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Retraction

Retracted: Metoprolol Improves Myocardial Remodeling and Cardiac Function in Patients with Permanent Pacemaker Implantation

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This article has been retracted by Hindawi following an investigation undertaken by the publisher [1]. This investigation has uncovered evidence of one or more of the following indicators of systematic manipulation of the publication process:

(1) Discrepancies in scope
(2) Discrepancies in the description of the research reported
(3) Discrepancies between the availability of data and the research described
(4) Inappropriate citations
(5) Incoherent, meaningless and/or irrelevant content included in the article
(6) Peer-review manipulation

The presence of these indicators undermines our confidence in the integrity of the article's content and we cannot, therefore, vouch for its reliability. Please note that this notice is intended solely to alert readers that the content of this article is unreliable. We have not investigated whether authors were aware of or involved in the systematic manipulation of the publication process.

In addition, our investigation has also shown that one or more of the following human-subject reporting requirements has not been met in this article: ethical approval by an Institutional Review Board (IRB) committee or equivalent, patient/participant consent to participate, and/or agreement to publish patient/participant details (where relevant).

Wiley and Hindawi regrets that the usual quality checks did not identify these issues before publication and have since put additional measures in place to safeguard research integrity.

We wish to credit our own Research Integrity and Research Publishing teams and anonymous and named external researchers and research integrity experts for contributing to this investigation.

The corresponding author, as the representative of all authors, has been given the opportunity to register their agreement or disagreement to this retraction. We have kept a record of any response received.

References

[1] L. Ye, G. Hu, H. Yu, J. Sun, and H. Yuan, "Metoprolol Improves Myocardial Remodeling and Cardiac Function in Patients with Permanent Pacemaker Implantation," *Journal of Healthcare Engineering*, vol. 2022, Article ID 7340992, 5 pages, 2022.

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Research Article

Metoprolol Improves Myocardial Remodeling and Cardiac Function in Patients with Permanent Pacemaker Implantation

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In China, the incidence of arrhythmia has also increased to approximately 20% of all cardiovascular diseases. The incidence of cardiovascular diseases in China has certain characteristics, which are generally low in the south and high in the north, and they tend to be younger and growing. Permanent pacemaker implantation is currently the most effective means of treating arrhythmia and preventing sudden death. To explore the clinical application value of metoprolol in patients after permanent pacemaker implantation. Ninety patients with permanent dual-chamber pacemaker implantation in our hospital are selected and divided into a metoprolol group and a control group according to whether metoprolol is used one week after the operation and 45 patients in each group. After one postoperative week, the LVEF%, LVEDd, LAD, and E/A of the metoprolol and the control groups had no statistically significant differences ($p > 0.05$). Twelve months postoperatively, the E/A of the metoprolol group is higher than that of the control group ($p < 0.05$), and LVEDd and LAD are lower than those of the control group ($P < 0.05$). The NT-proBNP and hs-CRP levels between the metoprolol and control groups had no significant differences ($p > 0.05$) in the values recorded immediately postoperatively. The NT-proBNP of the metoprolol group is lower than that of the control group ($p < 0.05$) at 12 months following pacemaker implantation. At one week after surgery, QTd, Pd, and Tp-Te are not significantly different ($P > 0.05$) between the metoprolol group and the control group, whereas the QTd and Pd times in the metoprolol group are lower than those in the control group ($p < 0.05$) at the 12-month follow-up. At one week postoperatively, the SDNN, SDANN, and RMSSD between the metoprolol and control groups did not show any statistically significant differences ($p > 0.05$). The SDANN of the metoprolol group is higher than that in the control group ($p < 0.05$) in the 12-month evaluation. One week after the operation, the serum IL-6 and TNF-α levels are not significantly different between the metoprolol and control groups ($p > 0.05$). At 12 months after surgery, the serum IL-6 and TNF-α levels in the metoprolol group are lower than those in the control group ($p < 0.05$). The incidence of adverse events in the metoprolol group is 9.30% lower than 26.83% in the control group within 12 months after the operation ($p < 0.05$). The use of metoprolol in patients with permanent pacemaker implantation after surgery can reduce the expansionary remodeling of the left atrium and have less impact on the QT-dispersion and Pd time.

