

Bioprosthetic Tricuspid Valve Regurgitation Associated With Pacemaker or Defibrillator Lead Implantation

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- Objectives** The goal of this study was to determine the impact of transvenous pacemaker and defibrillator leads on the incidence of bioprosthetic tricuspid valve (BTV) regurgitation compared with BTV patients without a transvalvular lead.
- Background** Although concern has been raised regarding the potential deleterious effect of permanent transvenous device leads on BTV function, little is known about the incidence of prosthetic tricuspid regurgitation (TR) after lead placement.
- Methods** A retrospective review of 58 patients who underwent BTV implantation and subsequently required endocardial pacemaker (n = 52) or defibrillator (n = 6) lead implantation across the BTV was conducted. Patient and prosthesis characteristics, lead type, and clinical events were collected. The incidence and severity of prosthetic TR, determined by Doppler echocardiography, was compared with 265 consecutive patients who underwent BTV implantation without undergoing subsequent transvalvular device lead implantation.
- Results** Over a mean follow-up of 25 months, in 5 patients (9%) with a transvalvular lead significant (moderate or greater) prosthetic TR developed compared with 12 patients (5%) in the control group (p = 0.20). Kaplan-Meier analysis revealed no significant difference in the incidence of TR in BTV patients with and without transvalvular leads (p = 0.45). Significant prosthetic TR in patients with and without a transvalvular lead more commonly occurred 2 years or later after lead or BTV implantation (4 of 5, 80% and 10 of 12, 83%, respectively).
- Conclusions** Transvalvular device lead implantation in BTV patients was not associated with an increased incidence of significant prosthetic TR (p = 0.45). Based on these data, transvalvular lead implantation appears to be an acceptable approach for patients with a BTV who require permanent pacemaker or defibrillator placement. (J Am Coll Cardiol 2012;59:813–8) © 2012 by the American College of Cardiology Foundation

Tricuspid valve replacement (TVR) with a bioprosthetic tricuspid valve (BTV) is an established treatment for severe tricuspid valve (TV) stenosis and tricuspid regurgitation (TR) related to a variety of disease states. Atrioventricular block and sinus node dysfunction are recognized postoperative complications in these patients, often necessitating permanent pacemaker implantation. In some cases, patients at increased risk of sudden cardiac death undergo defibrillator implantation. In contrast to mechanical TV prostheses, a bioprosthetic valve can in principle be crossed by transvenous leads. Concern has been raised regarding the potential deleterious effect of permanent transvenous device leads

on bioprosthetic tricuspid valve (BTV) function, yet few data exist pertaining to outcomes, specifically the occurrence of significant prosthetic TR after lead placement in this population.

Concern over transvalvular lead implantation has largely been derived from data pertaining to the native TV, in which transvalvular device leads appear to increase the risk of TR. Severe TR develops in some of these patients (1,2), with important clinical sequelae, including the development of right heart failure requiring surgical TV repair or replacement. Several mechanisms contribute to the development of severe TR in patients with device leads that pass through the native TV, including leaflet perforation, lead entanglement in the valve apparatus, lead impingement of leaflet excursion, and lead adherence to the valve (3).

Given the different anatomic structure of BTV, the mechanisms of lead-induced native TR may not be entirely relevant in this population. Most contemporary BTVs are composed of porcine tissue attached to a plastic and polyester cloth frame that is anchored to a sewing ring. If device leads were known

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Manuscript received August 4, 2011; revised manuscript received October 3, 2011, accepted October 19, 2011.

Abbreviations and Acronyms

- BTV** = bioprosthetic tricuspid valve
- LV** = left ventricular
- RV** = right ventricular
- TR** = tricuspid valve regurgitation
- TV** = tricuspid valve
- TVR** = tricuspid valve replacement

to have a significant negative impact on BTV function, alternative implantation strategies would have to be considered to avoid long-term BTV damage and dysfunction. Lower profile right ventricular (RV) leads and left ventricular (LV) pacing via the coronary sinus might potentially limit BTV dysfunction. The goal of this study was to determine whether transvalvular device leads promote significant BTV regurgitation.

