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Clinical Research

Prospective Study of Tricuspid Regurgitation Associated With Permanent Leads After Cardiac Rhythm Device Implantation

Caroline M. Van De Heyning, MD, PhD,[a] Esam Elbarasi, MD,[b] Simona Masiero, MD,[c] Michela Brambatti, MD,[d] Sami Ghazal, MD,[b] Said Al-Maashani, MD,[b] Alessandro Capucci, MD,[c] Darryl Leong, MD, PhD,[b] Bharati Shivalkar, MD, PhD,[a] Johan B. Saenen, MD, PhD,[a] Hielko P. Miljoen, MD,[a] Carlos A. Morillo, MD,[b] Syamkumar Divarakarmenon, MD, MSc,[b] Guy Amit, MD,[b] Sebastian Ribas, MD,[b] Erika Baiocco, MD,[c] Alessandro Maolo, MD,[c] Andrea Romandini, MD,[c] Simone Maffei, MD,[c] Stuart J. Connolly, MD,[b] Jeff S. Healey, MD, MSc,[b] and Hisham Dokainish, MD[b]

[a] *Department of Cardiology, Antwerp University Hospital, Edegem, Belgium*

[b] *Department of Cardiology, McMaster University, Hamilton, Ontario, Canada*

[c] *Department of Cardiology, Università Politecnica delle Marche, Ancona, Italy*

[d] *Division of Cardiology, University of California, San Diego, San Diego, California, USA*

ABSTRACT

Background: Tricuspid regurgitation (TR) has been associated with cardiac rhythm device (CRD) implantation with intracardiac lead insertion. However, data on the incidence of postdevice TR are limited and largely from retrospective studies. We hypothesized that permanent lead implantation would be associated with an increase in TR.

Methods: We prospectively included consecutive patients with a clinical indication for CRD. Patients underwent transthoracic echocardiography 1 month before and 1 year after CRD implantation.

Results: A total of 328 patients were prospectively enrolled (69 ± 15 years, 38% female). Echocardiograms before and 1 year after CRD were available in 290 patients (15 died, 23 lost to follow-up). Compared with baseline, there was a significant change in TR grade 1 year after CRD insertion (no/trivial TR: 66% vs 29%; mild TR: 29% vs

RÉSUMÉ

Introduction : La régurgitation tricuspidienne (RT) a été associée à l'implantation d'un dispositif cardiaque (DC) muni d'une sonde intracardiaque. Toutefois, les données sur l'incidence de la RT après l'implantation du dispositif sont limitées et proviennent en grande partie des études rétrospectives. Nous avons posé l'hypothèse que l'implantation d'une sonde permanente serait associée à une augmentation de la RT.

Méthodes : Nous avons inclus de manière prospective les patients consécutifs chez qui un DC était indiqué sur le plan clinique. Les patients ont subi une échocardiographie transthoracique 1 mois avant et 1 an après l'implantation du DC.

Résultats : Un total de 328 patients ont été inscrits de manière prospective (69 ± 15 ans, 38 % de femmes). Les échocardiogrammes de

Trace or mild tricuspid regurgitation (TR) is a common finding on transthoracic echocardiography and unlikely to be clinically relevant; however, moderate or severe TR is more likely to be clinically relevant and may be associated with reduced long-term survival.[1,2] In retrospective studies, cardiac rhythm device (CRD) implantation using an endocardial lead was associated with a 10% to 35% incidence of progression to moderate or severe TR.[3-7] A retrospective study by our group[8] reported a progression to moderate or severe TR of 11% after permanent endocardial lead implantation, whereas cardiac resynchronization therapy appeared to prevent this progression. A few small prospective studies (the largest included 61 patients) reported a lower but variable progression to moderate or severe TR (0% to 10%).[9-11] Therefore, there is uncertainty as to the presence and magnitude of a possible

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Corresponding author: Dr Hisham Dokainish, Department of Cardiology, McMaster University, 237 Barton St. E., CVSRI #C3 111, Hamilton, Ontario L8L 2X2, Canada. Tel.: +1-905-527-4322; fax: +1-905-577-1474.
E-mail: Hisham.Dokainish@phri.ca

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61%; moderate TR: 3% vs 8%; severe TR 2% vs 2%; $P < 0.001$ for an increase in TR by at least 1 grade). Compared with baseline, there was a higher prevalence of moderate or severe TR in the 247 patients with CRD without cardiac resynchronization therapy (4% vs 10%, $P = 0.004$), but no progression in the 43 patients who received cardiac resynchronization therapy (14% vs 11%, $P = 1$). Multivariable analysis in the patients with less than moderate TR at baseline (n = 274) showed that only a history of atrial fibrillation was independently associated with progression to moderate or severe TR after correction for baseline TR grade ($P = 0.013$).

