Left Ventricular Systolic Motion Pattern Differs Among Patients With Left Bundle Branch Block Patterns

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Research Article

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Abstract

Purpose: The study aimed to investigate left ventricular (LV) motion pattern in patients with LBBB patterns including patients with pacemaker rhythm (PM), type B Wolff-Parkinson-White syndrome (B-WPW), premature ventricular complexes originating from the right ventricular outflow tract (RVOT-PVC), and complete left bundle branch block (CLBBB).

Methods: Two-dimensional speckle tracking was used to evaluate peak value and time to peak value of the LV twist, LV apex rotation, and LV base rotation in patients with PM, B-WPW, RVOT-PVC, and CLBBB with normal LV ejection fraction, and in age-matched control subjects.

Results: The LV motion patterns were altered in all patients compared to the control groups. Patients with PM and CLBBB had a similar LV motion pattern with a reduced peak value of LV apex rotation and LV twist. Patients with B-WPW demonstrated the opposite trend in the reduction of LV rotation peak value, which was more dominant in the basal layer. The most impairment in the LV twist/rotation peak value was identified in patients with RVOT-PVC. Compared to the control group, the apical-basal rotation delay was prolonged in patients with CLBBB, followed by those with B-WPW, RVAP, and RVOT-PVC.

Conclusion: The LV motion patterns were different among patients with different patterns of LBBB. CLBBB and PM demonstrated a reduction in LV twist/rotation that was pronounced in the apical layer, B-WPW showed a reduction in the basal layer, and RVOT-PVC in both layers. CLBBB had the most pronounced LV apical-basal rotation dyssynchrony.

1. Introduction

Left bundle branch block (LBBB) is a common cardiac arrhythmia. The incidence of idiopathic LBBB in a general population is about 0.1%. It has been reported that approximately 90% of LBBB cases are associated with cardiovascular disease\cite{1}, and about 25% of heart failure patients have a history of LBBB\cite{2}. Wide QRS complex duration and deterioration of left ventricular (LV) systolic and diastolic functions occurring due to LBBB are risk factors for the development and progression of heart failure. Ventricular dysfunction caused by LBBB results in paradoxical motion of the septum, intra- and inter-ventricular mechanical dyssynchrony, and ultimately myocardial remodeling\cite{3}. The alterations in LV mechanical activation sequences in LBBB patients are attributed to abnormal electrical activation. Due to the blockage of the left bundle branch, electricity is conducted through normal cardiac myocytes in the LV free wall instead of Purkinje fibers. There are three other types of conduction disorders with a similar electricity conduction pattern—pacemaker rhythm (PM), type B Wolff-Parkinson-White syndrome (B-WPW), and premature ventricular complexes originating from the right ventricle (RVOT-PVC). Therefore, all four abnormal conditions were defined as LBBB pattern conduction disorders in the present study.

Two-dimensional speckle tracking echocardiography (2D-STE) is a noninvasive method used to analyze deformation of the myocardium without angle dependence. Good correlation between 2D-STE and cardiac magnetic resonance in the measurement of LV twist has been confirmed\cite{4,5}. A number of studies have assessed twist mechanisms of LV in patients with LBBB\cite{6-8}. However, none of the studies have evaluated and compared the torsion pattern in patients with LBBB pattern conduction disorders, including CLBBB, pacemaker rhythm, B-WPW, and RV-PVC. Therefore, the present study was designed to elucidate the varieties of twist patterns in the above four LBBB types.

2. Methods

2.1 Patient selection and data collection
The present study included 141 patients who underwent echocardiography in the First Affiliated Hospital of Nanjing Medical University between December 2010 and February 2018. A total of 28 patients with complete LBBB (CLBBB) and preserved LV ejection fraction (EF) were included using a conventional characteristic electrocardiogram (ECG) definition as follows: QRS duration ≥120 ms; absent Q waves in leads I, V5, and V6; presence of QS or rS in leads V1 and V2; and broad and notched R-waves in leads I, aVL, V5, and V6 (group CLBBB). There were 45 patients who underwent DDD pacemaker implantation due to a 3rd degree AV block (group PM). All patients in the PM group were pacemaker-dependent and the right ventricle apex served as the ventricle lead implantation location. A total of 38 patients with B-WPW, who underwent radiofrequency ablation with preoperative ECG characteristics including PR interval of <120 ms, QRS duration of >120 ms, and the presence of delta waves in QRS complexes, participated in the study. An electrophysiological examination demonstrated the existence of right accessory pathways (group B-WPW). Thirty patients had premature ventricular complexes originating from the right ventricular outflow tract (group RVOT-PVC). RVOT-PVC was defined as an ECG parameter of the LBBB contour in V1 and an inferior axis in the frontal plane with a frequency of >5 bpm (group RVOT-PVC)[9].

