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Original Article

The quality of life of patients with pacemaker-induced cardiomyopathy after they upgrade to left bundle branch pacing

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Abstract: Objective: To investigate the changes in the cardiac function and quality of life of patients with pacemaker-induced cardiomyopathy (PICM) after they upgrade to left bundle branch pacing (LBBP). Methods: Ten patients with PICM who upgraded to LBBP were recruited as the study cohort. The LBBP upgrade operations were all performed by the same cardiac intervention expert. The cardiac function index changes, including the left ventricular end-diastolic diameters, the cardiothoracic ratios, the left ventricular ejection fractions, the N-terminal brain natriuretic peptide levels, the 6 min walking test distances, and the quality of life changes, including the SF-36 scores, the European Five-Dimensional Health Scale (EQ-5D-3L) scores, and the Minnesota Heart failure Quality of Life Scale (MLHFQ) scores before and after the LBBP operations were analyzed. The incidences of adverse events during the postoperative follow-up were analyzed. Results: The ten patients were successfully upgraded to LBBP. Compared with before the operation, the left ventricular end-diastolic diameter levels and the cardiothoracic ratios decreased significantly, but the left ventricular ejection fractions and the 6 min walking test distances increased ($P<0.05$ or $P<0.01$). The SF-36 and EQ-5D-3L scores increased gradually, but the MLHFQ scores decreased gradually before the operations and at one month and 12 months after the operations. The physical functioning (PF), role-physical (RP), general health (GH), vitality (VT), and the social role (SR) scores of the SF-36 scale, the TTO index and the visual analog scale (VAS) of the EQ-5D-3L scale scores, and the MLHFQ scores at 12 months after the operations were significantly different from the scores before the operations (all $P<0.05$). In terms of safety, there were no adverse events such as pacemaker electrode dislocation or interventricular septal perforation during the postoperative follow-up. Conclusion: Upgrading to LBBP can effectively improve cardiac function and the quality of life in patients with PICM, and the operation is safe.

Keywords: Pacemaker-induced cardiomyopathy, left bundle branch pacing, cardiac function, quality of life, questionnaires

Introduction

Cardiac pacemaker implantation is an essential method for the clinical treatment of cardiac pacing conduction dysfunction. Traditional pacemaker implantation includes right ventricular septum pacing and right ventricular apical pacing [1]. However, studies have shown that long-term right ventricular pacing can lead to cardiac contraction asynchrony and local myocardial dysfunction, which in turn leads to decreased left ventricular ejection fraction, heart failure, atrial fibrillation, and even death [2, 3]. Pacemaker-induced cardiomyopathy (PICM) refers to patients who had normal left ventricular systolic function before pacemaker implantation and who have decreased left ventricular systolic function after pacemaker implantation when other heart diseases are excluded. A foreign study has pointed out that the clinical incidence of different degrees of PICM is as high as 20%, so we should pay more attention to it [4]. Safe and stable pacemaker implantation is the key to treating patients with cardiac pacing conduction dysfunction, which is of great significance in protecting patients' lives and improving their quality of their life.

With the advancement of cardiac pacemaker implantation research, scholars have found that His bundle pacing and left bundle branch pacing (LBBP) are more in line with patients' physiological needs [5, 6]. Compared with His bundle pacing, LBBP has the advantages of better perception, a more convenient operation, lower acute and long-term thresholds, lower requirements for operators, and a more comprehensive range of patients [7, 8]. At present, Professor Huang's team in China has tried to perform LBBP, improving the left bundle branch block, obtaining more stable pacing parameters, and protecting cardiac function by improving electromechanical synchronization [9]. In the clinic, the treatment of some patients was transformed into LBBP because of the occurrence of PICM after the pacemaker implantation. A follow-up study of this kind of patient can provide a basis for the treatment of clinical PICM. However, there is a lack of published research on this in China at present. So, our study intends to explore and evaluate the application value and safety of upgrading to LBBP in patients with PICM in terms of cardiac function, quality of life, and safety.

