Progressive Tricuspid Regurgitation and Elevated Tricuspid Regurgitation Pressure Gradient After Transvenous Permanent Pacemaker Implantation

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Abstract

Background

The association of post-implant tricuspid regurgitation (TR) and heart failure (HF) hospitalization in patients without HF and preexisting abnormal TR and TR pressure gradient (PG) remain unclear. This study aimed to explore the clinical outcomes about progressive post-implant TR after permanent pacemaker (PPM) implantation.

Methods

A total of 1,670 patients who underwent a single ventricular or dual-chamber transvenous PPM implantation at our hospital between January 2003 and December 2017 were included in the study. Patients with prior valvular surgery, heart failure (HF), and baseline abnormal TR and TRPG were excluded. Finally, a total of 1,075 patients were enrolled in this study. Progressive TR was defined as increased TR grade of ≥ 2 degrees and/or TRPG of >30 mmHg after implant.

Results

198 (18.4%) patients (group 1) experienced progressive post-implant TR and/or elevated TRPG. Group 1 had larger changes in post-implant TRPG (group 1 vs. group 2; 12.8 ± 9.6 mmHg vs. 1.1 ± 7.6 mmHg; $p < 0.001$) than group 2 without progressive post-implant TR. Group 1 had a higher incidence of HF hospitalization compared to group 2 (13.6% vs. 4.7%; $p < 0.001$). Pre-implant TRPG (HR: 1.075; 95% confidence interval (CI): 1.032-1.121; $p = 0.001$) and post-implant left atrial dimension (HR: 1.076; 95% CI: 1.038-1.114; $p < 0.001$) were independent predictors of progressive post-implant TR.

Conclusions

After a transvenous ventricular-based PPM implantation, 18.4% of patients experienced progressive post-implant TR and/or elevated TRPG. Higher pre-implant TRPG and larger post-implant LA dimension were independent predictors of progressive post-implant TR.

Background

In 1959, an endocardial transvenous lead was firstly introduced for permanent cardiac pacing, which has great benefits in reducing cardiac morbidity and mortality related to symptomatic bradycardia^{1,2}. However, the introduction of transvenous right ventricular pacing leads across the tricuspid valve can be associated with the development of tricuspid regurgitation (TR) and elevated tricuspid regurgitation pressure gradient (TRPG). Indeed, the prevalence of TR was increased in patients with transvenous permanent pacemaker (PPM) compared with the general population³. One previous report demonstrated that 21.2% of patients developed worsening TR degree after the transvenous lead implantation and a higher rate of worsening TR in patients with implantable cardioverter defibrillator (ICD) lead compared

with PPM ⁴. Another study showed that device type and number of leads placed did not affect the worsening degree of post-implant TR ⁵.

The underlying mechanisms of transvenous cardiac pacing-related TR is not fully understood. Several mechanisms have been proposed that included a mechanical effect of the lead interfering the motion of the tricuspid leaflets, RV pacing-induced desynchronization ^{6,7} and leads related tricuspid leaflet injury or perforation, entanglement, impingement, or adherence to the tricuspid valve ⁶. One study reported that worsening TR occurred only in the chronic phase over 2 years, whereas another study reported a temporal trend toward increasing TR both acutely and chronically over 4 years after cardiac devices implantation ^{5,8}. Therefore, the prevalence of increased degree of post-implant TR remains conflicting. Moreover, the association of post-implant TR and heart failure (HF) hospitalization in patients without HF and preexisting abnormal TR and abnormal TRPG remains unclear. Accordingly, we conducted this study to assess the prevalence of TR after cardiac device implantation and determine its clinical significance on HF hospitalization in a large retrospective cohort after transvenous ventricular-based PPM implantation.

Methods

Patient population

A total of 1,670 patients who underwent a single ventricular or dual-chamber transvenous PPM implantation at our hospital between January 2003 and December 2017 were included in this study. Patients with prior valvular surgery, HF and left ventricular ejection fraction (LVEF) < 50%, dilated cardiomyopathy, hypertrophic cardiomyopathy, and preexisting abnormal (mild-moderate, moderate or severe) TR and abnormal (> 30 mmHg) TRPG were excluded. Patients without follow-up records for PPM and without complete follow-up echocardiography were also excluded (Fig. 1). Finally, a total of 1,075 patients were enrolled in this study and were divided into two groups: group 1 consisted of 198 patients with increased degree of post-implant TR (≥ 2 degrees) and/or abnormal TRPG and group 2 consisted of 877 patients without increased degree of post-implant TR and abnormal TRPG.

