Unplanned, Postoperative Intubation in Pediatric Surgical Patients

Development and Validation of a Multivariable Prediction Model

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This article has been selected for the ANESTHESIOLOGY CME Program. Learning objectives and disclosure and ordering information can be found in the CME section at the front of this issue.

ABSTRACT

Background: To date, the independent predictors and outcomes of unplanned postoperative intubation (UPI) in pediatric patients after noncardiac surgery are yet to be characterized. The authors aimed to identify the incidence and predictors of this event and evaluated the effect of this event on postoperative mortality.

Methods: Data of 87,920 patients from the American College of Surgeons National Surgical Quality Improvement Program Pediatric database were analyzed and assigned to derivation (n = 58,614; 66.7%) or validation (n = 29,306; 33.3%) cohorts. The derivation cohort was analyzed for the incidence and independent predictors of early UPI. The final multivariable logistic regression model was validated using the validation cohort.

Results: Early UPI occurred with an incidence of 0.2% in both cohorts. Among the 540 patients who experienced a UPI, 178 (33.0%) were intubated within the first 72 h after surgery. The final logistic regression model indicated operation time, severe cardiac risk factors, American Society of Anesthesiologists physical status classification more than or equal to 2, tumor involving the central nervous system, developmental delay/impaired cognitive function, past or current malignancy, and neonate status as independent predictors of early UPI. Having an early UPI was associated with an increased risk of unadjusted, all-cause 30-day mortality, demonstrating an odds ratio of 11.4 (95% CI, 5.8 to 22.4).

Conclusions: Pediatric patients who experienced an early UPI after noncardiac surgery had an increased likelihood of unadjusted 30-day mortality by more than 11-fold. Identification of high-risk patients can allow for targeted intervention and potential prevention of such outcomes. **(ANESTHESIOLOGY 2016; 125:914-28)**

UNANTICIPATED postoperative intubation is a significant adverse event associated with increased cost, morbidity, and mortality.[1] Patients require an escalation in care, require admission to the intensive care unit (ICU), can experience prolonged intubation and, among adults, are at a greater risk of 30-day adjusted mortality.[2–4] However, for the pediatric population, little is yet known regarding unplanned intubation, its independent predictors, and its outcomes.

All studies evaluating unplanned intubation after pediatric noncardiac surgery have been limited to single-institution experiences, with an estimated incidence between 0.1 and 0.34%.[2,4–6] In these studies, unplanned intubations were captured only if they occurred immediately after surgery in the operating room or postanesthesia care unit. However, in adults, the first 72 h after anesthesia has been shown to impart the highest risk of hypoxemia as sleep-associated oxygen desaturation persists and peaks on the third postoperative day.[7–9] In one adult study, 49.4% of all 30-day

What We Already Know about This Topic

- Previous studies on unplanned postoperative intubation after pediatric noncardiac surgery have been limited to single-institution experiences and only collected the incidence up to immediately after surgery in the operating room or postanesthesia care unit

What This Article Tells Us That Is New

- Of 87,920 patients in a quality improvement database, 540 children experienced unplanned postoperative intubation (UPI) within the first 30 postoperative days, and 178 events (0.2%) occurred within the first 72 h after surgery
- Independent predictors of UPI within 72 h after surgery were operation time, severe cardiac risk factors, American Society of Anesthesiologists physical status classification more than 2, central nervous system tumor, developmental delay/impaired cognitive function, past or current malignancy, and neonate status
- When children experienced a UPI, unadjusted 30-day mortality increased by more than 11-fold

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 Anesthesiology 2016; 125:914-28

<zdoi;10.1097/ALN.0000000000001343>

postoperative intubations occurred within the first 72 h.[3] To date, no study has examined the incidence of unplanned intubation during the same period in the pediatric population nor have the independent predictors for pediatric intubation after noncardiac surgery been identified.

The primary objective of the current investigation was to identify the incidence of early unplanned intubation among pediatric patients after noncardiac surgery. We hypothesized that a significant proportion of postoperative intubations occurs in the first 72 h. We also sought to identify the independent risk factors for unplanned intubation and develop and validate a prognostic multivariable model. Finally, we hypothesized that postoperative intubation would be associated with increased mortality.