Exclusion criteria included congenital heart disease, valvular heart disease, and coronary heart disease. No antiarrhythmic drugs were taken before examination in all selected patients. During patient screening, it was discovered that demographic characteristic of the LBBB group were comparable to those of the PM group. Patients in the PM and LBBB groups were older than those in the RVOT-PVC group, and the average age in the B-WPW group was lowest among all groups. To reduce the influence of age, control subjects matched by age and gender in each group were selected. The characteristics of the Control Group 1 were compared to those of the CLBBB and PM groups. The characteristics of the Control Groups 2 and 3 were compared to those of the B-WPW and RVOT-PVC groups, respectively. Informed consent was obtained from all of the subjects. This study was approved by the institutional review board. All control subjects underwent ECG, echocardiography, and laboratory examinations. The gender, age, height (cm), weight (kg), heart rate (bpm), and QRS duration were recorded.

2.2 Image acquisition and standard echocardiography studies

Transthoracic echocardiograms were performed using Vivid E9 (GE Medical Systems, Milwaukee, WI, USA) with M5S probe. The frame rate (≥60 frames/s), probe frequency (range: 1.5–4.0 MHz), and depth (range: 15–17 cm) were adjusted at end-expiratory for better image quality. All subjects were examined in the left lateral decubitus position. The routine standard echocardiographic measurements included LV end-diastolic dimension (LVEDD) and end-systolic dimension (LVESD) from the M-mode or 2D imaging. LVEF was calculated using a biplane Simpson's method from images acquired in apical four- and two-chamber views. The 2D grayscale dynamic images were acquired in the parasternal short-axis view at the mitral valve and apex level for three consecutive cardiac cycles.

2.3 2D speckle tracking imaging analysis

All images were stored digitally on disks and then analyzed offline using dedicated software (EchoPac platform, Version 11.0.0, GE Vingmed). Endocardial borders were traced manually in both basal and apical levels of the parasternal short-axis view. LV torsion-time, apical rotation-time, and basal rotation-time curves were generated automatically. The following parameters were measured on the curves: peak basal rotation (Rot-B), time to peak basal rotation (T-RotB) (time from the onset of QRS complex to peak basal rotation), peak apical rotation (Rot-A), time to peak apical rotation (T-RotA) (time from the onset of QRS complex to peak apical rotation), peak LV twist (LVtwist), and time to peak LV twist (T-LVtwist) (time from the onset of QRS complex to peak LV twist). In order to reduce the influence of the heart rate, the above time interval parameters were expressed as percentages relative to the R-R interval (Figures 1 and 2). Time intervals between the peak apical and basal rotations were calculated.

2.4 Statistical analysis
Continuous variables were expressed as mean±standard deviation (SD), while categorical data were expressed as frequencies and percentages. Comparison of twist parameters between patients in each group and corresponding control groups was performed using an unpaired t-test. Comparison of categorical variables was performed using Pearson's chi-square test. All statistical tests were two-sided and performed using the SPSS software (SPSS version 22.0 for Windows), where p<0.05 was considered statistically significant.

Offline analysis of all subjects was performed by a single observer. LV twist parameters for 20 subjects selected randomly were reanalyzed by the same observer one week later. The 2D-STE analysis was repeated by another observer in these selected subjects at the same time. The intra- and inter-observer variability analysis was performed using Bland-Altman analysis. Peak LV twist showed a high inter- and intra-observer agreement on the Bland-Altman chart. The Bland-Altman drawing analysis method showed that the mean intra- and inter-observer differences in peak LV twist were -0.07° and 0.07°, respectively. The 95% confidence intervals (CIs) were in the range of -1.33° to 1.20° and -1.01° to 1.16°, respectively. It was demonstrated that the LV twist/rotation parameters had good intra- and inter-observer consistency (Figure 3).

