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Predictors of Operative Mortality in Cardiac Surgical Patients with Prolonged Intensive Care Unit Duration

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Abstract

Background—Several systems have been developed to predict mortality following intensive care unit (ICU) admission in medical and surgical patients. However, a similar tool specific to cardiac surgical patients with prolonged intensive care unit duration does not exist. The purpose of the present study was to identify independent perioperative predictors of operative mortality among cardiac surgical patients with prolonged ICU duration.

Study Design—From 2003–2008, 13,105 cardiac surgical patients with ICU durations greater than 48 hours were identified within a statewide database. Perioperative factors, including Society of Thoracic Surgeons Predicted Risk of Mortality (STS PROM), were evaluated. Univariate and multivariate analyses identified significant correlates of operative mortality and their relative strength of association as determined by the Wald χ^2 statistic.

Results—Mean patient age was 66.8 ± 11.2 years, median ICU duration was 76.5 [56.0–124.0] hours, and mean STS PROM was $4.4\% \pm 6.2\%$. Among preoperative and operative factors, intra-aortic balloon pump use, patient age, immunosuppressive therapy, hemodialysis requirement, cardiopulmonary bypass time, and heart failure proved to be the strongest correlates of mortality (all $p < 0.05$) on risk-adjusted multivariate analysis. Interestingly, type of cardiac procedure had no significant association with mortality after risk adjustment. Among postoperative complications, cardiac arrest, prolonged mechanical ventilation (>24 hours) and stroke were the strongest predictors of risk-adjusted mortality (all $p < 0.001$).

Conclusions—Operative mortality may be predicted by select risk factors for cardiac surgical patients with prolonged intensive care unit duration. Patient age, preoperative intra-aortic balloon pump, and postoperative cardiac arrest, prolonged ventilation and stroke have the strongest association with mortality. Identification of these factors in the perioperative setting may enhance resource utilization and improve mortality following cardiac surgery.

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Drs LaPar and Gillen contributed equally to this work.

INTRODUCTION

Patients in intensive care units (ICU) by definition have more severe physiologic derangement and consequentially a higher risk of mortality. Patients who require ICU care for an extended period of time have an even greater risk of succumbing to their illness.^{1,2} In medical and surgical ICU patients, there are a number of studies that have investigated the associations between various risk factors and mortality.³⁻⁷ However, there is a dearth of published series looking at factors that increase risk of mortality in cardiac surgical patients with prolonged ICU duration. Studies that have been published have suffered from relatively small study populations and have not reported the relative strength of association between observed risk factors and mortality.

The purpose of the present study was to identify independent perioperative (preoperative, operative, and postoperative) predictors of operative mortality among cardiac surgical patients with prolonged ICU duration. Prolonged ICU duration was defined as ≥ 48 hours as per the current Society of Thoracic Surgeons (STS) definition. Patients were identified from the Virginia Cardiac Surgical Quality Initiative (VCSQI) database, and univariate and multivariate risk-adjusted analyses were performed to quantify relative strength of association between various patient factors and mortality.

METHODS

This investigation was exempt from formal Institutional Review Board (IRB) review at each participating center as the data is collected for quality analysis and purposes other than research and because it represents a secondary analysis of the VCSQI data registry with the absence of Health Insurance Portability and Accountability Act (HIPAA) patient identifiers.

Patients and Data Acquisition

De-identified patient level data was obtained from the VCSQI database for the study period 1/1/2003 thru 12/31/2008. All records included those for patients undergoing cardiac surgical procedures who experienced postoperative intensive care unit lengths of stay (ICU LOS) ≥ 48 hours. Casewise deletion of incomplete records (< 5%) was performed to obtain a complete dataset for analysis. Patient records were then stratified into two comparison groups (survivors vs. decedents during index hospitalization) in order to identify associations between preoperative, operative and postoperative events and mortality. Standard STS variable definitions were utilized for examined variables.⁸ Patient preoperative risk was assessed by prevalence of patient comorbid disease, extent of operation, operative status (elective, urgent, or emergent) and individual calculated STS predicted risk of mortality (PROM).