Materials and Methods

Patients and Data Collection

The Ann & Robert H. Lurie Children's Hospital of Chicago Institutional Review Board (Chicago, Illinois) deemed this study as exempt from review, with waiver of signed patient consent (Institutional Review Board, 2016-89). Methods and reporting of the study adhered to the Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis statement.[10] The National Surgical Quality Improvement Program Pediatric (NSQIP-P) is a prospectively collected, multicenter clinical registry, which provides data on risk-adjusted outcomes to participating hospitals for the purpose of quality improvement. Details regarding this program have been described extensively in previous reports, but a brief overview is as follows.[11] Sponsored by the American College of Surgeons (ACS), trained surgical clinical reviewers collect thoroughly standardized and robust clinical data through an in-depth chart review and phone calls to patient families.[12] Institutional, provider, and patient anonymity is maintained by the omission of site- or region-specific data elements in the participant user file. The scope of patient data covers 147 different variables per patient, including patient demographics, preoperative risk factors, comorbidities, intraoperative factors, and outcomes until 30 days after an index procedure. The variables used in this analysis are listed with their definitions in appendix 1. Complications (including mortality) are captured regardless of whether they occur during an initial hospital stay or postdischarge. Trauma surgeries, surgeries involving the heart, or procedures requiring cardiopulmonary bypass are excluded.

Interrater reliability audits are conducted on all participating sites, with a disagreement rate of 5% or less being required for a site to continue participation in data submission. To date, the combined results of these audits revealed an overall disagreement rate of approximately 2% for all assessed program variables.[12]

Patients who underwent surgery at a continuously enrolled U.S. ACS NSQIP-P hospital from January 1, 2012, to December 31, 2013, were included in this study (n = 87,920). Cases excluded from the analysis were those with missing covariate or primary outcome data. Patients who were not classifiable by any of the provided race or ethnicity designations or who did not have race or ethnicity reported in the original patient chart were subsequently counted in this analysis as missing. Gestational age at birth was not a required entry until 2015, and any patients with unknown preterm birth statuses were also counted as missing. The impact of missing covariate data on our model was evaluated in a separate sensitivity analysis utilizing multiple imputation.

Outcomes

Unplanned intubations are defined by the NSQIP-P as the unanticipated, required placement of an endotracheal tube (nasal or oral) or supraglottic airway (SGA) with the initiation of ventilatory support. The SGA is used as a ventilatory rescue device in the setting of a difficult intubation and as a conduit for fiberoptic intubation. Thus, SGA placement was included in the unplanned intubation definition to allow for accurate capture of all intubations with subsequent mechanical ventilation. In patients intubated for surgery, unplanned intubation occurred at any time after the original extubation after the patient's departure from the operating room. If a patient was not intubated during surgery, intubation at any time after surgery was considered unplanned. Given the increased risk of respiratory complications in the first 72 h after surgery,[7–9,13] we defined unplanned intubation within 72 h after surgery (unplanned postoperative intubation [UPI]) as our primary outcome of interest. The secondary outcome of interest was all-cause, 30-day mortality after UPI.

Statistical Analysis

Cross-validation using the holdout method was used to assess the validity of a parsimonious multivariable logistic regression model to predict postoperative intubation. First, patients were randomly assigned to a derivation (66.7%) or a validation (33.3%) cohort. A derivation cohort is used to evaluate relationships between any particular risk factor and the defined outcome, in this case a UPI, and fit a model. The investigator then applies the model to the validation cohort and reassesses the relationships and the fit of model on the outcome of interest. Using the derivation cohort, univariable analyses were individually performed on preoperative characteristics and comorbidities of interest, as well as total operation time (z-score), to identify any associations with UPI. These variables included age, gender, race, ethnicity, cardiac risk factors, systemic inflammatory response syndrome/sepsis/septic shock, the American Society of Anesthesiologists (ASA) physical status classification, premature birth, asthma, cystic fibrosis, oxygen support, structural pulmonary/airway abnormalities, tumor involving the central nervous system (CNS), developmental delay/impaired cognitive function, neuromuscular disorder, weight loss or failure to thrive,

congenital malformation, past or current cancer, and neonate status at the time of surgery (specific definitions are given in appendix 1).

To identify independent predictors of UPI, the derivation cohort was used to fit a parsimonious multivariable logistic regression model using variables with an *a priori* basis for inclusion by two independent investigators (E.C.C. and N.J.). Patients in the validation cohort were not included in model development. Age was entered as a continuous variable. Total operation time was converted to a z-score for procedure as categorized by clinical classification software codes[14] as previously described.[15,16] White race was the referent group against black or African American, Asian, and other. Having no cardiac risk factors was the referent group *versus* minor, major, and severe cardiac risk factors. ASA physical status classification 4 and 5 were combined as one variable. This variable, along with ASA physical status classification 2 and 3, was compared against ASA physical status classification 1. Collinearity diagnostics and Spearman correlation matrix were performed for all variables entered into the model. Manual backward selection was used with a model entry criterion of 0.10 and evaluation of Akaike information criterion.