1. Introduction

Permanent pacemaker implantation effectively treats bradyarrhythmia and provides a prevention against sudden cardiac death. The pacemaker releases electrical pulses through pulse generators and stimulates myocardial contraction. In recent years, the indications for pacemaker implantation have been expanded to include vasovagal syncope, paroxysmal atrial fibrillation, refractory congestive heart failure, and hypertrophic cardiomyopathy [1]. However, the implantation of permanent pacemakers has been reported to affect the hemodynamics of patients, and the right ventricular apical pacing leads to the left and right ventricular asynchronous contraction and may even induce or aggravate the chronic heart failure. Therefore, after the implantation of permanent pacemaker, clinicians should focus on the improvement of cardiac function [1].

Metoprolol is a β-receptor blocker that is often used for the treatment of hypertension, angina pectoris, coronary heart disease, and supraventricular arrhythmia. It inhibits the activity of sympathetic nerves and the renin-angiotensin-aldosterone system, which reduces the myocardial oxygen consumption, improves the cardiac function, and reduces the atrial fibrillation load, while improving the QT-interval dispersion [2]. Metoprolol is reported to partially offset the adverse effects of long-term right ventricular apical pacing in a prior report [3]. However, some studies suggest that in patients with permanent pacemaker implantation, β-blockers cannot be used continuously [4]. Hence, in this paper, we explored the value of administering metoprolol to patients undergoing surgical implantation of permanent pacemakers [4–8].

2. The Proposed Scheme

We enrolled 90 patients who underwent permanent dual-chamber pacemaker implantation at the Department of Cardiovascular Medicine of our hospital. They are classified into the metoprolol and control groups, with 45 cases in each group. The hospitalization time of the paper subjects is from February 2015 to January 2018. The inclusion criteria for this paper are as follows: (1) atrioventricular block defined based on the 2014 EHRA/HRS/APHRS expert consensus on diagnosing ventricular arrhythmias; (2) third-degree atrioventricular block following the implantation of a permanent dual-chamber pacemaker; (3) patients with a ventricular electrode value located at the right ventricular apex; (4) patients with a good sinus-node heart function; and (5) patients who provided informed consent for the treatment plan. The exclusion criteria are as follows: (1) cardiomyopathy, heart valve disease, or congenital heart disease; (2) serious liver disease, kidney disease, or systemic infectious diseases; (3) blood system and immune system diseases; (4) connective-tissue diseases; (5) gastrointestinal ulcer bleeding and anemia; and (6) patients with chronic heart failure grade III and above, according to the New York Heart Association grading system.

The metoprolol group comprised patients aged between 33 and 65 years (average 43.2 ± 7.6 years, 25 men and 20 women; heart rate 81.6 ± 8.0 bpm). Additionally, diabetes ($n = 8$), dyslipidemia ($n = 11$), and hypertension ($n = 14$); qT duration: 22.6 ± 2.8 ms. The patients completed a follow-up period of 12 months, and 2 cases are lost to follow-up. The control group comprised patients aged 35–65 years (mean, 44.0 ± 7.0 years; 21 men, 24 women; heart rate of 83.0 ± 7.4 bpm; comorbidities: diabetes ($n = 5$), dyslipidemia ($n = 9$), and hypertension ($n = 16$); qT duration: 22.8 ± 2.5 ms). Following up for 12 months, 4 cases are lost. The above baseline data are compared between the two groups, and the difference is not statistically significant ($p > 0.05$).

