JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 66, NO. 20, 2015

ISSN 0735-1097/$36.00
PUBLISHED BY ELSEVIER INC. http://dx.doi.org/10.1016/j.jacc.2015.09.014

Early and Late Outcomes of Surgical Treatment in Carcinoid Heart Disease

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ABSTRACT

BACKGROUND Symptoms and survival of patients with carcinoid syndrome have improved, but development of carcinoid heart disease (CaHD) continues to decrease survival.

OBJECTIVES This study aimed to analyze patient outcomes after valve surgery for CaHD during a 27-year period at 1 institution to determine early and late outcomes and opportunities for improved patient care.

METHODS We retrospectively studied the short-term and long-term outcomes of all consecutive patients with CaHD who underwent valve replacement at our institution between 1985 and 2012.

RESULTS The records of 195 patients with CaHD were analyzed. Pre-operative New York Heart Association class was III or IV in 125 of 178 patients (70%). All had tricuspid valve replacement (159 bioprostheses, 36 mechanical), and 157 underwent a pulmonary valve operation. Other concomitant operations included mitral valve procedure (11%), aortic valve procedure (9%), patent foramen ovale or atrial septal defect closure (23%), cardiac metastasectomies or biopsy (4%), and simultaneous coronary artery bypass (11%). There were 20 perioperative deaths (10%); after 2000, perioperative mortality was 6%. Survival rates (95% confidence intervals) at 1, 5, and 10 years were 69% (63% to 76%), 35% (28% to 43%), and 24% (18% to 32%), respectively. Overall mortality was associated with older age, cytotoxic chemotherapy, and tobacco use; 75% of survivors had symptomatic improvement at follow-up. Presymptomatic valve operation was not associated with late survival benefit.

CONCLUSIONS Operative mortality associated with valve replacement surgery for CaHD has decreased. Symptomatic and survival benefit is noted in most patients when CaHD is managed by an experienced multidisciplinary team.
(J Am Coll Cardiol 2015;66:2189–96) © 2015 by the American College of Cardiology Foundation.

During the past 30 years, new medical and surgical treatments have emerged for malignant carcinoid syndrome. Medical therapies have targeted the symptom complex of carcinoid syndrome through the use of the somatostatin analogue octreotide. Surgical therapies have targeted hepatic metastases with dearterialization, resection, debulking, and liver transplantation. These treatments have improved symptoms and longevity in patients with carcinoid syndrome (1–7); however, for patients with cardiac involvement, right-sided heart failure worsens their quality of life and leads to excess mortality. Valve surgery is the only effective treatment option for patients with symptomatic carcinoid heart disease (CaHD) and improves survival (8). Without operation, only 10% of patients survive 2 years after the onset of New York Heart Association (NYHA) functional class III or IV symptoms (9).

In this study, we evaluated short-term and long-term outcomes after valve replacement surgery in 195 consecutive patients with CaHD at 1 institution,

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Manuscript received March 10, 2015; revised manuscript received July 24, 2015, accepted September 2, 2015.

ABBREVIATIONS AND ACRONYMS

CaHD = carcinoid heart disease

CI = confidence interval

NYHA = New York Heart Association

spanning a 27-year experience. We have previously reported our initial experience with 26 patients (9).

METHODS

PATIENTS. The Mayo Clinic Institutional Review Board approved the study. Between November 1985 and December 2012, 195 consecutive patients with CaHD underwent valve surgery at the Mayo Clinic, Rochester, Minnesota, in an attempt to improve symptoms and survival. We retrospectively reviewed the pre-operative characteristics, intraoperative management, and operative outcomes of these patients.

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CLINICAL AND LABORATORY FINDINGS. A comprehensive pre-operative clinical evaluation was performed that included echocardiography in all patients. All patients were cared for by a multidisciplinary team that included a medical oncologist, cardiologist, cardiac anesthesiologist, and cardiac surgeon. Coronary angiography was performed pre-operatively when applicable (10).

The usual initial pre-operative dose of octreotide was 150 μg, administered subcutaneously every 8 h. Since the introduction and use of the octreotide long-acting release formulation (Sandostatin, Novartis, Basel, Switzerland) in 1999 (11), most patients received this agent, typically 20 mg intramuscularly every 28 days, with higher long-acting release and supplementary short-acting doses administered for breakthrough symptoms or tachyphylaxis.