Measured Outcomes

The primary outcomes of interest included risk-adjusted associations between patient risk factors, operative features and postoperative events and observed mortality rate. Secondary outcomes included observed differences in patient risk factors, operative characteristics and postoperative complications among survivors and decedents. Operative mortality was defined as all patient deaths occurring during hospitalization as well those within 30 days of the date of surgery despite discharge status. Standard STS definitions for postoperative events and complications were utilized, including prolonged ventilation (>24 hours of mechanical ventilation), presence of any new onset atrial fibrillation, and renal failure (increase in serum creatinine level > 2.0 or a doubling (2x) of the most recent preoperative creatinine level).⁸

Statistical Analysis

All statistical analyses were designed to test the null hypotheses that operative mortality would not significantly differ as a function of patient preoperative risk factors, differences in operative characteristics or depending upon the presence of postoperative events among patients with prolonged ICU durations. Study outcomes and data comparisons were established *a priori* before data collection. Categorical variables are expressed as standard group percentages, while continuous variables are expressed as either mean $\pm$ standard deviation (SD) or median [25th, 75th percentile] depending upon overall variable distribution. Descriptive, univariate statistics included either Pearson's χ^2 or Fisher's Exact test for categorical variables and either independent sample single factor analysis of variance (ANOVA) for comparisons of normally distributed data or the Mann Whitney *U* test for non-normally distributed data comparisons. Calculated test statistics were utilized to derive all two-tailed *p*-values with standard statistical significance set to $\alpha < 0.05$.

Hierarchical multiple logistic regression models were used to estimate confounder-adjusted associations between patient preoperative factors, operative features and postoperative events and observed operative mortality. Two separate predictive models were analyzed. The first model included preoperative and operative risk factors for mortality, while the second model included postoperative events adjusted for the confounding influence of operation type, elective versus non-elective status, and patient age and gender. To account for inter-hospital variance in correlated events, clustering at the hospital level was considered in the hierarchical structure of each logistic regression model. Model covariates were selected *a priori* and included adjustment for patient risk using calculated STS PROM scores. Confounder adjusted measures of association are reported as odds ratios (OR) with a 95% confidence interval for all logistic regression models. The relative strength of association between each model covariate (clinical predictor) and mortality was determined by each factors likelihood ratio (Wald χ^2 test statistic) within the model. Model performance was assessed by three characteristics: 1) Area Under the Receiver Operating Characteristics curve (AUC) to determine the models ability to discriminate between survivors versus decedents, 2) the Hosmer-Lemeshow test to determine model calibration across deciles of observed and predicted risk, and 3) the Nagelkerke Pseudo R^2 test statistic to describe the degree of variance in operative mortality that is explained by the model.

Predictive Analytics SoftWare (PASW) with complex sampling module software, version 18.0.0 (IBM Corporation, Somers, NY) was used for all data manipulation and statistical analyses.

RESULTS

Significant Univariate Correlates of Operative Mortality

A total of 13,105 patients underwent cardiac operations resulting in prolonged ICU durations during the study period. This subset with prolonged ICU durations represents 50.3% of the total cardiac operations performed over the study period. Of the patients with prolonged ICU stays, 12,560 (95.8%) were survivors and 545 (4.2%) died. Overall, mean patient age was 66.8 ± 11.2 years, median ICU duration was 76.5 [56.0-124.0] hours, and mean STS PROM was $4.4\% \pm 6.2\%$. Severe chronic lung disease was observed in 3.5% of the patients. **Table 1** reports significant associations between operative mortality and patient characteristics. Among preoperative patient characteristics, presence of infective endocarditis, renal failure, need for hemodialysis, immunosuppression use, congestive heart failure, and intra-aortic balloon pump (IABP) requirement in the preoperative setting were among factors with the highest unadjusted associations with operative mortality. STS PROM was also significantly associated with mortality, with a mean of $4.1\% \pm 5.4\%$ in

survivors and $11.6\pm 13.5\%$ in decedents ($p<0.001$). **Table 2** shows operative factors that are related to mortality in the study cohort. Among operative factors, cardiac reoperation, non-elective (urgent or emergent) operative status, and performance of combined cardiac operations (valve/CABG) were associated with a higher incidence of mortality among patients with prolonged ICU durations. Of note, the large majority (91%) of the CABG operations in our cohort were performed using cardiopulmonary bypass (on-pump).