3. Pacemaker Implantation and Medications Administered

All patients underwent dual-chamber pacemaker implantation, followed by skin preparation, disinfection, and routine ECG monitoring. Antibiotics are administered 1 hour preoperatively. The pacemaker and electrodes are Medtronic Biotronik St. Jude. The patients are placed in the supine position and subcutaneously injected with 1% lidocaine for local anesthesia. Two J-shaped steel wires are inserted through the right subclavian vein puncture approach from the C-arm machine view to ensure the proper entry of the head of the steel wire through the inferior vena cava. A 5 cm incision is cut horizontally at 3 cm below the clavicle, and the individual layers of the fascia are separated. The surgical site is compressed with a gentamicin gauge to achieve hemostasis. The sheath tube is inserted along the wire; the guide wire and sheath core are pulled out. The atrial and ventricular electrode wires are inserted into the inferior vena cava along the sheath tube. Then, the ventricular electrode is sent to the right ventricular outflow tract and the head of the ventricular electrode is inserted into the trabecular muscles. After the head end of the ventricular electrode is fixed, the internal wire is retracted to the level of the right atrium, and the atrial electrode is retracted to the middle of the right atrium. The partial withdrawal of the guide wire bent the atrial electrode wire into a J-shape, and the head end of the electrode entered the right atrial appendage comb muscle. A good fixation of the head end of the electrode is confirmed. After a satisfactory pacing test, the built-in steel wire of the electrode is removed, and the electrode wire is fixed. The pacemaker is connected to the electrode wire and placed in the bag. The pacemaker is sutured and fixed; local compression is performed to achieve coagulation and hemostasis. The left shoulder is braked.

The control group received metoprolol after 1 week postoperatively. The metoprolol group received metoprolol on the same day postoperatively. The initial dose for both groups is oral, 12.5 mg/day, and gradually increased until the maximum tolerated dose of 25 mg.

4. Observation Indicators and Statistical Processing

The left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDd), right atrial diameter (LAD), maximum filling velocity ratio of E peak to/A peak (E/A), N-terminal probrain natriuretic peptide (NT-proBNP), high-sensitivity C-reactive protein (hs-CRP), QT-dispersion (QTd), P-wave duration, and its difference (Pd = maximum P-wave duration−minimum P-wave duration), Tp-Te interval, heart-rate variability (HVR), standard deviation of normal R-R interval (SDNN), standard deviation of normal R-R interval (SDNN) per 5 minutes within 24 hours, root mean square difference of adjacent normal R-R interval (RMSSD), serum interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and incidence of adverse events are compared between the two groups at 1 week and 12 months postoperatively.

LVEF, LVEDd, LAD, and E/A are detected by echocardiography (VIVID E9 Ultrasound Machine, General Electric, United States) at 1 week and 12 months postoperatively. QTd, Pd, and Tp-Te intervals are simultaneously detected by a conventional ECG standard 12-lead ECG. The parameters are a paper speed of 50 mm/s, fixed voltage of 10.0 m/V, continuous measurement of three cardiac cycles, and the average detection of heart-rate variability by the Holter system.

Table 1: Comparison of cardiac function indexes between two groups of patients, $\overline{X} \pm S$.

Group	n	LVEF (%)		LVEDd (mm)	
		1 week after operation	12 months after surgery	1 week after operation	12 months after surgery
Metoprolol group	43	54.62 ± 3.77	53.90 ± 4.01	39.51 ± 2.71	40.05 ± 2.86
Control group	41	54.35 ± 3.64	53.04 ± 3.85	39.24 ± 2.85	41.77 ± 2.50
T		0.334	1.002	0.445	−2.929
P		0.739	0.319	0.657	0.004
Group	n	LAD (mm)		E/A	
		1 week after operation	12 months after surgery	1 week after operation	12 months after surgery
Metoprolol group	43	32.60 ± 2.84	33.04 ± 2.75	1.75 ± 0.30	1.68 ± 0.28
Control group	41	32.84 ± 2.90	34.62 ± 2.88	1.71 ± 0.33	1.51 ± 0.24
t		−0.383	−2.572	0.582	2.981
P value		0.703	0.012	0.562	0.004

Table 2: Comparison of NT-proBNP, hs-CRP, and inflammatory factors between the two groups, $\overline{X} \pm S$.