Materials and methods

General information

Ten patients with PICM treated in Qingyang Second People's Hospital from March 2017 to March 2019 were recruited as the study cohort. All the patients underwent LBBP replacement surgery in Qingyang Second People's Hospital. Inclusion criteria: (1) Diagnostic criteria for PICM: The baseline of the left ventricular ejection fraction (LVEF) is no less than 50%, and the LVEF during follow-up is no more than 40%. The baseline of the LVEF is less than 50%, and the absolute value of the LVEF is reduced by more than 10% during follow-up. The total value of the LVEF is reduced by 10% regardless of the LVEF baseline. (2) All the patients successfully underwent an LBBP replacement operation. (3) The medical records were complete. Exclusion criteria: (1) Patients with other organic heart diseases, such as viral cardiomyopathy, hypertrophic cardiomyopathy, cardiac valvular disease, etc. (2) The medical records of patients related to this study are missing. (3) Patients have other chronic or severe illnesses that may affect the quality of life. (4) Patients need to take drugs that may affect cardiac function long after the operation. This study was approved by the Ethics Committee of Qingyang Second People's Hospital. All the patients in this study signed the informed consent form.

In this study, ten patients originally had right ventricular pacing, including three cases of right ventricular septum pacing and seven cases of right ventricular apical pacing. In terms of primary diseases, there were eight patients with hypertension and normal blood pressure control, two patients with coronary heart disease, no patients after the PCI operation, and eight patients with a standard or slow ventricular rate of atrial fibrillation, and no radiofrequency ablation was performed during the follow-up period.

Methods

The LBBP replacement in all the patients was performed by the same interventional cardiologist at Qingyang Second People's Hospital. The LBBP wire placement operation: The left axillary vein was selected for the puncture. The HisC315 sheath and the 3830 wire (both from Medtronic Company of the United States) were sent through the 8F sheath that can be torn off. And the His potential was found in the direction of 30° right anterior oblique. The head end of the 3830 wire was then sent by about 1-2 cm in the direction of the apical of the heart. When the output voltage was set to 5 V for pacing, the QRS wave in lead V1 showed a "W" shape and continued to spin into the lead, and the R wave appeared in the second half of the QRS wave in lead V1. The pacing conduction from the left bundle branch to the ventricle was measured using the pacing electrode with the voltage slightly higher than the pacing threshold and a frequency of 120-150 Hz, which was normal at 1:1. The electrode was fixed and the transport sheath was withdrawn after making sure that the end of the electrode was fixed firmly. An echocardiography and a 6 min walking test (6 MWT) were performed before and at 1 month after the operation. The indicators of the echocardiography included the left ventricular end-diastolic diameter (LVEDD), the cardiothoracic ratio (CTR), and the LVEF. The ultrasonic instrument used at Qingyang Second People's Hospital was a Mindray DC-N2S. The serum N-terminal brain natriuretic peptide (NT-proBNP) level was measured before and at 24 hours after the operation using a chemiluminescence enzyme immunoassay. The kit was purchased from Shanghai Enzymatic Biotechnology Co., Ltd., China. The measurement operation was carried out according to the kit's instructions. The SF-36, European five-dimensional Health scale (EQ-5D-3L) and Minnesota Heart failure Quality of Life Scale (MLHFQ) scores were completed before the operation, and at 1 month and 12 months after the operation. The SF-36 quality of life scale evaluates eight parameters, including physiological function (Physical Functioning, PF), physiological function (Role-Physical, RP), body pain (Bodily Pain, BP), general health status (General Health, GH), energy (Vitality, VT), social function (Social Role, SR), emotional function (Emotional Role, ER), and mental health (Mental Health, MH). The higher the score, the better the patient's quality of life. The EQ-5D-3L scale includes a five-dimensional scale and visual analog score scale (VAS). The five-dimensional scale covers five aspects: actionability, self-care ability, daily activity ability, pain or discomfort, anxiety or depression. The conversion of the TTO index was carried out using a Japanese utility conversion table and the conversion index was between 0.11 and 1.00. The higher the index value and VAS score, the better the patients' quality of life. The MLHFQ scale includes physical domain, emotional domain, and other areas, including 8, 5, 8 items, respectively. There are a total of 21 items and a total possible score ranging from 0-105. The higher the score , the worse the quality of life. The purpose and content of the scale were explained by the researchers in outpatient interviews or by telephone. They did it on their own or with the help of trained clinicians. The patients were followed up for at least 12 months, and any occurrence of pacemaker electrode dislocation or interventricular septal perforation was recorded.