Table 1
Baseline characteristics of the study patients

	Group 1 (N = 198)	Group 2 (N = 877)	P value
General demographics			
Age (years)	72.1 ± 9.4	71.9 ± 11.9	0.830
Female sex (%)	118 (59.6)	437 (49.8)	0.015
BMI (kg/m ²)	24.8 ± 3.9	25.0 ± 3.7	0.606
Risk factors			
Hypertension (%)	150 (75.8)	623 (71.0)	0.190
Diabetes mellitus (%)	68 (34.3)	299 (34.1)	0.934
Hyperlipidemia (%)	41 (20.7)	176 (20.1)	0.845
Prior stroke (%)	27 (13.6)	142 (16.2)	0.449
Atrial fibrillation (%)	74 (37.4)	249 (28.4)	0.016
ESRD (%)	15 (7.6)	41 (4.7)	0.110
PAOD (%)	5 (2.5)	18 (2.1)	0.595
CAD (%)	41 (20.7)	154 (17.6)	0.308
CKD stage > 3 (%)	45 (22.7)	189 (21.6)	0.704
Indication of PPM			0.022
Sick sinus syndrome	125 (63.1)	473 (53.9)	
AV block	73 (36.9)	404 (46.1)	
Lead position			0.474
Lower septum or apex (%)	56 (28.3)	225 (25.7)	
High septum or near RVOT region (%)	142 (71.7)	652 (74.3)	
Pacing QRS duration (msec)	152.7 ± 30.1	150.2 ± 28.1	0.305
> 150 msec (%)	109 (55.1)	451 (51.4)	0.387
Pacing percentage (%)	48.5 ± 43.4	53.9 ± 44.4	0.243
Data are expressed as mean ± standard deviation or as number (percentage).			
Abbreviation: BMI: body mass index; ESRD: end stage renal disease; CAD: coronary artery disease; PAOD: peripheral arterial occlusive disease; AV block: atrioventricular block; RVOT: right ventricular outflow tract; ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin receptor blocker.			

	Group 1 (N = 198)	Group 2 (N = 877)	P value
> 50%	51 (25.8)	214 (24.4)	0.715
Laboratory examination			
Creatinine (exclude ESRD) (mg/dL)	1.65 ± 1.12	1.50 ± 0.63	0.340
Medication			
ACEI/ARB use (%)	101 (51.3)	439 (50.9)	0.937
β-blocker use (%)	44 (22.3)	197 (22.8)	0.925
Data are expressed as mean ± standard deviation or as number (percentage).			
Abbreviation: BMI: body mass index; ESRD: end stage renal disease; CAD: coronary artery disease; PAOD: peripheral arterial occlusive disease; AV block: atrioventricular block; RVOT: right ventricular outflow tract; ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin receptor blocker.			

Table 2
Pre-implant and post-implant echocardiographic parameters of study patients

	Group 1 (N = 198)	Group 2 (N = 877)	P value
Pre-implant			
LA dimension (mm)	37.8 ± 6.6	36.7 ± 6.3	0.063
LVEDV (ml)	107.0 ± 31.9	106.9 ± 29.4	0.963
LVEF (%)	69.1 ± 9.0	69.7 ± 8.3	0.437
Average TRPG (mmHg)	23.1 ± 4.9	20.7 ± 6.1	< 0.001
The duration of follow-up (years)	4.7 (4.4–5.4)	4.5 (4.2–4.8)	0.610
Post-implant			
LA dimension (mm)	40.0 ± 6.4	37.2 ± 6.0	< 0.001
LVEDV (ml)	112.3 ± 41.8	111.0 ± 38.3	0.690
LVEF (%)	61.2 ± 13.2	64.2 ± 12.2	0.006
< 40%	13 (6.6)	26 (3.0)	0.020
TR grade			< 0.001
Severe (%)	21 (10.6)	0 (0)	
Moderate (%)	97 (49.0)	0 (0)	
Mild (%)	80 (40.4)	375 (42.8)	
Trivial or absence (%)	0 (0)	502 (57.2)	
Average TRPG (mmHg)	35.9 ± 9.1	21.8 ± 5.4	< 0.001
Categories of TRPG (%)			< 0.001
>55 mmHg	8 (4.0)	0 (0)	
55 – 40 mmHg	35 (17.7)	0 (0)	
40 – 30 mmHg	114 (57.6)	0 (0)	
<30 mmHg	41 (20.7)	0 (0)	
Changes in post-implant TRPG (mmHg)	12.8 ± 9.6	1.1 ± 7.6	< 0.001
Data are expressed as mean ± standard deviation or as number (percentage).			
Abbreviation: LA: left atrium; LVEDV: left ventricular end diastolic volume; LVEF: left ventricular ejection fraction; TRPG: tricuspid regurgitation pressure gradient.			