Because of the known poor prognosis of patients with severe symptomatic CaHD, patients were screened for cardiac disease. Valve surgery was offered to patients who had symptomatic severe CaHD, progressive right-sided cardiac chamber enlargement or dysfunction, or severe hepatic involvement requiring surgery with increased right atrial pressure (12).

Patients with CaHD and severe tricuspid valve regurgitation who underwent echocardiography at the Mayo Clinic during the same time period but did not have an operation were identified through the echocardiography laboratory database. The reason they did not have valve replacement at the Mayo Clinic was recorded.

SURGICAL MANAGEMENT. Treatment was not randomized. Initially, mechanical prostheses were recommended for tricuspid valve replacement because of the reported carcinoid involvement of a porcine bioprosthesis (13). Over time, bioprostheses were increasingly used in patients considered to be at high risk for anticoagulation-related complications; because of the generally favorable short-term outcomes in these patients, bioprostheses were used more frequently.

Pulmonary valve intervention was performed if pulmonary valve disease was present. In our early experience, pulmonary valvectomy was preferred. Subsequently, long-standing severe pulmonary valve regurgitation that occurred after this procedure was recognized to adversely affect right ventricular remodeling. Since 2002, the pulmonary valve has been routinely replaced when involved by CaHD (14).

Meticulous pre-operative planning and perioperative care were instituted for patients with CaHD to prevent life-threatening carcinoid crises (15) or to institute early therapy should a crisis occur intraoperatively. Anesthetic management aimed to limit hemodynamic perturbations associated with carcinoid reactions, primarily through the use of intravenous octreotide and vasopressors, as well as to initiate aggressive therapy for long-standing right-sided heart failure with hemofiltration and diuresis (15–17). Intravenous octreotide acetate was used if flushing, unexplained hemodynamic lability, or volume loss occurred during extracorporeal circulation (17).

PATHOLOGICAL FINDINGS. The surgical pathology reports were reviewed to assess the gross and microscopic pathology of the native valves and the explanted prostheses in patients who underwent reoperation (18).

OUTCOMES. Follow-up data were obtained by review of medical records. Perioperative death was defined as death within 30 days of operation or during the same hospital stay. The Social Security Index was used to determine whether patients who had not returned for follow-up were alive or dead.

STATISTICAL METHODS. Descriptive statistics for categorical variables are reported as frequency (percentage) and continuous variables as mean ± standard deviation or median and range. Thirty-day mortality was compared between surgical eras by use of the Fisher exact test.

The Kaplan-Meier method was used to calculate 1-, 5-, and 10-year survival and freedom from reoperation statistics. Cox regression models were used to find the univariate and multivariate predictors of overall mortality and reoperation. The multivariate model considered univariately significant variables ($p < 0.05$), with model selection using the stepwise method (backward and forward methods resulted in the same model). All statistical tests were 2-sided, and $p < 0.05$ was considered statistically significant. SAS software version 9.3 (SAS Institute, Inc., Cary, North Carolina) was used for statistical analysis.

RESULTS

CLINICAL AND DIAGNOSTIC DATA. During the study period, 195 patients with CaHD (98 men; mean age 61 ± 11 years) underwent valve surgery. Patients' preoperative clinical features are shown in Table 1. Most patients had primary carcinoid disease in the intestine with hepatic metastasis. Four patients had primary ovarian carcinoid tumor without hepatic metastasis (19,20). The mean time from diagnosis of carcinoid tumor to the valve operation was 4.7 ± 6.0 years. The NYHA functional class was III or IV in 125 patients (70%). Octreotide therapy was used before operation in 184 patients (94%) (Table 1).

All patients had severe tricuspid valve regurgitation. Pulmonary, mitral, or aortic valve disease that warranted intervention was detected in 157, 21, and 18 patients, respectively. Significant coronary artery disease (stenosis ≥50% diameter) was present in 27 patients who underwent pre-operative coronary angiography.