Methods

The medical records of all patients who underwent TVR with a BTV at our institution between January 1, 1997, and July 1, 2010, were reviewed after approval from the institutional review board. Patients who subsequently underwent transvalvular endocardial permanent pacemaker or defibrillator implantation were included in the study group. The medical records were reviewed longitudinally, and echocardiographic data were recorded. Patients without an echocardiographic follow-up examination after device lead implantation were excluded from the study group. Patients with preexisting transvenous leads undergoing BTV implantation in whom the ventricular lead was externalized between the BTV sewing ring and the TV annulus were also excluded from the study unless they subsequently underwent transvalvular lead implantation. A control group of patients who underwent TVR with a BTV and no subsequent transvalvular lead implantation was also followed longitudinally to determine the incidence and severity of prosthetic TR. Clinical variables including the indication for TVR, BTV type and size, concomitant cardiac surgery, indication for device implantation, transvalvular lead type, and RV lead implant location were collected for all patients.

2-dimensional and Doppler echocardiography. Transthoracic 2-dimensional and Doppler echocardiography was performed within 1 week of TVR and at follow-up for all patients. Echocardiographic studies were performed on commercially available ultrasound equipment (Acuson Sequoia, Siemens Medical, Mountain View, California; Vivid-7, GE Healthcare, Milwaukee, Wisconsin; and IE33, Phillips Healthcare, Andover, Massachusetts) according to the standard methods recommended by the American Society of Echocardiography (4,5). In accordance with these guidelines (5), the severity of TR was graded in the apical 4-chamber view based on TR jet length and jet area as estimated by color flow Doppler. TR severity was semiquantitatively classified as trivial, mild, moderate, or severe using a standard method (6,7). Continuous wave Doppler of the TR signal was recorded and the peak regurgitant velocity used to estimate RV systolic pressure using the modified Bernoulli equation. Inferior vena cava size and the degree of inspiratory collapse were used to

estimate right atrial pressure. When significant TR was suspected, pulse wave and color Doppler imaging was used to assess for alterations in hepatic vein flow patterns as seen in severe TR (8). RV and right atrial size were visually inspected and incorporated into the assessment of TR severity.

Intraoperative transesophageal echocardiography was also performed at the time of TVR in all subjects. None of the patients had more than mild TR immediately after BTV implantation.

Statistical analysis. Descriptive statistical analyses were performed. Data are reported as mean ± SD or total number and percentage. For independent groups (study and control), the Fisher exact test was used to compare categorical variables, whereas the Student *t* test was used for continuous variables. A Kaplan-Meier analysis was performed to compare the incidence of significant TR between the study and control groups. The log-rank test was used to compare the 2 groups. Statistical analysis was performed using SAS software (SPSS version 12.0, SAS Institute Inc., Cary, North Carolina).

Results

Transvalvular lead population. Fifty-eight patients with a permanent transvenous endocardial device lead placed across the BTV were included in the study group. Patient demographics are shown in Table 1, device lead characteristics in Table 2, and echocardiographic characteristics in Table 3. Fifty-four leads were placed at the RV apex, 3 leads along the mid-RV septum, and 1 lead in the RV outflow tract. All endocardial RV leads were steroid-eluting, active fixation models. Six of the transvalvular leads (10%) were defibrillator leads. Twenty-seven of the 58 patients (46%) had concomitant mitral, aortic, or pulmonary valve repair or replacement at the time of BTV implantation. The mean clinical and echocardiographic follow-up duration was 752 ± 1,042 days after lead implantation. Forty patients (69%) had >30 days of clinical

Table 1 Characteristics of 323 Patients With Bioprosthetic Tricuspid Valves

	BTV Lead (n = 58)	BTV Only (n = 265)	p Value
Age, yrs	65 ± 15	61 ± 17	0.11
Female	40 (69)	164 (62)	0.37
Indication for BTV			
TR (carcinoid syndrome)	4 (7)	44 (17)	0.07
TR (Ebstein anomaly)	6 (10)	43 (16)	0.32
TR (other causes)	48 (83)	178 (67)	0.02
BTV type			
Carpentier Edwards Perimount	2 (3)	4 (2)	0.29
St. Jude Medical Biocor	21 (36)	123 (46)	0.19
Medtronic Mosaic	5 (9)	57 (22)	0.03
Carpentier Edwards Duraflex	30 (52)	76 (29)	0.001
CarboMedics Mitroflow	0	5 (2)	0.59
BTV diameter, mm	31.6 ± 2.2	31.8 ± 1.9	0.37
Follow-up duration, days	752 ± 1,042	550 ± 734	0.19

Values are mean ± SD or n (%).
BTV = bioprosthetic tricuspid valve; Lead = pacemaker or defibrillator lead; TR = tricuspid regurgitation.