Table 3

Univariate and multivariate Cox regression analyses of predictors of progressive post-implant TR

Variables	Univariate analyses			Multivariate analysis		
	HR	95% CI	<i>p</i> value	HR	95% CI	<i>p</i> value
Female	1.485	1.086–2.031	0.013			
Age	1.001	0.988–1.015	0.830			
BMI	0.988	0.946–1.032	0.593			
Diabetes mellitus	1.011	0.731–1.399	0.947			
Hypertension	1.274	0.892–1.819	0.183			
CKD stage of > 3	1.071	0.740–1.549	0.717			
ESRD	1.671	0.906–3.084	0.100			
Atrial fibrillation	1.505	1.089–2.079	0.013			
Late-onset	1.179	0.533–2.606	0.685			
Coronary artery disease	1.226	0.834–1.802	0.300			
Pacing percentage	0.997	0.992–1.002	0.248			
> 50%	0.715	0.477–1.072	0.105			
Pacing QRS length	1.003	0.997–1.009	0.284			
> 150msec	1.172	0.845–1.626	0.342			
V lead position at the lower septum and apex	1.143	0.810–1.613	0.448			

Abbreviation: TR: tricuspid regurgitation; OR: odds ratio; CI: confidence interval; BMI: body mass index; CKD: chronic kidney disease; ESRD: end-stage renal disease; V: ventricular; LA: left atrium; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; TRPG: tricuspid regurgitation pressure gradient; ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin II receptor blocker.

	Univariate analyses		Multivariate analysis			
Pre-implant LA	1.026	1.000–1.054	0.054			
Pre-implant LVEDV	1.000	0.995–1.006	0.961			
Pre-implant LVEF	0.992	0.972–1.012	0.413			
Pre-implant TRPG	1.078	1.039–1.120	< 0.001	1.075	1.032–1.121	0.001
Post-implant LA	1.078	1.049–1.109	< 0.001	1.076	1.038–1.114	< 0.001
Post-implant LVEDV	1.001	0.997–1.005	0.677			
Post-implant LVEF	0.982	0.969–0.994	0.005			
Post-implant LVEF < 40%	2.300	1.160–4.560	0.017			
ACEI/ARB	1.016	0.746–1.385	0.919			
B-blocker	0.972	0.671–1.409	0.882			
Abbreviation: TR: tricuspid regurgitation; OR: odds ratio; CI: confidence interval; BMI: body mass index; CKD: chronic kidney disease; ESRD: end-stage renal disease; V: ventricular; LA: left atrium; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; TRPG: tricuspid regurgitation pressure gradient; ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin II receptor blocker.						

Table 4
Clinical outcomes of the study patients

	Group 1 (N = 198)	Group 2 (N = 877)	<i>P</i> value
Incidence of late-onset atrial fibrillation (%)	8 (6.5)	35 (5.6)	0.672
Incidence of HF hospitalization (%)	27 (13.6)	41 (4.7)	< 0.001
Incidence of sudden death or VTAs (%)	4 (2.1)	23 (2.6)	0.803
Incidence of cardiovascular mortality (%)	10 (5.7)	32 (4.1)	0.413
Incidence of all-cause mortality (%)	32 (16.2)	124 (14.1)	0.503
Data are expressed as number (percentage).			
Abbreviation: HF: heart failure; VTAs: ventricular tachyarrhythmias.			