Table 3 displays significant unadjusted associations between operative mortality and postoperative events encountered among cardiac surgery patients with prolonged ICU duration. Not surprisingly, almost all decedents encountered at least one primary postoperative complication prior to death. Among postoperative events, onset of sepsis, prolonged mechanical ventilation (> 24 hours), renal failure and new-onset hemodialysis requirement, myocardial infarction, and any episode of cardiac arrest were among the most frequent complications associated with mortality.

Significant Risk-Adjusted Predictors of Operative Mortality

Table 4 highlights multivariate risk-adjusted associations between preoperative and operative risk factors and operative mortality. In this mortality model, IABP use in the preoperative setting, advancing patient age, use of immunosuppression, preoperative hemodialysis requirements, prolonged cardiopulmonary bypass duration, and heart failure were among the strongest predictors of death as determined by each factors' likelihood ratio in cardiac surgical patients with prolonged postoperative ICU durations. The statistical strength of association with mortality was significantly less for the presence of preoperative renal failure, performance of cardiac reoperations, presence of infective endocarditis, and female gender. Importantly, although the unadjusted statistics (Table 1) revealed that overall, more males died than females, the female gender was associated with a 24% increase in the adjusted odds of death on multivariate analysis.

Table 5 describes significant risk-adjusted associations observed between postoperative events and operative mortality. Among postoperative complications, any episode of cardiac arrest was by far the most strongly associated event with operative mortality, while prolonged mechanical ventilation, postoperative stroke, new-onset renal dialysis, postoperative renal failure, onset of sepsis, or pulmonary embolism all increased the odds of death for those patients experiencing postoperative ICU durations in excess of 48 hours.

The statistical performance of each logistic regression model demonstrated good discrimination with AUC values of 0.75 and 0.93 for the preoperative and postoperative logistic regression models, respectively. AUC values of 1.0 indicate perfect model discrimination between dependent outcomes, while AUC values of 0.5 represent discrimination equal to chance. The calibration of each model was adequate across deciles of observed risk as reflected by Hosmer-Lemeshow p 0.05 for both models. The Nagelkerke Pseudo R^2 tests demonstrated the preoperative risk factor model explained 12% of the variance in mortality, while the postoperative event model explained 47% of mortality variance.

ICU Duration and Operative Mortality

Figure 1 displays the relationship between increasing ICU length of stay and operative mortality. With ICU LOS less than one week, operative mortality remained relatively low (2.1% for < 48 hours, 1.6% for 2-4 days, 3.3% for 5-7 days). However, with ICU durations greater than one week, operative mortality increased substantially, with a rate of 10% for ICU LOS of 1-2 weeks and 25.7% for ICU LOS greater than 2 weeks.

DISCUSSION

The present study evaluates the outcomes from 13,105 cardiac operations performed from 2003 through 2008 in the state of Virginia with prolonged ICU stay, defined as greater than 48 hours. This patient population is highly relevant as more than 50% of cardiac surgery patients have prolonged ICU stay with significant risk of morbidity and mortality. Therefore, identifying clinical features and postoperative characteristics associated with mortality in this surgical population has the potential to improve outcomes. The present multivariate risk-adjusted analyses identified several patient related and preoperative and operative factors and postoperative events that impact patient mortality. Most importantly, these analyses quantify the relative strength of association between patient factors and mortality to guide surgeons and critical care management to identify patients at risk for adverse outcomes. Finally, a strong association between duration of ICU stay and mortality is characterized.

Many of the risk factors associated with increased operative mortality in cardiac surgery patients are well defined. These factors include increasing patient age, female gender, low ejection fraction / congestive heart failure, diabetes, peripheral vascular disease, immunosuppressive therapy, renal insufficiency, urgent or emergent operation, and previous cardiac surgery.⁹⁻¹⁷ Among these risk factors, the most consistent and strongest correlations with increased mortality are seen with emergent cardiac surgery, patients with previous cardiac surgery, low ejection fraction, and renal insufficiency requiring dialysis.^{9,14-17} The present findings in patients with prolonged ICU duration corroborate these data, demonstrating that many of the factors associated with increased mortality are similar regardless of length of ICU stay. One notable discrepancy in our results compared with others was the lack of association between non-elective (urgent or emergent) operations and mortality after risk-adjustment for other variables. This finding is likely explained by the high proportion of non-elective cases (59.4%) included in this analysis and, as a result, a statistical difficulty in detecting differences between these patients as a function of operative status after effective risk-adjustment.