Conclusions: One year after endocardial lead insertion, there was a 5% increase in the prevalence of moderate or severe TR, which may be clinically relevant.

290 patients (15 sont morts, 23 ont été perdus de vue au cours du suivi) 1 mois avant et 1 an après l'implantation du DC étaient disponibles. Comparativement au début, nous avons observé un changement important dans le degré de RT 1 an après l'insertion du DC (aucune RT/RT insignifiantes : 66 % *vs* 29 %; RT minimes : 29 % *vs* 61 %; RT modérées : 3 % *vs* 8 %; RT importantes : 2 % *vs* 2 %; $P <$ 0,001 pour une augmentation de la RT d'au moins 1 degré). Comparativement au début, nous avons observé une prévalence de la RT modérée ou importante chez les 247 patients porteurs d'un DC sans thérapie de resynchronisation cardiaque (4 % *vs* 10 %, $P = 0{,}004$), mais aucune progression chez les 43 patients qui recevaient une thérapie de resynchronisation cardiaque (14 % *vs* 11 %, $P = 1$). L'analyse multivariable chez les patients qui avaient au début un degré inférieur à la RT modérée (n = 274) montrait que seuls des antécédents de fibrillation auriculaire étaient indépendamment associés à la progression de la RT modérée ou importante après la correction du degré initial de RT ($P = 0{,}013$).

Conclusions : Un an après l'insertion de la sonde endocardique, nous avons observé une augmentation de 5 % dans la prévalence de RT modérée ou importante, à savoir une augmentation qui peut être pertinente sur le plan clinique.

association of moderate or severe TR with endocardial lead insertion. In the present era of expanding indications of CRDs and the recent development of leadless and subcutaneous devices, a better understanding of the incidence and clinical relevance of lead-associated TR is needed.[12] We therefore performed a prospective study in which we hypothesized that CRD implantation would increase TR severity.

Material and Methods

The background, rationale, and design of this study have been previously published,[13] and are summarized below.

Study design

After informed consent, we prospectively included 328 consecutive patients aged 18 years and above with a clinical indication for CRD at 3 centres (Centre 1: McMaster University, Hamilton, Canada, n = 126; Centre 2: University Hospital of Antwerp, Edegem, Belgium, n = 100; Centre 3: Università Politecnica delle Marche, Ancona, Italy, n = 102) between March 2014 and April 2015. Patients with previous endocardial leads and patients with congenital heart disease were excluded. Eligible patients were scheduled for a comprehensive transthoracic echocardiography 1 month before and 1 year after CRD implantation.

The study complied with the Declaration of Helsinki[14] and was approved by the ethics committees of all 3 centres.

Echocardiography

A comprehensive 2-dimensional transthoracic echocardiography was performed at rest in the left lateral supine position using a Vivid 7 cardiovascular ultrasound system equipped with an M5S transducer (GE Healthcare, Milwaukee, WI). All echocardiographic studies were sent to the core echocardiography laboratory at the Population Health Research Institute (McMaster University, Hamilton, Canada) for central analysis by 2 experienced echocardiographers blinded to all clinical and CRD-related data. Conventional B-mode, colour Doppler, pulsed, and continuous wave Doppler images were acquired in still or cine format using electrocardiogram gating. All measurements were averaged over 3 consecutive cardiac cycles for patients in sinus rhythm and over 5 cycles for patients with atrial fibrillation. End-systolic and end-diastolic left ventricular (LV) diameters were measured with M-mode in the parasternal long-axis view according to current recommendations.[15] LV volumes and LV ejection fraction (LVEF) were quantified by the modified Simpson's method in the apical 4- and 2-chamber view. The left atrial volume was obtained by the area-length method and indexed for the body surface area. TR severity was graded qualitatively using a multi-integrative approach, by current guidelines, and was classified into 4 categories by consensus of the 2 readers: none or trivial ("physiological TR"), mild, moderate, or severe.[16] Right ventricular dimension was measured at the base at end diastole in a right ventricle-focused apical 4-chamber view. Right ventricular function was assessed by the measurement of tricuspid annular plane systolic excursion using M-mode. The transtricuspid pressure gradient was measured by continuous wave Doppler of the regurgitant tricuspid jet in the apical 4-chamber view. The right ventricular systolic pressure was calculated as the sum of the maximal transtricuspid pressure gradient and an estimate of the right atrial pressure based on inferior caval vein dimension and collapsibility.[17]

Statistical analysis

Results are reported as mean ± standard deviation or percentages unless otherwise specified.