Table 5
Univariate and multivariate Cox regression analyses of predictors of HF hospitalization

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	<i>p</i> value	HR	95% CI	<i>p</i> value
Female	0.951	0.591–1.530	0.836			
Age	1.061	1.032–1.091	< 0.001	1.073	1.037–1.110	< 0.001
BMI	1.145	1.082–1.211	< 0.001			
Diabetes mellitus	2.729	1.692–4.402	< 0.001			
Hypertension	1.588	0.882–2.859	0.123			
CKD stage of > 3	1.634	0.970–2.755	0.065	1.865	1.008–3.450	0.047
ESRD	1.292	0.405–4.119	0.665			
Atrial fibrillation	0.841	0.490–1.441	0.528			
Late-onset	0.976	0.303–3.138	0.967			
Coronary artery disease	2.773	1.685–4.562	< 0.001	1.790	0.986–3.251	0.056
Pacing percentage	1.003	0.994–1.012	0.476			
> 50%	1.363	0.618–3.002	0.443			
Pacing QRS length	1.013	1.004–1.013	0.008			
> 150msec	1.451	0.858–2.455	0.165			
V lead position at the lower septum and apex	1.812	1.107–2.968	0.018	1.713	0.952–3.082	0.072

Abbreviation: HF: heart failure; HR: hazard ratio; CI: confidence interval; BMI: body mass index; CKD: chronic kidney disease; ESRD: end-stage renal disease; V: ventricular; LA: left atrium; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; TRPG: tricuspid regurgitation pressure gradient; ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin II receptor blocker.

	Univariate analysis			Multivariate analysis		
Pre-implant LA	1.063	1.024– 1.102	0.001			
Pre-implant LVEDV	1.010	1.002– 1.017	0.014			
Pre-implant LVEF	0.971	0.945– 0.999	0.042			
Pre-implant TRPG	1.020	0.968– 1.075	0.448			
Post-implant LA	1.070	1.030– 1.111	< 0.001			
Post-implant LVEDV	1.017	1.013– 1.021	< 0.001	1.010	1.004– 1.017	0.001
Post-implant LVEF	0.923	0.907– 0.940	< 0.001	0.957	0.934– 0.980	< 0.001
Post-implant LVEF < 40%	13.045	7.662– 22.209	< 0.001			
Progressive post-implant TR	2.459	1.511– 4.000	< 0.001	1.694	0.959– 2.994	0.070
ACEI/ARB	1.600	0.975– 2.625	0.063			
B-blocker	1.329	0.781– 2.260	0.294			
Abbreviation: HF: heart failure; HR: hazard ratio; CI: confidence interval; BMI: body mass index; CKD: chronic kidney disease; ESRD: end-stage renal disease; V: ventricular; LA: left atrium; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; TRPG: tricuspid regurgitation pressure gradient; ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin II receptor blocker.						

Patients with dual-chamber PPM implantation underwent pacing in the dual chamber rate-adaptive mode, whereas patients with single ventricular PPM implantation underwent pacing in the ventricular-inhibited rate-adaptive mode. General demographics, comorbidities, lead positions, pacing QRS durations, pacing percentages, echocardiographic parameters, HF hospitalization, and cardiovascular and all-cause mortality were compared between the groups.

Baseline electrocardiographic (ECG) and echocardiographic parameters were obtained at nearest to the implant date. After implantation, pacing-lead locations were determined using anteroposterior, right-oblique, and left-oblique views under fluoroscopy. The pacing QRS duration was measured from the surface 12-lead ECG within 3 days after PPM implantation. Patients visited the outpatient department at regular intervals (3–6 months). PPM records were obtained at regular intervals, and the ventricular pacing percentage was obtained by telemetry.

Ethical statement

This study conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved for human research by the institutional review committee of Kaohsiung Chang Gung Memorial Hospital. All patients were informed to enroll our PPM registry when PPM implantation and did not need informed consent due to the retrospective study.

Echocardiography

Echocardiographic parameters, including left atrial (LA) dimension, LVEF, LV end-diastolic volume (LVEDV), and TR grade/TRPG, were measured using GE Vivid 9 or Philips IE33. LVEF and LVEDV were quantified by the M-mode and corrected by the two-dimensional guided biplane Simpson's method of disc measurements. Baseline echocardiography was performed before implantation. Follow-up echocardiography was performed at 2-year intervals thereafter in the absence of clinical events or at the onset of HF.