As expected, several studies have shown increased in-hospital mortality in patients with prolonged ICU stays.¹⁸⁻²² One issue in comparing these studies is the variability in how prolonged ICU stay is defined, with definitions ranging from greater than 48 hours to greater than one month or more. Most studies investigating prolonged ICU stay define this period as greater than one to two weeks, which is often less than 5% of the total cardiac surgery patient population.¹⁹⁻²¹ As a result, these studies report high in-hospital mortalities ranging from 15-33% among this population. As an example, one series by Gersbach et al. examined outcomes for cardiac surgical patients with an ICU stay greater than five days, reporting in-hospital mortality of 8.7%, as well as one-year and three-year mortalities of 14.4% and 24.9% respectively.²² In the present analysis, the definition of prolonged ICU LOS was based upon the established Society of Thoracic Surgeons (STS) definition, which is an ICU duration of greater than 48 hours. As a result, the observed 4.2% mortality reported herein likely reflects outcomes for a proportion of patients often overlooked in other reports and is consistent with expected mortality rates for this population with mean STS PROM of 4.4% $\pm$ 6.2%.

One similar report of outcomes for cardiac surgical patients with ICU duration > 48 hours was performed by Heimrath and colleagues.¹⁸ Reporting on 598 CABG patients with an ICU stay of more than 48 hours, this study population represented 19% of all CABG patients (n=3,139) at their institution from 1998 to 2002. Although their reported observed in-hospital mortality rate of 10% for patients with prolonged ICU stays was higher than that reported in the present population, this was compared to a mortality rate of 1.2% in patients

with an ICU stay of less than 48 hours. In addition, they reported significant associations between prolonged ICU stay and increased patient age, female gender, diabetes, recent MI, and urgent surgery, as well as a correlation with perioperative MI, stroke, and prolonged mechanical ventilation. These clinical predictors corroborate the observed associations for various risk factors and postoperative events noted in this investigation. Additionally, the 2.1% mortality rate in the present study for patients with an ICU stay of less than 48 hours mirrors the findings from Heimrath's analysis.

The present findings have significant clinical implications. The relatively low mortality rate reported in this series implies that even among patients with longer than anticipated intensive care unit stay, reasonable outcomes and acceptable mortality rates can be achieved with contemporary postsurgical care. Most importantly, however, these findings not only confirm important relationships between select patient-related and perioperative factors and mortality, but also extend the examination of these factors to address the relative strength of association between these factors and postoperative death. Few series report upon or address the significance of the strength of association between patient factors and outcomes during predictive modeling. In this series, each factor's likelihood ratio (or Wald χ^2 square test statistic) was utilized to quantify the strength of association between that factor and the dependent outcome of interest (operative mortality) after adjustment for the confounding influence of patient risk. As result, the important observations that intra-aortic balloon pump use (likelihood ratio = 115), advanced patient age (likelihood ratio = 99), and immunosuppressive therapy use (likelihood ratio = 35) were among the most strongly associated preoperative factors associated with mortality provides important prognostic information for cardiac surgical patients. Furthermore, while it was not surprising to see the strongest correlation between an episode of cardiac arrest (likelihood ratio = 398) and patient mortality, the observations of disproportionately strong associations between prolonged mechanical ventilation (likelihood ratio = 96) or stroke (likelihood ratio = 65) and mortality relative to that for renal failure (likelihood ratio = 23) or even new-onset hemodialysis (likelihood ratio = 28) requirement are noteworthy.

In our study design both preoperative and operative factors were considered as baseline characteristics at the time of their admission to the intensive care unit. Thus, clinicians can use these data to identify not only patients at risk for prolonged ICU durations based on these characteristics but also those who may be at increased risk for mortality. We then also considered postoperative events as potential risk factors for mortality in order to provide clinicians with a sense for which patients with ICU duration greater than 48 hours may be at increased risk for mortality with the onset of various complications. In these methods, we accounted for baseline patient risk and comorbid disease by including the STS PROM score as a model covariate in addition to adjusting for the confounding influence of operation type, operative status (elective vs. non-elective), and presence of an IABP. These results aid surgeons in early recognition of patients at high risk for mortality in order to target these areas to improve outcomes, and they assist in counseling families regarding potential outcomes for patients with complicated ICU courses.