Table 2 Device Lead Characteristics	
Lead type	
Pacemaker	52
Defibrillator	6
Lead external insulation	
Silicone	30
Polyurethane	23
Copolymer (silicone and polyurethane)	5
Active fixation	
RV apex	54
RV midseptum/RV outflow tract	4
Lead body size, F	
5.7	23
6.0	17
6.2	12
6.8	1
8.2	1
8.6	4

Values are n.
RV = right ventricular.

and echocardiographic follow-up after transvalvular lead implantation, with a mean follow-up duration of $1,018 \pm 1,046$ days.

Immediate and long-term findings after transvalvular lead placement. In 5 patients (9%) with a transvalvular lead, moderate or greater prosthetic TR developed (Fig. 1). Significant TR developed in none of the patients in the transvalvular lead group in the first week after BTV implantation. Moderate or greater TR was detected 1 month after lead implantation in 1 patient and >20 months later in 4 patients. The patient with early TR died 3 months after lead implantation of congestive heart failure due to restrictive cardiomyopathy. The remaining 4 cases survived >5 years after transvalvular device lead implantation, with 1 requiring repeat BTV implantation for severe TR. In the single patient that underwent repeat BTV implantation, pathological examination of the excised bioprosthesis showed no calcification, cusp tear, thrombus, or obstructive fibrous ingrowth (pannus).

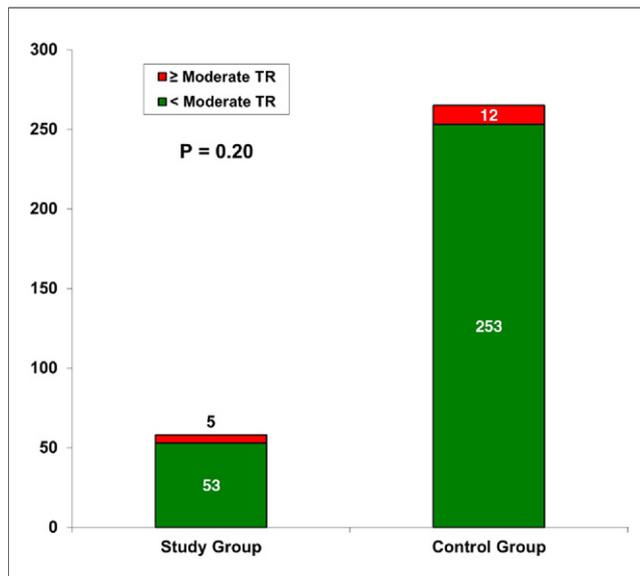


Figure 1 Incidence of Bioprosthetic TR in Patients With a Transvalvular Device Lead Compared With Controls

Patients with and without a transvalvular device lead had a similarly low incidence of prosthetic tricuspid regurgitation (TR) at follow-up ($p = 0.20$).

Control population. The control group included 265 patients who underwent TVR with a BTV and no subsequent implantation of a transvalvular device lead. The mean clinical and echocardiographic follow-up duration was 554 ± 734 days after BTV implantation. Clinical characteristics are shown in Table 1. Age, sex, and follow-up duration were similar in the control and study groups (all $p > 0.05$) (Table 1). Of the 265 control patients, 63 (24%) had an endocardial RV lead before TVR surgery that was subsequently externalized outside the sewing ring at the time of BTV implantation. In 4 patients (2%), an epicardial ventricular lead was placed at the time of TVR surgery. High-grade atrioventricular block developed in 6 patients (2%) after BTV implantation, and they underwent placement of an LV lead via the coronary sinus to avoid