Definition

Progressive TR was defined as increased TR grade of ≥ 2 degrees and/or TRPG of >30 mmHg after implant, and TRPG of >30 mmHg was suggestive of possible pulmonary hypertension⁹. Moderate TR (grade III) was defined as a regurgitant jet extending to less than half of the right atrium, whereas severe TR (grade IV) as a jet extending to more than half of the length of the right atrium¹⁰. HF hospitalization was defined as the occurrence of HF events according to a New York Heart Association functional class of III or IV in the absence of other alternative diagnoses. HF symptoms were classified as the New York Heart Association functional class II-IV required medical treatment. Cardiovascular mortality was defined as sudden death related to arrhythmias, HF, and myocardial infarction. All-cause mortality was defined as death related to any cause, such as sudden death with undefined reasons, natural course, sepsis, malignancy, and cardiovascular disease.

Study end-points

The primary study endpoint was TR progression (TR grade ≥ 3) and/or abnormal TRPG levels (PG >30 mmHg). The secondary study end-points were late-onset atrial fibrillation, HF hospitalization, sudden death or ventricular tachyarrhythmias, cardiovascular mortality, and all-cause mortality.

Statistical analysis

Data are presented as mean $\pm$ standard deviation or numbers (percentages). Clinical characteristics of the study groups were compared using the *t*-test for continuous variables and Chi-square test for categorical variables. Kaplan-Meier curve analysis was performed with the log-rank test for HF hospitalization and progressive TR in both groups during the follow-up period. Univariate and multivariate Cox regression analyses for HF hospitalization and progressive TR were performed to determine significant determinants. Multivariate Cox regression analysis included a hazard ratio (HR) < 0.100 for HF

hospitalization and progressive TR in univariate Cox regression analyses. Statistical analysis was performed using statistical software (SPSS for Windows, Version 22), and a two-sided p -value of <0.05 indicated statistical significance.

Results

Baseline characteristics of the study patients

Baseline characteristics of the study participants are listed in Table 1. During a median 4.9 (4.7-5.1) years follow-up, 198 (18.4 %) patients (group 1, mean age 72.1 ± 9 years; 59.6% female) experienced progressive post-implant TR, whereas 877 patients (group 2, mean age 71.9 ± 12 years; 49.8% female) did not have progressive post-implant TR. The percentage of female individuals was higher in group 1 than group 2. Additionally, the prevalence of atrial fibrillation (paroxysmal or non-paroxysmal) was also higher in group 1. A higher percentage of sick sinus syndrome for PPM was noted in group 1 (group 1 vs. group 2; 63.1% vs. 53.9%; $p=0.022$). There was no difference in the distribution of ventricular lead position, pacing QRS duration, ventricular pacing percentage, serum creatinine level and medication used between the 2 groups.

Pre-implant and post-implant echocardiographic parameters of study patients

At pre-implant, group 1 had significantly larger LA dimension (group 1 vs. group 2; 37.8 ± 6.6 mm vs. 36.7 ± 6.3 mm; $p = 0.063$) and significantly higher average TRPG (group 1 vs. group 2; 23.1 ± 4.9 mmHg vs. 20.7 ± 6.1 mmHg; $p < 0.001$) than group 1 (Table 2). The two groups did not differ in LVEDV and LVEF.

The median follow-up period was similar between the two groups (group 1 vs. group 2; 4.7 (4.4-5.4) years vs. 4.5 (4.2-4.8) years; $p = 0.610$). At post-implant, group 1 had significantly larger LA dimension, lower LVEF and more severe TR grade than group 2. Additionally, group 1 had significantly higher post-implant TRPG (group 1 vs. group 2; 35.9 ± 9.1 mmHg vs. 21.8 ± 5.4 mmHg; $p < 0.001$) and larger changes in post-implant TRPG (group 1 vs. group 2; 12.8 ± 9.6 mmHg vs. 1.1 ± 7.6 mmHg; $p < 0.001$) than group 2. Figure 2 showed the changes in pre-implant and post-implant TRPG in group 1 ($p < 0.001$).

Figure 3 shows the cumulative incident rate of progressive TR grade and/or abnormal TRPG from 1.3% in the first year to 18.4% in the sixth year in the study cohort.

Univariate and multivariate Cox regression analyses of predictors of progressive post-implant TR

Female gender, higher pre-implant TRPG, larger post-implant LA dimension, lower post-implant LVEF and post-implant LVEF <40 were significant predictors of progressive post-implant TR (Table 3). However, only pre-implant TRPG (HR: 1.075; 95% confidence interval (CI): 1.032-1.121; $p = 0.001$) and post-implant LA dimension (HR: 1.076; 95% CI: 1.038-1.114; $p < 0.001$) were independent predictors of progressive post-implant TR (Table 3).

