A Prospective Multi-Institutional Cohort Study of Mediastinal Infections After Cardiac Operations

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Background. **Mediastinal infections are a potentially devastating complication of cardiac operations. This study analyzed the frequency, risk factors, and perioperative outcomes of mediastinal infections after cardiac operations.**

Methods. **In 2010, 5,158 patients enrolled in a prospective study evaluating infections after cardiac operations and their effect on readmissions and mortality for up to 65 days after the procedure. Clinical and demographic characteristics, operative variables, management practices, and outcomes were compared for patients with and without mediastinal infections, defined as deep sternal wound infection, myocarditis, pericarditis, or mediastinitis.**

Results. **There were 43 mediastinal infections in 41 patients (cumulative incidence, 0.79%; 95% confidence interval [CI] 0.60% to 1.06%). Median time to infection was 20.0 days, with 65% of infections occurring after the index hospitalization discharge. Higher body mass index (hazard ratio [HR] 1.06; 95% CI, 1.01 to 1.10), higher creatinine (HR, 1.25; 95% CI, 1.13 to 1.38), peripheral vascular disease (HR, 2.47; 95% CI, 1.21 to 5.05), preoperative corticosteroid use (HR, 3.33; 95% CI, 1.27 to 8.76), and ventricular assist device or transplant surgery (HR, 5.81; 95% CI, 2.36 to 14.33) were associated with increased risk of mediastinal infection. Postoperative hyperglycemia (HR, 3.15; 95% CI, 1.32 to 7.51) was associated with increased risk of infection in nondiabetic patients. Additional length of stay attributable to mediastinal infection was 11.5 days (bootstrap 95% CI, 1.88 to 21.11). Readmission rates and mortality were five times higher in patients with mediastinal infection than in patients without mediastinal infection.**

Conclusions. **Mediastinal infection after a cardiac operation is associated with substantial increases in length of stay, readmissions, and death. Reducing these infections remains a high priority, and improving postoperative glycemic management may reduce their risk in patients without diabetes.**

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Major infection after cardiac operations remains a complication of significant concern to physicians and patients alike. Despite advances in care and multiple initiatives to decrease postoperative infections, nearly 5% of patients continue to experience major infection after their cardiac operation [1]. These infections have been shown to increase morbidity, death, and costs [1, 2].

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Efforts to eliminate the occurrence of mediastinal infection have been largely unsuccessful. The reported incidence of this serious complication after cardiac operations is 0.2% to 8.0%, with most estimates between 1% and 2%, and has remained stable over time [3–9]. Although a number of risk factors for mediastinal infection after cardiac operations have been described, most studies have been from a single center, retrospective, have not adjudicated infections, and lack follow-up past discharge or 30 days postoperatively [9]. In this study, we used prospective data collected by the Cardiothoracic Surgical Trials Network to characterize mediastinal infections in cardiac surgical patients and analyze patient risk factors and processes of care associated with these infections.

Patients and Methods

Patient Population

The study cohort included all patients at Cardiothoracic Surgical Trials Network sites (Appendix I and Consolidated Standards of Reporting Trials diagram) who participated in the prospective observational study "Management Practices and the Risk of Infection Following Cardiac Surgery" (NCT01089712) [1]. Participating sites enrolled patients consecutively between February and October 2010 who had a clinical indication for a cardiac operation, did not have an active systemic infection, were at least 18 years old, and provided written informed consent. The study was approved by Institutional Review Boards at each participating clinical center and at the data coordinating center.

Study Design

The primary outcome of interest in this analysis was the incidence of mediastinal infection, defined as deep sternal wound infection (DSWI), mediastinitis, pericarditis, or infectious myocarditis (Appendix II). Participants were monitored for up to 65 days to determine the incidence of major and minor infections, all-cause death, and hospital readmission. Infections were classified based on definitions from the Centers for Disease Control and Prevention and the National Healthcare Safety Network surveillance. All major infections, including mediastinal infections, and a subset of minor infections were adjudicated by an event adjudication committee that included 3 infectious disease experts [10].

Data were collected on comorbidities, procedure-related variables, and management practices. Postoperative hyperglycemia was defined as one or more blood glucose measurements above 180 mg/dL during the first 48 hours postoperatively.

Statistical Analysis

Univariable Cox proportional hazards regression models were used to assess differences in patient demographics, operative characteristics, and postoperative management by whether a mediastinal infection developed during the 65-day follow-up period. Factors with a p value of 0.15 or lower in univariable analyses were considered for inclusion in a multivariable model. A multivariable Cox proportional hazards regression model treating death as a competing risk was used to determine the cumulative incidence of mediastinal infection and the association of patient characteristics and management practices with mediastinal infection [11]. The interaction between diabetes and hyperglycemia was tested at the $p = 0.10$ threshold; all other variables included in the final model were tested at the $p = 0.05$ level.

Death by time-varying mediastinal infection was assessed by a Cox proportional hazards regression model adjusted for variables shown to be associated with death in the cohort as a whole [1].

Survival estimates for the average patient in the cohort (age, 64 years; creatinine, 1.165 mg/dL; no diabetes or heart failure) were generated from the proportional hazards regression model and plotted by time-varying mediastinal infection status.

A time-inhomogeneous multistate Markov model was used to determine the excess length of stay (LOS) of the index hospitalization resulting from mediastinal infection [12]. The model allowed transitions to multiple states from a single initial state (uninfected at the time of the index surgical procedure). State transitions could occur to death (competing risk), discharge (event of primary interest), or infection and then to death or discharge (Supplemental Fig 1). Transition hazards were calculated and used to estimate the excess LOS caused by infection. A bootstrap SE and 95% confidence interval (CI) for the excess LOS were computed based on 1,000 bootstrap samples. All analyses were conducted using SAS 9.4 (SAS Institute Inc, Cary, NC) and R 3.1.1 (The R Foundation for Statistical Computing, Vienna, Austria) software.

Results

Mediastinal Infection and Patient Characteristics

The study enrolled 5,158 patients, and 43 mediastinal infections were documented in 41 patients, for a cumulative incidence of 0.79% (95% CI, 0.60% to 1.06%; Fig 1). Of the 43 mediastinal infections, 26 were DSWIs (61%), 12 mediastinitis (28%), and 5 myocarditis or pericarditis (12%). In the patients with 2 mediastinal infections, 1 had a DSWI, followed by a later occurrence of mediastinitis, and 1 had 2 separate myocarditis or pericarditis events.

Compared with noninfected patients, patients with mediastinal infections typically had higher body mass index (BMI), higher creatinine, lower hemoglobin, and lower ejection fractions (Table 1). They were more likely to be receiving preoperative circulatory support (extracorporeal membrane oxygenation [ECMO], intraaortic balloon pump [IABP], or ventricular assist device [VAD]); to have diabetes, renal failure, or peripheral vascular disease; and to be receiving corticosteroids preoperatively. The most common procedures in both groups were isolated valve, isolated coronary artery bypass grafting (CABG), and combined CABG and valve procedures. A sternotomy approach was used in 90.5% of patients, and cardiopulmonary bypass was used in 91.1% of procedures. Increased operative and bypass time, packed red blood cell