Table 3 Echocardiographic and Hemodynamic Variables at Follow-Up	Study Group			Control Group		
	Moderate or Less TR (n = 53)	Moderate or Greater TR (n = 5)	p Value	Moderate or Less TR (n = 253)	Moderate or Greater TR (n = 12)	p Value
Body surface area, m ²	1.80 ± 0.21	1.78 ± 0.27	0.90	1.85 ± 0.26	1.76 ± 0.17	0.09
Ejection fraction, %	56 ± 14	64 ± 7	0.05	57 ± 12	61 ± 11	0.31
LV mass index, g/m ²	99 ± 32	114 ± 62	0.61	101 ± 34	82 ± 35	0.12
Bioprosthetic TV mean gradient, mm Hg	5.8 ± 2.1	6.2 ± 0.8	0.42	5.5 ± 2.4	6.3 ± 2.5	0.26
TV regurgitant velocity, m/s	2.8 ± 0.5	2.9 ± 0.5	0.59	2.5 ± 0.5	2.6 ± 0.9	0.78
Estimated right atrial pressure, mm Hg	11.6 ± 5.0	16.0 ± 5.5	0.15	11.5 ± 5.7	10.8 ± 5.0	0.69
Estimated right ventricular systolic pressure, mm Hg	45 ± 13	51 ± 14	0.44	37 ± 15	40 ± 19	0.66
Systolic blood pressure, mm Hg	117 ± 18	117 ± 24	0.96	116 ± 19	117 ± 16	0.88
Diastolic blood pressure, mm Hg	60 ± 10	72 ± 20	0.26	62 ± 11	70 ± 10	0.04
Heart rate, beats/min	74 ± 16	73 ± 15	0.85	75 ± 15	70 ± 14	0.30

Values are mean \pm SD.
LV = left ventricular; TR = tricuspid regurgitation; TV = tricuspid valve.

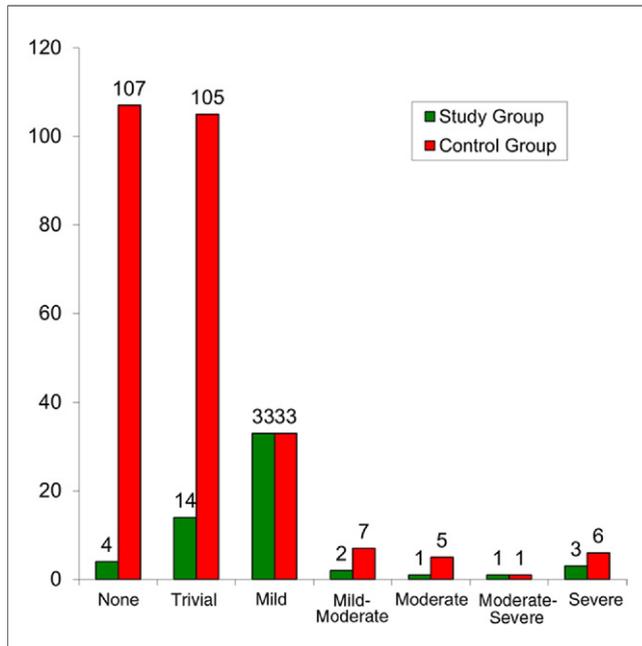


Figure 2 Severity of Prosthetic Regurgitation at Follow-Up

Distribution of prosthetic tricuspid regurgitation severity at follow-up in patients with and without a transvalvular device lead.

placement of the ventricular lead across the BTV. The remaining 192 patients (72%) did not require pacemaker or defibrillator implantation during the follow-up period.

During follow-up, moderate or greater BTV regurgitation developed in 12 control group patients (5%). In 10 patients,

moderate or greater TR was detected >2 years after BTV implantation. In 1 patient, TR was detected 1 year after TVR. In the last patient, moderate TR developed 1 week after BTV implantation and was probably related to thrombus formation on the prosthetic valve cusps because echocardiography demonstrated cusp thickening with reduced mobility. This patient was anticoagulated, and 4 months later, had only mild prosthetic regurgitation. The mean clinical follow-up duration for this group of 12 patients was 563 ± 784 days after the detection of moderate or greater BTV regurgitation by echocardiography. The majority of patients ($n = 9, 75\%$) remained asymptomatic at follow-up without signs or symptoms of right heart failure. Three patients required repeat BTV implantation for symptoms of right heart failure. Of these 3 patients, 1 subsequently underwent LV assist device implantation for end-stage ischemic cardiomyopathy and died of multiorgan failure 4 months after the detection of severe TR. The other 2 patients who had repeat BTV implantation were asymptomatic at follow-up.

