Left bundle branch area pacing improves functional tricuspid regurgitation in patients with persistent atrial fibrillation and bradycardia

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Abstract

Background Functional tricuspid regurgitation (FTR) is correlated with more symptoms and higher mortality. The purpose of this study was to analyze the effect of left bundle branch area pacing (LBBAP) on FTR in patients with persistent atrial fibrillation (AF) and bradycardia. **Methods** Consecutive patients with a pacemaker indication who underwent successful LBBAP were identified between July 2018 and March 2023. Patients who met the following criteria were included: 1) persistent AF; 2) mean heart rate (HR) $<$ 60 bpm; 3) moderate or severe FTR. The severity of FTR was graded qualitatively with a multi-integrative approach, classified into three grades: mild = 1, moderate = 2, and severe = 3. FTR improvement was defined as adding at least one grade of FTR level. Echocardiographic parameters were followed up for one week and 6 months. **Results** There were 29 patients enrolled. 17 (59%) patients were moderate FTR and 12 (41%) patients were severe FTR at baseline. The paced QRS duration showed no difference compared to baseline (112.9 $\pm$ 13.9 vs 113.8 $\pm$ 29.1 ms, P=0.856). The paced HR was 65.4 $\pm$ 6.9 bpm, was significantly higher than that of baseline (46.7 $\pm$ 8.0 bpm) (P $<$0.001). The VP percentage at one week was 85.9 $\pm$ 20.6%, and remained stable during 6 months follow-up (81.0 $\pm$ 19.2%) (P=0.159). One week after LBBAP, 15 (52%) patients had FTR improvement. The mean FTR degree was decreased from 2.4 $\pm$ 0.5 to 1.9 $\pm$ 0.7, P$<$0.001. Six months after LBBAP, 13 (45%) patients remained with FTR improvement. The mean FTR degree was decreased from 2.4 $\pm$ 0.5 to 2.0 $\pm$ 0.8, P$<$0.001. **Conclusion** LBBAP was able to improve FTR in persistent AF patients with bradycardia.

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Methods

Consecutive patients with a pacemaker indication who underwent successful LBBAP were identified between July 2018 and March 2023. Patients who met the following criteria were included: 1) persistent AF; 2) mean heart rate (HR) $<$ 60 bpm; 3) moderate or severe FTR. The severity of FTR was graded qualitatively with a multi-integrative approach, classified into three grades: mild = 1, moderate = 2, and severe = 3. FTR improvement was defined as adding at least one grade of FTR level. Echocardiographic parameters were followed up for one week and 6 months.

Results

There were 29 patients enrolled. 17 (59%) patients were moderate FTR and 12 (41%) patients were severe FTR at baseline. The paced QRS duration showed no difference compared to baseline (112.9 $\pm$ 13.9 vs 113.8 $\pm$ 29.1 ms, P=0.856). The paced HR was 65.4 $\pm$ 6.9 bpm, was significantly higher than that of baseline (46.7 $\pm$ 8.0 bpm) (P <0.001). The VP percentage at one week was 85.9 $\pm$ 20.6%, and remained stable during 6 months follow-up (81.0 $\pm$ 19.2%) (P=0.159). One week after LBBAP, 15 (52%) patients had FTR improvement. The mean FTR degree was decreased from 2.4 $\pm$ 0.5 to 1.9 $\pm$ 0.7, P<0.001. Six months after LBBAP, 13 (45%) patients remained with FTR improvement. The mean FTR degree was decreased from 2.4 $\pm$ 0.5 to 2.0 $\pm$ 0.8, P<0.001.

Conclusion

LBBAP was able to improve FTR in persistent AF patients with bradycardia.

Keywords: Atrial fibrillation; Bradycardia; Functional tricuspid regurgitation; Left bundle branch area pacing; ventricular pacing

INTRODUCTION

Atrial fibrillation (AF)-related functional tricuspid regurgitation (FTR) has been recognized. In AF patients without left heart disease, the prevalence of moderate or severe FTR ranges from 15% to 33.6%[1, 2]. The worsening FTR is associated with more symptoms such as edema, fatigue, exercise intolerance and adverse cardiovascular events[3]. Survival is significantly shorter in patients with moderate or severe FTR, even after adjustment for coexisting conditions[4]. Despite evidence suggesting atrial reverse remodeling and FTR reduction after restoring sinus rhythm[5], a considerable proportion of AF patients developed persistent AF[6, 7], and the FTR progresses over time.