The change in the prevalence of moderate or severe TR before and 1 year after CRD insertion was analysed using the McNemar test. Differences before and 1 year after CRD, and between patients with and without progression towards moderate or severe TR, were evaluated with the χ^2 test for categorical data, with the Student *t*-test for normally

Table 1. Baseline demographic and clinical factors in the study cohort

Variable (mean ± SD or %, N = 328)	
Age (y)	69 ± 15
Female	123 (38%)
Body mass index (kg/m^2)	28 ± 6
Hypertension	230 (70%)
Diabetes	84 (26%)
Smoking (past or current)	117 (35%)
Dyslipidemia	188 (57%)
History of prior myocardial infarction	94 (29%)
Prior revascularization (percutaneous or surgical)	98 (30%)
Prior aortic valve surgery	26 (8%)
Prior mitral valve surgery	12 (4%)
Prior tricuspid valve surgery	3 (1%)
New York Heart Association Class	
1	145 (44%)
2	116 (36%)
3	60 (18%)
4	7 (2%)
Heart rate (beats per minute)	63 ± 19
Systolic blood pressure (mm Hg)	133 ± 23
Diastolic blood pressure (mm Hg)	72 ± 12
Preprocedure electrocardiogram	
Sinus rhythm	231 (71%)
Atrial fibrillation or flutter	54 (16%)
Complete heart block	43 (13%)
Permanent pacemaker	174
Atrioventricular-node disease	119 (69%)
Sick sinus syndrome	51 (29%)
Other	4 (2%)
Implantable cardiac defibrillator	107
Primary prevention	47 (44%)
Secondary prevention	60 (56%)
Cardiac resynchronization therapy devices	47
Tricuspid regurgitation	
None/trivial	213 (65%)
Mild	94 (28%)
Moderate	12 (4%)
Severe	9 (3%)

Data are expressed as means ± standard deviation (SD) for continuous variables or as percentages for dichotomous variables.

distributed continuous data, and with the Mann-Whitney *U* test for non-normally distributed continuous data. Binary logistic regression analysis was performed to identify predictors of progression to moderate or severe TR. Subgroup analysis was performed for patients with and without cardiac resynchronization therapy. Statistical significance was set at a 2-tailed probability of $P < 0.05$. Patients who did not complete 1-year follow-up were excluded from further analysis. All statistical analyses were performed with IBM SPSS Statistics for Windows version 23.0 (IBM Corp, Armonk, NY).

Results

Study population

The mean age of the study population at baseline (n = 328) was 69 ± 15 years, 123 (38%) were female, with 94 (29%) having prior myocardial infarction, and 41 (13%) having prior valve surgery. A total of 174 patients (54%) underwent permanent pacemaker insertion, 107 (32%) implantable cardiac defibrillator implantation, and 47 (14%) underwent cardiac resynchronization therapy. Baseline demographic and clinical data are summarized in Table 1. Echocardiograms before and 1 year after CRD were available in 290 patients (15 patients died, and 23 patients were alive but were lost to follow-up; these 38 patients were excluded from further analysis). Time between CRD implantation and follow-up echocardiogram was 11 ± 2 months.

Echocardiographic variables before and 1 year after CRD insertion

There was an increase in TR grade from baseline to 1 year after CRD insertion. At baseline, 191 of 290 (66%) patients had none/trivial TR, decreasing to 83 of 290 (29%) at 1 year; mild TR was seen in 83 (29%) patients increasing to 177 (61%); moderate TR was observed in 9 (3%) patients increasing to 23 (8%); and severe TR was seen in 7 (2%) with no change at 1 year ($P < 0.001$ for increase in TR by at least 1 grade) (Table 2). This increase in TR grade was largely explained by progression from none/trivial TR to mild TR (Fig. 1). Five percent of patients had moderate or severe TR at baseline, which significantly increased to 10% one year after device insertion (absolute change = 5%; relative change = 88%; $P < 0.009$). Compared with baseline, there was a higher prevalence of moderate or severe TR after device implantation in the 247 patients with a pacemaker or implantable cardiac defibrillator without cardiac resynchronization therapy (4% vs 10%, $P = 0.004$) (Table 3). In contrast, there was no progression to moderate or severe TR in 43 patients who received cardiac resynchronization therapy (14% vs 11%, $P = 1$) (Table 4).

