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Short Communication

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Incidence of Atrioventricular Block After Valve Replacement in Carcinoid Heart Disease

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Abstract

Background: Carcinoid heart disease (CaHD) is a rare condition that has a high impact on the morbidity and mortality of its patients. Once heart failure symptoms develop in the patient with CaHD, cardiac valve surgery is often the only effective treatment. Although atrioventricular block (AVB) is a known postoperative complication of the valve surgery, the incidence of AVB in this population has not been well described.

Methods: Comprehensive records were collected retrospectively on consecutive patients with CaHD who underwent a valve surgery at a tertiary medical center from January 2001 to December 2015. We excluded patients with pre-existing permanent pacemaker (PPM).

Results: Nineteen consecutive patients were included in this study and 18 of them underwent at least dual valve (tricuspid and pulmonary valve) replacement surgery. Our 30-day post-surgical mortality was 0%. During the 6-month observation period following the surgery, 31.5% (n = 6) required PPM implantation due to complete AVB. There was no statistical difference in baseline characteristics and electrocardiographic and echocardiographic parameters between the patients who did or did not require PPM placement.

Conclusions: Our study revealed that almost one-third of CaHD patients who underwent a valve replacement surgery developed AVB requiring PPM implantation. Due to high incidence of PPM requirement, we believe that prophylactic placement of an epicardial lead during the valve surgery can be helpful in these patients to reduce serious complication from placement of pacemaker lead on a later date through a prosthetic valve.

Keywords: Carcinoid heart disease; Atrioventricular block; Pacemaker; Valve disease; Valve replacement surgery

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Introduction

Carcinoid heart disease (CaHD) is a fibrotic valvular process that occurs in patients with longstanding carcinoid syndrome and highly elevated levels of circulating serotonin [1]. Prior to development of effective systemic treatments for reduction of circulating serotonin levels, CaHD was reported to develop in approximately 50% of carcinoid syndrome patients [2]. In CaHD, the right-sided heart valves are primarily affected because of their direct exposure to circulating blood serotonin, leading to right heart failure. Once patients with CaHD develop heart failure symptoms, the only effective treatment option is valve surgery, which has shown to decrease mortality and improve functional symptoms [3-8]. Majority of those patients required both tricuspid valve (TV) and pulmonary valve (PV) surgeries, preferably replacement [7, 9]. In 1995, Connolly and colleagues reported that 30-day mortality in CaHD patients undergoing cardiac surgery was 35% [3]. Subsequent studies have demonstrated a decline in overall operative mortality to 10% or lower after 2000 [7, 10].

A potential complication of the valve surgery for CaHD patients is atrioventricular block (AVB). However, prior studies have not focused on the morbidity associated with this event and the appropriate management of this complication. We therefore sought to examine the incidence of AVB and permanent pacemaker (PPM) implantation following valve replacement in CaHD patients.

Materials and Methods

This retrospective chart review was conducted on consecutive patients with CaHD who were evaluated by a cardiothoracic surgeon for a valve replacement surgery at a tertiary medical

center between January 2001 and December 2015. This study was approved by Institutional Review Board of University of South Florida and Tampa General Hospital, and was conducted in accordance with the ethical standards of the institutions and with the Helsinki Declaration.

CaHD was diagnosed with echocardiography and presence of valvular thickening associated with regurgitation or stenosis. Valve surgery was recommended in stable CaHD patients if they had functional symptoms consistent with worsening heart failure or severe valvular dysfunction. Diagnoses of comorbid conditions were determined by the International Statistical Classification of Diseases and Related Health Problems (ICD)-9 or ICD-10 codes, with the exception of coronary artery disease, which had to be confirmed by left heart catheterization. Pre- and post-surgical electrocardiogram (EKG) and transthoracic echocardiogram data were collected and reviewed by an independent cardiologist.