3. Results

3.1. Baseline characteristics

The study comprised 141 patients with LBBB pattern (28 with CLBBB, 45 with pacemaker rhythm, 38 with B-WPW, and 30 with RVOT-PVCs), as well as 120 control subjects (49 in CON1 (control group 1), 31 in CON2 (control group 2), and 40 in CON3 (control group 3)). Compared to the corresponding control group, there was no significant difference in age, gender, height, and body weight in the arrhythmia group. Patients with pacemaker rhythm had a lower heart rate compared to the subjects in the CON1 group (64.4±8.0 bpm vs. 71.8±10.5 bpm, P<0.001; Table 1).
Table 1
Baseline characteristics in patients with LBBB patterns and controls.

| Groups          | CON1 (n=49) | CON2 (n=40) | CON3 (n=31) | CLBBB (n=28) | PM (n=45) | B-WPW (n=38) | RVOT-PVC (n=30) |
|-----------------|-------------|-------------|-------------|--------------|-----------|--------------|----------------|
| Male (%)        | 51          | 65          | 48          | 50           | 47        | 55           | 50             |
| Age (yrs)       | 70.6±10.0   | 36.7±12.6   | 47.5±18.7   | 69.6±9.6     | 69.3±10.5 | 34.0±14.5    | 51.2±18.9      |
| Height (cm)     | 163.0±7.3   | 167.3±8.9   | 163.1±5.4   | 165.7±7.6    | 162.2±7.2 | 166.7±5.8   | 164.5±7.2     |
| Weight (kg)     | 65.8±9.9    | 61.5±11.7   | 66.8±8.6    | 62.9±12.8    | 62.7±9.9  | 64.0±8.2     | 62.4±9.1      |
| HR (bpm)        | 71.8±10.5   | 71.9±11.2   | 70.8±10.6   | 70.8±9.4     | 64.4±8.0* | 73.0±10.3    | 73.0±12.2     |
| QRS (ms)        | 97.980±12.091 | 102.175±19.837 | 100.312±10.531 | 155.214*±13.543 | 176.978*±36.393 | 172.184*±37.971 | 169.358*±14.780 |

Note: Data in CON1 group were used to compare to patients with CLBBB and DDD PM implantation. Data in CON2 group were used to compare to patients with B-WPW. Data in CON3 group were used to compare to patients with RVOT-PVC. All data were compared to the corresponding control group. *represents P<0.05.

3.2. Standard echocardiographic parameters

Echocardiographic variables are summarized in Table 2. Patients in the CLBBB, PM, B-WPW, and RVOT-PVC groups showed enlarged LVEDD and LVESD compared to their corresponding control groups (all P<0.05). There were no differences in LVEF between the CLBBB, PM (65.2±3.9% and 63.9±4.8%), and CON1 (65.3±3.4%) groups. Patients with B-WPW had a significantly lower LVEF compared to those in the CON2 group (55.6±7.8% vs. 64.8±4.7%, P<0.001). Compared to the CON3 group, LVEF in the RVOT-PVC group was significantly lower (49.5±14.9% vs. 66.0±4.0%, P<0.001; Figure 4).
Table 2  
Standard echocardiographic parameters in patients with LBBB patterns and controls.

| Groups       | CON1   | CON2   | CON3   | CLBBB  | PM    | B-WPW  | RVOT-PVC | CLBBB vs. CON1 | PM vs. CON1 | B-WPW vs. CON2 | RVOT-PVC vs. CON3 |
|--------------|--------|--------|--------|--------|-------|--------|----------|---------------|--------------|----------------|------------------|
| LVEF (%)     | 65.3   | 64.8   | 66.0   | 65.2   | 63.9  | 55.6   | 49.5     | 0.587         | 0.923        | <0.001         | <0.001           |
| ±3.4         | ±4.7   | ±4.0   | ±3.9   | ±4.8   | ±7.8  | ±14.9  |          |               |              |                |                  |
| LVEDD(mm)    | 45.8   | 45.4   | 46.0   | 49.4   | 47.8  | 48.0   | 51.5     | 0.001         | 0.009        | 0.013          | <0.001           |
| ±3.4         | ±3.6   | ±2.9   | ±6.1   | ±3.4   | ±5.3  | ±4.3   |          |               |              |                |                  |
| LVESD(mm)    | 29.2   | 29.4   | 28.5   | 31.8   | 30.6  | 32.5   | 32.6     | 0.002         | 0.003        | 0.005          | <0.001           |
| ±2.1         | ±2.2   | ±2.1   | ±5.0   | ±2.4   | ±6.5  | ±3.2   |          |               |              |                |                  |

Note: Data in CON1 group were used to compare to patients with CLBBB and DDD PM implantation. Data in CON2 group were used to compare to patients with B-WPW. Data in CON3 group were used to compare to patients with RVOT-PVC. All data were compared to the corresponding control group.

