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Prolonged pulmonary support after cardiac surgery: incidence, risk factors and outcomes: a retrospective cohort study☆,☆☆,★

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ABSTRACT

Background: Post–cardiac surgery pulmonary dysfunction may be underreported. Therefore, we evaluated associated risk factors for prolonged pulmonary support after cardiac surgery.

Methods and materials: We conducted a retrospective, observational study of consecutive patients undergoing coronary artery bypass grafting or coronary artery bypass grafting plus valve repair/replacement between Jan 1, 2005, and Dec 31, 2010, at an academic medical center. Using multivariate logistic regression and Cox proportional hazards modeling, we identified risk factors associated with prolonged mechanical ventilation and supplemental O_2 support as well as in-hospital mortality.

Results: Overall, 33% (1298/3881) of patients required more than 2 days of mechanical ventilation and/or more than 5 days of supplemental O_2 (prolonged support). Independent risk factors included age, weight, pre-existing lung disease, cardiac or renal dysfunction, emergent status, transfusion and cardiopulmonary bypass duration. Prolonged support was associated with increased mortality (OR, 4.75; 95% CI, 2.95-7.95; $P < .001$). Radiological evidence of persistent pulmonary edema 2 days after surgery was found in 4% of controls and 27% of prolonged support cases.

Conclusions: We identified risk factors for prolonged mechanical ventilation and supplemental O_2 use, described an association with increased adverse outcomes, and determined that persistent pulmonary edema on day 2 was the most likely radiological finding.

1. Introduction

One of the leading causes of prolonged intensive care unit (ICU) stay, morbidity, and mortality after cardiac surgery are pulmonary complications, with acute respiratory distress syndrome (ARDS) being reported as a rare but highly morbid outcome [1–6]. While rare (0.4%-2.5%), these retrospective reports may underestimate the true incidence of pulmonary dysfunction after cardiac surgery [4]. A more recent multicenter, prospective study diagnosed 10% of patients after cardiac surgery with ARDS, and the associated morbidity was far higher than that of unaffected patients [5,7]. In fact, perioperative organ injury may be the third leading cause of death in the United States [8].

Currently, the incidence of Society of Thoracic Surgeons (STS) defined, specifically post-cardiac surgery respiratory complications including ARDS and acute pulmonary dysfunction, is reported as relatively low (7.5%-12%), albeit highly morbid, with 20% in-hospital mortality [9,10]. The list of pulmonary complications recorded in the STS national database is broad and includes pneumothorax, pulmonary embolus, pleural effusion, pneumonia, cardiogenic pulmonary edema, as well as ARDS (http://www.sts.org/sites/default/files/documents). Although extensive, this list misses more subtle, clinically relevant forms of pulmonary dysfunction that can lead to prolonged mechanical ventilation and a requirement for supplemental oxygen. Prior investigations suggest that approximately 65% of patients meet oxygenation criteria for mild ARDS (Pa_{O_2}/F_{IO_2} 200-300 mmHg) after cardiac surgery [3]. In most cases, mild ARDS after cardiac surgery rapidly improves, may not fulfill specific STS diagnostic categories, and therefore evades database capture with its true incidence being unknown. We propose that subtle lung injury after cardiac surgery, as defined by the de novo need for supplemental oxygen, is worth capturing as it represents residual hypoxemia requiring considerable resource utilization, delaying mobilization, recovery, and eventual hospital discharge.

We hypothesized that the extent and etiology of postoperative pulmonary support required after cardiac surgery may not be fully

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appreciated and is greater than what current studies suggest. We therefore determined the incidence and risk factors associated with a prolonged need for mechanical ventilation and/or supplemental oxygen and describe the radiographic appearances associated with this more broadly defined outcome of prolonged pulmonary support.

2. Materials and methods

2.1. Patient selection

We completed an institutional review board–approved, retrospective observational cohort study on 3881 consecutive patients who underwent coronary artery bypass grafting (CABG) or CABG/valve procedures at Duke University Medical Center between Jan 1, 2005, and Dec 31, 2010. Procedural data including the duration of cardiopulmonary bypass (CPB) and aortic cross-clamp application, number of bypass grafts, and intraoperative blood product transfusion were obtained from an automated intraoperative anesthesia record-keeping system. The respiratory therapy billing records were sourced for the duration of mechanical ventilation and supplemental oxygen requirements (in days) in the setting of a strict protocol for aggressive extubation and weaning of supplemental oxygen (Supplemental Digital Content—Appendix 1). Patient demographics, operative details, and mortality were collected from data entered into the STS database and sourced from electronic medical records, custom datasheets, and records of laboratory results. Quality assurance involved random chart review for data confirmation and assessment of data completeness; incomplete fields are updated on a chart review basis. Long-term complication and mortality follow-up were recorded by the Duke Clinical Research Institute Follow-up Service group, as previously described [11].

2.2. Procedural characteristics

Typical practice included general anesthesia with invasive hemodynamic monitoring and standardized conduct of CPB. Intraoperative mechanical ventilation was typically adjusted to maintain a normal arterial pH, $Pa{CO_2}$ and $Pa{O_2}$, using a plateau pressure no greater than 30 cm H_2O. Throughout CPB, targets included a $Pa{CO_2}$ between 35 and 40 mmHg and a $Pa{O_2}$ between 150 and 290 mm Hg. Mean arterial pressure during CPB was maintained between 50 and 70 mmHg using vasoactive agents as required.

