Early Assessment of Ventricular Synchronization and Function After Left Bundle-Branch-Area Pacing with Right Bundle-Branch Block

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Research Article

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Abstract

Aim

To evaluate ventricular synchronization and function in patients with right bundle-branch block after left bundle-branch-area pacing (LBBAP) by echocardiography.

Methods

Forty patients who successfully received LBBAP were selected and divided into the right bundle-branch block group (RBBB group) and the non-RBBB group by pre-operation ECG. Echocardiography and follow-up were performed 1 month after operation. Interventricular synchronization was evaluated by tissue Doppler (TDI), tissue mitral annular displacement (TMAD), and interventricular mechanical delay (IVMD). The tricuspid annular plane systolic excursion (TAPSE), right ventricular fractional area change(RVFAC), tricuspid annulus sidewall systolic velocity (TV-s') ,global ventricular longitudinal strain(GLS) ,right ventricular free wall longitudinal strain(LS-RV) , standard deviation of left ventricular 18 segments peak time difference(SDt-L) and standard deviation of right ventricular free wall 3 segments peak time difference(SDt-R) were applied to evaluate intraventricular synchronization and ventricular function.

Results

The deviation of displacement peak time of the tricuspid and mitral valves, namely $\Delta PT_{TV\text{-}MV}$ measured by TMAD, the deviation of systolic time to peak of the tricuspid and mitral valves, namely $\Delta Ts_{TV\text{-}MV}$ measured by TDI, were statistically different between the two groups ($P < 0.05$). (2) Compared with the non-RBBB group, there were no statistically significant differences in the GLS, RVFAC, LS-R,TAPSE, TV-s', SDt-L, SDt-R ($P > 0.05$).

Conclusion

Echocardiography technology including two-dimensional speckle tracking imaging (2D-STI), TDI, and TMAD can effectively analyze interventricular synchronization, intraventricular synchronization, and ventricular function. Although the movement of the right ventricular myocardium in the RBBB group was slightly later than that of the left ventricular myocardium after LBBAP, LBBAP could still be applied in RBBB patients with pacing indication.

Introduction

Left bundle-branch-area pacing (LBBAP) is a kind of physiological pacing with a low and stable pacing threshold [1]. After LBBAP, the patient's ECG often shows a complete or an incomplete right bundle-branch block (RBBB) pattern [2, 3]. After optimizing the atrioventricular interval, right bundle branch conduction can merge with the pacing signals, so that RBBB morphology can be eliminated. However, for patients with intrinsic RBBB, the conduction of the right bundle branch is delayed or blocked. Although the duration of QRS after LBBAP is shorter than before, and the RBBB morphology of the electrocardiogram is improved[3, 4], there is still a difference in the optimal atrioventricular interval between the RBBB and non-RBBB group[5]. On the premise of atrioventricular interval optimization, whether the right bundle-branch block will cause ventricular asynchrony and decline in ventricular function in RBBB patients after LBBAP has not been discussed yet. This study is conducted to explore the interventricular and intraventricular synchronization and ventricular function of RBBB patients after LBBAP, compared with non-RBBB patients.

Materials And Methods

1.1 Subjects

The ethics committee of The Third People's Hospital of Chengdu approved to carry out the study within its facilities, and all methods were performed in accordance with the relevant guidelines and regulations. Informed consent was obtained from all subjects. This study was carried out in Chengdu Third People's Hospital in patients who were indicated for pacing therapy according to 2013 ESC/EHRA Guideline. The criteria for exclusion were as follows: 1) Patients with a left ventricular ejection fraction of less than 50%; 2) Patients with arrhythmia, such as atrial fibrillation; 3) Patients with congenital heart disease, valvular heart disease, and myocardial disease; 4) Unclear acoustic window. Patients completed an electrocardiogram to confirm whether they had RBBB (Figure. 1) and then were divided into the RBBB group or the non-RBBB group.