Impact of transvalvular device leads on prosthetic TR.

The severity of BTV regurgitation in patients with and without transvalvular leads is shown in Figure 2. Kaplan-Meier analysis for the incidence of significant TR in the study versus control group is shown as a failure plot in Figure 3. Comparison of the 2 groups revealed no significant difference in the incidence of TR ($p = 0.45$). A reassessment after excluding patients with <30 days of echocardiographic follow-up ($n = 18$) after transvalvular lead placement likewise showed no significant difference in the incidence of TR (Fig. 4) ($p = 0.19$).

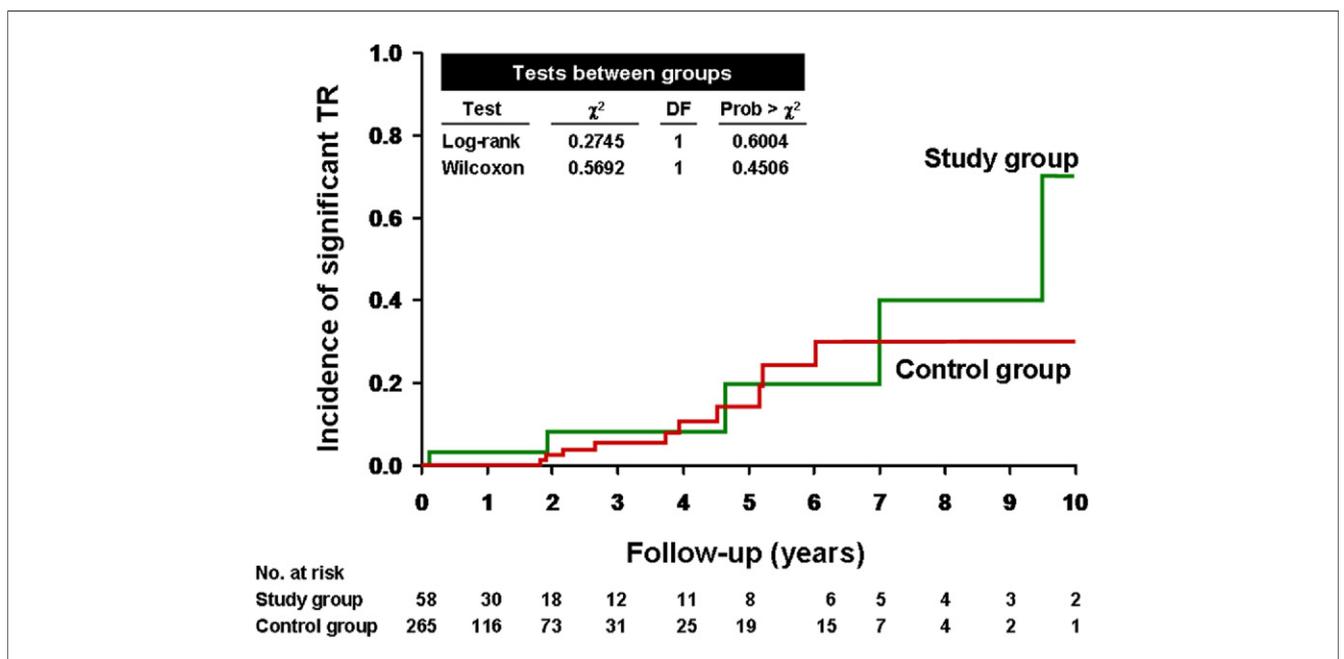


Figure 3 Product-Limit Survival Fit Failure Plot for All Subjects

Kaplan-Meier product-limit failure plot for significant prosthetic tricuspid regurgitation (TR) in bioprosthetic tricuspid valve recipients with and without transvalvular lead implantation showed no significant difference between the 2 groups ($p = 0.45$).