Although the majority of persistent AF patients often manifest a fast heart rate[8], some of them manifest a slow heart rate and are indicated for pacemaker[9]. Irregular rhythm and slow heart rate may contribute to FTR in these patients[10]. As the previous study demonstrated the tricuspid regurgitation (TR) deterioration following a pacemaker[11], the coexistence of AF and a pacemaker may accelerate the FTR deterioration. Right ventricular pacing has shown FTR deterioration in AF patients with bradycardia even in the absence of lead[12, 13], and the main mechanism was considered to be pacing-induced ventricular dyssynchrony[14]. Left bundle branch area pacing (LBBAP) is a physiological pacing method with excellent electrical and mechanical synchrony[15], but the data about FTR in patients with bradycardia responding to LBBAP is rare. The purpose of this study was to explore the change of FTR after LBBAP implantation in patients with persistent AF and bradycardia.

METHODS

Study population

This was a retrospective study. Consecutive patients with a pacemaker indication who underwent successful LBBAP were identified from the First Affiliated Hospital of Nanjing Medical University between July 2018 and March 2023. Patients who met the following criteria were included: 1) persistent AF; 2) mean heart rate (HR) < 60 bpm; 3) moderate or severe FTR. Patients with tricuspid valve replacement surgery, primary tricuspid valvular diseases[16] and lost follow-up (defined as without having a follow-up of both one week and 6 months) were excluded. Patients with heart failure and complete left bundle branch block who were candidates for cardiac resynchronization therapy (CRT) were also excluded [17]. All the patients included in the study were provided with written informed consent. And the study protocol was approved by the Institutional Review Board of the First Affiliated Hospital of Nanjing Medical University.

LBBAP implantation procedure

Details of the LBBAP procedure have been described before[18]. The ventricular pacing lead (Medtronic Inc. 3830 lead) was introduced via a 7-Fr guiding sheath (Medtronic Inc. C315 HIS). After mapping the His-potential, the 3830 lead was advanced 15-20 mm towards the cardiac apex. The lead was screwed into the interventricular septum and finally fixed at the left bundle branch area when there was a right bundle branch block (RBBB) pattern in the V1 lead. Successful LBBAP is defined[19] as the capture of the subendocardial area on the left side of the interventricular septum, with or without simultaneous conduction system capture, and includes left bundle branch pacing (LBBP), left fascicular pacing (LFP), and left ventricular septal pacing (LVSP). The lower rate of the pacemaker was set at 60, 70, or 75 bpm based on the condition of the patients, and was not changed during follow-up.

Data collection

Baseline characteristics were collected, including sex, age, and medication history. The 2020 ESC guidelines[20]were followed when making the diagnosis of persistent AF. Other electrocardiogram (ECG) parameters such as the intrinsic QRS duration (QRSd), the paced QRSd, and the stimulus to left ventricular activation time (s-LVAT) were measured. A 24-hour Holter electrocardiogram and device interrogation were used to collect the mean ventricular rate and pacing percentage. Pacing parameters, including pacing threshold, R-wave sensing and impedance were also recorded.

Echocardiographic parameters

Echocardiographic parameters, including left atrial diameter (LAD), right atrial diameter (RAD), left ventricular end-diastolic diameter (LVEDD), right ventricular end-diastolic diameter (RVEDD), pulmonary artery systolic pressure (PASP), left ventricular ejection fraction (LVEF) and degree of FTR, were measured at baseline and each follow-up. The proximal iso-velocity surface area method was used to evaluate the degree of TR. Per current guidelines, the severity of FTR was graded qualitatively with a multi-integrative approach, classified into three grades[21]: mild = 1, moderate = 2, and severe = 3. FTR deterioration or improvement was defined as adding or decreasing at least one grade of FTR level.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD). Differences within groups were compared using paired t-test. An independent sample t-test was used to compare the differences between the two groups. Non-normally distributed parameters were expressed as the median with an interquartile range (IQR) and compared by Mann-Whitney U-tests. Categorical variables were expressed as numbers and percentage values, and compared using chi-square or Fisher's exact test. A 2-tailed P-value < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 25.0 software (IBMCorp., Armonk, NY, US).