1.2 Image acquisition

Conventional echocardiography was performed by the Philips IE Elite color Doppler ultrasound diagnostic apparatus, equipped with an S5-1 probe, a frequency of 1~5MHz, and a Qlab13 workstation. One month after the implantation, the programmer set the pacing mode to the DDD unipolar pacing mode, and we optimized the atrioventricular interval according to LVEF, aortic velocity time integral, mitral regurgitation and tricuspid regurgitation. Under the optimal atrioventricular interval, the patient took the left side decubitus, synchronously connecting it to the electrocardiogram, and then performed image acquisition. The specific operations were as follows:1) conventional echocardiographic parameters: left atrial volume index(LAVI), right atrial diameter (RAD), left ventricular end-systolic Volume (LVESV), left ventricular end-diastolic Volume (LVEDV), left ventricular ejection fraction (LVEF), measured by Simpson method, right ventricular fractional area change(RVFAC); 2) We obtained the forward blood flow spectrum of the patient's aortic valve and pulmonary valve; 3) The M-mode cursor was oriented to the junction of the tricuspid valve plane with the RV free wall using the apical four-chamber view.

imaging plane is then prescribed from the RV apex through the anterolateral tricuspid annulus, the distance traveled by the tricuspid annulus is reported as the tricuspid annular plane systolic excursion (TAPSE) ; 4) We measured tricuspid annulus sidewall systolic velocity (TV-s') by tissue Doppler (TDI); 5) We acquired apical four-chamber, three-chamber, and two-chamber images for three consecutive cardiac cycles, where the image completely contained the left and right ventricles, and the frame rate was >100 f/s; 6) We acquired continuous acquisition of three cardiac cycles of the apical four-chamber TDI dynamic image.

1.3 Image analysis

We used echocardiographic technique, such as blood flow spectrum, 2DQ and TDI to evaluate interventricular synchronization. The parameters were measured as follows: 1) We measured the time from the beginning of QRS to the beginning of the blood flow spectrum on the pulmonary valve (pulmonary pre-ejection interval, PPEI), and the time from QRS to the beginning of the blood flow spectrum on the aortic valve (artery pre-ejection interval, APEI). The deviation of PPEI and APEI is IVMD; 2) We selected the apical four-chamber TDI dynamic image and entered the SQ plug-in, outlined the tricuspid valve (TV) sidewall and mitral valve (MV) sidewall, and obtained the myocardial motion curve of the right ventricular basal segment and the left ventricular basal segment. The deviation of systolic time to peak of TV and MV were recorded as ΔTs_{TV-MV} (Figure. 2A, B); 3) We selected apical four-chamber two-dimensional dynamic image and entered the 2DQ plug-in TMAD mode. Then, we placed the fixed points on the TV sidewall, MV sidewall and the left ventricular apex respectively. The software would automatically generate two simultaneous displacement curves of sampling points. We measured the displacement peak time of the MV and TV, namely PT_{MV} and PT_{TV} (Figure. 2C, D), and recorded deviation of PT_{MV} and PT_{TV} as ΔPT_{TV-MV}.

The evaluation of intraventricular systolic synchronization and systolic function was as follows: Two-dimensional speckle tracking imaging (2D-STI) of the Qlab 13 workstation was used to analyze the left ventricular global longitudinal strain (GLS) and longitudinal strain of right ventricular free wall(LS-RV) (Figure. 3A, D) to reflect the ventricular function. The standard deviation of systolic peak time was calculated to reflect the asynchrony index of the left (SDt-L) and right ventricles(SDt-R) to reflect the intraventricular synchronization.

1.4 Statistical methods

SPSS23.00 software was used for statistical analysis. Continuous variables are presented as the mean ± standard deviation. Categorical variables are expressed as percentages. The differences between two groups were assessed with the chi-square analysis for categorical variables and the t-test or non-parametric tests for continuous data at baseline. $P < 0.05$ was considered statistically significant.

