Pneumonia after cardiac surgery: Experience of the National Institutes of Health/Canadian Institutes of Health Research Cardiothoracic Surgical Trials Network

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ABSTRACT

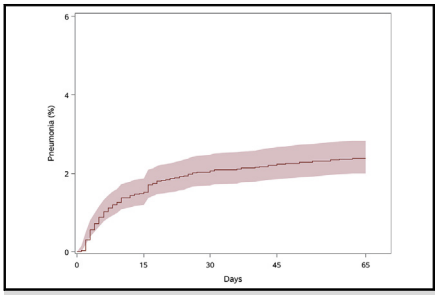
Rationale: Pneumonia remains the most common major infection after cardiac surgery despite numerous preventive measures.

Objectives: To prospectively examine the timing, pathogens, and risk factors, including modifiable management practices, for postoperative pneumonia and estimate its impact on clinical outcomes.

Methods: A total of 5158 adult cardiac surgery patients were enrolled prospectively in a cohort study across 10 centers. All infections were adjudicated by an independent committee. Competing risk models were used to assess the association of patient characteristics and management practices with pneumonia within 65 days of surgery. Mortality was assessed by Cox proportional hazards model and length of stay by a multistate model.

Measurements and Main Results: The cumulative incidence of pneumonia was 2.4%, 33% of which occurred after discharge. Older age, lower hemoglobin level, chronic obstructive pulmonary disease, steroid use, operative time, and left ventricular assist device/heart transplant were risk factors. Ventilation time (24-48 vs $\leq$24 hours; hazard ratio [HR], 2.83; 95% confidence interval [95% CI], 1.72-4.66; >48 hours HR, 4.67; 95% CI, 2.70-8.08), nasogastric tubes (HR, 1.80; 95% CI, 1.10-2.94), and each unit of blood cells transfused (HR, 1.16; 95% CI, 1.08-1.26) increased the risk of pneumonia. Prophylactic use of second-generation cephalosporins (HR, 0.66; 95% CI, 0.45-0.97) and platelet transfusions (HR, 0.49, 95% CI, 0.30-0.79) were protective. Pneumonia was associated with a marked increase in mortality (HR, 8.89; 95% CI, 5.02-15.75) and longer length of stay of 13.55 $\pm$ 1.95 days (bootstrap 95% CI, 10.31-16.58).

Conclusions: Pneumonia continues to impose a major impact on the health of patients after cardiac surgery. After we adjusted for baseline risk, several specific management practices were associated with pneumonia, which offer targets for quality improvement and further research. (J Thorac Cardiovasc Surg 2017;153:1384-91)



Cumulative incidence of pneumonia over 65 days.

Central Message

Pneumonia is the most common infection after cardiac surgery. Several specific modifiable management practices were associated with pneumonia, which offer targets for quality improvement.

Perspective

Pneumonia is a common complication after cardiac surgery, and previous studies have identified several patient-specific risk factors. Ours, however, is the first multicenter, prospective study of both risk factors and management practices on the risk of pneumonia. This analysis provides knowledge and targets for future quality improvement initiatives.

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Abbreviations and Acronyms

CI = confidence interval
COPD = chronic obstructive pulmonary disease
CTSN = Cardiothoracic Surgical Trials Network
HAI = healthcare-associated infection
HR = hazard ratio
LOS = length of stay
NG = nasogastric
SCIP = Surgical Care Improvement Project

Scanning this QR code will take you to the online appendices for this article.

Healthcare-associated infections (HAIs) represent the leading cause of noncardiac morbidity after cardiac surgery,[1] and pneumonia particularly is common and responsible for adverse patient outcomes.[2-4] Moreover, pneumonia frequently is cited as among the most costly and resource-intensive of all HAIs.[5-7]

