Right ventricular pacing increases tricuspid regurgitation grade regardless of the mechanical interference to the valve by the electrode

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Aims
The effect of right ventricular (RV) pacing on tricuspid regurgitation (TR) is debatable and is presumed to be related to an interference with valve closure by the electrode. The aim of the study was to determine the impact of pacing per se on TR grade.

Methods and results
The study group included 23 clinically stable patients (13 males; mean age 78 ± 12 years) with a permanent pacemaker at the RV apex (83% DDD mode) and normal left ventricular function. They were all non-dependent on pacing and were otherwise in sinus rhythm. None had a primary dysfunction of the tricuspid valve. TR grade and RV size were assessed in two consecutive echo studies with and without active RV pacing. Results showed that active RV pacing was associated with an increase in TR severity (TR vena contracta: 0.4 ± 0.2 vs. 0.2 ± 0.2 cm, \(P = 0.001\); TR jet area: 4.1 ± 2.3 vs. 2.3 ± 1.8 cm², \(P < 0.001\)). This was also reflected in a significant decrease in the number of patients with mild TR \((P = 0.003)\) and increase in the number with moderate regurgitation \((P = 0.02)\). There was no change in RV areas with pacing.

Conclusion
Active RV pacing is associated with a significant increase in TR grade. This effect is not induced by acute changes in the RV area and is unrelated to an interference with leaflet closure by the electrode.

Keywords
Right ventricle • Pacemaker • Tricuspid regurgitation

Introduction
Mild tricuspid regurgitation (TR) is a common echocardiographic finding which is usually devoid of clinical relevance. However, more advanced grades of TR are associated with a poor prognosis.\(^1\) It is therefore important to focus on the causes of significant TR.

Endovascular cardiac pacing is a known cause of TR, but the underlying mechanism has not been fully elucidated. Some researchers suggested that the presence of the endovascular pacemaker electrode at the right ventricle (RV) interferes with the motion of the tricuspid leaflets.\(^2\)–\(^5\) Others explained findings of an association of late TR with the presence of an endovascular pacemaker by a delay in activation within the RV or alteration in RV geometry by a remote factor (such as aortic valve replacement).\(^6\)–\(^8\) In contrast, several studies reported no significant change in TR grade following pacemaker implantation.\(^9\)–\(^11\) It is noteworthy, however, that these studies did not distinguish patients by pacemaker function at the time of assessment (i.e. active ventricular pacing or sensing mode) and that the assessment of TR is preload sensitive which could bias the findings before and after device implantation in the same patient.

The aim of the present study was to examine whether active RV pacing by itself has a direct impact on TR grade, regardless of the potential interference with valve function by the presence of an electrode.

Methods
The study group consisted of outpatients of the Pacemaker Service Clinic at Rabin Medical Center. We included only patients who had
a permanent pacemaker with an endovascular electrode located at the RV; in all cases, the tip was at the RV apex. The fundamental inclusion criterion was non-dependent on constant pacing. Other inclusion criteria were age over 18 years, stable clinical state at the time of recruitment, normal left ventricular function, sinus rhythm (when not paced), and the absence of organic tricuspid valve disease or previous tricuspid valve surgery.

After routine check-up of the pacemaker, a transthoracic echocardiography (TTE) study was performed. In patients who were in active pacing mode, TTE was followed by inactivation of the pacemaker, so that the intrinsic rhythm would take over. If the baseline rhythm was sinus, the pacemaker was programmed to take over the intrinsic rhythm by either shortening or prolonging the atrioventricular (AV) delay. After pacemaker reprogramming, a second TTE study was performed, within 5 min of the first, and the pacemaker was then reprogrammed to restore the baseline mode. The difference in heart rate between the intrinsic and paced rhythm did not exceed 5 bpm.

The TTE study included the routine views. TR was graded by the TR jet area in the apical view (at a Nyquist limit of 50–60 cm/s) and the vena contracta.12 The vena contracta value was averaged between the jet at the RV inflow and the apical view: a value of \( \leq 0.2 \) cm was graded as mild TR, 0.2–0.6 cm moderate TR, and \( \geq 0.7 \) cm severe TR. TR flow was sampled by Doppler to measure RV systolic pressure (RVSP), which reflects the pulmonary systolic pressure in the absence of RV outflow obstruction. The RV area was traced at end-systole (RVES) and end-diastole (RVED) in the apical view. The RV shortening area fraction was calculated with the following formula: \( \frac{RVED_{area} - RVES_{area}}{RVED_{area}} \). The fraction was measured with and without active pacing.