Results

2.1 General situation analysis

A total of 40 patients who successfully underwent left bundle-branch pacing were included in this study, including 22 males and 18 females. The average age of the enrolled patients was (70.88 ± 12.95) years; there were 26 patients with hypertension, 11 patients with diabetes, and 6 with coronary heart disease. Moreover, for the indication of pacemaker implantation, 10 patients are owing to high-grade atrioventricular block, 19 patients owing to third-degree atrioventricular block, 11 patients owing to a second-degree type II atrioventricular block. After LBBAP treatment, the pacing parameters were satisfied. According to the preoperative electrocardiogram, the patients were divided into two groups, including 19 people in the RBBB group and 21 people in the non-RBBB group. There was no statistical difference between the two groups in terms of age, gender, comorbidities, etiology, pacemaker parameters, or preoperative cardiac color Doppler ultrasound parameters (P > 0.05). See Table 1 for details.

Table 1 General condition of the patient

Parameters		total (n=40)	RBBB group (n=19)	Non-RBBB group (n=21)	P
Age/y		70.88 ± 12.95	74.71 ± 9.68	69.39 ± 14.00	0.37
Male/n (%)		22 (55%)	8 (42.1%)	14 (66.7%)	0.08
Complication/n (%)	Hypertension	26 (65%)	12 (63.2%)	14 (67.7%)	0.17
	Diabetes	11 (28%)	5 (26.3%)	6 (28.6%)	0.28
	Coronary heart disease	6 (15%)	2(10.5%)	4 (19.0%)	0.69
pathogen /n (%)	High-grade atrioventricular block	10 (25%)	6 (28.6%)	4(19.0%)	0.71
	Third degree atrioventricular block	19 (48%)	8 (42.0%)	11 (52.3%)	
	Second degree type II atrioventricular block	11 (28%)	6 (31.6%)	5 (23.8%)	
Ventricular perception /mV		10.95 ± 5.43	9.53 ± 3.25	11.58 ± 6.13	0.42
Ventricular capture /V		0.73 ± 0.40	0.67 ± 0.35	0.76 ± 0.42	0.62
Impedance /Ω		752.96 ± 214.89	818.14 ± 234.76	724.44 ± 206.96	0.35
LAVI /ml/m2		22.74±9.26	21.86±9.23	23.13±9.55	0.77
Transverse diameter of right atrium /mm		38.4 ± 4.00	38.71 ± 4.19	38.27 ± 4.04	0.81
Right Atrium Vertical Diameter /mm		48.08 ± 4.7	49.00 ± 4.93	47.72 ± 4.70	0.55
LVEDV /ml		68.49±20.77	72.80±30.80	66.61±15.52	0.52
LVESV/ml		29.16±10.32	32.10±12.29	27.88±9.48	0.38
LVEF/%		58.84 ± 5.07	60.00 ± 3.74	58.39 ± 5.53	0.49

2.2 TMAD, IVMD, and TDI assess left and right ventricular synchrony.

There was no significant difference in IVMD between the two groups ($P > 0.05$). $\Delta Ts_{TV\text{-}MV}$ between two groups has statistical difference between the two groups ($P < 0.05$). The $\Delta Ts_{TV\text{-}MV}$ of RBBB group and non-RBBB group were (47.29 ± 58.45) ms,(−12.00 ± 49.91) ms respectively (Figure2A and2 B).$\Delta PT_{TV\text{-}MV}$ measured was statistically different between two groups ($P < 0.05$). Moreover, the RBBB group was (28.14 ± 39.04) ms, and the non-RBBB Group was (−28 ± 48.26) ms (Figure. 2C, D). See Table 2 for details.