RESULTS

Baseline characteristics

From July 2018 to March 2023, a total of 52 LBBAP patients with persistent AF and bradycardia were identified. Among whom, 37 patients were with moderate to severe FTR. 8 patients were excluded (2 with primary tricuspid valve disease, 1 with tricuspid valve surgery, 1 with a CRT indication and 4 with lost follow-up. Finally, 29 patients were enrolled. The baseline characteristics are shown in Table 1. The patients were characterized by a majority of males (76%) with the age of (76.3 ± 9.0 years). Three patients were of LVEF <50%. There were 1 patient of hypertrophic cardiomyopathy, 1 patient of ischemic cardiomyopathy and 1 patient of dilated cardiomyopathy. Seventeen (59%) patients were moderate FTR and 12 (41%) patients were severe FTR.

Pacing parameters

Pacing parameters were summarized in Table 2. The pacing threshold, R-wave sensing, and pacing impedance were 0.64 ± 0.18 V/0.4ms, 10.3 ± 4.1 mV, and 766.2 ± 150.2 Ω, respectively. The paced QRS duration showed no difference compared to baseline (112.9 ± 13.9ms vs 113.8 ± 29.1ms, P=0.856). The stimulus to left ventricular activation time was 82.6 ± 17.4ms. There were no complications related to the implementation of LBBAP (formation of hematomas, infection, pneumothorax, lead dislocation). The lower rate of the pacemaker was set at 60, 70, or 75 bpm in 19, 8, and 2 patients, respectively.

Heart rate changes and LBBAP percentage

The VP percentage at one week was 85.9 ± 20.6%, and remained stable during 6 months follow-up (81.0 ± 19.2%) (P=0.159). The paced HR was 65.4 ± 6.9 bpm, which was significantly higher than that of baseline (46.7 ± 8.0 bpm) (P <0.001). The percentage of HR change was 43.5 ± 24.6% (see Table 3). One patient had premature ventricular contraction (PVC) burden of 10.1%. The other patients had relatively low PVC burden ([?]2%).

Follow up of echocardiographic parameters

At one week, 15 (52%) patients had FTR improvement. FTR degree was decreased from moderate to mild in 9 (31%) patients, and decreased from severe to moderate in 6 (21%) patients (Figure 1). The mean FTR degree was decreased from 2.4 +- 0.5 to 1.9 +- 0.7, P<0.001. No patients had FTR deterioration. Meanwhile, RAD decreased from 45.7 +- 5.5 mm to 44.4 +- 5.8 mm (P =0.057), and PASP reduction was observed (44.8 +- 11.8 vs 33.8 +- 8.2, P<0.001). There were no differences in LVEF and LVEDD between baseline and after LBBAP. During 6 months follow-up, 13 (45%) patients remained with FTR improvement (Figure 1). With 9 (31%) patients had mild FTR. The mean FTR degree was decreased from 2.4 +- 0.5 vs 2.0 +- 0.8, P<0.001. There were no changes in the pharmacotherapy during follow-up period.

Factors predict FTR improvement

At one week, there were 15 patients had FTR improvement and 14 patients did not have FTR improvement. The baseline characteristics and pacing parameters were not different between the two groups except for VP percentage (93.7 +- 9.1% vs 77.6 +- 26.1, P=0.044) (Table 4).

DISCUSSION

The main findings of this study were: 1) LBBAP may improve FTR in patients with persistent AF and bradycardia; 2) A high ventricular pacing percentage of LBBAP maybe needed to improve FTR.

Long-term hemodynamic disturbance resulting from an irregular and slow heart rate may be the main mechanism of FTR in patients with persistent AF and bradycardia. Compared to regular rhythm, irregular rhythm leads to hemodynamic effects including cardiac output decreases, capillary wedge pressure increases and right atrial pressure increases in AF patients[10, 22, 23]. And the slow heart rate causes a prolonged diastole phase, resulting in ventricular filling pressure increasing, which is correlated with a higher PASP and right atrial pressure. Those hemodynamic disturbances may contribute to RAV enlargement, PASP increase, and FTR development subsequently. Preclinical and exploratory clinical studies suggested that pacing at moderately accelerated heart rates was able to decrease ventricular filling pressures and improve hemodynamic effects[24-26]. Besides, the clinical trial also demonstrated the benefits of moderately accelerated heart rate compared to usual care[27]. In our study, LBBAP elevated and regularized the heart rate, and the RAV and PASP reduction were observed, which may contribute to the FTR improvement.