Patients undergoing cardiac surgery are highly susceptible to pneumonia. Many patients present with cardiac symptoms requiring hospitalization before urgent surgery, predisposing them to pathogens. Common risk factors among cardiac surgery patients, such as chronic obstructive pulmonary disease (COPD), heart failure, and advanced age, result in a greater risk profile for pneumonia. Moreover, cardiopulmonary bypass, with its effect on systemic inflammatory mediators and its potential for lung injury, may further contribute to the risk of developing pneumonia.[8] Significant fluid shifts in the perioperative setting often leading to pulmonary edema, combined with the frequent need for transfusion of blood products, may affect a patient's risk for pneumonia.[9] Any prolonged use of mechanical ventilation also places patients at increased risk for pneumonia.[10,11] Finally, postoperative pain due to sternotomy or thoracotomy can affect pulmonary mechanics. Variations in management practices, such as fluid administration and ventilator management, are likely to affect the incidence of pneumonia,[12,13] but few insights exist about the relationship between these "process of care" variables and pneumonia.

The purpose of this study was to examine the time course, pathogens, and risk factors, including modifiable management practices, for postoperative pneumonia in patients undergoing cardiac surgery. This study is a substudy of a larger prospective cohort study conducted within centers participating in the Cardiothoracic Surgical Trials Network (CTSN), looking at all serious postoperative infections.[14]

PATIENTS AND METHODS

Study Design and Patients

The primary objective of this CTSN observational study was to identify management practices associated with the risk of infection after cardiac surgery. This study was conducted in 10 centers from the CTSN. The patient population included all adults receiving cardiac surgical interventions, excluding those with active systemic infections, including endocarditis.

We targeted a minimum sample size of 5000 patients to obtain at least 200 patients with major infections. This sample size was based not on explicit statistical criteria but on acquiring an adequate number of events (at least 10 per variable) to ensure stability of coefficient estimates in our models.[15,16] Patients were followed for up to 60 ± 5 days after surgery, with 2 planned postdischarge assessments at 30 and 60 days after surgery; the last date of follow-up was November 29, 2010. We collected data on patient characteristics (demographics, baseline laboratory values, comorbidities), surgery-related factors (such as previous intra-aortic balloon pump, surgery time, operative procedure), and management practices (such as antimicrobial prophylaxis, glycemic control, line management) (see Appendix E1). Data were transmitted from sites electronically to a secure server administered by the Data Coordinating Center. Participating institutional review boards approved the protocol (see Appendix E2 for participating sites), and the study was overseen by a National Heart, Lung, and Blood Institute–appointed Data Safety and Monitoring Board. All patients provided written informed consent to participate and release their medical information.

Endpoints

The primary endpoint for this analysis was pneumonia within 65 days of the index cardiac surgery. Pneumonia was classified according to definitions from the Centers for Disease Control and the National Healthcare Safety Network surveillance (see Appendix E1). Other secondary endpoints included all-cause mortality, reoperation, and hospital readmissions. All pneumonias were reviewed by an independent event adjudication committee. The date of final event adjudication was June 2011.

Data Analysis

We used the proportional subdistribution hazards model,[17] a variant of the Cox proportional hazards model, to account for death as a competing event when assessing the effect of baseline characteristics and management practices on pneumonia. Model building proceeded in 2 stages. We first identified patient- and procedure-related risk factors that were associated individually (at $P < .10$) with pneumonia and remained significant (at $P < .05$) in the multivariable model using a backward selection procedure. We then evaluated the additional contribution of management practices used before the first pneumonia (see Appendix E1 for details), except for postoperative transfusions, where the exact timing could not always be ascertained. Management practices that were associated individually with pneumonia (at $P < .10$) were placed in a multivariable model that contained all the patient- and procedure-specific variables in the first stage. With the use of a backward selection approach, the final competing risk model for pneumonia consisted of only management practices with a $P < .05$, adjusting for all the first stage baseline risk factors.

The standard Cox proportional hazards model was applied to the mortality analysis, with pneumonia treated as a time-dependent covariate. Patient characteristics that are known risk factors for mortality in the elderly cardiac surgery population and that were significant in our model were controlled for in the analysis.

To estimate the incremental length of stay (LOS) due to pneumonia, we used a multistate approach that treats pneumonia as a time-dependent exposure and mortality as a competing risk.[18] LOS was defined as the time from index procedure to hospital discharge or death. The model assumed a time-inhomogeneous Markov process with 1 initial state (index surgery), 1 intermediate state (pneumonia), and 2 absorbing states (death and discharged