Among the 274 patients who had less than moderate TR at baseline, 20 (7%) progressed to moderate or severe TR. Of these patients, 25% had no or trivial TR at baseline, whereas 75% had mild TR before device implantation. Patients with mild or less TR at baseline who progressed to moderate or severe TR after 1 year were older, more often had a history of atrial fibrillation, had a larger left atrial volume index, and had higher right ventricular systolic pressures at baseline (Table 5). Sex, arterial hypertension, diabetes, LVEF, percentage of right ventricular pacing, and parameters of right ventricular function and dimension were not associated with progression towards significant TR. In multivariable analysis in this group, including history of atrial fibrillation, indexed left atrial volume and right ventricular systolic pressures, and after correction for baseline TR grade (mild vs none/trivial), only a history of atrial fibrillation was independently associated with progression to moderate or severe TR ($P = 0.013$). Interestingly, 6 of 16 patients with at least moderate TR at baseline had a decrease towards mild (n = 5) or no/trivial TR (n = 1) after 1 year.

There was a significant improvement in LVEF in patients with cardiac resynchronization therapy ($P < 0.001$), in contrast to patients without cardiac resynchronization therapy in whom a decrease of LVEF was noted ($P = 0.007$). In both groups, there was no difference before compared with 1 year after device implantation in right ventricular function as assessed by tricuspid annular plane systolic excursion.

Discussion

Our study is the largest prospective study to date assessing the impact of permanent endocardial lead implantation on TR severity. We observed a significant increase in TR grade at 1 year after CRD, largely explained by progression to mild TR,

Table 2. Echocardiographic variables before and 1 year after device implantation

Variable (mean ± SD or %, N = 290)	Baseline	1 year	*P* value
Left ventricular ejection fraction (%)	49 ± 16	49 ± 13	0.671
Left atrial volume index (mL/m^2)	39 ± 17	39 ± 15	0.577
Right ventricular diastolic diameter (cm)	3.7 ± 0.6	3.6 ± 0.6	0.002
Tricuspid annular plane systolic excursion (cm)	1.9 ± 0.4	1.9 ± 0.4	0.836
Right ventricular systolic pressure (mm Hg)	35 ± 13	31 ± 10	< 0.001
Tricuspid regurgitation			< 0.001
None/trivial	191 (66%)	83 (29%)	
Mild	83 (29%)	177 (61%)	
Moderate	9 (3%)	23 (8%)	
Severe	7 (2%)	7 (2%)	

Data are expressed as means ± standard deviation (SD) for continuous variables or as percentages for dichotomous variables.

and unlikely to be clinically important. However, 7% of patients with baseline less than moderate TR progressed to moderate or severe TR, which may be clinically relevant. This proportion is lower than that previously reported in retrospective studies. Cardiac resynchronization therapy may prevent significant TR progression. Progression towards moderate or severe TR was independently associated with a history of atrial fibrillation.

The absolute change in the prevalence of moderate or severe TR in our study was 5%, which is lower than that reported by several recent retrospective studies. Studies by Höke et al.[3] (n = 239) and Fanari et al.[5] (n = 206) showed an increase in moderate or severe TR after CRD implantation in 35% and 20% of patients, respectively. Lee et al.[4] (n = 328) observed an increase in TR severity of 2 grades in 10% of their study population. Likewise, a small prospective study by Kucukarslan et al.[10] (n = 61) reported a 5% increase in prevalence of moderate or severe TR, whereas another smaller prospective study by Leibowitz et al.[9] (n = 35) found no progression of TR after CRD insertion. Although these small prospective studies might have been underpowered to detect TR worsening, the prior larger retrospective studies might have overestimated increases in TR because of selection bias. That is, echocardiography may have been more likely to be performed in patients after CRD who presented with clinical symptoms or signs of heart failure and/or tricuspid valve dysfunction.

Several studies have endeavoured to identify risk factors of TR progression after cardiac rhythm device implantation. In a recent retrospective study comprising 382 patients with a pacemaker or cardiac implantable defibrillator, Lee et al.[4] found that atrial fibrillation, age, and systolic pulmonary artery pressure were univariable predictors of a 2-grade increase of TR, whereas only systolic pulmonary artery pressure was an independent predictor after multivariable analysis. Likewise, a retrospective study comparing 26 patients with and 26 patients without severe TR after pacemaker or cardiac defibrillator implantation found that atrial fibrillation was associated with severe TR.[18] Similarly, in our study, atrial fibrillation and right ventricular systolic pressures were associated with significant TR progression (Fig. 2, example), although atrial fibrillation remained the only independent variable after adjustment for baseline TR grade. In patients without CRDs, both atrial fibrillation and elevated systolic pulmonary artery pressures secondary to left heart disease are well-known determinants of functional TR severity. A recent comprehensive 3D-transesophageal study by Utsunomiya et al.[19] showed that patients with functional TR and atrial fibrillation had larger tricuspid valve areas and right atrial volumes, whereas functional TR in the context of left heart disease with pulmonary hypertension was associated with larger tricuspid valve tenting volumes and right ventricular volumes. These mechanisms may play a role in progression of TR severity after lead implantation although our study was not designed to specifically address the specific mechanisms leading to TR after CRD insertion.