The physiological pacing effect of LBBAP was essential for FTR improvement. Lead interference and pacing-induced ventricular dyssynchrony were considered to be the main mechanisms of TR deterioration following right ventricular pacing[11]. With a thinner pacing lead and physiological pacing mode, LBBAP has the potential to preserve tricuspid valve function during long-term follow-up[28-30]. Lead interference was avoidable, as relevant studies[29, 30] showed that farther distance from the electrode fixation site to the tricuspid annulus (Lead-TA-dist) was correlated with a lower incidence of TR worsening after LBBAP. With the Lead-TA-dist of 19.7 +- 5.0 mm in our study, the interference of 3830 lead on tricuspid valve (TV) was relatively small. And pacing effect of LBBAP could preserve tricuspid valve function in the acute phase also had been proved[31]. Taken together, the effect of a high percentage of LBBAP on FTR in persistent AF patients with bradycardia challenged the old belief that pacemaker implantation was correlated with TR deterioration only. PVC burden can decrease VP percentage and impact the improvement of FTR. Drugs such as beta blocker or catheter ablation could be considered to eliminate PVC burden.

Limitations

First, this is a retrospective study with small sample size, a prospective study with larger sample size is needed to confirm the finding. Besides, this study is lack of directly comparison between the LBBAP and right ventricular pacing on the FTR. Second, we did not differentiate LBBP from LVSP. However, LVSP was supposed to have the same effect as LBBP[32]. Third, dimensions of the tricuspid annulus, peak tricuspid regurgitation jet velocity, the right atrial pressure and other parameters were crucial for assessing the right ventricular and TV performance. However, it is time consuming to acquire these parameters in daily work. As a retrospective study, these data were not recorded and difficult to trace. Finally, the mean HR of LBBAP was 65.4bpm, a higher HR (such as 70bpm) may result in a better outcome, which should be demonstrated in the future.

CONCLUSION

LBBAP was able to improve FTR in persistent AF patients with bradycardia. In this special population, LBBAP could be chosen as an appropriate pacing site and a high ventricular pacing percentage may be needed to improve FTR.

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DATA AVAILABILITY STATEMENT

Data available on request from the authors.

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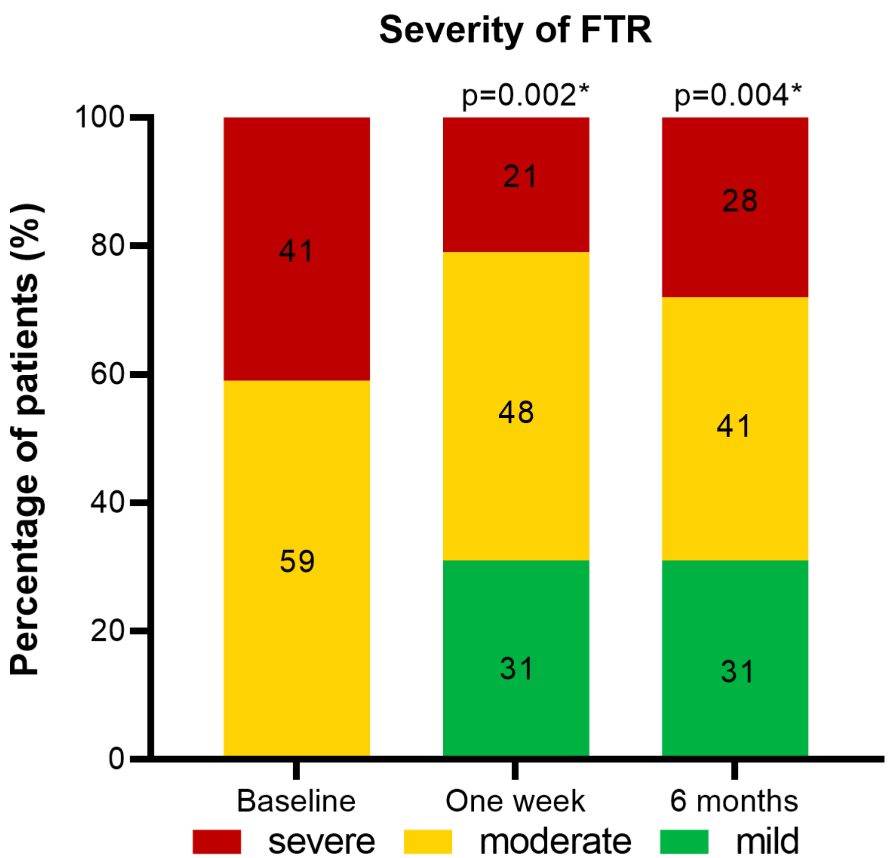
Figure 1. Severity of functional tricuspid regurgitation (FTR) in total patients (n=29) during follow up. * There was a significant difference compared to the baseline.



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