Table 2 TMAD, IVMD and TDI to assess the synchrony of the left and right ventricles

Parameters	RBBB group	Non-RBBB group	t	P
APEI/ms	185.2 ± 80.63	117.70 ± 11.88	2.7	0.02*
PPEI/ms	177.60 ± 81.52	117.40 ± 20.09	2.28	0.04*
IVMD/ms	7.60 ± 6.77	0.20 ± 20.44	0.78	0.45
PT_{TV}/ms	355.29 ± 71.12	385.25 ± 78.22	−0.87	0.40
PT_{MV}/ms	327.14 ± 77.15	413.25 ± 73.78	−2.54	0.02*
$\Delta PT_{TV\text{-}MV}$/ms	28.14 ± 39.04	−28.00 ± 48.26	2.70	0.01*
$\Delta Ts_{TV\text{-}MV}$/ms	47.29 ± 58.45	−12.00 ± 49.91	2.49	0.02*

2.3 Ventricular systolic synchronization and systolic function

Compared with the non-RBBB group, the LVEF, GLS, RVFAC, LS-R, TAPSE, TV-s’, SDt-L, SDt-R in the RBBB group were not statistically different ($P > 0.05$) (Figure. 3). See Table 3 for details.

Table 3 Assessment of ventricular synchronization and ventricular function

	parameter	RBBB group	non-RBBB group	t	P
LV	LVEF/%	60.00 ± 3.74	58.39 ± 5.53	0.71	0.49
	GLS/%	−19.43 ± 2.63	−17.75 ± 3.27	−0.48	0.64
	SDt-L/ms	47.57 ± 17.28	32.19 ± 22.74	1.59	0.13
RV	TAPSE/mm	16.33±1.15	19.27±2.24	-2.15	0.06
	TV-s'/cm/s	13.86±3.39	13.19±2.86	0.49	0.63
	RVFAC/%	49.86±7.37	52.37±8.05	-0.71	0.49
	LS-RV/%	−20.57 ± 10.21	−19.65 ± 12.50	0.72	0.87
	SDt-R/ms	65.43 ± 40.34	66.56 ± 37.22	−0.07	0.95

Discussion

The right bundle branch originates from the His bundle and forms three branches at the base of the tricuspid anterior papillary muscle. It runs on the low position of the ventricular septum and the anterior wall of the right ventricle, the free wall of the right ventricle and the posterior papillary muscle, and the lower right posterior part of the ventricular septum. The electrical excitement is quickly transmitted to each segment of the right ventricular wall through the three branches, ensuring the interventricular and intraventricular synchronous contraction. However, because the right bundle branch is slender, superficial, mostly supplied by a single branch of the left anterior descending branch, the right bundle-branch conduction system is prone to conduction disorders. Therefore, RBBB is common in clinical practice, with an incidence of 8%, which increases with age[6, 7]. Herein, the incidence of RBBB in patients undergoing pacemaker implantation is not supposed to be low. The optimal pacing method for bradyarrhythmia with RBBB remains to be explored. His-Bundle pacing, cardiac resynchronization therapy, and right bundle-branch pacing can correct RBBB morphology, but it has the disadvantages of a complicated operation, an unstable pacing threshold, and a low success rate[8-10]. At present, LBBAP is a pacing method with a high success rate, a stable pacing threshold, and physiological pacing for bradyarrhythmia. A case report showed that LBBAP could eliminate the RBBB morphology in patient with RBBB[11]. However, there is currently a lack of echocardiographic techniques to study the ventricular function and synchronization of RBBB patients after LBBAP.

