

RESEARCH ARTICLE

The deleterious effect of intracardiac pacing leads on right ventricular function

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ABSTRACT

Aim: The aim of this study was to evaluate the progression of tricuspid regurgitation (TR) in patients with pacemaker leads across the tricuspid valve and assess the clinical effect on right ventricular (RV) function.

Methods: Patients who had undergone permanent pacemaker implantation at our institution over an 8-year period were identified. Those who had an echo (for any indication) pre- and postdevice implantation were included in this study, and their data assessed. Clinical information was obtained from their medical records. A total of 65 patients (mean age 70 ± 13 years, 31 (48%) males, and 34 (52%) females) were enrolled in the study.

Results: The median interval of echo after implantation was 12 (12 to 24) months. Before implantation, 29 patients had TR, which increased to 51 (78%) during follow up, indicating that 22 patients developed new TR. Of those with preexisting TR, the grade of TR had worsened by at least one grade in 17 patients. RV function as measured by tricuspid annular plane systolic excursion (TAPSE) had decreased from 1.87 ± 0.44 to 1.68 ± 0.42 ($p = 0.002$). Eighteen patients had developed signs of right heart failure (either breathlessness with raised jugular venous pressure or pedal edema or both), of which 13 had only new pedal edema.

Conclusion: There is a definite progression of TR in patients with a pacing lead across the tricuspid valve (TV) associated with an increase in the incidence of right heart failure. Patients with a pacing lead across the TV should be followed closely for signs of right heart failure.

Keywords: pacemaker, tricuspid regurgitation, right heart failure

INTRODUCTION

With an ageing population and with improvements in technology and the changes to the indications for cardiac implantable electronic devices (CIED) including cardiac resynchronization therapy (CRT) and implantable cardiac defibrillators (ICDs), the rates of implantation of these devices are increasing.¹ There have been numerous studies to understand the effect of right ventricular (RV) pacing on left ventricular (LV) function and on the tricuspid valve (TV) itself.²⁻⁶ Most of these studies have demonstrated that the presence of a pacing lead across the TV either resulted in new tricuspid regurgitation (TR) or worsened preexisting TR.^{2,3} The underlying mechanism, however, is not clear as it has been demonstrated to be a late phenomenon and is not present immediately after CIED implantation.^{4,5} It has been suggested that valve damage during lead implantation might play an important role in future TR.^{6,7} Another hypothesis is that TR worsens due to a mechanical effect caused by the physical presence of the pacemaker electrode across the TV that interferes with the motion of the tricuspid leaflets and prevents closure.⁸ The pacemaker electrode may also induce fibrosis and affect the mobility of the leaflet.⁹ Another hypothesis is that this is due to the dyssynchrony induced by RV pacing,¹⁰ and the development of new TR corresponds to the level of ventricular pacing.¹¹⁻¹³ Others suggest that the pacemaker electrodes act as a nidus for the formation of microthrombi within the RV which leads to recurrent micro-pulmonary emboli that induces pulmonary hypertension which in turn causes TR.^{14,15}

The clinical effect of this mechanical TR is, however, uncertain, with some studies showing poor long-term prognosis.³ The aim of our study was to assess the incidence of new TR, or the worsening of preexisting TR in patients undergoing CIED implantation at our institution, and to study the factors affecting it. We also aimed to assess the clinical impact of this on new or worsening TR.

METHODS

This was a retrospective case-based study. From our records, we identified 131 patients who had CIED implantation between January 2011 and May 2018 at our institution. We then reviewed their electronic records and echocardiography reports. Patients were included in the study if they had a baseline echo and a

follow-up study after CIED implantation. Patients with either a dual or single chamber pacemaker were included. We excluded patients that did not have an echo either before or after the implant. We also excluded patients who were not followed up in the pacemaker clinic. A total of 65 patients (mean age 70 ± 13 years; 31 (48%) males) fulfilled our criteria and were included in the study.

At our institution, we do not implant ICDs or CRTs. Therefore, all the patients included in our study had permanent pacemakers (PPMs).

The echocardiograms were reviewed. The data regarding RV size, RV function in terms of the tricuspid annular plane systolic excursion (TAPSE), the grade of TR, and pulmonary artery pressure were noted.

