outside the field.<sup>5</sup> Recent studies have also demonstrated that HPCSP significantly improved heart function in heart failure patients with left bundle branch block (LBBB),<sup>6-8</sup> and even better than BVP.<sup>9,10</sup> Theoretically, HBP is the most physiological pacing mode and it could achieve the same narrow QRS complex as the intrinsic and correct LBBB or right bundle branch block (RBBB) as well. However, pacing safety concerning high pacing threshold and low R wave amplitude of HBP limits its application in all pacing candidates, especially in infra-Hisian block cases.<sup>11</sup> While pacing captures the left conduction system more distal than His bundle, LBBP offers a low and stable threshold and high R wave amplitude comparable to RVP and its feasibility has been confirmed in large-scale studies with mid-long term follow-up.<sup>12-14</sup> LBBP activates the left ventricle earlier than the right ventricle through the left conduction system. Although paced QRS of LBBP is narrower than RVP from the literature, it shows an RBBB morphology that is different from the intrinsic.

Consequently, it remains unknown that its RBBB shape would result in ventricular mechanical desynchrony as compared to HBP though previous case-controlled studies have demonstrated its synchrony similar to HBP and superior to RVP.<sup>15,16</sup> However, the definitions of LBBP in these studies were not unified and the study populations were not ventricular pacing dependent. It would be more reliable to compare electromechanical synchrony at different pacing sites in each case in typically ventricular pacing dependent patients. Whereas, till now, direct comparisons of electromechanical effects in HPCSP and conventional RVP have not been well estimated. Additionally, an inpatient analysis focusing on solely atrioventricular block (AVB) patients to balance individual differences has never been performed in previous research. Moreover, it is also unclear which electrophysiological value has the best correlations with ventricular synchrony and left ventricular function. Hence, the purpose of our present study is to draw meaningful comparisons between the electrophysiological and echocardiographic parameters during HPCSP and conventional RVP in AVB from an inpatient analysis to further assess the relationship between electrical and mechanical synchrony.

## 2 | METHODS

### 2.1 | Study population

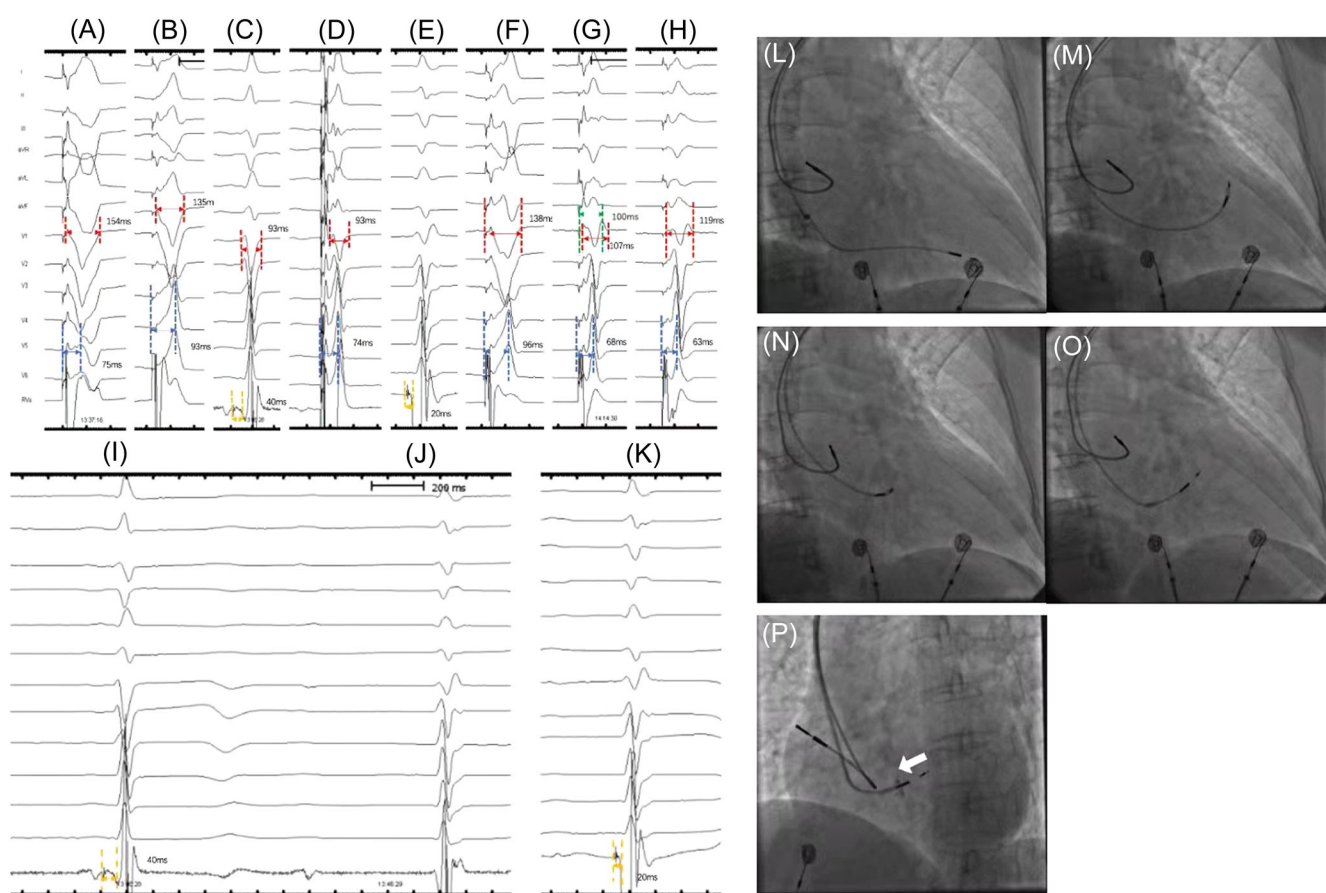
Twenty patients with complete AVB indicated for dual-chamber pacemaker implantation were included in the study. Exclusion criteria included persistent atrial fibrillation, escape beat of intraventricular conduction defect (IVCD) morphology, and left ventricular ejection fraction (LVEF) < 50%. Written informed consent was obtained from

all of the participants and the study was approved by the Institutional Review Board of Zhongshan Hospital, Fudan University, Shanghai, China.