In this study, we performed LBBAP on patients with and without RBBB who had no statistical difference in general conditions. After optimization of the atrioventricular interval, we used the IVMD, TMAD, and TDI to evaluate the synchronization of left and right ventricular myocardial movements. Through these three methods, we found the following: 1) The movement of the right ventricular myocardium in the RBBB group after LBBAP treatment was slightly later than that of the left ventricular myocardium; 2) TMAD and TDI techniques are easier to find a nuance of biventricular desynchrony than IVMD. In this study, we used unipolar LBBAP pacing. There are two possibilities for pacing signals to be transmitted to the right ventricle: 1) The right ventricular myocardium in the region of the left bundle branch is stimulated, and the right ventricle is stimulated through intercellular conduction. This conduction method may cause asynchrony between the right and left chambers (Figure. 4A); 2) In previous studies, the existence of interconnection fibers (TFs) between the left and right bundle branches was also proposed. The pacing signal of the left ventricle may be transmitted to the right bundle branch through TFs, which in turn stimulates the right ventricle physiologically (Figure 4B)[11]. However, in the presence of RBBB, the pacing signal of the left ventricle may not be able to transmit to the right ventricle through TFs to achieve physiological pacing of the right ventricle (Figure. 4C), so the synchronization of the two ventricles will be inconsistent. This argument was verified by our study. By the application of TMAD and TDI, we detected a slight difference between RBBB group and non-RBBB group. The maximum systolic displacement time and peak time of systolic velocity of TV side wall is slow than that of MV in RBBB group in the same cardiac cycle. The reasons why IVMD did not find the discrepancy are probably as follows: 1) PPEI and APEI come from different cardiac cycles, which is an important cause of error. 2) IVMD evaluates biventricular synchronization by hemodynamic method. While TMAD and TDI directly evaluate the mechanical myocardial synchronization of the ventricles. We supposed that the desynchrony of biventricular myocardial movement happen before the biventricular hemodynamics. Through this study, we found that patients with RBBB still had asynchrony of left and right ventricular contractions after LBBAP.

According to the study by Mou Junyu et al, SDt-R of complete RBBB is different from that of the control group, with 49.89±4.79ms VS 8.90±1.67 respectively[12].Compared with this study, our data did not find a distinct difference in right ventricular asynchrony in two groups. Nor did we find difference in two groups in the aspect of right ventricular function, namely TAPSE, TV-s’, RVFAC and LS-RV, as well as in the aspect of left ventricular function and intraventricular asynchrony, namely LVEF, GLS and SDt-L. It suggests that at least RBBB did not exacerbate the asynchrony and dysfunction of right ventricle in LBBAP patients. This may be because of the activation of right ventricular myocardial cells in the adjacent area during LBBAP pacing, which accelerates the depolarization process of the right ventricle and thereby may help to ameliorate right ventricle desynchrony in RBBB patients. A lot of researches have testified that LBBAP could ensure the physiological pacing of the left ventricle. The morphology and function of the left and right ventricles affect each other. Insufficiency or asynchronization of the left heart can cause changes in the pulmonary artery pressure due to the increase in left atrial pressure, leading to an increase in the afterload of the right heart; Insufficiency or asynchrony of the right heart can cause the right heart to enlarge. In the limited volume of the pericardium, the enlarged right heart causes the diastolic restriction of the two ventricles. Studies have shown that right ventricular dysfunction or asynchrony of exercise is an early warning indicator of poor prognosis for heart failure and non-response of CRT[13, 14].Herein, in the selection of pacing strategy, the function and synchronization of the two ventricular should all be taken into account. In the context of that RBBB do not bring more damage to right ventricular synchronization and function to RBBB patient receiving LBBAP than those without RBBB, LBBAP could realize the left ventricular physiological pacing of RBBB patients. From this early assessment, we deduce that LBBAP could be safely applied in the patients with RBBB.

This study also had certain limitations. First, the small sample size may have caused some errors in statistics. Second, because the right ventricle has an irregular crescent shape, we only studied the strain of the right ventricle in the apical four chambers; Finally, the follow-up time was short, so this study could only reflect the short-term impact of LBBAP on right ventricular function and synchronization. With a prolonged implantation time, whether the mechanical and electrical remodeling of the heart will have a long-term improvement effect on RBBB remains unknown. Whether it can reduce atrial fibrillation and cardiovascular adverse events caused by RBBB [7, 15] also remains to be further studied.

Conclusion

In summary, after LBBAP, RBBB patients had a certain degree of asynchrony of left and right ventricular movements, but postoperative RBBB patients' right ventricular synchronization and right ventricular longitudinal strain were not statistically significant compared with the non-RBBB group. It indicates that LBBAP is an optional pacing strategy for RBBB patients with pacing indications.