Outcome measures

(1) The changes in the echocardiographic parameters, the blood NT-proBNP levels and the 6 MWT distances before and after operations, (2) the changes in the SF-36, EQ-5D-3L, and MLHFQ scores before and after the operations, (3) the occurrence of any postoperative adverse events.

Statistical methods

The statistical analysis was carried out using SPSS 25.0. The measurement data were expressed as the mean ± standard deviation ($\bar{x} \pm sd$), and paired sample t-tests were carried out before and after the comparisons. The test level was taken as bilateral $\alpha=0.05$. $P<0.05$ meant that a difference was statistically significant.

Results

Baseline patient data

See **Table 1**.

Changes in the cardiac echocardiographic parameters, the blood NT proBNP levels and the 6 MWT before and after the operations

The LVEDD, CTR, and blood NT-proBNP levels decreased, and the LVEF and 6 MWT levels increased after the operations. There were significant differences in the LVEDD, CTR, LVEF, and 6 MWT levels before and after the operations ($P<0.05$ or $P<0.01$). See **Table 2** and **Figure 1**.

Changes in the SF-36, EQ-5D-3L and MLHFQ scores before and after the operation

The scores on all the dimensions of the SF-36 scale increased gradually at 1 month and 12 months after the operations. The PF, RP, GH, VT, and SR scores on the SF-36 scale at 12 months after operations were significantly higher than they were before the operations ($P<0.05$). See **Table 3** and **Figure 2**.

The TTO index and the VAS scores of the postoperative EQ-5D-3L scale increased gradually at 1 and 12 months after the operations, and the MLHFQ scores decreased gradually at 1 and 12 months after the operations. The EQ-5D-3L scores at 12 months after the operations were significantly higher than they were before the operations, but the MLHFQ scores were significantly lower than they were before the operation ($P<0.05$). See **Table 4** and **Figure 3**.

Postoperative adverse events

All the patients were followed up for at least 12 months, and no pacemaker electrode dislocation or interventricular septal perforation was found.

Table 1. Baseline patient information

Indexes	Range	$\bar{x} \pm sd$	n, (%)
Age (years)	59-85	70.8±7.9	
Sex (male/female)			5 (50.00%)/5 (50.00%)
Duration of VP (mo)	23-192	82.76±45.21	
RVP percentage (%)	40-99	83.96±17.87	
Pre-LBBAP EF (%)	31-70.2	47.58±15.27	
Systolic BP (mmHg)	101-160	131.72±19.63	
Diastolic BP (mmHg)	45-97	72.60±14.17	
Blood glucose (mmol/L)	5.2-7.1	6.45±0.64	
Creatinine (μmol/L)	63-139	81.54±24.32	
Beta natriuretic peptide (pg/mL)	220-13482	2863.77±3935.68	
Medical history information			
Hypertension			7 (70.00%)
Hypercholesterolemia			1 (10.00%)
Type 2 diabetes mellitus			1 (10.00%)
Prior myocardial infarction			0 (0.00%)
History of atrial fibrillation			5 (50.00%)
Percutaneous coronary intervention			1 (10.00%)
Coronary artery bypass surgery			0 (0.00%)
Previous ICD			0 (0.00%)
Valve surgery			1 (10.00%)
NYHA heart failure class			
Class II			6 (60.00%)
Class III-IV			4 (40.00%)
Medications			
Beta blockers			4 (40.00%)
Aspirin/antithrombotics			2 (20.00%)
Lipid lowering agents			3 (30.00%)
Diuretics			4 (40.00%)
ACEI/ARB			7 (70.00%)
Digoxin			1 (10.00%)
Hypoglycemics			1 (10.00%)
Antidepressants/antianxiety			0 (0.00%)
Vasodilators			10 (100.00%)