## 2.2 | Implantation procedure

Unipolar pacing at different sites, including right ventricular apex pacing (RVAP), right ventricular septum pacing (RVSP), HBP, LBBP, and unipolar pacing from the ring electrode of LBBP lead (RVSP<sub>ring</sub>) were successively performed in each patient (Figure 1A–P). HBP and LBBP were attempted according to the literature by the lead (Mode 3830 69 cm; Medtronic) together with the sheath (Mode

C315His; Medtronic) during the implantation procedure.<sup>17,18</sup> Briefly, His bundle potential was mapped around the atrioventricular groove with the pacing lead connection to the electrophysiology (EP) recording system (GE CardioLab EP Recording System 2000 GE Inc.) through the sheath (Model 3830, C315His; Medtronic Inc.) at RAO 30°. The lead was then turned four to five times clockwise for fixation. Afterward, the paced 12-lead ECG was the same as the intrinsic during unipolar pacing, which confirmed His bundle capture (Figure 1I–J). LBBP was performed according to the His bundle location at RAO 30°. The pacing lead was moved toward the ventricular side about 1 cm across the tricuspid along the line between His location and RV apex and was deeply screwed into the subendocardium of the left ventricular septum. The criteria of successful LBBP were as follows



**FIGURE 1** The 12-lead ECG, EGM, and fluoroscopic images during pacing at different sites. (A) The 12-lead ECG and the EGM recorded during RVAP: The paced QRSd was 154 ms while Sti-LVAT was 75 ms. (B) The 12-lead ECG and the EGM recorded during RVSP: The paced QRSd 135 ms was while Sti-LVAT was 93 ms. (C)  $Po_{His}$  during the intrinsic rhythm with the potential to ventricle interval were 40 ms. (D) The 12-lead ECG and the EGM recorded during HBP: The paced QRSd was 93 ms while Sti-LVAT was 74 ms. (E)  $Po_{LBB}$  during the intrinsic rhythm with the potential to ventricle interval were 18 ms. (F) The 12-lead ECG and the EGM recorded by unipolar pacing from the ring electrode of the LBBP lead (RVSP ring): The paced QRSd was 138 ms while Sti-LVAT was 96 ms. (G) The 12-lead ECG and the EGM recorded by the LBBP lead (Nonselective LBBP): The paced QRSd was 107 ms while Sti-LVAT was 68 ms and Sti-RVAT was 110 ms. (H) The 12-lead ECG and the EGM recorded by the LBBP lead (Selective LBBP): The paced QRSd was 119 ms while Sti-LVAT was 63 ms. (I)  $Po_{His}$  obtained during the intrinsic rhythm of a narrow QRS with an HV interval of 40 ms. (J) No  $Po_{His}$  recorded during escape beat of an RBBB morphology. (K)  $Po_{LBB}$  obtained with the LBB potential to ventricle interval of 20 ms. Fluoroscopic images at RAO 30° of: (L) RVAP; (M) RVSP; (N) HBP; (O) LBBP; at LAO 35° of (P) LBBP (white arrow depicted the depth of LBBP lead inside the septum via angiography through the sheath). HBP, his bundle pacing; LAO, left anterior oblique; LBB, left bundle branch; LBBP, left bundle branch pacing; RAO, right anterior oblique; RVAP, right ventricular apex pacing; RVSP, right ventricular septum pacing; Sti-LVAT, stimulus to left ventricular activation time.

according to our previous studies: (1) paced QRS of an RBBB pattern; (2) confirmation of selective LBBP (paced QRS of a typical RBBB pattern and a discrete component between stimulus and ventricle activation in intracardiac electrogram); and (3) the stimulus to left ventricular activation time (Sti-LVAT) (Figure 1), which is defined as the interval from the pacing stimulus to the peak of the R wave in lead V5, shortening abruptly by increasing output or remaining shortest and constant at the final depth. The lead depth inside the interventricular septum was measured via angiography through the sheath at LAO 35° (Figure 1P). During the procedure, the atrial lead placed at the right atrium appendage and ventricular lead at different pacing sites above were temporarily connected to the programmer (Medtronic 2290) with DDD mode, AV delay of 150 ms, and pacing output of 3.5 V/0.5 ms during unipolar configuration at different sites above in each patient.

## 2.3 | Data collection

QRS duration was measured from the onset to the end of the QRS wave and was compared during the intrinsic rhythm and different pacing sites. Sti-LVAT and pacing stimulus to right ventricular activation time (Sti-RVAT) (Figure 1G), defined as the interval from the pacing stimulus to the peak of R' wave in lead V1, were recorded and compared during pacing at different sites. The transthoracic echocardiogram was used during the procedure. Echocardiographic parameters, including LVEF, left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), interventricular mechanical delay (IVMD), and standard deviation (SD) of the time-to-peak myocardial sustained velocity of 12 left ventricular segments (TS-12-SD), tricuspid annular plane systolic excursion (TAPSE), were measured after 10 min of pacing at each site with a washout period of 5 min. IVMD was determined as the delay between left and right ventricular pre-ejection intervals by Doppler (Figure S1). For TS-12-SD, pulsed-wave Doppler and tissue synchronization imaging (Figure S2) were used to measure the left ventricular synchrony. All echocardiograms of our study were assessed by two experienced echocardiographers blinded to our study design. The fluoroscopy time of positioning the ventricular lead at different sites was also collected and compared. After collecting these parameters, LBBP lead was finally implanted together with the atrial lead connected to the ventricular and atrial port of the generator, respectively. Sensed/paced AV delay of 150/180 ms with pacing output of 3.5 V/0.5 ms by unipolar configuration were set in each case.