Abbreviations

left bundle-branch-area pacing (LBBAP)

right bundle-branch block (RBBB)

tissue Doppler (TDI)

tissue mitral annular displacement (TMAD)

interventricular mechanical delay (IVMD)

tricuspid annular plane systolic excursion (TAPSE)

right ventricular fractional area change (RVFAC)

tricuspid annulus sidewall systolic velocity (TV-s')

global ventricular longitudinal strain (GLS)

right ventricular free wall longitudinal strain (LS-RV)

standard deviation of left ventricular 18 segments peak time difference (SDt-L)

standard deviation of right ventricular free wall 3 segments peak time difference (SDt-R)

left atrial volume index(LAVI)

right atrial diameter (RAD)

left ventricular end-systolic Volume (LVESV)

left ventricular end-diastolic Volume (LVEDV)

left ventricular ejection fraction (LVEF)

pulmonary pre-ejection interval (PPEI)

(artery pre-ejection interval (APEI）

tricuspid valve (TV)

mitral valve (MV)

Two-dimensional speckle tracking imaging (2D-STI)

left ventricular global longitudinal strain (GLS)

interconnection fibers (TFs)

His bundle (HB)

right bundle branch (RBB)

left anterior branch (LAF)

left posterior branch (LPF)

right ventricle (RV)

interventricular septum (IVS)

left ventricle (LV)

Declarations

- Ethics approval and consent to participate：The ethics committee of The Third People's Hospital of Chengdu approved to carry out the study within its facilities. Informed consent was obtained from all subjects.
- Availability of data and materials: The datasets generated and/or analyzed during the current study are not publicly available due to the ongoing project but are available from the corresponding author on reasonable request.
- Competing interests: none.
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- Authors' contributions: Ruohan Zhao made contributions to the conception and design of the work, analysis and interpretation of data, writing the manuscript.

Feng Xiong provided the fund supports and conception of the work.

Xiaoqi Deng was in charge of the LBBAP operation.

MinXu and Kunyue Tan made contributions to the conception and design of the work.

Shuzhen Wang and Xiuxiu Wang made contributions to the image acquisition.

All of the authors have approved the submitted version and have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work.