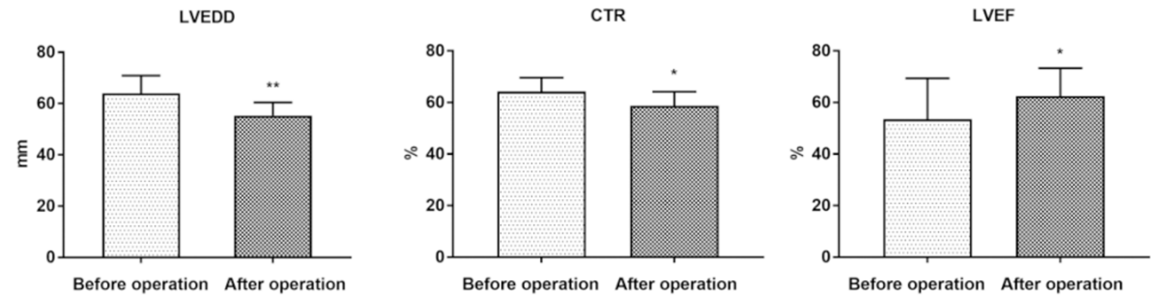
Table 2. Comparison of the cardiac ultrasound parameters and blood NT-proBNP levels before and after the operations ($\bar{x} \pm sd$)

Time	n	LVEDD (mm)	CTR (%)	LVEF (%)	NT-proBNP (pg/mL)	6 MWT (m)
Before the operation	10	63.98±6.82	64.25±5.34	47.57±15.25	93.84±41.87	267.94±84.57
1 month after the operation	10	55.24±5.15	58.72±5.47	62.53±10.74	88.42±36.64	395.62±64.37
t		3.237	2.299	2.552	0.592	3.799
P		0.005	0.035	0.021	0.562	0.001

Note: LVEDD: left ventricular end-diastolic diameter; CTR: cardiothoracic ratio; LVEF: left ventricular ejection fraction; NT-proBNP: N-terminal brain natriuretic peptide; 6 MWT: 6 min walking test distance.

Discussion

It was found that long-term right ventricular pacing can lead to cardiac electrophysiological changes, delay the activation of the left ventricular free wall, affect the synchronization of the electrical and mechanical activity of the ventricles, lead to cardiomyocyte degenerative



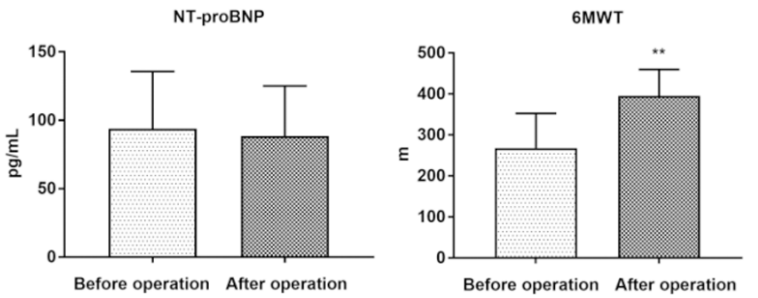


Figure 1. Changes in the cardiac echocardiographic parameters, the blood NT-proBNP levels, and the 6 MWT before and after the operations. Compared with before the operation, *P<0.05, **P<0.01. LVEDD: left ventricular end-diastolic diameter; CTR: has a heart-to-heart ratio; LVEF: left ventricular ejection fraction; NT-proBNP: terminal brain natriuretic peptide; 6 MWT: 6 min walking test.