During the same time period, 108 patients had CaHD and severe tricuspid valve regurgitation identified by echocardiography at our institution but did not have an operation at the Mayo Clinic. Of those 108 patients, 39 (36%) were asymptomatic or minimally symptomatic, 6 (6%) underwent valve replacement elsewhere, 10 (9%) died before cardiac consultation or intervention, 9 (8%) were lost to follow-up, and 8 (7%) declined intervention. Thirty-six (33%) were not believed to be surgical candidates for the following reasons: comorbid conditions (n = 17), extensive metastatic disease (n = 14), left ventricular dysfunction (n = 3), age (n = 1), or religious objections (n = 1).

TABLE 1 Pre-Operative Clinical Features (N = 195)

Men	98 (50)
Age at cardiac surgery, yrs	61 ± 11 62 (25–87)
NYHA functional class (n = 178)	
I or II	53 (30)
III or IV	125 (70)
Creatinine, mg/dl	1.2 ± 0.4
Other chemotherapy for carcinoid disease	47 (24)
Octreotide therapy	184 (94)
Dose per 24 h	
Short-acting, μg	750 (200–3,000)
LAR, mg	30 (20–120)
Time from carcinoid diagnosis to valve surgery, yrs (n = 118)	4.7 ± 6 2.4 (0–41)

Values are n (%), mean ± SD, or median (range).
LAR = octreotide long-acting release formulation; NYHA = New York Heart Association.

SURGICAL MANAGEMENT. Surgical data are presented in Table 2. Tricuspid valve replacement involved bioprostheses in 159 patients and mechanical valves in 36; median valve size was 31 mm. Pulmonary valve intervention was performed in 157 patients: 50 had pulmonary valvectomy with outflow tract enlargement, and 107 had pulmonary valve replacement.

Concomitant CaHD with moderate or greater regurgitation prompted mitral valve repair in 5 patients and mitral valve replacement in 16 patients. Three patients had aortic valve repair, and 15 had aortic valve replacement. Seven patients underwent quadruple valve replacement (21). Coronary artery bypass grafting surgery was also performed in 22 patients. Eleven patients (6%) required permanent pacemaker implantation for persistent post-operative heart block.

The mean cardiopulmonary bypass time was 88 ± 37 min, and cross-clamp time was 30 ± 30 min. Large doses of octreotide were often required; the

TABLE 2 Surgical Features (N = 195)

CPB time, min	88 ± 37 (16–205)
Tricuspid valve replacement only	83 ± 34
Tricuspid valve replacement with other valve operation	127 ± 37
Tricuspid valve replacement	
Mechanical	36 (18)
Bioprosthesis	159 (82)
Tricuspid valve size, mm	31 (25–34)
Pulmonary valve replacement	107 (55)
Mechanical	6 (6)
Bioprosthesis	101 (94)
Pulmonary valve size, mm	25 (19–31)
Pulmonary valvectomy	50 (26)
Mitral valve prosthesis	16 (8)
Mechanical	5 (31)
Bioprosthesis	11 (69)
Mitral valve size, mm	27 (25–29)
Mitral valve repair	5 (3)
Aortic valve prosthesis	15 (8)
Mechanical	5 (33)
Bioprosthesis	10 (67)
Aortic valve size, mm	21 (19–27)
Aortic valve repair	3 (2)
PFO or ASD closure	45 (23)
Cardiac metastasis biopsied or removed	8 (4)
Simultaneous coronary artery bypass surgery	22 (11)
Octreotide dose during operation, mg	0.5 (0.0–2.1)
Pacemaker	11 (6)
Time in hospital, days	9 ± 7
Death in hospital or within 30 days	20 (10)

Values are mean ± SD (range), n (%), or median (range).
ASD = atrial septal defect; CPB = cardiopulmonary bypass; PFO = patent foramen ovale.