Cardiopulmonary bypass was preformed through midline sternotomy. Inflow arterial cannula was placed in the ascending aorta and outflow cannulas placed in the superior and inferior vena cava. Operation was performed on a beating heart at normothermia. Bioprosthetic valve was used due to favorable outcomes without need for lifetime anticoagulation [7]. The biggest valve possible on the pulmonic position was used in order to maximize the unload of the weak right ventricle (RV). Our valve of choice was a 29-mm freestyle bioprosthesis. In order to fit the valve, the RV outflow track was consistently enlarged with a patch.

Difference in categorical and continuous variables was analyzed using Fisher's exact test or Chi-square test and *t*-tests, respectively. Data were presented as mean ± standard deviation (SD) or as proportion (%). All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and STATA version 12.1 (Stata Corp., College Station, TX, USA). Reported probability values were two-sided and a $P < 0.05$ was considered statistically significant.

Results

In total, 27 patients were identified with CaHD seeking surgical evaluation for valve replacement during the study period. Among them, seven patients did not undergo surgery due to extensive metastatic disease or comorbid conditions. One patient was excluded due to the presence of a PPM upon initial preoperative evaluation. After these exclusions, 19 patients were finally included in this study.

Table 1 demonstrates characteristics of study participants. The average age was 60.4 ± 1.9 years old and 57.9% were male gender. All 19 patients had symptomatic heart failure (New York Heart Association class III/IV) and were on octreotide therapy prior to the surgery. Two patients had had prior valve replacement and underwent redo valve surgery as a result of worsening disease. Sixteen patients underwent dual valve replacement (TV and PV), two patients underwent triple valve replacement (TV, PV, and aortic valve), and the other one underwent PV replacement.

During the 6-month observation period following surgery, 31.5% (n = 6) required PPM implantation due to complete AVB. There was no statistically significant difference in demographic and comorbidity profile, pre-procedural EKG parameters, and pre- and post-procedural echocardiographic parameters between PPM and non-PPM groups. Also, there was no significant difference in type of surgery between the two groups (P = 0.088). All two patients who underwent triple valve replacement developed AVB and required PPM placement, but number was too small to detect statistical difference. Our 30-day surgical mortality was 0%. Two patients died during the follow-up period, approximately 4 months after the surgery.

Table 2 demonstrates characteristics of patients who developed AVB and required PPM placement following the valve surgery. The mean time to PPM implantation after the surgery was 6.3 ± 0.5 days (median, 6.5 days). Device interrogation done in at least 4 months after the PPM implantation revealed that all patients were still dependent to the PPM except one patient whose interrogation result was not available.

Discussion

The majority of CaHD patients develop heart failure symptoms as a result of tricuspid and pulmonary insufficiency leading to right heart chamber dilation. Once they develop heart failure symptoms, the only effective treatment option is a valve surgery, and both TV and PV are usually replaced [7, 10]. In our retrospective study that included 19 patients with CaHD who underwent valve surgery, most patients (n = 18) had at least dual valve replacement (TV and PV), and 30-day operative mortality was 0%. Incidence of complete AVB requiring PPM placement after the surgery was 31.5% during the 6-month follow-up.

The incidence of PPM requirement after TV operation has been known to be higher than that after other valve interventions [11]. During replacement of the TV, independent of valve size, stitches are placed through the TV annulus, which is in close proximity to the AV node. Despite all efforts to avoid surgical injury to the AV node, injury to the node or even edema of the surrounding tissue could cause temporary or permanent AVB. In our study, the incidence of PPM requirement after valve replacement in patients with CaHD was even higher than that after overall TV operations performed in the same hospital during 2014 - 2015 (unpublished data; 24%) or other experienced centers (21-22%) [11, 12]. Although number of cases from our study was not enough to detect statistical significance of such difference, it should be noticed that almost one-third of CaHD patients required PPM placement after the valve replacement. Part of the reason is that those patients required multiple valve replacement, and multivalve surgery is a well-known risk factor for post-operative PPM requirement [13]. In addition, valve replacement is known to be associated with significantly higher risk of post-operative PPM requirement compared with valve repair [13], and all of our patients received valve replacement surgery.