Table 3. Changes in the SF-36 scale scores before and after the operations ($\overline{x}$ ± sd, score)

Subjects	Baseline	1 month after the operation	12 months after the operation	P (12 months after the operation vs baseline)
PF	67.17±22.48	74.24±15.86	85.37±9.83[a]	0.037
RP	60.07±40.02	75.39±19.43	95.57±10.06[a]	0.022
BP	94.53±12.16	95.23±7.34	96.83±6.45	0.604
GH	56.65±21.22	66.39±15.01	77.82±10.92[a]	0.015
VT	79.35±11.22	83.55±11.29	89.52±10.32[a]	0.049
SR	82.55±13.52	90.09±13.55	96.36±8.03[a]	0.015
ER	76.72±30.40	90.06±15.34	96.22±10.07	0.083
MH	92.16±7.29	93.28±6.20	92.43±7.75	0.929

Note: Compared with before the operation, [a]P<0.05. PF: physical functioning; RP: role-physical; BP: bodily pain; GH: general health; VT: vitality; SR: social role; ER: emotional role; MH: mental health.

fibrosis and mitochondrial variation, cause disorganized arrangement of muscle fiber, which then affects cardiac function and even leads to the occurrence of atrial fibrillation [10, 11]. Studies have found that his bundle pacing can avoid the adverse effects of right ventricular pacing and realize the synchronization of cardiac electrophysiology and mechanical activation, which then reduces the incidence of heart failure and fibrillation [12-14]. However, the operation has a high threshold at the time of implantation, and there is a possibility of a further increase in the later stage [15]. Especially when the patient's block size develops further, there is still a risk of loss and capture [16]. The operation is difficult and requires a highly-skilled surgeon. There are also some problems, such as low ventricular perception, atrial overperception, and so on. All these problems limit the clinical application of His bundle pacing to a great extent. The appearance of LBBP makes up for the deficiency of His bundle pacing to a great extent and further improves the comprehensive level of treatment of cardiac pacemaker implantation. As early as 1997, Narula et al. realized that bundle branch block mostly occurs inside the His bundle through His bundle stimulation [17]. Stimulation of the left bundle branch area at the distal end of the His bundle can eliminate the right bundle branch block, the left bundle branch block, the left anterior branch block, and so on. Laske et al. paced different regions of the interventricular septum of a pig heart and found that His parafascicular pacing