TAPSE is a measurement of longitudinal systolic performance of the right ventricle. It is measured according to the American Society of Echocardiography recommendations.¹⁶ In the M-mode apical four-chamber view, an M-mode cursor was aligned along the RV free wall as perpendicular to the lateral tricuspid annulus as possible (and as parallel as possible to the movement of the TV annulus). The distance moved by the leading edge of the annulus from the end-diastole toward the apex at the end-systole is measured. The RV midcavity dimension was calculated in mid-diastole with a cursor drawn at the midpoint of the septum to the midpoint of the RV free wall in the apical four-chamber view.

TR was graded according to the European Society of Echocardiography Guidelines,¹⁷ which are 0 if absent, 1 for mild, 2 for moderate, and 3 for severe.

Clinical data regarding any symptoms and signs of heart failure were obtained from the electronic case records. The data was primarily collected by one of the authors but checked for consistency by a senior member of the team. A power calculation was not required, as this is a retrospective analysis of the outcomes of patients.

Ethical approval was obtained from the Ethics Committee of our institution before commencing this study.

The collected data were analyzed using statistical software SPSS Statistics (SPSS Inc., Chicago, US), version 22. A descriptive analysis of the categorical variables was presented as proportions, and continuous variables were presented as the mean and standard deviation. The Kolmogorov-Smirnov test

was used to assess normality. The Wilcoxon signed rank test and the paired t-test were used to study the pre- and post-associations. The Chi-square test, Student's t-test, and Mann-Whitney U test were used to assess other unpaired differences. Binary logistic regression was performed with the "development of new TR or worsening of preexisting TR" as the outcome measure, and demographic features, comorbidities, and type of pacemaker were used as input variables. These variables were chosen since they potentially affect TR. A value of $p < 0.05$ was considered significant.

RESULTS

We identified 131 patients who had a PPM implanted during the study period. Of these patients, only 65 met our inclusion criteria and were enrolled in the study. The excluded patients did not have an echocardiogram available either before or after PPM implantation or were not followed up in the outpatient clinic. Table 1 shows the basic demographic characteristics of the patients enrolled in the study.

The mean age of the study group was 70 ± 13 years, with 31 (48%) males and 34 (52%) females. The main

comorbidities were ischemic heart disease 9 (13%), chronic obstructive pulmonary disease (COPD) 7 (10%), hypertension 48 (73.8%), and diabetes 39 (60%). The indication for pacemaker implantation was complete heart block 36 (55%), sick sinus syndrome 28 (43%), and asystole 1 (2%). More than half the patients (35% or 54%) had a single chamber (ventricular) pacemaker, whereas the remaining had a dual-chamber pacemaker. The mean duration of follow up for the postimplant echo was 12 months. All patients had the ventricular lead placed in the RV apex. There were no septal or outflow tract lead placements.

Table 2 documents the changes in echocardiographic findings before and after pacemaker implantation. Before the pacemaker implantation, TR was present in 29 patients, with nine patients having grade 1, 17 patients having grade 2, and three patients having grade 3 TR. During follow up, the number of patients with TR increased to 51, with three patients having grade 1, 31 patients having grade 2, and 18 patients having grade 3 severity. This change was statistically significant ($p = 0.008$). The RV was normal (midRV dimension < 3.5 cm) in 60 patients at baseline but reduced to 54 patients during follow up. However, the mean RV size increased significantly from 2.94 ± 0.30 to 3.26 ± 0.44 cm ($p < 0.001$) during follow up. RV function, as measured by TAPSE, also fell from a preimplant TAPSE of 1.87 ± 0.44 to a postimplant TAPSE of 1.68 ± 0.42 ($p = 0.002$). There was a significant increase in the pulmonary artery (PA) pressure measured as the sum of the pressure gradient across the TV and the right atrial (RA) pressure (10 (5–12) mmHg vs. 30 (23–41) mmHg $p < 0.001$). There was a significant change in the grade of mitral regurgitation (MR) postpacemaker implantation. Sixteen (24%) patients had a worsening of MR by at least one grade ($p = 0.005$).

On follow up, clinical signs of presumed right heart failure were seen in 18 patients, with all having breathlessness, but pedal edema was seen only in 13 (20%) patients. All 18 patients with these symptoms had a worsening of preexisting TR.