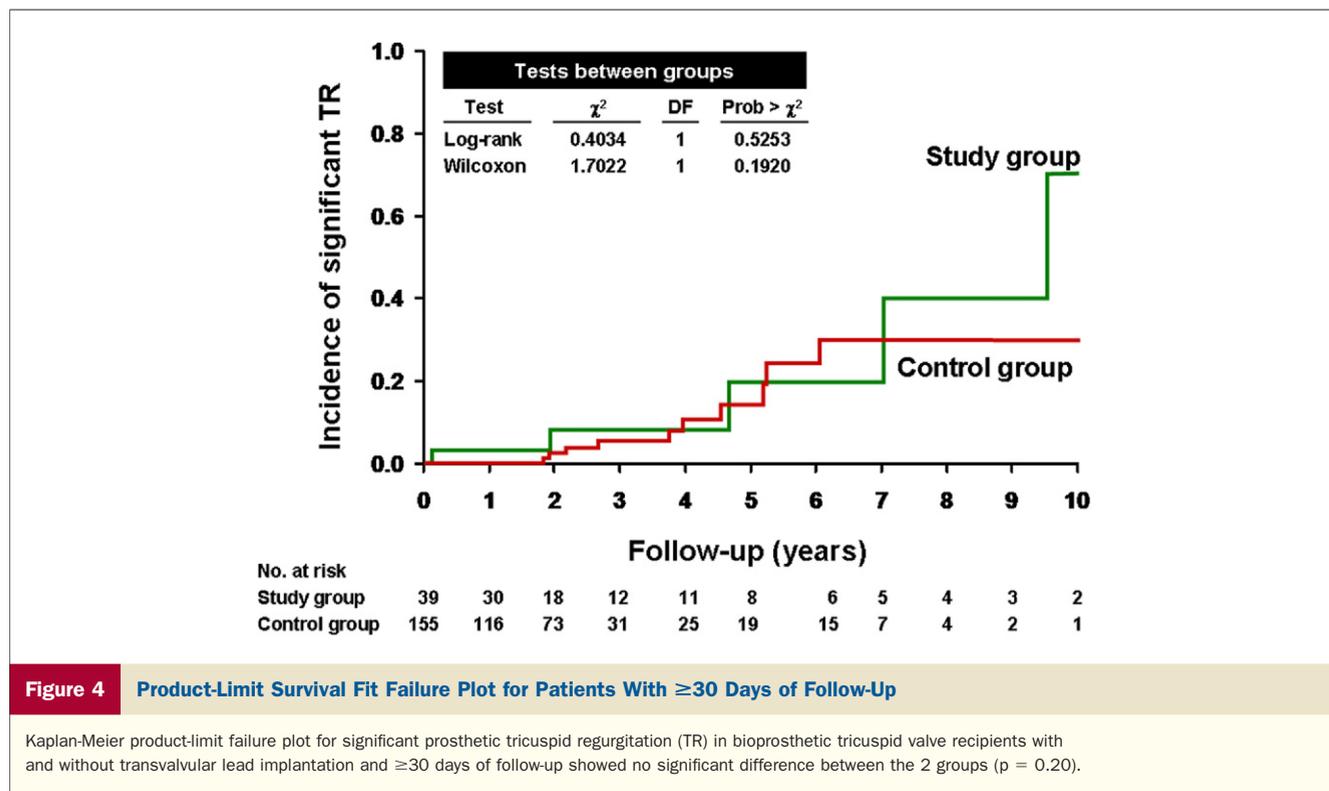


Figure 4 Product-Limit Survival Fit Failure Plot for Patients With ≥ 30 Days of Follow-Up

Kaplan-Meier product-limit failure plot for significant prosthetic tricuspid regurgitation (TR) in bioprosthetic tricuspid valve recipients with and without transvalvular lead implantation and ≥ 30 days of follow-up showed no significant difference between the 2 groups ($p = 0.20$).