Postoperative mechanical ventilation was provided according to a standardized protocol using either pressure assist-control or pressure support ventilation modes, as detailed in Supplemental Digital Content—Appendix 1. Respiratory therapists present in the ICU and step-down units on a 24-hour basis aggressively pursued early extubation, and adherence to this protocol including the weaning of supplemental O_2 to maintain an O_2 saturation above 90% with activity impeded the ability to discharge patients home.

2.3. Definition of prolonged pulmonary support

We chose a statistical approach to define prolonged pulmonary support using (1) the uppermost quartile (>75th percentile) of the duration of postoperative mechanical ventilation and/or (2) the uppermost quartile (>75th percentile) of the duration of the requirement for supplemental O_2 therapy after extubation to keep an O_2 saturation above 90% with activity; (3) in-hospital death given respiratory complications could not be excluded. Patients on home O_2 prior to surgery were excluded from the analysis.

Candidate variables for risk factor analysis associated with prolonged pulmonary support were based on analysis of the literature, including age, sex, history of smoking, chronic obstructive pulmonary disease (COPD), urgent or emergent procedure, pre-existing congestive heart failure (CHF), hypertension, history of myocardial infarction (MI), preoperative diuretic use, restrictive lung disease, CPB time, body mass index, left ventricular ejection fraction (LVEF), preoperative serum creatinine level, preoperative hemoglobin concentration, and aortic cross clamp time.

Chest radiograph (CXR) data were obtained for a nested, matched case-control subset of patients from routine CXR taken immediately after surgery and on the mornings of the following 2 postoperative days. Patients with pre-existing conditions that may have predisposed them to pulmonary complications were excluded from this analysis; cases were patients requiring prolonged pulmonary support, and controls were patients not requiring prolonged pulmonary support matched to within 1 year of age. Patients identified as having suffered stroke or coma in the postoperative period were also excluded from this analysis due to the potential confounding of a neurological, not primarily respiratory, indication for prolonged pulmonary support. The CXR abnormalities recorded were atelectasis, pneumothorax, pleural collection (either effusion or hemothorax), and pulmonary edema as described on radiology reports read by board-certified, attending radiologists on the day of imaging. Our hypothesis was that prolonged pulmonary support was the result of persistent pulmonary edema; therefore, pulmonary edema on day 2 was our primary variable for this sub-analysis.

2.4. Statistical analysis

Continuous variables were described as means (± SD) or medians (interquartile range), as appropriate; categorical variables were described as a percentage. A univariate association with a $P < .1$ by Student 2-tailed t tests for continuous and χ^2 or Fisher's exact tests for categorical variables merited inclusion in a multivariable model of risk factors for prolonged pulmonary support. For short and long-term outcomes, a logistic regression model adjusting for EuroSCORE [12,13] and CPB duration was performed; hazard ratios were calculated using Cox proportional hazards models. A 2-sided P of .05 was considered statistically significant, and all analyses were performed using SAS version 9.2 (SAS Inc, Cary, NC).

3. Results

Respiratory billing data were available for 3881 patients, and complete intraoperative and follow-up data were available for 2995 patients.

3.1. Defining prolonged pulmonary support

The mean duration of mechanical ventilation was 1.9 (SD 2.6) days presenting a skewed distribution with a fifth centile of 1 day and a 95th centile of 6 days (see Fig. 1A). Similarly, the mean duration of supplemental oxygen requirement was 4.1 (SD 3.6) days, again with a skewed distribution ranging from a fifth centile of 1 day to a 95th centile of 14 days (see Fig. 1B). Our uppermost quartiles used for the definition of prolonged pulmonary support was, therefore, more than 2 days on a mechanical ventilator and/or more than 5 days of supplemental oxygen requirement: 588 were on a ventilator for more than 2 days (15.2%); 990 were on oxygen for more than 5 days (25.5%); overall, 1289 (33.2%) patients met the definition of prolonged pulmonary support with either more than 2 days of mechanical ventilation and/or more than 5 days of supplemental oxygen requirement.

3.2. Association with prolonged pulmonary support

Mean patient age in those who met our definition for prolonged respiratory support was 65.2 (SD 11.9) compared with 62.6 (SD 12.7) years old ($P < .0001$) and fewer patients in the prolonged pulmonary support were white (80.4% vs 76.5%; $P = .0059$). In univariate analysis, comparing preoperative characteristics with or without the need for prolonged pulmonary support included the presence of a diagnosis of diabetes (17.2% vs 10.8%; $P < .0001$), a history of smoking (33.8% vs 25.8%; $P < .0001$), a prior history of stroke (6.7% vs 4.5%; $P < .038$), a diagnosis of COPD (26.6% vs 19.2%; $P < .0001$), a prior history of MI (36.7% vs 27%; $P < .001$), an increased preoperative creatinine (1.5 vs 1.2; $P < .0001$), a reduced LVEF (47%, vs. 52.7%; $P < .0001$), and an increased EuroSCORE (3.1 vs. 2.8; $P < .0001$), see Table 1. To our surprise, the addition