When analyzed by binary logistic regression, no factors were identified that predicted the new onset of TR or the worsening of preexisting TR. Table 3 shows the difference between the patients who had a worsening of TR or the development of new TR with those in whom the severity of TR remained the same. The only factor that appeared to be statistically

Table 1. Baseline patient characteristics

Characteristic	Number n (%)
Age	70 ± 13
Sex	
Male	31 (48%)
Female	34 (52%)
Comorbidities	
IHD	9 (13%)
COPD	7 (10%)
Hypertension	48 (73.8%)
Diabetes	39 (60%)
Indication for pacemaker	
CHB	36 (55%)
SSS	28 (43%)
Asystole	1 (2%)
Type of device	
Single chamber	35 (54%)
Dual chamber	30 (46%)
Medications	
Beta-blockers	33 (50%)
ACE-inhibitors	27 (41%)
Statin	27 (41%)

IHD-ischemic heart disease; COPD-chronic obstructive pulmonary disease; CHB-complete heart block; SSS-sick sinus syndrome; ACE-angiotensin-converting enzyme

Figures are mean + standard deviation or number (%)

Table 2. Echo parameters before and after pacemaker implantation

	Prepacemaker (n = 65)	Postpacemaker (n = 65)	p-value
Presence of TR (n)	29	51	0.018
RV dilatation (n)	5	11	0.01
TAPSE (mm)	1.87 ± 0.44	1.68 ± 0.42	0.002
Presence of pedal edema (n)	5	13	0.01
TR grade			
0	36	14	
1	9	3	
2	17	31	0.008
3	3	17	
RV size	2.94 ± 0.30	3.26 ± 0.44	<0.001
PA pressure	10 (5–23)	30 (23–41)	<0.001
MR grade			
0	44 (67%)	40 (61%)	
1	8 (12%)	7 (11.5%)	
2	11 (16%)	11 (16%)	0.005
3	2 (3%)	7 (11.5%)	

TR-tricuspid regurgitation; TAPSE-tricuspid annular plane systolic excursion; RV-right ventricle; PA-pulmonary artery; MR-mitral regurgitation. Figures are number (%) or mean + standard deviation. The analysis was performed either by a paired sample t-test or Wilcoxon signed rank test.

Table 3. Characteristics of patients with and without worsening of TR

	No worsening of TR (n = 26)	Worsening of TR (n = 39)	p-value
Age (years)	70 ± 14	69 ± 13	0.97
Gender			
Male	11	20	
Female	15	19	0.47
Comorbidities			
IHD	5	4	0.24
COPD	3	4	0.72
Hypertension	18	30	0.50
Diabetes	12	27	0.06
Dyslipidemia	7	9	0.51
Atrial fibrillation	2	1	0.22
Indication			
Complete heart block	14	22	
Sick sinus syndrome	11	10	
Asystole	0	1	0.26
Bradycardia	1	6	
Type of pacemaker			
Single chamber	10	25	
Dual chamber	16	14	0.04
% pacing	99 (78–100)	95 (35–99)	0.153
Drugs			
Beta-blocker	13	20	0.91
ACE-inhibitors	9	18	0.64

TR-tricuspid regurgitation; IHD-ischemic heart disease; COPD-chronic obstructive pulmonary disease; ACE-angiotensin-converting enzyme. Analysis with Chi-square test, Students t-test, or Mann-Whitney U test as appropriate.

significant was whether the patient had a single or dual-chamber pacemaker; those with a dual-chamber pacemaker were less likely to have a worsening of their TR ($p = 0.04$). The use of beta-blockers or ACE-inhibitors did not affect either new-onset TR or the progression of preexisting TR.

DISCUSSION

The rate of implantations of CIED is increasing.¹ Although they are generally safe and potentially lifesaving procedures, their effect on the right ventricle is of concern. Despite a few studies to the contrary,^{18,19} many studies have demonstrated a worsening of TR or the development of new TR with the presence of a pacing lead across the TV.^{20,21} Our study is in keeping with existing literature. We found that the presence of a pacemaker lead across the TV led to the development of new TR or the worsening of preexisting TR. This was associated with an increase in RV size, a worsening of RV function, and an increase in PA pressure.