In a substudy of the PROTECT-PACE (Protection of Left Ventricular Function During Right Ventricular Pacing) study

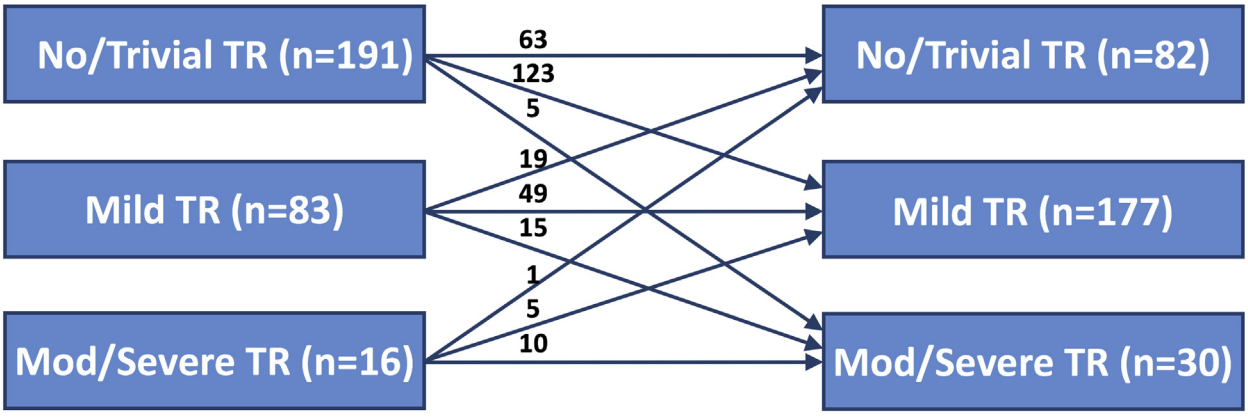

Figure 1. Change in tricuspid regurgitation (TR) severity from baseline to 1 year after device implantation.

Table 3. Echocardiographic variables before and 1 year after pacemaker or cardiac defibrillator implantation without cardiac resynchronization therapy

Variable (mean ± SD, N = 247)	Baseline	1 year	*P* value
Left ventricular ejection fraction (%)	53 ± 14	51 ± 13	0.005
Left atrial volume index (mL/m^2)	39 ± 17	38 ± 14	0.650
Right ventricular diastolic diameter (cm)	3.7 ± 0.6	3.5 ± 0.6	0.003
Tricuspid annular plane systolic excursion (cm)	1.9 ± 0.4	1.9 ± 0.4	0.758
Right ventricular systolic pressure (mm Hg)	35 ± 13	31 ± 9	< 0.001
Tricuspid regurgitation			< 0.001
None/trivial	165 (67%)	72 (29%)	
Mild	72 (29%)	150 (61%)	
Moderate	4 (2%)	19 (8%)	
Severe	6 (2%)	6 (2%)	

Data are expressed as means ± standard deviation (SD).

designed to evaluate the effect of right ventricular pacing on ventricular function,[20] echocardiography was performed immediately after and 24 months after pacemaker implantation. This study found no effect of pacing site (right ventricular apex vs non-apex site). However, the authors of the PROTECT-PACE substudy observed that right ventricular pacing might increase TR by deterioration of LV function with subsequent elevation of LV filling pressures, with subsequent back-pressure on the right heart. Vaturi et al.[21] showed in 23 clinically stable patients, none of whom were pacemaker dependent, that TR severity acutely increased during active pacing.

Overall, these findings may suggest that TR progression may not be entirely lead related (ie, direct structural damage to or interference with tricuspid valve leaflets) but may also be "functional" in nature (ie, deterioration of ventricular function with such as tricuspid annular dilation leading to malcoaptation of physically unaffected tricuspid valve leaflets). With the advent of leadless pacemakers[22] and subcutaneous implantable cardiac defibrillators,[23] which would, by definition, not result in direct interference with tricuspid valve leaflets (but may still lead to functional TR from right ventricular pacing), it is important to further understand the association of TR with "traditional" lead-based CRDs. Ongoing randomized controlled trials comparing traditional pacemakers and leadless pacemakers might further clarify the role of a lead across the tricuspid valve in TR progression.