## 2.4 | Follow-up

During follow-up (1, 3, 6, 12, and 18 months postprocedure), QRS durations and echocardiographic parameters, including LVEF, LVEDV, and LVESV were collected and compared. The procedure-related complications, including lead dislodgement, perforation, device, or lead infection, pericardial effusion, and thromboembolism were also collected.

## 2.5 | Statistical analysis

Continuous variables were expressed as mean  $\pm$  SD and paired Student's *t*-test was used to compare the difference between baseline and 6-month follow-up in each group. Analysis of variance test was used to perform comparison among more than two groups and was followed by the least significant difference test for multiple comparisons. Categorical variables were presented as numbers (percentages) by using Pearson's  $\chi^2$  test or Fisher's exact test. The correlations between electrophysiological characteristics and echocardiographic parameters were performed by Pearson's analysis. All analyses were performed by SPSS version 22.0 (SPSS, Inc.) and a two-sided  $p < .05$  was considered statistically significant.

## 3 | RESULTS

### 3.1 | Electromechanical parameters during pacing at different sites

A total of 20 patients (mean age:  $66.15 \pm 13.65$  years, 15 male) with complete AVB were enrolled and their baseline characteristics are shown in Table 1. Dual-chamber pacemaker implantation with recordings of unipolar pacing at different sites was successfully achieved in all patients (Table 1) without procedure-related complications. The mean depth of the lead was measured as  $12.80 \pm 0.89$  mm into the interventricular septum. Pacing parameters during different pacing sites

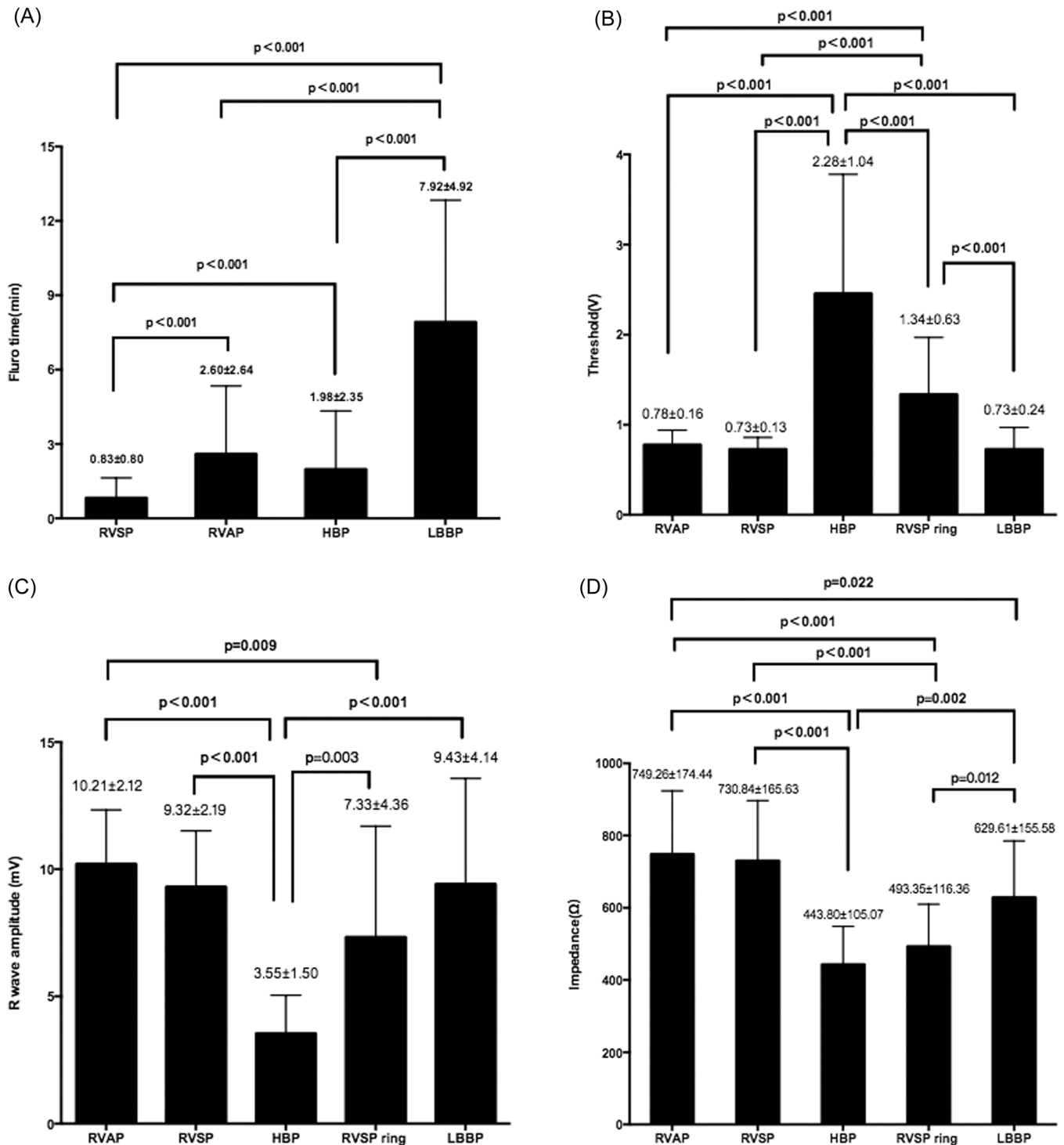
**TABLE 1** Baseline characteristics.