AVB after valve surgery can be transient and recovery of conduction usually occurs before the seventh postoperative day [13, 14]. However, since there are risks of delayed PPM implantation (e.g. prolonged immobilization and hospital

Table 1. Characteristic of Patients With Carcinoid Heart Disease Who Underwent a Valve Replacement Surgery According to Post-Surgical Permanent Pacemaker Placement

	Overall (n = 19)	Post-surgical PPM placement		
		PPM (n = 6)	No PPM (n = 13)	P value[a]
Demographic and comorbidity profile				
Age[b], years	60.4 ± 1.9	63.2 ± 1.9	59.2 ± 2.6	0.331
Male	11 (57.9)	1 (16.7)	10 (76.9)	0.041
Hypertension	12 (63.2)	1 (16.7)	11 (84.6)	0.010
Diabetes mellitus	3 (15.8)	1 (16.7)	2 (15.4)	1.000
Hyperlipidemia	4 (21.1)	1 (16.7)	3 (23.1)	1.000
Coronary artery disease[c]	2 (10.5)	1 (16.7)	1 (7.7)	1.000
Atrial fibrillation	7 (36.9)	4 (66.7)	3 (23.1)	0.129
Obesity[d]	4 (21.1)	0 (0.0)	4 (33.8)	0.255
NYHA class III/IV	19 (100)	6 (100)	13 (100)	-
Prior treatment				
Prior valve surgery	2 (10.5)	1 (16.7)	1 (7.7)	1.000
Prior octreotide treatment	19 (100)	6 (100)	13 (100)	-
Pre-surgical EKG parameters				
First degree AVB	3 (15.8)	0 (0.0)	3 (23.1)	0.522
≥ Second degree AVB	0 (0)	0 (0)	0 (0)	-
RBBB	3 (15.8)	0 (0.0)	3 (23.1)	0.517
Left fascicular block	2 (10.5)	1 (16.7)	1 (7.7)	1.000
PR interval (ms)	167.6 ± 13.0	158.8 ± 9.8	171.6 ± 18.6	0.660
QRS interval (ms)	102.3 ± 4.0	104.2 ± 10.7	101.5 ± 3.7	0.765
Pre-surgical TTE parameters				
LVEF (%)	54.6 ± 1.2	56.8 ± 1.9	53.5 ± 1.5	0.236
Reduced RV function	15 (79.0)	4 (66.7)	11 (84.6)	0.557
RVSP (mm Hg)	32.0 ± 3.0	35.0 ± 9.1	30.9 ± 2.8	0.566
Pulmonary insufficiency, moderate to severe	12 (63.2)	2 (33.3)	10 (76.9)	0.129
Pulmonary stenosis	11 (58.9)	3 (50.0)	8 (61.5)	1.000
Tricuspid regurgitation, moderate to severe	18 (94.7)	6 (100.0)	12 (92.3)	1.000
Tricuspid stenosis	6 (31.6)	1 (16.7)	5 (38.5)	0.605
Post-surgical TTE parameters[a]				
LVEF (%)	55.6 ± 2.2	55.8 ± 4.0	55.5 ± 2.8	0.945
Reduced RV function	7 (43.8)	3 (50.0)	4 (40.0)	1.000
RVSP (mm Hg)	30.3 ± 2.5	36.0 ± 5.1	28.0 ± 2.7	0.161
Type of surgery				0.088
PVR	1 (6.3)	0 (0.0)	1 (7.7)	
PVR + TVR	16 (84.2)	4 (66.7)	12 (92.3)	
PVR + TVR + AVR	2 (10.5)	2 (33.3)	0 (0.0)	
Post-surgical mortality	2 (10.5)	1 (16.7)	1 (7.7)	1.000
Operative (30 days)	0 (0.0)	0 (0.0)	0 (0.0)	-
During 6-months follow up	2 (10.5)	1 (16.7)	1 (7.7)	1.000