Group	n	NT-proBNP (pg/mL)		Hs-crp (mg/L)		IL-6 (ng/mL)		TNF-α (pg/mL)	
		1 week after operation	12 months after surgery	1 week after operation	12 months after surgery	1 week after operation	12 months after surgery	1 week after operation	12 months after surgery
Metoprolol group	43	2325.6 ± 440.1	1786.2 ± 300.5	6.65 ± 2.20	2.85 ± 0.78	32.88 ± 6.53	18.77 ± 5.00	3.90 ± 0.96	1.88 ± 0.56
Control group	41	2289.4 ± 410.8	1951.7 ± 332.8	6.27 ± 1.96	3.04 ± 0.91	34.16 ± 7.76	23.55 ± 6.84	3.76 ± 1.10	2.30 ± 0.74
t		0.389	−2.394	0.834	−1.029	−0.819	−3.669	0.622	−2.942
P value		0.698	0.019	0.406	0.307	0.415	0	0.535	0.004

Table 3: Comparison of ECG indexes and HVR indexes between the two groups, $\overline{X} \pm S$.

Group	n	QTd (ms)		Pd (ms)		Tp-Te (ms)	
		1 week after operation	12 months after surgery	1 week after operation	12 months after surgery	1 week after operation	12 months after surgery
Metoprolol group	43	22.5 ± 2.4	23.1 ± 2.6	25.1 ± 5.8	31.6 ± 6.6	123.6 ± 13.0	125.4 ± 12.8
Control group	41	22.8 ± 2.6	25.0 ± 3.1	25.7 ± 4.6	35.0 ± 7.0	121.3 ± 11.5	124.0 ± 13.1
t		−0.550	−3.049	−0.524	−2.291	0.857	0.495
P value		0.584	0.003	0.602	0.025	0.394	0.622
Group	N	SDNN (ms)		SDANN (ms)		RMSSD (ms)	
		1 week after operation	12 months after surgery	1 week after operation	12 months after surgery	1 week after operation	12 months after surgery
Metoprolol group	43	103.21 ± 16.74	124.26 ± 19.53	92.80 ± 8.55	117.42 ± 11.07	35.48 ± 5.81	46.68 ± 8.64
Control group	41	101.55 ± 18.32	120.74 ± 16.88	94.55 ± 8.81	111.75 ± 13.26	37.11 ± 7.03	43.52 ± 9.41
t		0.434	0.882	−0.924	2.131	−1.161	1.604
P value		0.666	0.380	0.358	0.036	0.249	0.112

Blood samples are taken at 1 week and 12 months postoperatively to detect NT-proBNP and hs-CRP. Venous blood samples are collected from the patients who fasted for at least 8 h before blood sampling; the samples are centrifuged within 1 h. Serum is collected to detect NT-proBNP, IL-6, and TNF-α by enzyme-linked immunosorbent assay, and hs-CRP is detected by immunoturbidimetry (Shenzhen Mindray Medical Electronics Co., Ltd). The RT-96A microplate reader is purchased from Shanghai Enzyme Biotechnology Co., Ltd.

SPSS software (version 21.0) is used for statistical analysis. The measurement indexes such as LVEF%, LVEDd, LAD, E/A, NT-proBNP, and hs-CRP of the two groups are expressed as means ± standard deviations, and the independent sample *t*-test is used for comparison between the two groups. The $\chi 2$ test is used to compare the numerical data (gender, incidence of adverse events). A p value <0.05 is used to indicate statistically significant differences. Table 1 is the comparison of cardiac function indexes between two groups of patients. Table 2 is the comparison of NT-proBNP, hs-CRP, and inflammatory factors between the two groups. Table 3 is the comparison of ECG indexes and HVR indexes between the two groups. Table 4 is the comparison of the incidence of adverse events between the two groups.

Table 4: Comparison of the incidence of adverse events between the two groups.