Variables	Results
Age (years)	$66.15 \pm 13.65$
Male, <i>n</i> (%)	15 (75)
Body mass index (kg/m <sup>2</sup> )	$24.58 \pm 3.14$
Hypertension, <i>n</i> (%)	10 (50)
Baseline electrocardiogram	
QRS durations (ms)	$118.75 \pm 24.63$
Complete AVB, <i>n</i> (%)	20 (100)
Narrow QRS, <i>n</i> (%)	9 (45)
LBBB, <i>n</i> (%)	2 (10)
RBBB, <i>n</i> (%)	9 (45)
Baseline echocardiography	
Left atrium (mm)	$40.30 \pm 5.32$
LVEDD (mm)	$49.15 \pm 5.46$
LVEF (%)	$62.12 \pm 13.83$
Ventricular septum (mm)	$9.80 \pm 1.58$

Abbreviations: AVB, atrioventricular block; LBBB, left bundle branch block; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; RBBB, right ventricular branch block.

are shown in Figure 2B–D. The highest threshold ( $2.28 \pm 1.04$  V) and lowest R-wave amplitude ( $3.55 \pm 1.50$  mV), as well as impedance ( $443.80 \pm 105.07 \Omega$ ), were achieved in HBP among all the pacing sites (all  $p < .01$ ). Threshold in LBBP ( $0.73 \pm 0.24$  V) was similar to RVAP ( $0.78 \pm 0.16$  V,  $p = .633$ ) and RVSP ( $0.73 \pm 0.13$  V,  $p = .954$ ) but significantly lower than RVSP<sub>ring</sub> ( $1.34 \pm 0.63$  V,  $p < .001$ ). For R-wave amplitude, there was no difference between LBBP ( $9.43 \pm 4.14$  mV)

and RVAP ( $10.21 \pm 2.12$  mV,  $p = .474$ ) or RVSP ( $9.32 \pm 2.19$  mV,  $p = .914$ ). With regard to impedance, LBBP ( $629.61 \pm 155.58 \Omega$ ) is relatively lower than RVAP ( $749.26 \pm 174.44 \Omega$ ,  $p = .022$ ) but similar to RVSP ( $730.84 \pm 165.63 \Omega$ ,  $p = .064$ ). Moreover, higher impedance was demonstrated in LBBP when compared to RVSP<sub>ring</sub> ( $493.35 \pm 116.36 \Omega$ ,  $p = .012$ ). As for LBBP, LBB potential was recorded in 15 cases (75%) and 16 cases (80%) achieved selective LBBP during the procedure.

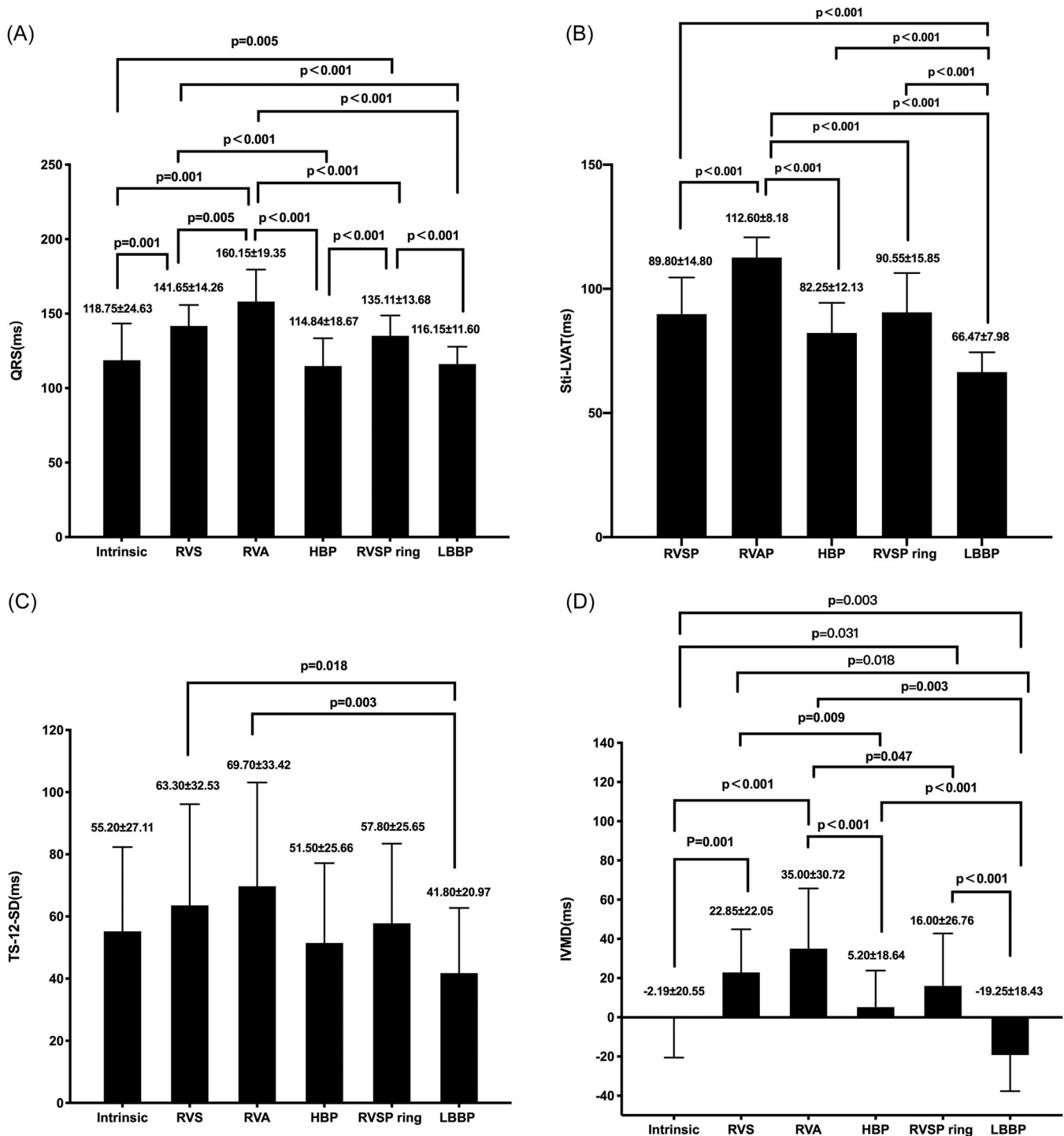


**FIGURE 2** Fluoroscopic time and pacing parameters during pacing at different sites: (A) Fluoroscopic time; (B) Threshold; (C) R wave amplitude; (D) Impedance.