Values are number (%) or mean ± standard deviation. [a]Fisher's exact test or *t*-test. [b]Average age in years at time of surgery or during last visit. [c]Diagnosed via left heart catheterization. [d]Body mass index ≥ 30 kg/m^2. AVB: atrioventricular block; AVR: aortic valve replacement; EKG: electrocardiogram; LVEF: left ventricular ejection fraction; ms: millisecond; NYHA: New York Heart Association; PPM: permanent pacemaker; PVR: pulmonary valve replacement; RBBB: right bundle branch block; RV: right ventricle; RVSP: right ventricular systolic pressure; TTE: transthoracic echocardiogram; TVR: tricuspid valve replacement.

Table 2. Characteristics of Patients With Carcinoid Heart Disease Who Required Post-Surgical Pacemaker Placement

Patient	Surgery	Year of surgery	Prior valve surgery	Reason for PPM	Time to PPM (days)	PPM type	PPM burden in several months
1	TVR, PVR	2012	Yes (TVR, PVR)	CHB	6	Dual-chamber	100% V-paced
2	TVR, PVR, AVR	2014	None	CHB	8	Dual-chamber	NA
3	TVR, PVR	2015	None	CHB	7	Dual-chamber	33% A-paced
4	TVR, PVR	2015	None	CHB	7	Dual-chamber	19% A-paced, 100% V-paced
5	TVR, PVR	2004	None	CHB	5	Dual-chamber	100% V-paced
6	TVR, PVR, AVR	2012	None	CHB	5	Dual-chamber	87% A-paced, 11% V-paced

AVR: aortic valve replacement; CHB: complete heart block; NA: not available; PPM: permanent pacemaker: PVR: pulmonary valve replacement; TVR: tricuspid valve replacement; A: atrial; V: ventricular.

stay), the best timing of permanent pacing is still controversial. Per literature review, it is generally recommended to defer the PPM placement no earlier than 5 - 7 days after the surgery [13-15]. In our study, the mean time to PPM implantation after the surgery was 6.3 ± 0.5 days (median, 6.5 days), which was not quite different from what was recommended. Furthermore, device interrogation done in several months after the PPM implantation revealed that those patients continued to be dependent on the PPM.

After TV replacement, placement of an endocardial ventricular pacemaker lead could be difficult. The lead, if placed at a later time through the prosthetic valve, will damage the prosthetic valve with time. It can also increase the risk of prosthetic endocarditis. To prevent such complications, preemptive placement of an epicardial right ventricular pacemaker lead was advised by our team. Therefore, all 19 patients in our study had a bipolar epicardial ventricular lead placed and tunneled underneath the left chest. These leads were well tolerated and relatively easy to connect if PPM needs to be utilized.

This study has several limitations. First, it was a single-center, retrospective study with a small sample size. Secondly, our study period extends over 14 years in which changes in the care of cardiac disease patients in general may have affected the results. Despite above limitations, this is the first study to investigate the incidence of AVB requiring PPM placement after valve replacement surgery in CaHD patients.

Conclusions

In conclusion, our study found that almost one-third of CaHD patients who underwent a valve replacement surgery required post-operative PPM placement due to AVB. Therefore, we believe that prophylactic placement of an epicardial lead during the valve surgery could be helpful in these patients to reduce serious complications that can result from repeat thoracotomy or placement of pacemaker lead on a later date through a prosthetic valve.

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Financial Disclosure

None to declare.

Conflict of Interest

All authors have nothing to disclose.

Informed Consent

This study was approved to waive informed consent process by the IRB committee.

Author Contributions

IS and D Sayad contributed to conceptualization; IS, D Shin, KMS, and TT contributed to data curation; IS, D Shin, KMS, and TT contributed to writing and original draft preparation; IS, D Shin, KMS, JVP, SHC, CCC, JRS, and D Sayad contributed to writing, critical review and editing.

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