Predictors of TR. Univariate analysis of the clinical and echocardiographic variables shown in Tables 1 and 2 revealed no significant predictors of TR in the study or control groups, including prosthetic valve type ($p = 0.65$ and $p = 0.46$, respectively), indication for TVR ($p = 0.33$ and $p = 0.45$, respectively), or right ventricular systolic pressure ($p = 0.44$ and $p = 0.66$).

Discussion

The present study is the first to examine the incidence of significant prosthetic TR after transvalvular pacemaker or defibrillator lead implantation in patients with a BTV compared with prosthetic TR in patients who have not undergone transvalvular lead implantation. In this population, we found no significant difference in the incidence of early or late prosthetic TR between the 2 groups over a mean follow-up of 2 years. These results provide reassurance that implantation of a transvalvular device lead across a BTV does not significantly increase the risk of prosthetic regurgitation.

The clinical implications of these findings are substantial because patients who require a pacemaker or defibrillator after BTV implantation may undergo more complex or less durable device implantation procedures, such as placement of an epicardial ventricular lead or transvenous LV lead via the coronary sinus, in an attempt to avoid damaging the BTV (9-13). Epicardial leads generally have poorer longevity compared with endocardial leads due to higher chronic thresholds (i.e., exit block) and lead fracture (12), whereas the long-term stability of leads placed via the coronary sinus is less than that of leads placed in a conventional endocardial

RV location (14,15). A transvenous endocardial system may even be placed before TVR and then exteriorized to the prosthesis at the time of TVR. This exteriorized lead approach is particularly relevant to defibrillator implantation, in which endocardial systems with an RV lead are optimal for the integrity of pacing and defibrillation. Unfortunately, such recently placed leads are more prone to dislodgment intraoperatively and cannot readily be repositioned. The findings of this study suggest that such efforts to avoid transvalvular lead placement may be unnecessary.

Our data highlight the fact that BTV regurgitation may occur early or late, with or without a transvalvular lead, thereby suggesting varied mechanisms of prosthesis dysfunction. In the present study, there was no increased incidence of early or late significant BTV regurgitation in the study group after transvalvular lead implantation compared with controls. In a study of 61 patients with native TV referred for transvenous device implantation, no significant worsening in the severity of native TR was noted early after endocardial lead implantation (16). Furthermore, TR severity did not change at a mean follow-up of 6 ± 3 months (16). In another study of patients with severe symptomatic native TR due to device leads, the average time from pacemaker or defibrillator placement to TV surgery was 6 years (range: 2 months to 19 years), with lead adherence and impingement of the tricuspid valve leaflets more common (30 of 41, 73%) than perforation or entanglement (11 of 41, 27%) (3). The authors did not describe the temporal evolution of severe TR in their patients and instead emphasized the obstacles to timely recognition of this disorder. In

the one patient in the present study with a transvalvular lead and severe prosthetic regurgitation who underwent repeat BTV replacement, pathological examination of the excised valve was inconclusive regarding the mechanism of TR. The overall incidence of TR was low in the BTV group with a transvalvular lead. It is possible that BTV may be less vulnerable to lead-induced regurgitation than the native TV. They have smaller and thicker cusps, and glutaraldehyde fixation may have leaflet-stabilizing properties, potentially contributing to the observed low incidence of TR in this study.

Study limitations. Although the present study provides important long-term follow-up data on the incidence of BTV regurgitation in association with transvalvular pacemaker or defibrillator leads in a large series of patients, limitations exist. The data were collected retrospectively, and only patients with echocardiographic follow-up were included, which may introduce selection bias. The number of patients with a transvalvular lead was relatively small, and event rates were low, which may limit the ability to detect a statistically significant difference in the incidence of BTV regurgitation compared with controls. Furthermore, although the mean follow-up duration was favorable, several patients had relatively short follow-up, which may limit the capacity of the study to identify a greater tendency for TR over the long term after device lead implantation. For this reason, a separate Kaplan-Meier analysis was performed that included only patients with >30 days of follow-up. A prospective study with more uniform and longer follow-up would more accurately quantify the risk of significant BTV regurgitation in the setting of transvalvular pacemaker or defibrillator leads, but would also be difficult to perform. In the current study, the majority (69%) of study group patients had at least 30 days of follow-up, with a median follow-up duration of 655 days. As such, it represents a robust analysis of the incidence of BTV regurgitation in the first 2 years after transvalvular lead implantation. Further investigation will be required to more fully judge the incidence of BTV regurgitation beyond 2 years after lead implantation. Finally, a relatively small number of defibrillator leads were implanted, thus limiting inferences that can be made regarding the risk of TR from transvalvular defibrillator leads in this BTV population.