Clinical outcomes of the study patients

During the follow-up period, group 1 had a significantly higher incidence of HF hospitalization compared to group 2 (13.6% vs. 4.7%; $p < 0.001$) (Table 4 and Figure 4). However, the incidence of late-onset atrial fibrillation, sudden death or ventricular tachyarrhythmias, cardiovascular mortality, and all-cause mortality did not differ between the two groups (Table 4).

Univariate and multivariate Cox regression analyses of predictors of HF hospitalization

By univariate Cox regression analyses, older age, high body mass index, diabetes mellitus (DM), coronary artery disease (CAD), longer pacing QRS length, ventricular lead position at the lower septum and apex, larger pre-implant LA dimension, larger pre-implant LVEDV, larger post-implant LA dimension, larger post-implant LVEDV, lower post-implant LVEF, post-implant LVEF $< 40\%$, and progressive post-implant TR were significant predictors of HF hospitalization (Table 5). However, by multivariate Cox regression analyses, only older age (HR: 1.073; 95% CI: 1.037-1.110; $p < 0.001$), CKD stage of > 3 (moderate to severe CKD) (HR: 1.865; 95% CI: 1.008-3.450; $p = 0.047$), and larger post-implant LVEDV (HR: 1.010; 95% CI: 1.004-1.017; $p = 0.001$) were independently associated with HF hospitalization. Post-implant LVEF (HR: 0.957; 95% CI: 0.934-0.980; $p < 0.001$) was independently inversely associated with HF hospitalization. Progressive post-implant TR (HR: 1.694; 95% CI: 0.959-2.994; $p = 0.070$) had a non-significant trend toward HF hospitalization.

Discussion

In the present study, the cumulative rate of progressive TR ranged from 1.3% in the first year to 18.4% in the sixth year. Higher pre-implant TRPG and larger post-implant LA dimension were positively associated with progressive post-implant TR, which was associated with a trend toward HF hospitalization.

TR occurs mainly due to annular dilation and right ventricular enlargement, often secondary to LV dysfunction from myocardial or valvular causes, right ventricular volume and pressure overload, and cardiac chamber dilations¹¹. Lead-related TR is an underdetermined problem and may be caused by lead-related tricuspid leaflet injury or perforation or lead entanglement, impingement, or adherence to the tricuspid valve⁶. However, lead-related tricuspid valve injury could not be fully detected and was only observed in 12% of patients with PPM-related severe TR by transthoracic echocardiography⁶. Kim et al. reported that abnormal TR developed in 21.2%, worsened TR by ≥ 1 grade in 24.2%, and progressed to severe TR in 3.9% of patients with initially normal TR⁴. However, Al-Bawardy et al. reported a small but significant increase in the prevalence of moderate and severe TR, both acutely and chronically after a cardiac device implantation⁵. Arabi et al. reported that TR was worsened by 1 grade in 70.8% and 2 grades in 17.1% of patients, and 19.5% of patients without baseline TR developed new-onset TR after the lead implantation in the follow-up period¹². In this study, the cumulative rate of progressive post-implant TR (increased TR grade of ≥ 2 degrees and/or TRPG of > 30 mmHg) was from 1.3% in the first year to 18.4% in the sixth year. Moreover, higher pre-implant TRPG and larger post-implant LA dimension were independent predictors of progressive post-implant TR. Pacing-induced electrical and mechanical dyssynchrony of LV can also result in TR and MR¹³. However, in this study, pacing percentage and

pacing QRS length was not associated with the development of progressive post-implant TR. In this study, larger post-implant LA size was an independent predictor of progressive post-implant TR. Our previous study showed that right and left atrial sizes were larger in patients with atrioventricular dyssynchrony after pacing¹⁴. Atrial enlargement is a well known predictor of atrial fibrillation. Utsunomiya et al reported that functional TR with a structurally normal tricuspid valve may occur secondary to chronic atrial fibrillation and is associated with advanced age and right atrial enlargement¹⁵.