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Figures

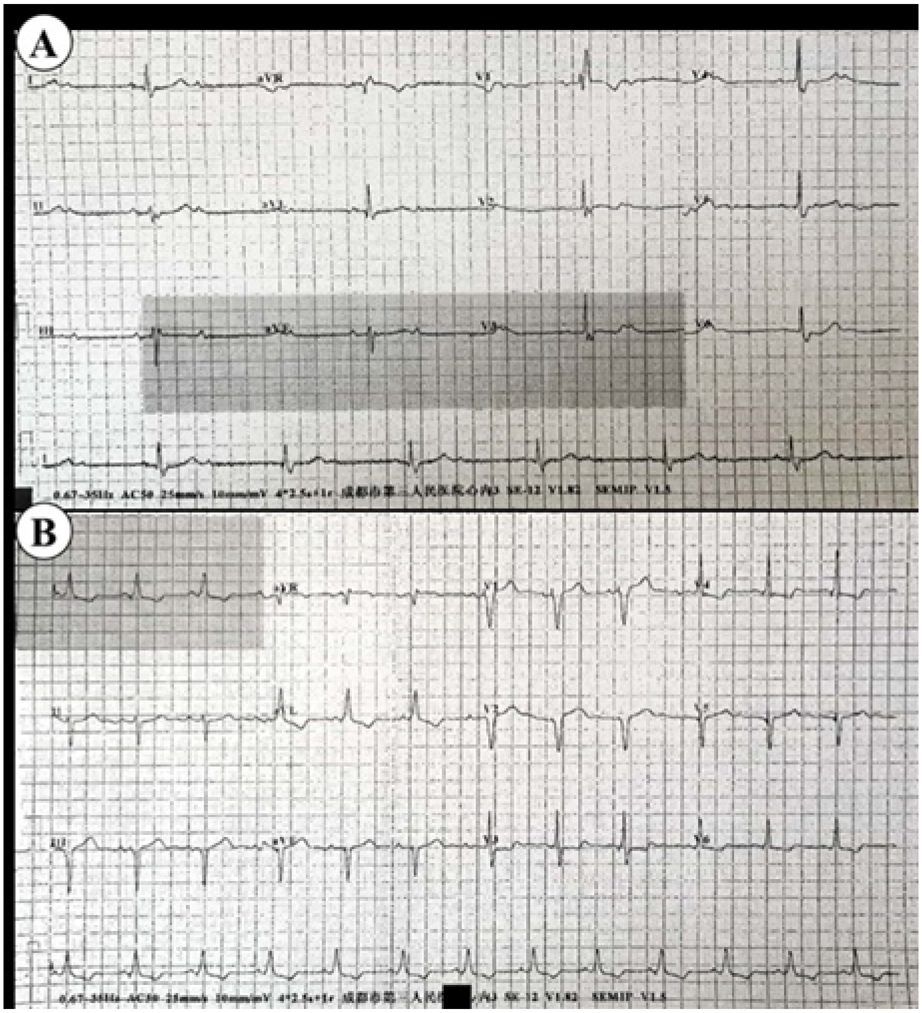

Figure 1

ECG of patients with right bundle-branch block before LBBP (Figure. A) and after (Figure. B)

Figure 2

A, B: TDI measurement of left and right ventricular lateral wall basal segment myocardial contraction velocity peak time, where A is non-RBBB, and B is RBBB. The difference in the contraction velocity peak time of RBBB group’s left and right ventricular lateral wall basal segment is greater than that of the non-RBBB group (arrows indicate the peak position); C, D: TMAD measures the average displacement peak time of the mitral and tricuspid annulus sidewalls. Figure C shows the non-RBBB group, and Figure. D shows RBBB. For the RBBB group, the peak time of the maximum displacement of the mitral and tricuspid valve annulus is quite different.

Figure 3

A, D: 2D-STI measures the peak time of LS and LS of each wall of the right ventricle, A is non-RBBB, D is RBBB; B, E: the peak time of LS of each wall of the left ventricle, B is non-RBBB, E is RBBB; C, F: LS of each wall of the left ventricle, B is non-RBBB, E is RBBB. There is no difference between the two groups.

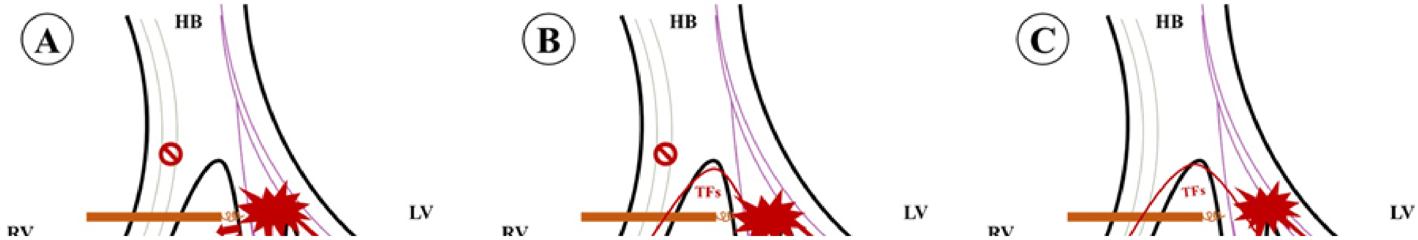

Figure 4

A. When accompanied by RBBB, LBBAP stimulates the right ventricular myocardial cells in the left bundle-branch area, and the right ventricle is activated through intercellular conduction; B. When RBBB is located in front of TFs, the left ventricular pacing signal is transmitted to the right bundle through TFs C. When the RBBB is located at the distal end of the TFs, the pacing signal of the left ventricle is not always transmitted to the right ventricle through the TFs to achieve physiological pacing of the right ventricle. (HB: His bundle; RBB: right bundle branch; LAF: left anterior branch; LPF: left posterior branch; RV: right ventricle; IVS: interventricular septum; LV: left ventricle)