TABLE 3 Univariate and Multivariate Predictors of Overall Mortality

Predictor	Univariate		Multivariate	
	HR (95% CI)	p Value	HR (95% CI)	p Value
Age	1.03 (1.01–1.04)	<0.001	1.02 (1.01–1.04)	<0.01
Higher pre-operative creatinine	1.70 (1.04–2.79)	0.03		
Longer time from carcinoid diagnosis to valve operation	1.02 (0.99–1.04)	0.25		
Higher EF	0.99 (0.97–1.00)	0.13		
Female	0.77 (0.55–1.08)	0.13		
Year of surgery				
1990–1999	0.73 (0.37–1.44)	0.37		
2000–2009	0.56 (0.29–1.10)	0.09		
2010–2012	0.79 (0.32–1.94)	0.61		
Pre-operative NYHA functional class III or IV	1.63 (1.07–2.49)	0.02		
Loop diuretic agents				
Not used	0.81 (0.58–1.14)	0.23		
Higher dose	1.16 (0.83–1.61)	0.40		
Higher oral dose	0.95 (0.67–1.34)	0.77		
IV furosemide	1.67 (1.08–2.58)	0.02		
Somatostatin therapy	2.15 (0.94–4.88)	0.07		
Pre-operative chemotherapy	1.48 (1.04–2.11)	0.03	1.48 (1.03–2.11)	0.03
Nonpharmacological treatment of metastatic disease	0.78 (0.55–1.10)	0.15		
Ascites	1.48 (1.06–2.08)	0.02		
Leg edema	1.32 (0.90–1.94)	0.16		
Pre-operative diabetes mellitus	1.88 (1.05–3.34)	0.03		
Pre-operative hypertension	1.06 (0.76–1.49)	0.71		
Pre-operative tobacco use	1.96 (1.40–2.75)	<0.001	1.71 (1.21–2.42)	<0.01
Pre-operative CAD	1.39 (0.95–2.04)	0.09		
PVR	0.82 (0.59–1.15)	0.26		
Mechanical valve	1.43 (0.96–2.11)	0.08		
Moderate or greater MV or AV regurgitation	1.69 (1.08–2.64)	0.02		
Larger RV size	0.50 (0.30–0.83)	0.008		
Reduced RV systolic function	1.59 (1.00–2.52)	0.049		
Moderate or greater PV regurgitation	1.15 (0.75–1.76)	0.52		
Higher Charlson index	1.02 (0.96–1.08)	0.52		
Isolated TVR	0.98 (0.54–1.78)	0.95		

AV = aortic valve; CAD = coronary artery disease; CI = confidence interval; EF = ejection fraction; HR = hazard ratio; IV = intravenous; MV = mitral valve; NYHA = New York Heart Association; PV = pulmonary valve; PVR = pulmonary valve replacement; RV = right ventricle; TVR = tricuspid valve replacement.

median octreotide dose administered during the perioperative period was 0.5 mg (range 0 to 2.1 mg). The overall mean hospital stay was 9 ± 7 days.

VALVE PATHOLOGY. Examination of the explanted valves demonstrated gross cusp thickening without calcification. Thickening was attributable to cellular proliferation and deposition of extracellular matrix, which comprised collagen, myxoid ground substance, and elastin. Carcinoid plaque involved the tricuspid and mitral valve leaflets, tendinous cords, and papillary muscles. Excised pulmonary and aortic valve cusps also demonstrated carcinoid plaques.

Microscopic examination of the explanted tricuspid bioprostheses demonstrated degenerating and organizing thrombus without typical carcinoid plaques in 4 patients, pannus in 1 patient, and normal appearance in 2 patients (whose bioprostheses were replaced at the time of pulmonary valve replacement for pulmonary valve regurgitation). One patient had microscopic features of bioprosthetic carcinoid plaque deposition with associated prosthetic valve dysfunction at the time of reoperation, more than 8 years after initial valve replacement.

SURVIVAL AND OUTCOMES. Univariate predictors of perioperative death included era of operation (higher mortality before 2000), need for pre-operative loop diuretic therapy, mechanical valve replacement, and longer cardiopulmonary bypass time (data not shown). By multivariate analysis, era of operation and need for intravenous loop diuretic therapy were related to perioperative mortality (data not shown).

The overall operative mortality was 10%. The surgical deaths were not equally distributed over the 27-year period: mortality was highest before 1990 (2 of 10, or 20%) and decreased in each subsequent decade. Of the 20 perioperative deaths, 12 occurred in the first 71 patients (before 2000; 17%). Since 2000, 8 perioperative deaths occurred in 124 patients (6%): 7 of 97 (7.2%) occurred between 2000 and 2009, and 1 of 27 (3.7%) occurred between 2010 and 2012.