Group	n	Low blood pressure	Ventricular velocity	Difficulty breathing	Adverse events (%)
Metoprolol group	43	2 (4.65)	2 (4.65)	0 (0.00)	4 (9.30)
Control group	41	4 (9.76)	5 (12.2)	2 (4.88)	11 (26.83)
χ^2					4.395
P value					0.036

5. Experimental Results Analysis

Cardiac pacemakers are precise electronic devices that are implanted into the heart. They stimulate the cardiac muscle fibers in contact with the electrode through regular electrical impulses, causing cardiac contraction, and have a good therapeutic effect on symptomatic bradycardia and third-degree atrioventricular block. Swedish scholars had reported a complete permanent pacemaker implantation performed first in the 1950s, after which clinical application of the device is started. There have been rapid developments in pacemaker devices, which have improved their pacing to the levels close to physiological pacing; however, their application inevitably affects the hemodynamics in most cases. When pacing, electrical stimulation starts at the apex of the right ventricle, transmits along the ventricular septum, and slowly spreads from the myocardium to the whole heart. Asynchronous left and right ventricular stimulation can increase mitral regurgitation, which has adverse effects on the systolic and diastolic functions. At present, there are few clinical studies on the safety and effectiveness of changing pacing sites with no consensus.

The enhancement of cardiac stress and activation of the renin-angiotensin-aldosterone system after pacemaker implantation causes postoperative myocardial remodeling. Angiotensin can increase the synthesis of myocardial contractile proteins, and aldosterone can promote the generation of collagen fibers, increase myocardial collagen fibers and myocardial interstitial fibrosis, and aggravate the deterioration of cardiac function. Metoprolol can inhibit the renin-angiotensin-aldosterone system and delay the process of myocardial remodeling. Some scholars have found that metoprolol combined with amiodarone in the treatment of chronic heart failure complicated by ventricular arrhythmia can effectively improve cardiac function, maintain sinus rhythm, improve the therapeutic effect, and have good safety.

The HRV index (change in the difference in the successive heartbeat cycle) explains the regulation of neurohumoral factors in the cardiovascular system and can be useful to predict the prognosis of cardiovascular diseases. In this paper, metoprolol is used for permanent pacemaker implantation. At the 12-month postoperative evaluation, the cardiac function index and HRV of patients treated with metoprolol are better, and the incidence of adverse events within 12 postoperative months is also lower, which indicated an effective use of metoprolol after permanent pacemaker implantation in improving the cardiac pump function of patients, regulating the function of the sympathetic and vagus nerves, and reducing the risk of adverse events (including postoperative hypotension, ventricular tachycardia, and dyspnea. This is because the sympathetic nerve is overexcited after pacemaker implantation, and the excitability of the sinus node is enhanced. Metoprolol acts on the β receptor, inhibits sympathetic-nerve excitability, reduces the ventricular damage, and protects cardiac function. Metoprolol can also delay cardiac electrical-mechanical remodeling and reduce ventricular damage caused by long-term high proportion ventricular pacing.

NT-proBNP is an endogenous hormone secreted by ventricular myocytes after injury, and its serum level is related to the degree of myocardial injury. hs-CRP is a sensitive inflammatory indicator that is often used as a predictor of cardiovascular and cerebrovascular diseases in clinical practice. IL-6 and TNF-α play an important role in promoting cardiovascular disease, can promote the activation of monocytes and macrophages, causing or aggravating the inflammatory response, and can induce oxidative stress response. This paper found that the NT-proBNP, IL-6, and TNF-α levels are lower in patients treated with metoprolol after 12 months following pacemaker implantation, suggesting the myocardial protective properties of metoprolol, ventricular myocardial injury reduction, and inhibition of excessive inflammatory response in patients with permanent pacemaker implantation.

6. Conclusion

QTd reflects the course of myocardial repolarization and action potential, with a good prediction effect on the ventricular arrhythmia. Pd indicates the atrial conduction state and sinus conduction synchronization; its elevated level suggests a decrease in atrial conduction compliance. The Tp-Te interval is a newly discovered predictor of ventricular arrhythmia. This paper revealed that the QTd and Pd time of patients treated with metoprolol at 12 months after surgery are lower, suggesting that the use of metoprolol after permanent pacemaker implantation could improve the atrial conduction compliance and prevent ventricular arrhythmia.

In summary, metoprolol in patients with permanent pacemaker implantation after surgery can reduce the expansionary remodeling of the left atrium and have less impact on QTd and Pd time.

Data Availability

The simulation experiment data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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