3.3. LV twist parameters

3.3.1 LV twist/rotation parameters in patients with LBBB
Compared to the CON1 group, a significant reduction was found in peak apical rotation (6.0±4.5° vs. 9.6±4.2°, P=0.001) and LV twist (10.4±5.9° vs. 16.1±5.6°, P<0.001) in the CLBBB group. Peak basal rotation remained unaltered. T-RotA and T-LVtwist were longer than those in the CON1 group. The time interval between peak apical and basal rotation was significantly longer in the CLBBB group compared to the control group (17.2±13.3% vs. 6.6±6.3%, P<0.001; Table 3).
Table 3
LV twist parameters in patients with LBBB patterns and control subjects.

| Groups               | CON1  | CON2  | CON3  | CLBBB | PM    | B-WPW | RVOT-PVC | CLBBB vs. CON1 | PM vs. CON1 | B-WPW vs. CON2 | RVOT-PVC vs. CON3 |
|----------------------|-------|-------|-------|-------|-------|-------|----------|-----------------|-------------|----------------|-----------------|
| Rot-B(°)             | -7.1  | -7.0  | -5.3  | -7.2  | -6.0  | -3.0  | -0.6     | 0.921           | 0.127       | <0.001          | <0.001          |
|                      | ±3.4  | ±3.3  | ±3.8  | ±3.1  | ±3.6  | ±3.6  | ±4.4     |                 |             |                 |                 |
| TTP-B(%)             | 48.6  | 48.9  | 48.0  | 59.9  | 53.1  | 41.8  | 40.5     | 0.057           | 0.950       | 0.004           | 0.050           |
|                      | ±11.2 | ±9.2  | ±8.9  | ±12.6 | ±11.9 | ±11.7 | ±18.6    |                 |             |                 |                 |
| Rot-A(°)             | 9.6   | 10.3  | 9.5   | 6.0   | 6.2   | 7.2   | 3.9      | 0.001           | 0.001       | 0.011           | <0.001          |
|                      | ±4.2  | ±4.2  | ±3.2  | ±4.5  | ±5.2  | ±6.2  | ±7.2     |                 |             |                 |                 |
| TTP-A(%)             | 47.8  | 46.2  | 46.3  | 62.0  | 53.5  | 46.7  | 38.6     | 0.016           | 0.698       | 0.878           | 0.015           |
|                      | ±10.1 | ±8.6  | ±8.6  | ±17.7 | ±11.9 | ±16.6 | ±16.0    |                 |             |                 |                 |
| Twist(°)             | 16.1  | 16.9  | 14.0  | 10.4  | 11.2  | 8.5   | 4.4      | <0.001          | <0.001      | <0.001          | <0.001          |
|                      | ±5.6  | ±4.3  | ±4.1  | ±5.9  | ±5.1  | ±9.0  | ±9.6     |                 |             |                 |                 |
| TTP-LV(%)            | 46.3  | 46.2  | 45.2  | 63.2  | 54.3  | 48.0  | 39.3     | <0.001          | <0.001      | 0.478           | 0.058           |
|                      | ±7.9  | ±7.5  | ±6.3  | ±12.2 | ±9.3  | ±13.6 | ±15.4    |                 |             |                 |                 |
| TD_A-B(%)            | 6.6   | 7.1   | 7.9   | 17.2  | 10.4  | 14.0  | 9.3      | <0.001          | 0.042       | 0.008           | 0.599           |
|                      | ±6.3  | ±8.0  | ±8.1  | ±13.3 | ±8.2  | ±13.4 | ±11.9    |                 |             |                 |                 |

Note: Data in CON1 group were used to compare to patients with CLBBB and DDD PM implantation. Data in CON2 group were used to compare to patients with B-WPW. Data in CON3 group were used to compare to patients with RVOT-PVC. All data were compared to the corresponding control group.

3.3.2 LV twist/rotation parameters in patients with pacemaker rhythm

In patients with pacemaker rhythm, peak apical rotation (6.2±5.2° vs. 9.6±4.2°, P=0.001) and peak LV twist (11.2±5.1° vs. 16.1±5.6°, P<0.001) were reduced, accompanied by a longer T-TLVTWIST (54.3±9.3° vs. 46.3±7.9°, P<0.001) compared to the control subjects. In addition, the time interval between peak apical and basal rotations was significantly longer (10.4±8.2° vs. 6.6±6.3°, P=0.042; Table 3).

3.3.3 LV twist/rotation parameters in patients with B-WPW

Compared to the CON2 group, a significant reduction was observed in peak apical rotation (7.2±6.2° vs. 10.3±4.2°, P=0.011), basal rotation (-3.0±3.6° vs. -7.0±3.3°, P<0.001), and twist (8.5±9.0° vs. 16.9±4.3°, P<0.001) in the B-WPW group. The TTP-B was shorter (41.8±11.7% vs. 48.9±9.2%, P=0.004) than that in the CON2 group subjects. The time interval between peak apical and basal rotations was prolonged significantly (14.0±13.4% vs. 7.1±8.0%, P=0.008; Table 3).