Survival at 1, 5, and 10 years was 69% (95% confidence interval [CI]: 63% to 76%), 35% (95% CI: 28% to 43%), and 24% (95% CI: 18% to 32%), respectively. Maximal survival to date is 19.5 years after valve replacement for CaHD. Univariate predictors of mortality included patient age, pre-operative serum creatinine value, pre-operative NYHA functional class, use of intravenous furosemide, pre-operative chemotherapy, presence of ascites, diabetes mellitus, pre-operative tobacco use, left-sided valve disease, and right-sided heart size and function (Table 3). By multivariate analysis, older age, pre-operative chemotherapy, and pre-operative tobacco use remained significant predictors of mortality during follow-up. Survival did not differ by type of valve used ($p = 0.08$) (Figure 1).

During follow-up, 17 patients had reoperation, with some patients having more than 1 procedure: 8 tricuspid bioprosthesis replacements, 8 pulmonary valve replacements (3 after initial pulmonary valvectomy), 5 pericardiectomies, 1 mechanical tricuspid prosthesis replacement, and 1 emergent pulmonary valve replacement for pulmonary artery rupture during attempted homograft balloon valvuloplasty. Survival free from reoperation was not related to prosthesis type ($p = 0.22$) (Figure 2). At reoperation for bioprosthesis dysfunction, 7 valves were replaced

with mechanical prostheses. One of the patients included in this series had percutaneous valve-in-valve tricuspid and pulmonary valve replacement for prosthesis dysfunction.

In 1 patient, a thrombus developed on a mechanical tricuspid prosthesis related to inadequate systemic anticoagulation; this caused dyspnea and an increase in transvalvular gradient. The thrombus was successfully treated with intravenous thrombolytic therapy.

Among patients with significant limiting preoperative symptoms (NYHA functional class III or IV), symptomatic improvement was noted in 69 of 92 patients (75%), and 118 of 155 patients (76%) were in NYHA functional class I or II at follow-up.

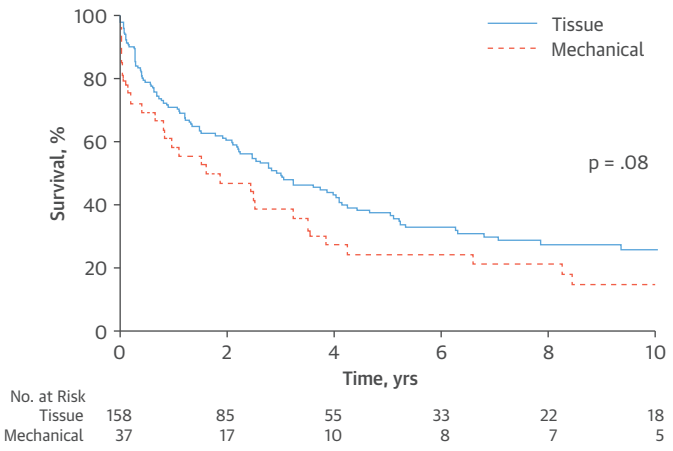
DISCUSSION

In this series of 195 consecutive surgically treated patients with CaHD, operative risk, patient selection, post-operative symptoms, and long-term survival have improved with time and experience of our specialized multidisciplinary team. In our initial surgical experience with CaHD (9) and in reports from other centers (22-24), the perioperative risk of valve replacement in patients with CaHD was high. We subsequently refined our approach to carcinoid syndrome and CaHD. With increased experience and a multidisciplinary approach, operative mortality decreased in our series from 20% before 1990 to <5% (**Central Illustration**). Our operative mortality compares favorably with reports from before 2012, which ranged from 18% to 63% (22-24).

Post-operative survival among patients with CaHD has also improved over time. Survival is markedly improved compared with medically managed historical control subjects with NYHA functional symptoms greater than class II: only 10% of those patients survived 2.5 years (8,9). The current series also demonstrates favorable survival (**Figure 1**) compared with our early surgical series (9). Post-operatively, most patients had symptomatic improvement, with survival up to 19.5 years after valve replacement. Lack of improvement in functional status after operation was related to tumor progression in some patients; others appeared to have systolic or diastolic right-sided heart failure with or without pericardial effusion or constriction.