As mentioned earlier, many theories have attempted to explain this worsening of TR and have been extensively reviewed recently.²² The most likely explanation is the mechanical effect of the lead across the TV leading to mal-coaptation and interference with valve function. Fibrosis and adhesions along the path of the pacemaker lead, especially across the TV, also contribute to this valve dysfunction.²³ Postmortem studies have shown that this fibrosis, which is the body's reaction to the foreign body, can start as early as five days after implantation.²⁴ A series of 41 patients who had undergone surgery for TR after pacemaker implantation revealed that the TV was damaged more often than previously believed. Leaflet perforation, leaflet impingement, and leaflet adherence were noted.²⁵ Other studies had noted that when the distal lead was placed apically rather than at the septum, there was a higher chance of valve tethering.²⁶

The only factor in our study that appeared to predict worsening of TR was the presence of a single chamber pacemaker as opposed to a dual-chamber pacemaker. This may tie in with the theory that RV/LV dyssynchrony leads to LV dysfunction and MR, which in turn cause a secondary TR.²⁷⁻³⁰ However, both single and dual-chamber pacemakers would cause the same amount of RV/LV dyssynchrony, but the former might cause atrioventricular dyssynchrony. Our study also found a slight, but statistically significant, increase in the grade of MR.

It is well known that comorbidities, such as systemic hypertension and COPD, can elevate PA pressure, a common cause of TR, causing annulus enlargement. However, we did not find any correlation between any coexisting condition, including COPD, and the worsening of TR.

We also found a significant increase in the PA pressure with pacing, along with dilatation of the RV and RV dysfunction. It is difficult to know whether this is the cause or the effect of TR. It is likely a combination of both, whereby the pacing lead and the dyssynchronous pacing causes RV dysfunction and RV dilatation. This, along with the mechanical interference and/or associated fibrosis, leads to TR, thereby potentially setting up a vicious cycle that could lead to further RV dilatation and RV dysfunction.

There are no studies to assess the effect of medications, such as angiotensin-converting enzyme (ACE) inhibitors, on the development of TR in patients with pacemaker leads. Our study did not find any difference between patients on ACE-inhibitors or beta-blockers on the development of TR. However, randomized controlled trials are required to confirm or refute the hypothesis that these medications can alter the progression of TR.

The progression of TR in patients with intracardiac leads is not benign as in our study; all those who developed symptoms had a worsening of their TR or new TR. Therefore, additional studies are required to elucidate the long-term prognosis of these patients and the effect of medications as outlined above.

Our study has several strengths that set it apart from similar studies. It is the only study where RV function (TAPSE) and RV dimensions, along with clinical implications, are studied. No other previously reported studies, to the best of our knowledge, assess clinical findings. We included a complete data set on the subjects in the analysis. In addition, in our study, we looked at the effect of different medications on RV that was not performed in other studies.

Our study has a few limitations. First, the retrospective design of this study, as in other retrospective studies, is dependent on the quality of the data entered. Our sample size was small, as we only used patients with a complete data set. The clinical findings were documented during a clinic visit, and these were not documented by follow-up phone calls or further visits. The average interval between pacemaker implantation and the follow-up echo was approxi-

mately 12 months. This interval is longer than that of some other studies,²⁰ but perhaps it was not long enough to ascertain the true clinical effects of this pacemaker-induced TR.

CONCLUSION

CIED lead implantation worsens TR, increases PA pressure, causes RV dilatation, impairs RV function, and appears to worsen MR. These effects are probably induced by mechanical interference with the TV closure and are consistent regardless of the indication or degree of RV pacing. We recommend that patients with a CIED implant be closely monitored both clinically and by echocardiography to look for signs of right heart failure.

Declarations

Ethics approval and consent to participate- Ethical approval was obtained from the Medical Research Ethics Committee of the Sultan Qaboos University Hospital (MREC approval number 1415/16), and consent was not required as it was a retrospective analysis.

Consent for publication

Not applicable.

Availability of data and material

Data will be available at request.

Competing interests

Not applicable.

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Authors' contributions

SN- data analysis, manuscript writing, MMS- data collection. Manuscript editing, SJ- data collection, manuscript editing, MR- manuscript editing, data analysis, all authors have read and approved the manuscript.

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