Conclusions

In a group of BTV patients who received transvalvular pacemaker and defibrillator lead systems postoperatively, the incidence of moderate or greater prosthetic TR was not significantly different from that of BTV controls without a transvalvular lead. Thus, in patients who require a permanent pacemaker or defibrillator after BTV implantation, use of an endocardial lead system that crosses the BTV appears to be an acceptable approach.

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REFERENCES

1. Kim JB, Spevack DM, Tunick PA, et al. The effect of transvenous pacemaker and implantable cardioverter defibrillator lead placement on tricuspid valve function: an observational study. *J Am Soc Echocardiogr* 2008;21:284-7.
2. Paniagua D, Aldrich HR, Lieberman EH, Lamas GA, Agatston AS. Increased prevalence of significant tricuspid regurgitation in patients with transvenous pacemakers leads. *Am J Cardiol* 1998; 82:1130-2.
3. Lin G, Nishimura RA, Connolly HM, Dearani JA, Sundt TM 3rd, Hayes DL. Severe symptomatic tricuspid valve regurgitation due to permanent pacemaker or implantable cardioverter-defibrillator leads. *J Am Coll Cardiol* 2005;45:1672-5.
4. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005;18: 1440-63.
5. Cheitlin MD, Armstrong WF, Aurigemma GP, et al. ACC/AHA/ ASE 2003 guideline update for the clinical application of echocardiography: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASE Committee to Update the 1997 Guidelines for the Clinical Application of Echocardiography). *J Am Coll Cardiol* 2003;42:954-70.
6. Miyatake K, Okamoto M, Kinoshita N, et al. Evaluation of tricuspid regurgitation by pulsed Doppler and two-dimensional echocardiography. *Circulation* 1982;66:777-84.
7. Suzuki Y, Kambara H, Kadota K, et al. Detection and evaluation of tricuspid regurgitation using a real-time, two-dimensional, color-coded, Doppler flow imaging system: comparison with contrast two-dimensional echocardiography and right ventriculography. *Am J Cardiol* 1986;57:811-5.
8. Sakai K, Nakamura K, Satomi G, Kondo M, Hirose K. Evaluation of tricuspid regurgitation by blood flow pattern in the hepatic vein using pulsed Doppler technique. *Am Heart J* 1984;108:516-23.
9. Grimard C, Clementy N, Fauchier L, Babuty D. Ventricular pacing through coronary sinus in patients with tricuspid prosthesis. *Ann Thorac Surg* 2010;89:e51-2.
10. Davidson NC, Mond HG. Ventricular pacing in the presence of tricuspid valve disease. *Pacing Clin Electrophysiol* 2002;25:129-31.
11. Hansky B, Guldner H, Vogt J, et al. Coronary vein leads for cardiac pacing in patients with tricuspid valve replacement. *Thorac Cardiovasc Surg* 2002;50:120-1.
12. Nguyen LS, Swaroop S, Prejean CA. Pacing in the middle cardiac vein in a patient with tricuspid prosthesis. *Pacing Clin Electrophysiol* 2002;25:243-4.
13. Cooper JP, Jayawickreme SR, Swanton RH. Permanent pacing in patients with tricuspid valve replacements. *Br Heart J* 1995;73: 169-72.
14. Lin G, Anavekar NS, Webster TL, Rea RF, Hayes DL, Brady PA. Long-term stability of endocardial left ventricular pacing leads placed via the coronary sinus. *Pacing Clin Electrophysiol* 2009;32: 1117-22.
15. Bulava A, Lukl J. Single-centre experience with coronary sinus lead stability and long-term pacing parameters. *Europace* 2007;9:523-7.
16. 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.

Key Words: bioprosthetic tricuspid valve ■ pacemaker ■ prosthetic tricuspid regurgitation.