### 3.2 | Electrical and mechanical synchrony

The electrocardiographic parameters during pacing at different sites are summarized in Table S1. RVSP ( $141.65 \pm 14.26$  ms,  $p = .001$ ), RVAP ( $160.15 \pm 19.35$  ms,  $p = .001$ ), as well as RVSP<sub>ring</sub> ( $135.11 \pm 13.68$  ms,  $p = .005$ ) resulted in a remarked increase in QRS duration compared to

the baseline ( $118.75 \pm 24.63$  ms) (Figure 3A). QRS duration during HBP ( $114.84 \pm 18.67$  ms) and LBBP ( $116.15 \pm 11.60$  ms) was comparable to the intrinsic and hence, was both significantly narrower than RVSP, RVAP, and RVSP<sub>ring</sub> (all  $p < .001$ ). Concerning Sti-LVAT, LBBP ( $66.47 \pm 7.98$  ms) showed the shortest Sti-LVAT compared with RVSP ( $89.80 \pm 14.80$  ms,  $p < .001$ ), RVAP ( $112.60 \pm 8.18$  ms,  $p < .001$ ),



**FIGURE 3** Electrical and mechanical synchrony during pacing at different sites: (A) QRSd; (B) Sti-LVAT; (C) TS-12-SD; (D) IVMD.

IVMD, interventricular mechanical delay; QRSd, QRS duration; Sti-LVAT, stimulus to left ventricular activation time; TS-12-SD, standard deviation of the time-to-peak myocardial sustained systolic velocity of 12 left ventricular segments.

HBP ( $82.25 \pm 12.13$  ms,  $p < .001$ ), and  $RVSP_{ring}$  ( $90.55 \pm 15.85$  ms,  $p < .001$ ) (Figure 3B).

Among all the different pacing sites, there was no significant difference in TS-12-SD as compared to baseline ( $55.20 \pm 27.11$  ms) while a decreasing trend could be seen during HBP ( $51.50 \pm 25.66$  ms) and LBBP ( $41.80 \pm 20.97$  ms) (Figure 3C). Whereas, TS-12-SD was significantly lower in LBBP compared with RVSP ( $p = .029$ ) and RVA ( $p = .004$ ). Significant negative means of IVMD was demonstrated in LBBP ( $-19.25 \pm 18.43$ ) than RVSP ( $22.85 \pm 22.05$  ms), RVAP ( $35.00 \pm 30.72$  ms), HBP ( $5.20 \pm 18.64$  ms), and  $RVSP_{ring}$  ( $16.00 \pm 26.76$  ms) (all  $p < .05$ ) (Figure 3D). IVMD during HBP was similar to baseline and were significantly lower than RVSP ( $p = .009$ ) and RVA ( $p < .001$ ).

### 3.3 | Evaluation of cardiac function during pacing at different sites

LVEF in HBP ( $62.71 \pm 7.69\%$ ) and LBBP ( $62.93 \pm 6.09\%$ ) was comparable to baseline ( $62.12 \pm 13.83\%$ ) while a significantly decreased LVEF was identified in RVSP ( $59.40 \pm 9.81\%$ ,  $p = .016$ ), RVAP ( $60.47 \pm 8.00\%$ ,  $p = .040$ ), and  $RVSP_{ring}$  ( $58.50 \pm 7.21\%$ ,  $p = .008$ ) (Table S1). For other echocardiographic parameters, a trend toward decreased LVEDV and LVESV compared to baseline was indicated in HBP and LBBP but the difference did not reach statistical significance. TAPSE was significantly lower in RVSP ( $17.70 \pm 3.06$  mm,  $p = .004$ ), RVAP ( $17.35 \pm 2.82$  mm,  $p = .001$ ), and  $RVSP_{ring}$  ( $18.37 \pm 2.81$  mm,  $p = .033$ ) compared with baseline ( $20.33 \pm 2.54$  mm) while HBP ( $19.53 \pm 2.65$  mm,  $p = .352$ ) and LBBP ( $18.75 \pm 2.65$  mm,  $p = .069$ ) remained stable.

### 3.4 | Correlation between electrophysiological characteristics and echocardiographic parameters

Correlations between electrophysiological characteristics and echocardiographic parameters are summarized in Table S3. Notable positive linear correlations could be observed between Sti-LVAT and QRS duration ( $r = 0.612$ ,  $p < .001$ ), LVEDV ( $r = 0.348$ ,  $p = .003$ ), LVESV ( $r = 0.338$ ,  $p = .004$ ), TS-12-SD ( $r = 0.241$ ,  $p = .016$ ), and IVMD ( $r = 0.440$ ,  $p < .001$ ), while a negative relationship between Sti-LVAT and LVEF ( $r = -0.245$ ,  $p = .035$ ) was demonstrated (Figure 4A-F). However, QRS duration was not significantly correlated to the echocardiographic parameters except for IVMD ( $r = 0.388$ ,  $p < .001$ ). No significant association between Sti-RVAT and echocardiographic parameters were confirmed, either.

### 3.5 | Pacing parameters and echocardiographic outcomes at follow-up

Follow-up echocardiograms were obtained at least 18 months after the initial pacemaker implant in each patient. Stability was maintained

in LBBP capture ( $0.81 \pm 0.23$  V,  $p = .300$ ) and sensed R-wave amplitude ( $10.98 \pm 4.56$  mV,  $p = .295$ ) during unipolar configuration (Table S2). For unipolar pacing impedance, a significant decrease was found 6 months ( $510.61 \pm 88.29 \Omega$ ,  $p = .008$ ) after implantation and it was maintained till 18 months follow-up ( $455.78 \pm 73.68 \Omega$ ,  $p < .001$ ) (Table S2). Neither LVEF ( $62.80 \pm 6.01\%$ ,  $p = .952$ ) nor QRS duration ( $113.75 \pm 11.36$  ms,  $p = .512$ ) showed significant difference during follow-up and none of the complications, including lead dislodgement, perforation, device or lead infection, pericardial effusion, or thromboembolism were reported.