In the present study, there was an increase in moderate or greater TR in patients undergoing CRD implantation without cardiac resynchronization therapy, whereas in the cardiac resynchronization therapy subgroup, there was no such association. This observation is consistent with prior retrospective data.[12] Possible explanations for this latter finding include: (a) an increase in ventricular dyssynchrony in patients with pacemakers and implantable cardiac defibrillators during active pacing with subsequent malcoaptation of the tricuspid valve leaflets, with no such dyssynchrony in the cardiac resynchronization therapy patients;[21] (b) an increase in TR caused by elevated filling pressures due to LV dysfunction in patients with chronic right ventricular pacing;[20] and (c) improved right ventricular function and reverse remodelling in the cardiac resynchronization therapy subgroup with subsequent improvement in tricuspid valve function, analogous to that seen after improvement in LV function in patients with functional mitral regurgitation.[24,25] Moreover, there might be a potential impact of lower rates of atrial fibrillation in these patients, although there was no difference in prevalence of atrial fibrillation between patients with and without cardiac resynchronization therapy (24% vs 31%, $P = 0.602$) in our study cohort. Given the limited number of patients with cardiac resynchronization therapy and follow-up data (n = 43), further studies are needed to confirm whether biventricular pacing might prevent significant TR progression.

LV dysfunction might occur after CRD implantation due to right ventricular pacing inducing LV dyssynchrony.[26] Superiority of biventricular pacing over right ventricular pacing for LV function has been documented.[27] Our findings may reflect this, as LVEF in the cardiac resynchronization therapy subgroup increased, whereas it decreased in the pacemaker and defibrillator subgroup; however, our study was not designed to assess changes in LV function *per se*. The impact of CRD implantation on right ventricular function is less well understood. Despite observing an increase in TR, we did not observe a decline in right ventricular function as assessed by

Table 4. Echocardiographic variables before and 1 year after device implantation with cardiac resynchronization therapy

Variable (mean ± SD, N = 43)	Baseline	1 year	*P* value
Left ventricular ejection fraction (%)	30 ± 10	38 ± 13	< 0.001
Left atrial volume index (mL/m^2)	43 ± 18	42 ± 18	0.703
Right ventricular diastolic diameter (cm)	3.7 ± 0.6	3.7 ± 0.6	0.305
Tricuspid annular plane systolic excursion (cm)	1.9 ± 0.4	1.8 ± 0.4	0.806
Right ventricular systolic pressure (mm Hg)	35 ± 15	32 ± 12	0.205
Tricuspid regurgitation			0.003
None/trivial	26 (60%)	11 (26%)	
Mild	11 (26%)	27 (63%)	
Moderate	5 (12%)	4 (9%)	
Severe	1 (2%)	1 (2%)	

Data are expressed as means ± standard deviation (SD).

Table 5. Comparison of clinical and echocardiographic data between patients with and without progression towards moderate or severe tricuspid regurgitation

Variable	Progression TR (n = 20)	No progression TR (n = 254)	*P* value
Gender (M/F)	11/9	160/94	0.482
Age (y)	75 ± 11	68 ± 15	0.036
Hypertension	16 (80%)	176 (69%)	0.448
Diabetes	7 (35%)	60 (24%)	0.281
History of AF	14 (70%)	68 (27%)	< 0.001
Left atrial volume index (mL/m^2)	51 ± 24	38 ± 17	0.001
LVEF (%)	51 ± 16	50 ± 16	0.846
Grade TR (0/1)	5/15	186/68	< 0.001
RV end-diastolic diameter (mm)	36 ± 7	36 ± 6	0.686
TAPSE (mm)	19 ± 4	19 ± 4	0.396
RV systolic pressure (mm Hg)	42 ± 14	33 ± 12	0.002
RV pacing (% of time)	41 ± 44	32 ± 41	0.623
CRT (no/yes)	20/0	217/37	0.066

Patients with moderate or severe tricuspid regurgitation at baseline excluded.

AF, atrial fibrillation; CRT, cardiac resynchronization therapy; LVEF, left ventricular ejection fraction; RV, right ventricular; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.

measurement of tricuspid annular plane systolic excursion, which is in agreement with a recent small prospective study.[11] The PROTECT-PACE substudy[20] did not observe an overall decrease of right ventricular function after 2 years of right ventricular pacing, although there was an association between a decrease of tricuspid annular plane systolic excursion and LV deterioration and right ventricular dyssynchrony. However, this is an observation that requires further study with longer patient follow-up.