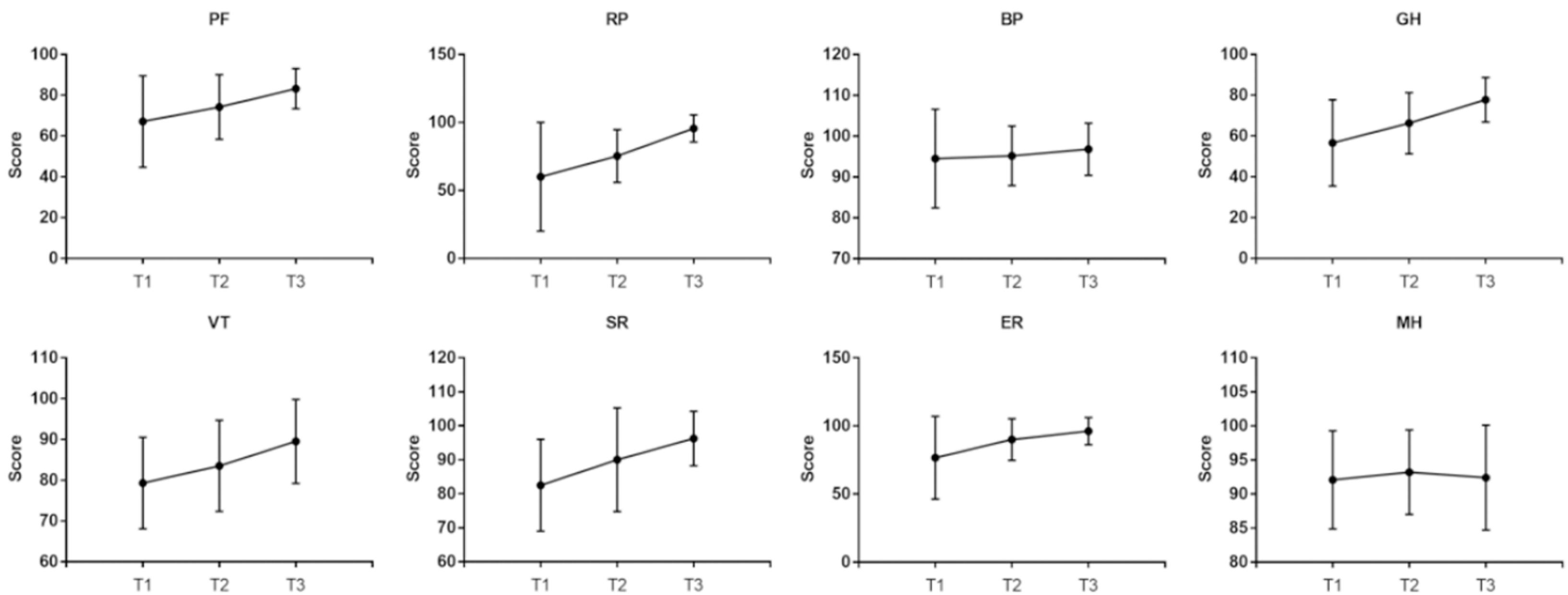


Figure 2. Changes in the SF-36 scores before and after the operation. T1: Baseline; T2: 1 month after the operation; T3: 12 months after the operation; PF: physical functioning; RP: role-physical; BP: bodily pain; GH: general health; VT: vitality; SR: social role; ER: emotional role; MH: mental health.

Table 4. Changes in the EQ-5D-3L and MLHFQ scale scores before and after the operations ($\overline{x}$ ± sd)

Time	n	Total scale index	EQ-VAS (score)	MLHFQ (score)
Baseline	10	0.82±0.12	81.54±5.08	25.08±11.29
1 month after the operation	10	0.87±0.14	82.99±7.66	22.30±8.73
12 months after the operation	10	0.95±0.11[a]	87.14±4.66[a]	13.34±3.65[a]
P (12 months after the operation vs baseline)		0.021	0.018	0.010

Note: Compared with before the operation, [a]P<0.05. VAS: visual analog scale score; MLHFQ: Minnesota Heart Failure Quality of Life Scale.

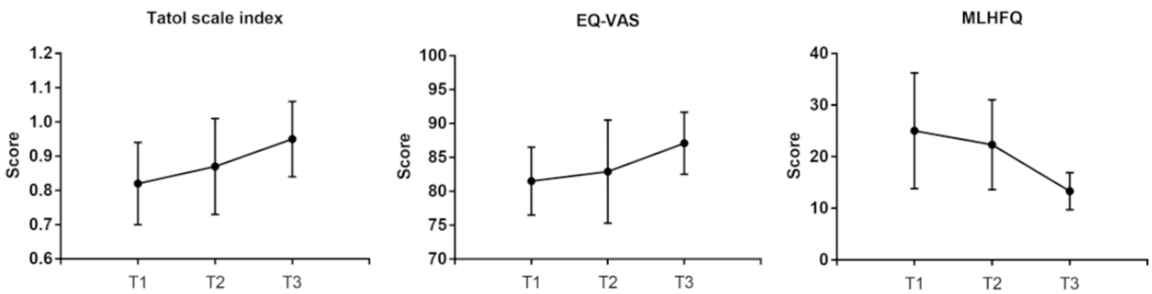


Figure 3. Changes in the EQ-5D-3L and MLHFQ scores before and after the operations. T1: Baseline; T2: 1 month after the operation; T3: 12 months after the operation. Total scale index: five-dimensional scale TTO conversion index; EQ-VAS: EQ-5D-3L scale visual analog score; MLHFQ: Minnesota heart failure quality of life scale.

can produce physiological ventricular activation similar to sinus conduction [18]. With the introduction of LBBP by Professor Huang Weijian's team, LBBP has become a hot topic in related fields [19]. The tree structure of the left hip system provides more pacing sites. And the presence of ventricular muscle tissue helps to reduce the threshold and increase the stability of the threshold, so it may have long-term safety and stability [20-22].