## 4 | DISCUSSION

The present study directly compared electrophysiological characteristics and echocardiographic parameters at different pacing sites in each patient during the procedure and the main findings were as follows: (1) similar to HBP, LBBP preserved better electrical and LV mechanical synchrony compared with conventional RV pacing (RVAP or RVSP); (2) our research provided the initial evidence of earlier LV electrical activation than RV during LBBP in accordance with interventricular synchrony (negative values of IVMD in LBBP); (3) there were significant correlations between Sti-LVAT and echocardiographic parameters, including LVEDV, LVESV, LVEF, TS-12-SD, and IVMD.

### 4.1 | Electrical synchrony

Paced QRS duration is demonstrated to be narrower in LBBP<sup>12,17</sup> and left ventricular septal pacing<sup>19</sup> as compared to RVP. Wide QRS duration might be associated with ventricular dyssynchrony and heart failure.<sup>20</sup> During HBP and LBBP, the heart was activated fast through the conduction system, showing a significantly narrower QRS duration than RVAP or RVSP. When the comparison between HBP and LBBP, HBP showed a narrower QRS duration similar to the intrinsic than LBBP, and LBBP performed an RBBB pattern of paced QRS. Moreover, Sti-LVAT, which is often used to reflect the lateral precordial myocardium depolarization time, was significantly decreased in HBP and LBBP than RVAP or RVSP. These findings demonstrated that HBP was the most physiological pacing strategy, which activated both ventricles fast through His bundle (LBB and RBB) while LBBP preserved physiological LV activation before RV through LBB. These findings were consistent with the literatures<sup>18</sup>: LBBP showed significantly reduced QRS duration and sti-LVAT than RVSP in different individuals while our study further demonstrated it in each ventricular pacing dependent patient suffering from complete AVB during the implantation procedure.

A novel pacing site of the present study was  $RVSP_{ring}$ , a specific RVSP during unipolar pacing from the ring electrode of LBBP lead. It might be a better pacing site than conventional RVAP or RVSP since the mean QRS duration during  $RVSP_{ring}$  was significantly decreased than RVAP and the trend was confirmed

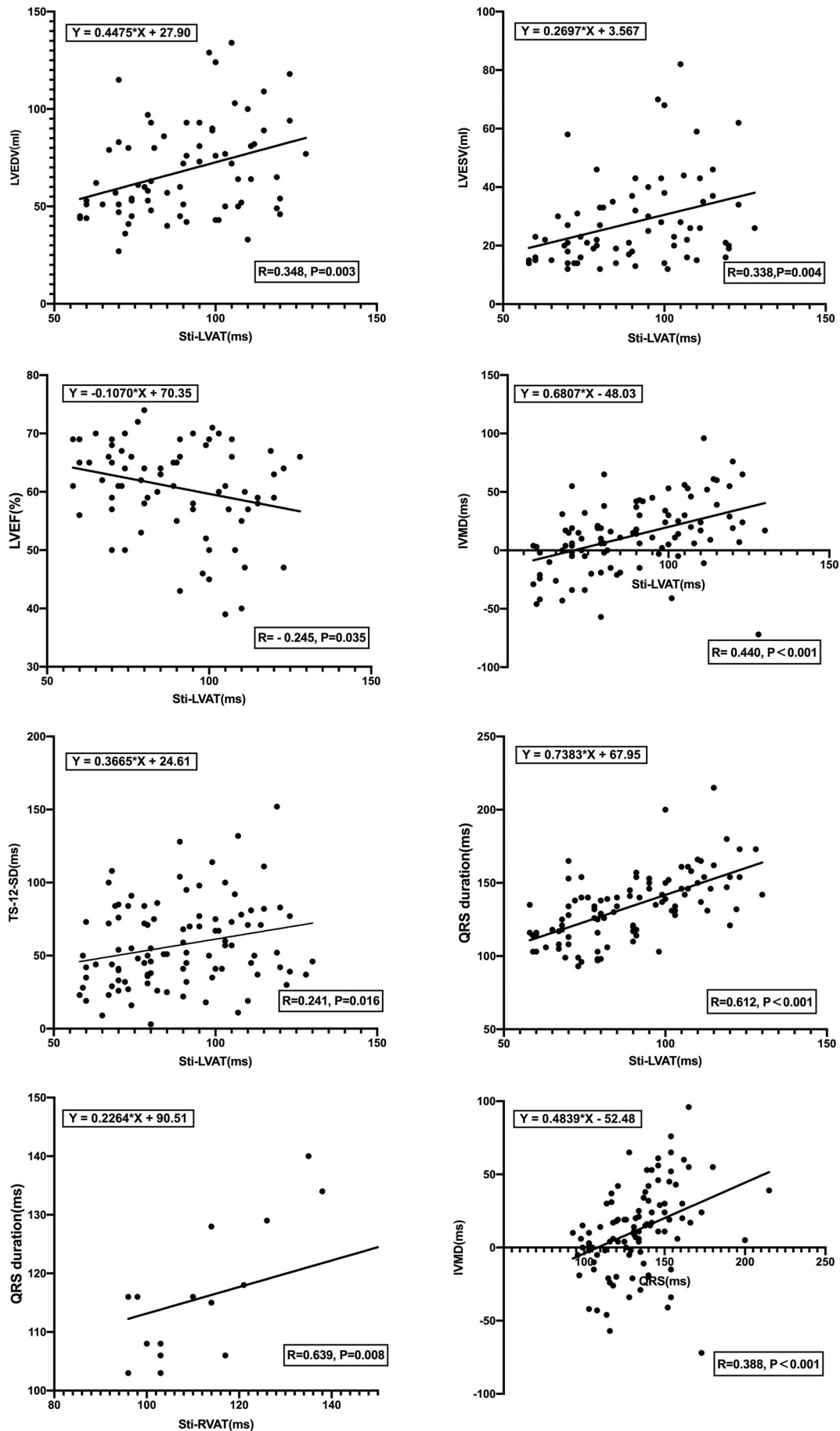


FIGURE 4 (See caption on next page)



when comparing with RVSP but no statistical significance was found. Since the length between the tip and the ring of the lead (Mode 3830) was 10.8 mm, the pacing site of RVSP<sub>ring</sub> was still RVS in most cases and might be a little bit deeper than conventional RVSP when the lead screwed deep inside the septum. Hence, the mean QRS duration and sti-LVAT during RVSP<sub>ring</sub> were significantly increased than LBBP, though they showed a decreased trend than RVAP or RVSP. And the pacing parameters were good as well during RVSP<sub>ring</sub>. Dual cathodal lead might be designed in the future to give an additional pacing option.