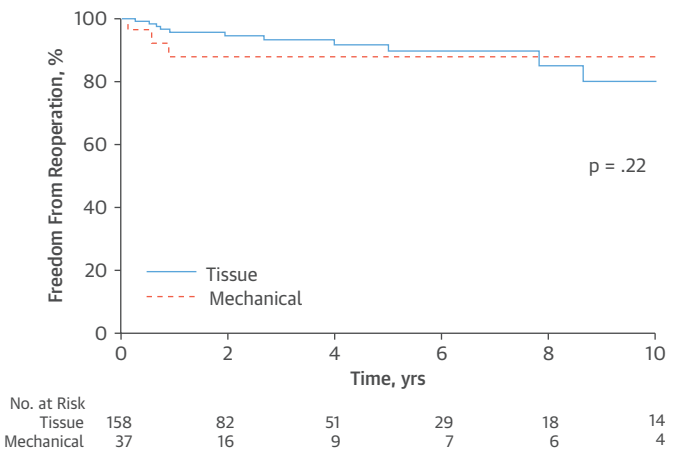
Because of the known poor prognosis related to severe symptomatic CaHD, we decided to evaluate patients annually for cardiac involvement. Echocardiography was performed in patients with signs or symptoms of cardiac disease. A multidisciplinary team approach (8) allowed us to refine indications for operation. We offered valve surgery to both symptomatic patients with severe CaHD and asymptomatic or minimally symptomatic patients with progressive right-sided heart enlargement or dysfunction. We also referred some asymptomatic patients with severe CaHD for correction of valve regurgitation before partial hepatectomy or liver transplantation. Liver operation carries excess risk in patients with CaHD with high right atrial pressure (12). We avoid valve replacement surgery in patients with end-stage metastatic disease and in those with poorly controlled systemic carcinoid symptoms despite octreotide therapy or hepatic dearterialization.

FIGURE 1 Survival by Tricuspid Valve Prosthesis Type



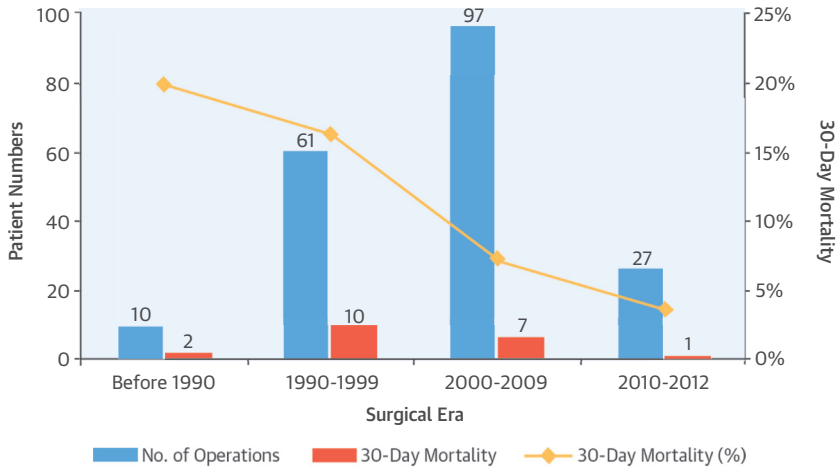
Kaplan-Meier overall survival.

FIGURE 2 Freedom From Reoperation by Valve Type



Kaplan-Meier survival free from reoperation.

CENTRAL ILLUSTRATION Surgical Treatment Outcomes in Carcinoid Heart Disease: 30-Day Mortality by Surgical Era



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30-day cardiac surgical mortality attributable to carcinoid heart disease according to era of operation.

A major clinical challenge in patients with CaHD is the difficulty distinguishing symptoms of right-sided heart failure from end-stage metastatic carcinoid disease, because both can present with progressive fatigue, edema, and ascites. Clinical status after valve replacement serves as the confirmatory clinical tool, but operation carries an excess risk of morbidity and decreased post-operative survival when pre-operative symptoms are primarily related to advanced metastatic disease. Improved pre-operative tools are needed for continued refinement of risk stratification. This will most likely require a comprehensive assessment of tumor burden, nutritional status, cardiac disease, and the potential for future tumor management.

Mechanical valve prostheses were used for tricuspid valve replacement in our early experience because of the reported carcinoid involvement of a porcine bioprosthesis (13). Over time, we used bioprostheses more often in patients considered to be at higher than normal risk for anticoagulation-related complications; the generally favorable short-term outcome in these patients led us to use bioprostheses more liberally. In addition, pathological review of explanted bioprostheses suggested that carcinoid involvement was an uncommon reason for valve dysfunction requiring reoperation; it was found in only 1 explanted bioprosthesis in our series.