Limitations

Although this is the largest prospective study regarding lead-related TR progression and follow-up was complete on 290 of 313 patients (93%) who were alive at 1-year follow-up, 15 patients died in this time period. Therefore, TR progression may be underestimated.

The readers were blinded to baseline TR severity grading and CRD implantation status, when classifying TR severity at follow-up. Nevertheless, a lead is usually seen in the right ventricle, which is an inherent bias of echocardiographic studies examining TR after CRD implantation.

This study was not designed to identify specific mechanisms of TR progression. Interim cardiac events might have played a role on the observed fluctuations in TR severity. Furthermore, right ventricular dimensions did not increase after CRD implantation and were not associated with progression towards significant TR in this study. This may be mainly due to the 1-year follow-up in these patients, as significant TR would likely require a longer time to result in right ventricular dilatation, and an even longer time to result in clinical symptoms or events. In addition, because of its complex shape, echocardiographic evaluation of the right ventricle can be challenging.[17] Right ventricular remodelling after CRD implantation on TR progression may be more ideally performed using cardiac magnetic resonance. However, this imaging technique is more technically challenging in patients with CRDs, and was not performed in our study.

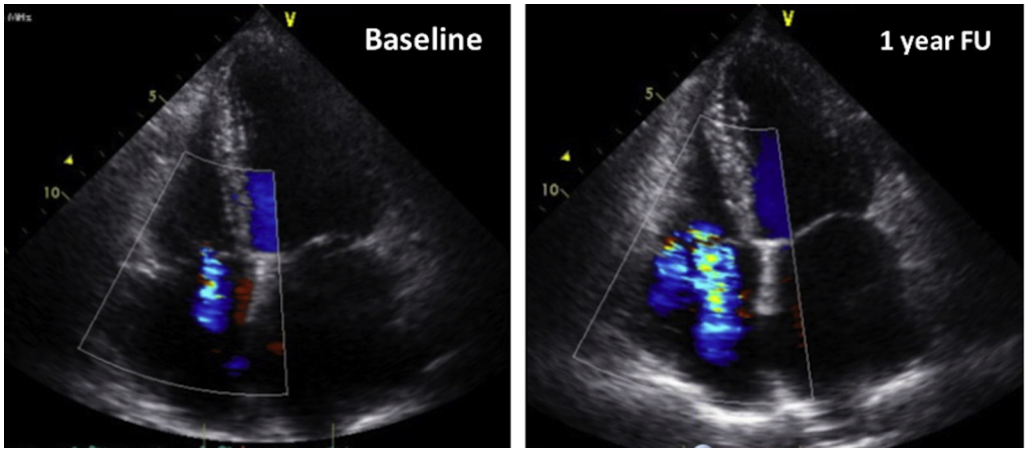

Figure 2. Example: patient with an increase in tricuspid regurgitation after pacemaker implantation. An 83-year-old female patient with a history of atrial fibrillation and moderate pulmonary hypertension (estimated pulmonary artery systolic pressure of 54 mm Hg). She was referred for single-chamber pacemaker implantation for third-degree heart block. Baseline echocardiography showed enlarged atria and mild tricuspid regurgitation. At 1 year after device insertion, there was progression to moderate tricuspid regurgitation.

Larger prospective studies with longer follow-up (5-10 years) are likely needed to evaluate the potential clinical impact of TR progression.

Conclusions

One year after endocardial lead insertion, there was a 5% increase in the prevalence of moderate or severe TR, which may be clinically relevant. A history of atrial fibrillation was the only independent predictor for TR progression. Larger prospective studies with long-term follow-up are needed to assess the potential clinical impact of these findings.

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Disclosures

The authors declare that they have no relevant conflicts of interest to disclose.