In one small retrospective cohort study, significant lead-induced TR was associated with a significantly increased incidence of all-cause mortality and HF events in patients after PPM implantation¹⁶. Other studies also reported post-implant TR to be an independent risk factor for late death^{5,13}. However, a significant proportion of patients in previous studies included patients with HF and receiving ICD and cardiac resynchronization therapy (CRT). Patients with ICDs and/or CRT devices usually have poor LVEF and advanced HF and consequently, higher incident HF hospitalization and mortality. In our study, we only enrolled patients receiving PPM implantation and excluded patients receiving ICD or CRT and those with prior history of HF, valvular heart disease and preexisting abnormal (mild-moderate, moderate or severe) TR and abnormal (>30 mmHg) TRPG. In this large cohort study, progressive post-implant TR was significantly associated with HF hospitalization in univariate analysis and was associated with a non-significant trend toward HF hospitalization ($p = 0.070$) in multivariate analysis (Table 5), and progressive post-implant TR was not associated with cardiovascular and all-cause mortality. Therefore, patients with preserved LV function and without valve disease underwent transvenous ventricular-based pacemaker implantation should have baseline echocardiography evaluation before implant and those with higher pre-implant TRPG should have more vigorously echocardiographic follow-up for the development of progressive post-implant TR.

Study Limitations

One limitation of this study is its retrospective nature, including data from only one medical center. Because of older age, the all-cause mortality rate was relatively high in this study. Another limitation was the absence of baseline and follow-up right heart size and function by echocardiography. However, we still provided important information about lead-related post-implant TR progression and its associated outcomes in patients with transvenous ventricular-based PPM.

Conclusions

After a transvenous ventricular-based PPM implantation, 18.4% of patients experienced progressive post-implant TR and/or elevated TRPG. Patients with progressive post-implant TR had a higher incidence of HF hospitalization. Higher pre-implant TRPG and larger post-implant LA dimension were independent predictors of progressive post-implant TR.

Abbreviations

TR

tricuspid regurgitation; TRPG:tricuspid regurgitation pressure gradient; PPM:permanent pacemaker; ICD:implantable cardioverter defibrillator; HF:heart failure; LVEF:left ventricular ejection fraction; ECG:electrocardiographic; LA:left atrial; LVEDV:LV end-diastolic volume; DM:diabetes mellitus; CAD:coronary artery disease; CRT:cardiac resynchronization therapy.

Declarations

Ethics approval and consent to participate

All procedures were following the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later revisions. This study was already approved for human research by the institutional review committee of Kaohsiung Chang Gung Memorial Hospital and did not need informed consent due to the retrospective study.

Consent for publication

All authors agree with this publication.

Availability of data and material

The data was available when request to corresponding author.

Competing interests

None

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None

Authors' contributions

Data curation, HC Chen and HY Fang; formal analysis, WC Lee; investigation, WC Lee; methodology, WC Lee; project administration, WC Lee; resources, YL Chen, TH Tsai, KL Pan, YS Lin, WH Liu, MC Chen; supervision, MC Chen; validation, WC Lee; visualization, WC Lee; writing original draft, WC Lee; writing, reviewing and editing, MC Chen. All authors have read and approved the manuscript.

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Figures

Figure 1

Flowchart of the study enrollment. Abbreviations: HF: heart failure; LVEF: left ventricular ejection fraction; DCM: dilated cardiomyopathy; TR: tricuspid regurgitation; TRPG: tricuspid regurgitation pressure gradient; TV: tricuspid valve.

The change of TRPG

Figure 2

Changes of the tricuspid regurgitation pressure gradient in group 1. In group 1, the post-implant TRPG was significantly higher than pre-implant TRPG ($p < 0.001$).

Figure 3

The cumulative incident rate of progressive post-implant tricuspid regurgitation. The cumulative rate of progressive post-implant TR increased from 1.3% in the first year to 18.4% in the sixth year.

HF hospitalization

Number at risk

Group: 1

198 190 179 162 147 128

Group: 2

877 776 707 586 481 377

Figure 4

A Kaplan-Meier curve analysis for heart failure hospitalization. Group 1 (with progressive post-implant tricuspid regurgitation and/or elevated tricuspid regurgitation pressure gradient) had a significantly higher incidence of heart failure hospitalization compared to group 2 (without progressive post-implant tricuspid regurgitation and/or elevated tricuspid regurgitation pressure gradient) (log-rank $P < 0.001$).