3.3.4 LV twist/rotation parameters in patients with RVOT-PVCs
Compared to the control subjects, RVOT-PVC patients showed a significantly lower peak basal rotation (-0.6±4.4° vs. -5.3±3.8°, *P*<0.001), apical rotation (3.9±7.2° vs. 9.5±3.2°, *P*<0.001), and LV twist (4.4±9.6° vs. 14.0±4.1°, *P*<0.001). However, the time interval between peak apical and basal rotations showed no significant difference (Table 3).

### 3.5 Comprehensive analysis of LV twist parameters

#### 3.5.1 Twist/rotation changes in different LV layers

The LV twist/rotation curves of the control group were characterized. The global LV and LV apex twists/rotates counterclockwise (black and blue positive curves in Figure 5), while the LV base rotates clockwise (red negative curves in Figure 5) during systole. The twist/rotation reaches peak value at the end of the contraction and then gradually untwist back to the baseline during diastole. Compared to the control groups, LV motion pattern was altered in all patients, including the reduction in peak LV twist, peak apical/basal rotation, and dyssynchrony of LV apical-basal rotation (Figure 5). Patients with LBBB or pacemaker rhythm presented with a similar LV motion pattern, where reduced rotation was more dominant in the apical layer. In contrast, patients with B-WPW demonstrated the opposite trend with a reduction in LV rotation peak value, which is more dominant in the basal layer. The most predominant impairment in the peak value of the LV twist/rotation was found in patients with RVOT-PVC, which was prominent in both apical and basal layers (Figure 6).

#### 3.5.2 Synchrony of LV rotation in different layers

In the control groups, the rotation of LV base and apex reached the peak value synchronously (Figure 4). In patients with CLBBB, time to peak LV twist was prolonged (63.2±12.2% vs. 46.3±7.9%, *P*<0.001), which manifested as the prolonged time to peak apical rotation (62.0±17.7% vs. 47.8±10.1%, *P*=0.016). The apical and basal rotation movements were out of sync, which manifested as a prolonged TDA-B (17.2±13.3% vs. 6.6±6.3%, *P*<0.001). In patients with pacemaker rhythm, the rotation of the apex and base was not synchronized, presenting with a prolonged TDA-B (10.4±8.2% vs. 6.6±6.3%, *P*=0.042). Time to peak basal rotation in patients with B-WPW was shortened (41.8±11.7% vs. 48.9±9.2%, *P*=0.004) and had a prolonged TDA-B, which represented the dyssynchrony of the apical and basal rotations (14.0±13.4% vs. 7.1±8.0%, *P*=0.008). Patients with RVOT-PVC showed a synchronous rotation of the apex and base accompanied by a change in TDA-B (9.3±11.9% vs. 7.9±8.1%, *P*=0.599). This association was not significant (Figure 7).

### 3.4 QRS complex duration

Patients in the CLBBB, PM, B-WPW, and RVOT-PVC groups had a prolonged QRS complex duration compared to their corresponding control groups (all *P*<0.001; Figure 8).

### 4. Discussion

Coordinated contraction of myocardial fibers in different directions leads to normal ventricular contraction. Contractions of oblique myocardial fibers constitute the main mechanism of LV twist, which is characterized by the opposite rotation of the apex and base. As observed from the apex, the LV base rotates clockwise during systole, while the LV apex rotates counterclockwise. LV twist was calculated as the instantaneous net difference between basal and apical rotations. In addition to the shortening and thickening of the myocardial fibers, the LV twist plays an important role in cardiac systolic function.

LVEF is the most commonly used parameter for LV systolic function and is identified as a cornerstone of clinical therapeutic strategies. It is load-dependent and prone to inaccuracies, especially in patients with LBBB. Asynchronous activation of LV among these patients can lead to subtle abnormalities in LV systolic function, which has a low sensitivity when using LVEF as the assessment indicator. LVEF relies on geometric assumptions and alterations in LV
volumes and dimensions. Therefore, it indirectly reflects LV systolic function rather than the intrinsic myocardial contractility[^10].