References

1. Nath J, Foster E, Heidenreich PA. Impact of tricuspid regurgitation on long-term survival. J Am Coll Cardiol 2004;43:405-9.
2. Topilsky Y, Nkomo VT, Vatury O, et al. Clinical outcome of isolated tricuspid regurgitation. JACC Cardiovasc Imaging 2014;7:1185-94.
3. Höke U, Auger D, Thijssen J, et al. Significant lead-induced tricuspid regurgitation is associated with poor prognosis at long-term. Heart 2014;100:960-8.
4. Lee RC, Friedman SE, Kono AT, Greenberg ML, Palac RT. Tricuspid regurgitation following implantation of endocardial leads: Incidence and predictors. Pacing Clin Electrophysiol 2015;38:1267-74.
5. Fanari Z, Hammami S, Hammami MB, Hammami S, Shuraih M. The effects of right ventricular apical pacing with transvenous pacemaker and implantable cardioverter defibrillator on mitral and tricuspid regurgitation. J Electrocardiol 2015;48:791-7.
6. Al-Bawardy R, Krishnaswamy A, Rajeswaran J, et al. Tricuspid regurgitation and implantable devices. Pacing Clin Electrophysiol 2015;38:259-66.
7. Delling F, Hassan Z, Piatkowski G, et al. Tricuspid regurgitation and mortality in patients with transvenous permanent pacemaker leads. Am J Cardiol 2016;117:988-92.
8. Sadreddini M, Haroun MJ, Buikema L, et al. Tricuspid valve regurgitation following temporary or permanent endocardial lead insertion, and the impact of cardiac resynchronization therapy. Open Cardiovasc Med J 2014;8:113-20.
9. Leibowitz D, Rosenheck S, Pollak A, Geist M, Gilon D. Transvenous pacemaker leads do not worsen tricuspid regurgitation: a prospective echocardiographic study. Cardiology 2000;93:74-7.
10. Kucukarslan N, Kirilmaz A, Ulusoy E, et al. Tricuspid insufficiency does not increase early after permanent implantation of pacemaker leads. J Card Surg 2006;21:391-4.
11. Arabi P, Özer N, Ateş AH, et al. Effects of pacemaker and implantable cardioverter defibrillator electrodes on tricuspid regurgitation and right sided heart functions. Cardiol J 2015;22:637-44.
12. Chang JD, Manning WJ, Ebrille E, Zimetbaum PJ. Tricuspid valve dysfunction following pacemaker or cardioverter-defibrillator implantation. J Am Coll Cardiol 2017;69:2331-41.
13. Dokainish H, Elbarasi E, Masiero S, et al. Prospective study of tricuspid valve regurgitation associated with permanent leads in patients undergoing cardiac rhythm device implantation: background, rationale, and design. Glob Cardiol Sci Pract 2015;41.
14. Assembly WMAG. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. J Int Bioethique 2004;15:124-9.
15. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015;28:1-39.
16. Lancellotti P, Tribouilloy C, Hagendorff A, et al. Recommendations for the echocardiographic assessment of native valvular regurgitation: an executive summary from the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 2013;14:611-44.
17. Rudski LG, Lai WW, Afilalo J, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography. J Am Soc Echocardiogr 2010;23:685-713.
18. Najib MQ, Vittala SS, Challa S, et al. Predictors of severe tricuspid regurgitation. Tex Heart Inst J 2013;40:529-33.
19. Utsunomiya H, Itabashi Y, Mihara H, et al. Functional tricuspid regurgitation caused by chronic atrial fibrillation: a real-time 3-dimensional transesophageal echocardiography study. Circ Cardiovasc Imaging 2017;10:e004897.
20. Saito M, Iannaccone A, Kaye G, et al. Effect of right ventricular pacing on right ventricular mechanics and tricuspid regurgitation in patients with high-grade atrioventricular block and sinus rhythm (from the Protection of Left Ventricular Function During Right Ventricular Pacing Study). Am Heart J 2015;116:1875-82.
21. Vaturi M, Kusniec J, Shapira Y, et al. Right ventricular pacing increases tricuspid regurgitation grade regardless of the mechanical interference to the valve by the electrode. Eur J Echocardiogr 2010;11:550-3.
22. Tjong FV, Reddy VY. Permanent leadless cardiac pacemaker therapy: a comprehensive review. Circulation 2017;135:1458-70.
23. Boersma L, Barr C, Knops R, et al. Implant and midterm outcomes of the subcutaneous implantable cardioverter-defibrillator registry: the EFFORTLESS study. J Am Coll Cardiol 2017;70:830-41.
24. van Bommel RJ, Marsan NA, Delgado V, et al. Cardiac resynchronization therapy as a therapeutic option in patients with moderate-severe functional mitral regurgitation and high operative risk. Circulation 2011;124:912-9.
25. Porciani MC, Macioce R, Demarchi G, et al. Effects of cardiac resynchronization therapy on the mechanisms underlying functional mitral regurgitation in congestive heart failure. Eur J Echocardiogr 2006;7:31-9.
26. Tops LF, Schalij MJ, Bax JJ. The effects of right ventricular apical pacing on ventricular function and dyssynchrony. J Am Coll Cardiol 2009;54:764-76.
27. Curtis AB, Worley SJ, Adamson P, et al. Biventricular pacing for atrioventricular block and systolic dysfunction. N Engl J Med 2013;368:1585-93.