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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.
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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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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.