## 4.2 | Mechanical synchrony

Better LV mechanical synchrony has been previously confirmed during LBBP than RVSP using SPECT MPI and echocardiogram.<sup>15,16</sup> The latter study by Cai et al.<sup>15</sup> demonstrated that LV mechanical synchrony during LBBP was similar to that of native-conduction concerning LV systolic dyssynchrony index and the SD of TS in the 12 segments, and the LV synchrony in LBBP was superior to the RVSP significantly in sick sinus syndrome patients. Consistently, our results showed the similarity of TS-12-SD between HBP, LBBP, and the intrinsic while increased TS-12-SD during RVP indicated LV dyssynchrony, showing preserved LV mechanical synchrony in HPCSP. Whereas, the biggest advantage of the present inpatient-controlled study in AVB was that the baseline difference between individuals had been minimized to the utmost extent to facilitate the measurement and comparison of the echocardiographic results at different pacing sites. However, there was no significant difference concerning TS-12-SD between LBBP and RVSP<sub>ring</sub>. It might be attributed to the study population (AVB patients without heart failure) and small-sample-sized study design.

Furthermore, IVMD was measured and compared in the study and showed a significant difference between LBBP and HBP or RVAP or RVSP or RVSP<sub>ring</sub>. IVMD evaluates the mechanical synchrony between LV and RV and is recognized as a predictive factor in CRT response.<sup>21</sup> During LBBP, earlier LV activation than RV was confirmed by pacing activating LV before RV through LBB, showing an RBBB morphology of paced QRS. Consequently, significant negative means of IVMD during LBBP were confirmed as compared to positive ones at other pacing sites, indicating mechanical contraction of LV earlier than RV. Earlier LV electrical activation than RV during LBBP as an RBBB paced morphology in accordance with interventricular synchrony (shown as negative values of IVMD) was initially demonstrated in our research.

Concerning our findings of TS-12-SD and IVMD, HBP maintained inter and intraventricular synchrony while LBBP preserved LV synchrony with delayed RV activation. Conversely, RVP resulted in earlier RV activation and deteriorated LV synchrony.

## 4.3 | Correlations between electrophysiological characteristics and echocardiographic parameters

To maintain satisfied heart function and mechanical synchrony after implantation, it is of significant importance to confirm a simple and reliable electrophysiological value correlated to echocardiographic parameters during pacing. Sti-LVAT is indicated for the depolarization duration of the LV wall. Hence, a shorter Sti-LVAT may represent rapid propagation of LV activation leading to synchronous LV contraction. During LBBP, Sti-LVAT has been reported to be a useful parameter to determine LBB capture according to electrophysiological mapping while QRS duration failed to act as an ideal diagnostic value for LBB capture due to its delayed RV activation.<sup>22</sup> As a main and novel finding, our research further confirmed that Sti-LVAT was also notably correlated with LV systolic function (LVEDV, LVESV, and LVEF) and mechanical synchrony (TS-12-SD and IVMD), while QRS duration failed except for IVMD, indicating that Sti-LVAT might be a better variable correlated to LV-related echocardiographic parameters than QRS duration. Since a positive relationship was also shown between Sti-LVAT and QRS duration, shorter Sti-LVAT could be reasonably proposed to depict both favorable electrical synchrony and LV systolic function and mechanical synchrony. As for RV function, no remarkable correlations were shown in our study between Sti-RVAT and TAPSE. Since our study was performed based on small sample size and merely TAPSE was included as RV-related echocardiographic parameters, the correlation between Sti-RVAT and RV function might be highly underestimated. In the future, further analysis of RV function (RV fractional area change, Tei index, speckle tracking derived free wall strain, and so forth.) was warranted to specifically evaluate the correlation with Sti-RVAT during LBBP.

## 4.4 | Limitations

The study focused on the electrical and mechanical synchrony at different pacing sites during the procedure. These findings were acute hemodynamic results. Thus, the long-term hemodynamic effects of LBBP remain uncertain. In addition, it is a single-center, self-controlled observational study, with relatively small sample size.

**FIGURE 4** Linear correlations between electrical synchrony and echocardiographic parameters (A) Sti-LVAT versus LVEDV; (2) Sti-LVAT versus LVESV; (3) Sti-LVAT versus LVEF; (4) Sti-LVAT versus IVMD; (5) Sti-LVAT versus TS-12-SD; (6) Sti-LVAT versus QRS duration; (7) Sti-RVAT versus QRS duration; (8) QRS duration versus IVMD. IVMD, interventricular mechanical delay; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; Sti-LVAT, stimulus to left ventricular activation time; TS-12-SD, standard deviation of the time-to-peak myocardial sustained systolic velocity of 12 left ventricular segments; Sti-RVAT, stimulus to right ventricular activation time.

The main study population was AVB with narrow QRS or RBBB and normal LVEF. Consequently, the results of the study could not be generalized to patients with IVCD or heart dysfunction.