The present study has select limitations. First, a secondary analysis of the VCSQI data registry and STS data limited the performed analyses to de-identified data, which limited the ability to scrutinize data further than what was originally captured during the initial data extraction. Therefore, further investigation into the details surrounding cardiac arrest events or the differences between university and community-based ICU environments, for example, was unable to be performed. Second, inherent selection bias in reported results must be considered in a retrospective study design. The definition of prolonged ICU length of stay differs from many other series, which may account for discrepancies between the superior results reported herein. Furthermore, the influence of differences in postoperative critical

care management including criteria for ICU care between the included institutions can also not be fully accounted for in these analyses. The hierarchical structure of the performed regression analyses, however, likely mitigated such influence as they were designed to account for variance in correlated events between hospitals. All analyses were limited to short-term, operative outcomes, and intermediate or long-term follow-up data were not available. Finally, the potential for unrecognized miscoding of data must also be considered in any secondary analysis of a data registry.

CONCLUSIONS

Based upon the present results, operative mortality following cardiac surgery may be predicted by select risk factors for patients with prolonged intensive care unit duration. Preoperative factors with the strongest association with mortality include intra-aortic balloon pump use and increasing patient age. Postoperatively, cardiac arrest, prolonged ventilation and stroke have the strongest association with mortality. Moreover, the operative mortality increases as the ICU duration increases, with particular high mortality in patients who require more than 14 days in the ICU. Identification of these factors in the perioperative setting may enhance resource utilization and improve mortality following cardiac surgery.

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Figure 1.

Relationship between ICU length of stay and mortality. With ICU length of stay greater than one week, risk of operative mortality increases substantially.

Table 1

Significant Preoperative Risk Factors for Mortality on Univariate Analyses

Variable	Overall (n=13,105), %	Survivors (n=12,560), %	Decedents (n=545), %	UOR [95% CI]	p Value
Renal failure requiring dialysis	3.8	3.5	11.4	3.54 [2.68, 4.69]	<0.001
Immunosuppression	2.9	2.7	7.9	3.10 [2.23, 4.31]	<0.001
Intra-aortic balloon pump	13.8	13	30.8	2.97 [2.46, 3.59]	<0.001
Renal failure	8.0	7.6	18.3	2.74 [2.18, 3.43]	<0.001
Infectious endocarditis	1.5	1.4	3.7	2.74 [1.71, 4.40]	<0.001
Heart failure	24.3	23.4	45.3	2.71 [2.28, 3.22]	<0.001
Peripheral arterial disease	18.0	17.5	29.5	1.98 [1.63, 2.39]	<0.001
Cerebrovascular disease	16.9	16.4	27.3	1.91 [1.58, 2.32]	<0.001
Cerebrovascular accident	8.7	8.5	14.3	1.80 [1.41, 2.31]	<0.001
Hypertension	80.3	80.1	84.8	1.39 [1.09, 1.76]	0.008
Diabetes	39.7	39.5	45.3	1.23 [1.07, 1.51]	0.007
Sex				0.74 [0.62, 0.88]	0.001
Female	34.9	34.6	41.8		
Male	65.1	65.4	58.2		

UOR, unadjusted odds ratio.

Table 2

Significant Operative Risk Factors for Mortality on Univariate Analyses

Variable	Overall (n=13,105), %	Survivors (n=12,560), %	Decedent (n=545), %	UOR [95% CI]	p Value
Intra-aortic balloon pump	13.8	13.0	30.8	2.97 [2.46, 3.59]	<0.001
Reoperation	10.7	10.4	18.2	1.85 [1.50, 2.28]	<0.001
Operative status				n/a	<0.001
Elective	40.6	41.0	31.9		
Urgent	53.8	53.8	54.7		
Emergent	5.3	5.1	11.6		
Emergent salvage	0.3	0.2	1.8		
Operation type				n/a	<0.001
CABG	78.0	78.5	65.9		
AV Replacement	7.3	7.2	9.0		
AV Replacement + CABG	8.8	8.6	13.2		
MV Repair	0.3	0.3	0.2		
MV Repair + CABG	0.6	0.5	0.7		
MV Replacement	2.7	2.6	4.6		
MV Replacement + CABG	2.4	2.2	6.4		

UOR, unadjusted odds ratio; CABG, coronary artery bypass grafting; AV, aortic valve; MV, mitral valve.