In this study, we explored the changes in cardiac function and quality of life in patients with PICM after they upgraded to LBBP. The echocardiography results showed that one month after their operations, the patients' LVEDD and CTR were significantly lower than they were before the operation. At the same time, the LVEF was significantly higher than it was before the operation. An increase in the LVEDD indicates ventricular enlargement and impaired cardiac function. CTR refers to the ratio of the transverse diameter of the heart (the sum of the maximum distance from the left and right cardiac margin to the midline of the body) to the transverse diameter of the chest (the horizontal internal thoracic meridian through the top of the right diaphragm) on X-ray, and it is closely related to cardiac function. When the CTR increases, it suggests that the heart is dilated and cardiac function may be impaired [23]. LVEF is a commonly-used clinical index to directly reflect the ventricular systolic function. Therefore, the results of ultrasound examinations suggested that the cardiac function of the patients was significantly improved. The increase of the 6 MWT also indicates that the heart failure is relieved and the cardiac function is significantly improved. As mentioned earlier, the desynchrony of cardiac electrophysiological and mechanical activation is the main reason for the decline of cardiac function in patients with PICM. Therefore, combined with the results of this study and the mechanism of LBBP, it can be considered that LBBP can effectively restore the synchronization of electrophysiological and mechanical activation in patients. In a study by Chen et al., LBBP and RVP were used in patients with cardiac pacemaker indications [24]. The ECG characteristics, the pacing parameters, the pacing sites, and the safety events were evaluated during implantation and at three months' follow-up. The results showed that the LBBP group had shorter QRS pacing durations and lower and stable pacing thresholds, in which the QRS pacing duration was an important index to reflect ventricular systolic synchronization. It is related to the incidence of heart failure and mortality after an operation [25]. And no adverse events were found during the follow-up period, indicating that LBBP is better and safer. In this study, 10 patients were successfully upgraded to LBBP, and no adverse events were found during their surgeries and postoperative follow-ups. This study's cardiac function and safety are consistent with those of Chen et al. [24]. Huang et al. used LBBP in a patient with dilated cardiomyopathy with a complete left bundle branch block [26]. The threshold was only 0.5 V/0.5 ms. During the 1-year follow-up, the symptoms gradually improved, and the threshold was stable, suggesting that LBBP is very effective at improving cardiac function.

After the implantation of a pacemaker, it will accompany the patient for a long time. In addition to considering that a pacemaker is an important guarantee of a patient's cardiac health, it is also necessary to consider the patient's quality of life. A study suggested that the type of pacemaker implantation is an important factor affecting patients' quality of life after an operation [27]. With the further popularization of the physiological-psychological-social medical model, a large number of studies have included patients' quality of life and psychological problems such as anxiety and depression into the important indicators to evaluate the efficacy of cardiac pacemaker implantation [28]. A study showed that pacemaker implantation can improve patients' quality of life [29]. And another study pointed out that pacemaker implantation may lead to anxiety and depression in patients after their operations and reduce the quality of life [30]. In this study, the SF-36, EQ-5D-3L and MLHFQ scales were used to evaluate the changes in the patients' quality of life. The results showed that the SF-36 and EQ-5D-3L scores increased gradually after the operations, and the MLHFQ scores decreased gradually after the operations. SF-36 is an important way of evaluating the quality of life of patients with cardiac insufficiency, and it can be assessed comprehensively from the aspects of physical pain, physiological function, mental health, emotional function, and social function [31]. The EQ-5D-3L and the MLHFQ are also common ways of evaluating quality of life, and they also have the advantage of a comprehensive evaluation. The results of this study suggest that the quality of life of patients has been significantly improved after they upgraded to LBBP.

To sum up, upgrading the pacemaker to LBBP can effectively improve PICM patients' cardiac function and quality of life, and it is very safe.

Disclosure of conflict of interest

None.

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