## 5 | CONCLUSIONS

HPCSP provided better electrical and mechanical left ventricular synchrony than conventional RVP. While interventricular synchrony during LBBP was significantly different as compared to HBP, RVAP, and RVSP, showing earlier LV activation than RV, which was consistent with the RBBB pattern of paced QRS during LBBP. Sti-LVAT might be a good electrophysiological parameter correlated to LV systolic function and mechanical synchrony.

### AUTHOR CONTRIBUTIONS

All authors have read and approved the manuscript. Methodology and manuscript writing: Xueying Chen, Qinchun Jin, Yanan Wang, Xiaolan Zhou. Data collection and pacing performance: Yufei Chen, Jingfeng Wang, Shengmei Qin, Jin Bai, Wei Wang, Yixiu Liang. Conceptualization and supervision: Haiyan Chen, Yangang Su, Junbo Ge.

### CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

### DATA AVAILABILITY STATEMENT

The datasets generated and/or analysed during the current study are not publicly available due but are available from the corresponding author on reasonable request.

### ORCID

Junbo Ge  <http://orcid.org/0000-0002-8765-4941>

### REFERENCES

- Curtis AB, Worley SJ, Chung ES, Li P, Christman SA, St John Sutton M. Improvement in clinical outcomes with biventricular versus right ventricular pacing: the BLOCK HF study. *J Am Coll Cardiol*. 2016;67:2148-2157.
- Cicchitti V, Radico F, Bianco F, et al. Heart failure due to right ventricular apical pacing: the importance of flow patterns. *Europace*. 2016;18:1679-1688.
- Pastore G, Zanon F, Baracca E, et al. The risk of atrial fibrillation during right ventricular pacing. *Europace*. 2016;18:353-358.
- Sharma PS, Vijayaraman P, Ellenbogen KA. Permanent His bundle pacing: shaping the future of physiological ventricular pacing. *Nat Rev Cardiol*. 2020;17:22-36.
- Huang WJ, Huang DJ, Zhang S, et al. Chinese Society of Pacing and Electrophysiology, Chinese Society of Arrhythmias. Chinese expert consensus on His-Purkinje conduction system pacing. *Zhonghua Xin Lv Shi Chang Xue Za Zhi*. 2021;25:10-36.
- Huang W, Su L, Wu S, et al. Long-term outcomes of His bundle pacing in patients with heart failure with left bundle branch block. *Heart*. 2019;105:137-143.
- Ji W, Chen X, Shen J, Zhu D, Chen Y, Li F. Left bundle branch pacing improved heart function in a 10-year-old child after a 3-month follow-up. *Europace*. 2020;22:1234-1239.

- Huang W, Wu S, Vijayaraman P, et al. Cardiac resynchronization therapy in patients with nonischemic cardiomyopathy using left bundle branch pacing. *JACC Clin Electrophysiol*. 2020;6:849-858.
- Wu S, Su L, Vijayaraman P, et al. Left bundle branch pacing for cardiac resynchronization therapy: nonrandomized on-treatment comparison with His bundle pacing and biventricular pacing. *Can J Cardiol*. 2021;37:319-328.
- Chen X, Ye Y, Wang Z, et al. Cardiac resynchronization therapy via left bundle branch pacing vs. optimized biventricular pacing with adaptive algorithm in heart failure with left bundle branch block: a prospective, multi-centre, observational study. *Europace*. 2021; euab249. doi:10.1093/europace/euab249
- Chen X, Wei L, Bai J, et al. Procedure-related complications of left bundle branch pacing: a single-center experience. *Front Cardiovasc Med*. 2021;8:645947.
- Chen X, Jin Q, Bai J, et al. The feasibility and safety of left bundle branch pacing vs. right ventricular pacing after mid-long-term follow-up: a single-centre experience. *Europace*. 2020;22:ii36-ii44.
- Su L, Wang S, Wu S, et al. Long-term safety and feasibility of left bundle branch pacing in a large single-center study. *Circ Arrhythm Electrophysiol*. 2021;14:e009261.
- Chen X, Jin Q, Li B, et al. Electrophysiological parameters and anatomical evaluation of left bundle branch pacing in an in vivo canine model. *J Cardiovasc Electrophysiol*. 2020;31:214-219.
- Cai B, Huang X, Li L, et al. Evaluation of cardiac synchrony in left bundle branch pacing: insights from echocardiographic research. *J Cardiovasc Electrophysiol*. 2020;31:560-569.
- Hou X, Qian Z, Wang Y, et al. Feasibility and cardiac synchrony of permanent left bundle branch pacing through the interventricular septum. *Europace*. 2019;21:1694-1702.
- Huang W, Chen X, Su L, Wu S, Xia X, Vijayaraman P. A beginner's guide to permanent left bundle branch pacing. *Heart Rhythm*. 2019; 16:1791-1796.
- Chen X, Wu S, Su L, Su Y, Huang W. The characteristics of the electrocardiogram and the intracardiac electrogram in left bundle branch pacing. *J Cardiovasc Electrophysiol*. 2019;30:1096-1101.
- Mafi-Rad M, Luermans JG, Blaauw Y, et al. Feasibility and acute hemodynamic effect of left ventricular septal pacing by transvenous approach through the interventricular septum. *Circ Arrhythm Electrophysiol*. 2016;9:e003344.
- Sandhu R, Bahler RC. Prevalence of QRS prolongation in a community hospital cohort of patients with heart failure and its relation to left ventricular systolic dysfunction. *Am J Cardiol*. 2004;93:244-246.
- Risum N. Assessment of mechanical dyssynchrony in cardiac resynchronization therapy. *Dan Med J*. 2014; 61: B4981.
- Wu S, Chen X, Wang S, et al. Evaluation of the criteria to distinguish left bundle branch pacing from left ventricular septal pacing. *JACC Clin Electrophysiol*. 2021;7:1166-1177.

### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Chen X, Zhou X, Wang Y, et al. Evaluation of electrophysiological characteristics and ventricular synchrony: An inpatient-controlled study during His-Purkinje conduction system pacing versus right ventricular pacing. *Clin Cardiol*. 2022;45:723-732. doi:10.1002/clc.23837