Demographic data, medical history, and pacemaker-related data were obtained from the medical records.

The study protocol was approved by the Rabin Medical Center Committee on Human Research.

Statistical analysis

The results are presented as mean (SD) for continuous variables and as total patients (percentage of total patients) for categorical data. The Wilcoxon matched-pairs signed-rank test was used to determine differences between groups of paired data. Spearman’s rank correlation was used to determine the association between TR vena contracta and QRS width (at the pacing mode) and between TR severity and AV delay. The Mann–Whitney test was used to analyse the relationship between the presence of bundle branch block prior to pacemaker implantation and TR severity. A two-sided \( P \)-value of \( <0.05 \) was considered statistically significant.

Results

The study group included 23 patients (13 males) of mean age 78 ± 12 years (range: 41–92). The pacing mode was DDD in 83% and VDD in the remainder. The indication for pacing was sick sinus syndrome.
(52%) or advanced AV block (48%). The average time from pacemaker implantation to the study was 48.6 ± 32.7 months. Most of the patients (61%) had bundle branch block prior to pacemaker implantation. The mean AV delay during active pacing was 162.4 ± 34.8 ms (range: 110–240) and in sensing mode, 262.9 ± 59.2 ms (range: 160–350). The average baseline heart rate was 66 ± 12 bpm. RV global contraction was estimated (visually) as normal in all patients. The RV area shortening fraction (area change in the apical view) measured 0.44 ± 0.12. The mean RVSP was 32 ± 10 mmHg (without changes between pacing modes).

Active RV pacing was associated with an increase in TR (Figure 1), as indicated by the increase in both the vena contracta (0.4 ± 0.2 vs. 0.2 ± 0.2 cm, P < 0.001) and TR jet area (4.1 ± 2.3 vs. 2.3 ± 1.8 cm², P < 0.001). TR was mild or absent in 61% of the patients in sensing mode and in 21% during active pacing (Figure 2). This shift in distribution was related to a decrease in the number of patients with mild TR (z = −2.95, P = 0.003) and an increase in those number with moderate TR (z = −2.37, P = 0.02). The switch in pacing mode was not associated with acute changes in either end-systolic or end-diastolic RV areas (Table 1).

Active pacing was associated with significant widening of the QRS complex, from 84 ± 18 ms (range: 60–120) before pacing to 168 ± 25 ms (range: 120–200) after (P < 0.0001). TR severity (graded by the vena contracta) was inversely correlated with the QRS width during active pacing (Spearman’s correlation r = −0.502, P = 0.015) (Figure 3). The presence of bundle branch block on the electrocardiogram prior to pacemaker implantation was not significantly associated with TR severity (graded by the vena contracta) (P = 0.76, z = −0.306).

**Discussion**

The present study shows that TR grade increases significantly with active RV pacing. This effect of pacing could not be attributed to acute changes in the RV area or to a possible interference with valve closure by the presence of an endovascular electrode.

Anatomically, the tricuspid valve is anchored by chords at three separate sites in the RV. It is reasonable to assume that any change in the timing of contraction of these sites (e.g., RV mechanical dysynchrony) may alter the competent closure of the tricuspid leaflets, ultimately leading to TR or exacerbating existing TR. The variability in interventricular septal motion according to the origin of electrical activation was supported by the study of Little et al., who noted different patterns of interventricular septal motion during RV pacing compared with ventricular premature beat or normal sinus beat. As such, septal motion may differ between patients with active RV pacing and patients in whom the pacemaker is in standby mode. Given that the septum is part of the subvalve apparatus, this difference may be reflected by differences in tricuspid valve function.

Prompted by findings that high TR grades (moderate or worse) may serve as a negative prognostic factor, regardless of the pulmonary pressure or left ventricular systolic function, we sought to identify factors that could increase TR grade. We found that the majority of patients had mild TR in the non-pacing mode. However, active pacing shifted the TR grade, mostly towards the moderate range (Figure 1).

The explanation for our finding of a negative correlation between TR severity and QRS width during active pacing was beyond the scope of the present study. This observation warrants further validation.
In conclusion, active RV pacing may increase the severity of TR, independently of the potential interference of the endovascular electrode with valve closure. Further study is needed to determine the mechanism as well as the clinical impact of this phenomenon.

Conflict of interest: none declared.

References