The LV twist is a sensitive indicator of LV systolic function, which has been established in various populations with multifarious diseases[^11–14]. Heart failure patients scheduled for cardiac resynchronization therapy (CRT) were prospectively studied by Chiara et al.[^15]. They found that alterations in LV twist take place earlier than variations in LV volumes and LVEF. Patients who experience a greater acute modification of twist when switching from CRT-off to CRT-on will benefit more from LV reverse remodeling. This indicates that LV twist parameters can help in prognosis during early follow-up in heart failure patients with CRT. Mohamed et al. have investigated LV twist in patients with non-ischemic dilated cardiomyopathy (DCM). They showed that patients with reduced LV twist and apical rotation at baseline were more often hospitalized for worsening cardiac events during the follow-up period than patients with relatively preserved rotational mechanics, suggesting that LV twist has prognostic relevance in non-ischemic DCM patients. The reduced LV twist indicated a more rigid ventricle, which appropriately reflects the greater disease severity[^16]. In addition to cardiac disease, LV twist parameters are also used for early detection of myocardial dysfunction in other diseases. Fu-Wei et al. have investigated LV twist in patients with non-ischemic dilated cardiomyopathy (DCM). They showed that patients with reduced LV twist and apical rotation at baseline were more often hospitalized for worsening cardiac events during the follow-up period than patients with relatively preserved rotational mechanics, suggesting that LV twist has prognostic relevance in non-ischemic DCM patients. The reduced LV twist indicated a more rigid ventricle, which appropriately reflects the greater disease severity[^16]. In addition to cardiac disease, LV twist parameters are also used for early detection of myocardial dysfunction in other diseases. Fu-Wei et al. have investigated LV twist in patients with non-ischemic dilated cardiomyopathy (DCM). They showed that patients with reduced LV twist and apical rotation at baseline were more often hospitalized for worsening cardiac events during the follow-up period than patients with relatively preserved rotational mechanics, suggesting that LV twist has prognostic relevance in non-ischemic DCM patients. The reduced LV twist indicated a more rigid ventricle, which appropriately reflects the greater disease severity[^16]. In addition to cardiac disease, LV twist parameters are also used for early detection of myocardial dysfunction in other diseases. Fu-Wei et al. have investigated LV twist in patients with non-ischemic dilated cardiomyopathy (DCM). They showed that patients with reduced LV twist and apical rotation at baseline were more often hospitalized for worsening cardiac events during the follow-up period than patients with relatively preserved rotational mechanics, suggesting that LV twist has prognostic relevance in non-ischemic DCM patients. The reduced LV twist indicated a more rigid ventricle, which appropriately reflects the greater disease severity[^16].

The components of a normal conducting system include the sinoatrial node, atrioventricular node, bundle of His, right and left branches, and Purkinje fibers. The electrical impulse is first picked up by pacemaker cells in the sinoatrial node due to its rapid inherent rhythm and movement to the atrioventricular node through internodal pathways. Then, it passes the bundle of His and onward to the right and left bundle branches. The impulse eventually quickly and almost uniformly spreads out to the ventricular muscle.

In patients with LBBB, the impulse travels from the atrioventricular node to the right bundle branches, and the septum is activated from right to left. Then, activation of LV free wall occurs slowly via ordinary ventricular muscle instead of Purkinje fibers. Myocardium at the apex layer is activated earlier, and the posterior lateral wall at base layer is the latest excitation location. The rotation at that apex that contracted earlier decreases. At the same time, dyssynchrony of intraventricular excitation results in a decrease in LV twist. LV twist can be used as a potential clinical marker of myocardial dysfunction in isolated LBBB patients with preserved LVEF[^6]. Patients with heart failure accompanied by LBBB who received resynchronization therapy showed a shorter delay time between the septum and left posterior wall, as well as significantly improved LVEF and mitral regurgitation[^18,19]. The other three types of conduction disorders, including pacemaker rhythm, B-WPW, and RVOT-PVC, show an LV electrical activation pattern similar to that of CLBBB demonstrated in clinical work.

4.1. Right ventricular apical pacing

Right ventricular apex has been the most common pacing location due to the abundant trabeculae, which is convenient for electrode fixation. Various clinical and animal studies have shown that long-term right ventricular apical pacing can increase the incidence of atrial fibrillation, lead to LV remodeling, and eventually decrease cardiac function[^20–24]. The present study found that LV twist and apical rotation decreased significantly in patients with pacemaker rhythm. The time interval between apical and basal rotations was prolonged, which may lead to uncoordinated contraction of the LV myocardium. These findings were consistent with the study by Koh et al.[^25]. The abnormal electrical activation sequence is key for the inhibition of LV twist in such patients. The pacemaker lead inserts were first excited in the right ventricular apex. Electrical excitation is transmitted from the apex to the septum contrary to the sinus rhythm pattern and then
propagates through the myocardium to the LV free wall. The abnormal activation process in pacemaker rhythm is similar to that in LBBB. This pacemaker rhythm is known as iatrogenic LBBB. The decreased LV twist in RVAP patients is related to perfusion defects mainly over the inferior and apical segments\[^{26}\]. Long-term regional perfusion defects may lead to decreased contractility of myocardial fibers in the apex, thereby inhibiting rotation in the apex of the heart. Studies on the His bundle pacing revealed that electrical activation expands uniformly along the bundle of His and Purkinje fibers to both right and left ventricles, which can reduce ventricular dyssynchrony and reverse ventricular remodeling in comparison to right ventricular apex pacing\[^{27,28}\].