The most frequent cause of tricuspid bioprosthesis dysfunction in our patients was thrombus. Identification of thrombus on dysfunctional explanted bioprostheses resulted in a protocol change. We now recommend post-operative vitamin K antagonist anticoagulation for 3 months and periodic echocardiographic surveillance of the prosthetic valves after cessation of anticoagulation. Reversal of bioprosthesis dysfunction has been noted in patients with CaHD with reinitiation of vitamin K antagonist anticoagulation (25). When reoperation is required for bioprosthetic valve dysfunction related to carcinoid or thrombus formation, a mechanical prosthesis is advised when vitamin K antagonist anticoagulation can be tolerated (26). Alternatively, percutaneous valve-in-valve replacement may be considered for select patients (27).

Since 2002, we have routinely replaced the pulmonary valve when CaHD affected it because of the incomplete right ventricular remodeling recognized in patients with long-standing severe pulmonary valve regurgitation (14). Homografts were used to replace the pulmonary valve early in our experience; however, in several patients, we identified premature dysfunction related to constriction of the homograft. We now favor placement of a large stented bioprosthesis, facilitated with patch enlargement of the pulmonary valve annulus and outflow tract. Rarely, a mechanical prosthesis is used for tricuspid valve replacement (26). In this setting when pulmonary valve replacement is indicated, a mechanical pulmonary prosthesis is preferred over bioprosthesis (28).

In our patients with CaHD, multivariate analysis showed that perioperative mortality was related to the era of operation and the need for pre-operative intravenous diuretic therapy. These findings demonstrate that surgical survival has improved during our experience. This likely reflects a combination of improved patient selection, experience of the multidisciplinary team, progress in the management of the underlying malignancy, and possible advances in surgical and valve technology. In the past, right-sided valve surgery was performed relatively late in the natural history of the disease and on patients with features of advanced right-sided heart failure (10,29).

Increasingly, data suggest survival benefit with presymptomatic surgical intervention for left-sided valve disorders (10). By univariate analysis, advanced NYHA functional class was associated with decreased long-term survival in our series. However, by multivariate analysis, long-term survival benefit was not detected with presymptomatic surgical intervention. This most likely reflects the comorbid malignancy that independently decreases life expectancy.

Our multivariate analysis suggests that patients with carcinoid disease and anasarca who require hospitalization and intravenous diuretic treatment before operation have decreased perioperative survival. In addition, older patients, those with a history of tobacco use, and those with carcinoid disease treated with chemotherapy other than octreotide before valve operation also had reduced survival. These patients represent the group with the most advanced disease and highest risk. Some of these patients have end-stage metastatic carcinoid disease that affects survival more than right-sided heart failure from CaHD.

STUDY LIMITATIONS. These data must be interpreted in light of the retrospective, nonrandomized study design and a component of referral bias. Patients with carcinoid syndrome pose a clinical challenge, because it is often difficult to objectify pre-operative functional status as a result of isolated right-sided heart disease and comorbid malignancy. Unfortunately, a subset of the patients referred to our center for consideration of valve surgery are severely symptomatic with advanced carcinoid disease and anasarca, which results in poor operative risk and decreased post-operative survival.

CONCLUSIONS

CaHD decreases survival in patients with carcinoid syndrome. These patients have multivalve disease and comorbid conditions. Despite this complexity, symptomatic patients with CaHD and controlled systemic disease who are referred for valve surgery have an acceptable perioperative risk when treated at an experienced center by a multidisciplinary team. Valve operation before the onset of advanced symptoms carries a survival benefit for this population compared with operation performed for more advanced symptoms. Symptomatic improvement is noted in the majority.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Most patients with symptomatic carcinoid valvular heart disease benefit from valve replacement surgery in terms of both survival and symptoms.

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: Valve replacement surgery should be considered for patients with symptomatic carcinoid heart disease before they develop advanced right-sided heart failure.

TRANSLATIONAL OUTLOOK: Future studies should seek to define imaging and biomarker strategies to distinguish right-sided heart failure from end-stage metastatic carcinoid disease and to guide timing of valve replacement surgery.

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KEY WORDS carcinoid syndrome, right-sided heart failure, valve replacement