Table 3
Significant Associations between Postoperative Events and Mortality on Univariate Analyses

Variable	Overall (n=13,105), %	Survivors (n=12,560), %	Decedents (n=545), %	UOR [95% CI]	p Value
Cardiac arrest	2.6	1.1	36.1	49.16 [38.66, 62.05]	<0.001
Renal failure requiring dialysis	3.6	2.3	34.3	22.1 [17.88, 27.31]	<0.001
Sepsis	2.4	1.6	20.2	15.32 [11.92, 19.68]	<0.001
Prolonged mechanical ventilation	23.5	21.1	79.6	14.65 [11.84, 18.12]	<0.001
Renal failure	8.9	7.1	49.5	12.86 [10.73, 15.41]	<0.001
Myocardial infarction	0.5	0.3	3.3	10.43 [5.95, 18.28]	<0.001
Gastrointestinal event	4.0	3.2	24	9.67 [7.76, 12.05]	<0.001
Pneumonia	7.0	5.8	33.4	8.09 [6.67, 9.81]	<0.001
Deep sternal infection	0.8	0.7	4.4	7.01 [4.41, 11.14]	<0.001
Permanent stroke	2.8	2.3	14.3	6.97 [5.34, 9.09]	<0.001
Pulmonary embolism	0.6	0.5	2.4	4.56 [2.50, 8.31]	<0.001
Tamponade requiring reoperation	3.9	3.6	9.7	2.89 [2.14, 3.89]	<0.001
Atrial fibrillation	23.6	23.0	38.2	2.07 [1.73, 2.47]	<0.001

UOR, unadjusted odds ratio.

Table 4**Multivariate Risk-Adjusted Preoperative and Operative Predictors of Mortality**

Factor	Likelihood Ratio (Wald χ^2)	AOR [95% CI]	p Value
Intra-aortic balloon pump	115.908	3.163 [2.565, 3.900]	<0.001
Patient age, y	98.899	1.048 [1.039, 1.058]	<0.001
Immunosuppression	35.479	2.878 [2.032, 4.075]	<0.001
Hemodialysis requirement	31.187	2.800 [1.951, 4.018]	<0.001
Cardiopulmonary bypass time	29.699	1.005 [1.003, 1.006]	<0.001
Heart failure	29.168	1.713 [1.409, 2.083]	<0.001
Renal failure	12.862	1.688 [1.268, 2.248]	<0.001
Cardiac reoperation	12.603	1.552 [1.218, 1.978]	<0.001
Infective endocarditis	6.138	1.998 [1.156, 3.455]	0.013
Female sex	5.384	1.24 [1.034, 1.492]	0.02

Model performance: area under ROC = 0.75; Nagelkerke Pseudo R^2 = 0.12; Hosmer and Lemeshow Test: p = 0.15. Model adjusted for: renal failure, renal failure requiring dialysis, immunosuppression, infectious endocarditis, heart failure, intra-aortic balloon pump, type of operation, elective status, redo status, perfusion time.

AOR, adjusted odds ratio.

Table 5**Multivariate Risk-Adjusted Associations between Postoperative Events and Mortality**

Factor	Likelihood Ratio (Wald χ^2)	AOR [95% CI]	p Value
Cardiac arrest	398.935	21.57 [15.958, 29.157]	<0.001
Prolonged mechanical ventilation	95.932	3.84 [2.933, 5.026]	<0.001
Stroke	65.309	4.235 [2.984, 6.009]	<0.001
Renal Failure requiring dialysis	28.333	2.814 [1.922, 4.118]	<0.001
Renal failure	23.119	2.242 [1.613, 3.115]	<0.001
Sepsis	17.538	2.108 [1.487, 2.988]	<0.001
Pulmonary embolism	4.166	2.37 [1.035, 5.428]	0.041

Model performance: area under ROC = 0.93; Nagelkerke Pseudo R^2 = 0.47; Hosmer and Lemeshow Test: p = 0.05. Model covariates adjusted for: age, gender, procedure type, elective vs. non-elective status, intra-aortic balloon pump, STS Predicted Risk of Mortality, tracheostomy, sepsis, stroke, myocardial infarction, reoperation due to tamponade, anticoagulation complications, cardiac arrest, renal failure, renal failure requiring dialysis, prolonged mechanical ventilation, pulmonary embolism, gastrointestinal events, pneumonia.

AOR, adjusted odds ratio.