4.2. B-WPW

The B-WPW is a congenital heart disease with an incidence of 1–3‰\[^{29}\]. The incidence of preexcitation cardiomyopathy is highest in B-WPW patients with right septal accessory pathways\[^{30}\]. The present study found that LV twist, apical rotation, and basal rotation were all reduced in patients with B-WPW. Compared to the reduction at the apex, the rotation decreased more at the base. Time to peak basal rotation was shorter than that at the apex, which suggests dyssynchrony of intraventricular contraction, accompanied by wider QRS duration and reduced LVEF. In patients with B-WPW, right ventricular anterior wall is first activated via the right accessory pathway. Then, electrical activation is transmitted from the right ventricle to the left slowly, similar to the LBBB pattern. Our previous studies\[^{31}\] have revealed that LV diameter and LVEF can be reversed in patients with B-WPW after successful radiofrequency ablation. The LV twist, apical and basal rotation, as well as apical-basal rotation synchrony improved significantly after ablation.

4.3. Premature ventricular complexes from the right ventricular outflow tract (RVOT-PVC)

Frequent PVC is one of the most common arrhythmias. More than 80% of idiopathic ventricular tachycardia or PVC cases originate from the RVOT, and about 16% of them develop into polymorphic ventricular tachycardia and ventricular fibrillation. The present findings revealed that during PVC originating from RVOT, both apical and basal rotations were much more altered and accompanied by a wide QRS duration and significant decrease in LVEF. In RVOT-PVC, the septum is close to the ectopic excitation points and is therefore excited first. Then, the electrical activation transmits from right to left through the ventricular muscle. The electricity conduction pattern during RVOT-PVC was similar to that during LBBB. Frequent PVCs are believed to cause a significant decrease in LVEF, as well as pacing from the right ventricular apex in patients with pacemaker dependency\[^{32}\]. Clinical studies have found that long-term frequent RVOT-PVCs reduce stroke volume, aggravate LV remodeling and mitral regurgitation, and finally lead to the reduction in LVEF. Patients with frequent PVCs were associated with LV dilation and reduced LVEF. After a successful radiofrequency ablation, both LV dimension and LVEF improved significantly\[^{33,34}\].

The characteristics of the above LBBB pattern conduction disorders can be summarized as shown further. First, the electrical activation of LV is not transmitted through the His bundle and Purkinje fibers rapidly and uniformly, but slowly through the ordinary ventricular muscle from right to left. Second, LV twist motion shows heterogenetic alteration in the four types of conduction disorders. Patients with LBBB or pacemaker rhythm manifested as having decreased apical rotation, while patients with B-WPW were mainly characterized by the reduction in basal rotation and a prolonged peak value time. The attenuation in rotation for both basal and apical layers in RVOT-PVC patients was the most significant among all groups. By analyzing the characteristics of the electricity conduction pattern, it was found that in patients with LBBB or pacemaker rhythm, LV apex myocardium was excited and contracted earlier than the rest of the LV muscle. Then, the impulse gradually expanded through the LV free wall, while the basal LV layer was excited later. In patients with B-WPW, myocardium at the base layer close to the right accessory pathway was activated first. Then, electrical activation was slowly transmitted from the right ventricle to the left. The apical layer was activated relatively late. Prinzen et al have investigated dogs with different pacing patterns and found that the fiber strain and blood flow are both impaired in the early excited myocardium\[^{35}\]. Our previous study on the influence of pacing location on cardiac
motion pattern and function found that the earlier contracting segment resulted in a reduced peak longitudinal strain\textsuperscript{[36]}. When the regional myocardium activates in advance, the blood flows to the excitation site relatively slowly. Rotation is decreased at the myocardium with poor perfusion according to the Frank-Starling mechanism. At the same time, the pressure in the LV cavity remains low when regional myocardium is activated in advance. Myocardial fibers in areas that activated late are passively elongated with relatively enhanced contractility. The reduction in the regional myocardium in patients with LBBB pattern conduction disorders was a consequence of reduced perfusion and myocardial fiber contractility. In patients with LBBB pattern conduction disorders, regional myocardium (apex or base layer) is activated in advance. The decrease in rotation in pre-excited myocardium and intraventricular dyssynchrony leads to a reduction in global LV twist and myocardial contracting efficiency, which eventually results in a decrease in stroke volume and cardiac function. In patients with LBBB pattern conduction disorders, slight changes in myocardial movements can lead to large alterations in LV twist prior to LVEF. Early quantification of impaired LV twist parameters can assist with clinical vigilance and therapeutic decisions, especially in patients with LBBB pattern conduction disorders and preserved LVEF.

4.4 Study limitations

There are several limitations that need to be acknowledged in the present study. First, the enrollment in this case-control study was relatively low. Second, the influence of the subjects’ medication use was not considered. Third, the endocardial borders were manually traced when the LV cavity was occluded at the end of the contraction at the apical short-axis level and its consistency could not be ensured among all subjects.

5. Conclusions

The present investigation represents the first case-control study to compare different LBBB pattern conduction disorders with age-matched control subjects in aspects of LV twist motion pattern.

LV twist motion shows heterogenous alteration in four types of conduction disorders. Patients with LBBB or pacemaker rhythm manifested as having decreased apical rotation, while patients with B-WPW were mainly characterized by the reduction in basal rotation and a prolonged peak value time. The attenuation in rotation for both basal and apical layers in RVOT-PVC patients was the most significant among all groups. Quantification of LV twist parameters analyzed using 2D-STE enables a detailed characterization of the contraction pattern in patients with LBBB pattern conduction disorders.

Declarations

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Conflict of Interest: All authors have no conflict of interest and have full control of all primary data. All authors agree to allow the journal to review their data if requested.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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Figures

Figure 1

Endocardial borders were traced at basal (A) and apical (B) levels of parasternal short-axis view and rotation-time curves were generated. Color-coded solid curves represent different layer segments, and white-dotted curve represents layer value.
Figure 2

Basal rotation-time curve (pink), apical rotation-time curve (blue), and LV twist-time curve (white) were obtained using 2D-STE. Peak of basal rotation (Rot-B), apical rotation (Rot-A), LV twist (LV twist), and time to peak value were measured on corresponding curves. Time to peak values was standardized using R-R interval. LV: left ventricle; STE: speckle tracking echocardiography.
Figure 3

Intra- and inter-observer consistency of LV twist parameters. Note: Bland-Altman analysis for estimating the accuracy of peak LV twist measurements by a single observer (A) and two different observers (B). Blue solid line indicates mean, and red dotted lines indicates two SD limits.
LVEF in patients with LBBB patterns and control subjects. Note: Data in CON1 group were used to compare to patients with CLBBB and DDD PM implantation. Data in CON2 group were used to compare to patients with B-WPW. Data in CON3 group were used to compare to patients with RVOT-PVC. All data were compared to the corresponding control group. *represents P<0.05.
| Group     | Schematic diagram | ECG | Twist/rotation-time curve |
|-----------|-------------------|-----|---------------------------|
| Control   | ![Control schematic](image) | ![Control ECG](image) | ![Control twist/rotation-time curve](image) |
| LBBB     | ![LBBB schematic](image) | ![LBBB ECG](image) | ![LBBB twist/rotation-time curve](image) |
| PM       | ![PM schematic](image) | ![PM ECG](image) | ![PM twist/rotation-time curve](image) |
| B-WPW    | ![B-WPW schematic](image) | ![B-WPW ECG](image) | ![B-WPW twist/rotation-time curve](image) |
| RVOT-PVC | ![RVOT-PVC schematic](image) | ![RVOT-PVC ECG](image) | ![RVOT-PVC twist/rotation-time curve](image) |

**Figure 5**

"See image above for figure legend."
Figure 6

Peak value of LV twist (A), apical rotation (B), and basal rotation (C) in patients with LBBB pattern and control subjects. Note: Data in CON1 group were used to compare to patients with CLBBB and DDD PM implantation. Data in CON2 group were used to compare to patients with B-WPW. Data in CON3 group were used to compare to patients with RVOT-PVC. All data were compared to the corresponding control group. *represents P<0.05.
Figure 7

Time to peak value of LV twist (A), apical rotation (B), and basal rotation (C), and time interval between apical and basal rotation (D) in patients with LBBB patterns and control subjects Note: Data in CON1 group were used to compare to patients with CLBBB and DDD PM implantation. Data in CON2 group were used to compare to patients with B-WPW. Data in CON3 group were used to compare to patients with RVOT-PVC. All data were compared to the corresponding control group. *represents P<0.05.

Figure 8
QRS complex duration in patients with LBBB patterns and control subjects Note: Data in CON1 group were used to compare to patients with CLBBB and DDD PM implantation. Data in CON2 group were used to compare to patients with B-WPW. Data in CON3 group were used to compare to patients with RVOT-PVC. All data were compared to the corresponding control group. *represents P<0.05.