The area under the curve (AUC) of the receiver operating characteristic curves was used to assess the predictive value of the final model in the derivation and validation cohorts. The validation cohort was used to cross-validate the model by comparing model-estimated regression coefficients across models for each parameter. A relative percent difference of 10% between the derivation and validation β-coefficients was chosen as the validation threshold. Incidence of UPI was analyzed based on the number of risk factors present. Risk factors were defined as operation time z-score more than 1, any cardiac risk factors, ASA physical status classification greater than or equal to 2, structural pulmonary/airway abnormalities, tumor involving the CNS, developmental delay/impaired cognitive function, past or current malignancy, and neonate status as determined by the final multivariable model.

Proportions of missing data between patients with UPI and patients without UPI were assessed using chi-square or Fisher exact tests. In a sensitivity analysis, our analysis methods were replicated using multiple imputation. We randomly assigned patients to derivation (66.7%) and validation cohorts (33.3%) and used the PROC MI procedure to generate 10 multiple imputed datasets within each cohort. Parameter estimates from logistic regression models in the imputed training datasets were synthesized using the SAS procedure PROC MI ANALYZE (SAS Institute, USA), and parameter estimates were compared to those from our initial final model derived from our complete case training dataset. The AUC of the receiver operating characteristic curves for the multivariate imputed prediction model and completed case final model was also evaluated.

A univariable logistic regression model was used to assess for a relationship between UPI and all-cause 30-day postoperative mortality. Results are reported as an odds ratio (OR) with 95% CI with $P < 0.05$ being considered statistically significant. All analyses were performed using SAS versions 9.3 and 9.4. Save for multiple imputation, all statistical analyses were planned before accessing the data. The original statistical plan is outlined in appendix 2.

Results

Data of 87,920 patients were used for the final analysis. Figure 1 displays the exclusion process for the cohort as a whole. Of these patients, 58,614 were allocated to the derivation cohort and 29,306 were allocated to the validation cohort, with no differences between cohorts in terms of demographics, predictors, or outcomes (appendix 3). There were 119 (0.20%) cases of UPI in the derivation cohort and 59 (0.20%) in the validation cohort. A total of 540 patients experienced a UPI within the first 30 postoperative days, with 178 (33.0%) of these patients having their UPI event within the first 72 h after surgery. A histogram illustrating days to UPI *versus* percent total is shown in figure 2.

Collinearity diagnostics and Spearman correlation matrix showed no evidence of strong correlation, and all variables remained in the model. The variables listed in table 1 were inputted into the multivariable parsimonious logistic regression model. The final logistic regression model obtained through backward selection indicated operation time (z-score), severe cardiac risk factors, ASA physical status classification greater than or equal to 2, structural pulmonary/airway abnormalities, tumor involving the CNS, developmental delay/impaired cognitive function, past or current malignancy, and neonate status as independent predictors of UPI (table 2).

Forcing the derivation final model on the validation cohort using model parameter estimates yielded an AUC of 0.85 (0.78 to 0.91). The AUC of the final logistic regression model (appendix 4) in the derivation cohort was 0.87 (95% CI, 0.84 to 0.90). The AUC of the final logistic regression model in the validation cohort was 0.90 (95% CI, 0.87 to 0.94), indicating strong discriminant value of the final model in both cohorts. Relative differences between model-estimated regression coefficients in the derivation and validation cohorts ranged from 0.07 to 2.98%, indicating little change in coefficients across cohorts. The likelihood ratio test indicated a chi-square value of 406.24 with 17 degrees of freedom and $P < 0.0001$, indicating that at least one of the predictors in our final model had a regression coefficient not equal to zero. In the derivation cohort, patients with 0 to 1 risk factors had an incidence of UPI of 0.04%: two risk factors, 0.32%; three risk factors, 0.67%; 4 to 5 risk factors, 1.34%; and greater than or equal to six risk factors, 2.46%. Table 3 lists the ORs for UPI based on the number of risk factors present. In the total sample, there were 418 deaths (0.48%). Univariable logistic regression showed UPI to be associated

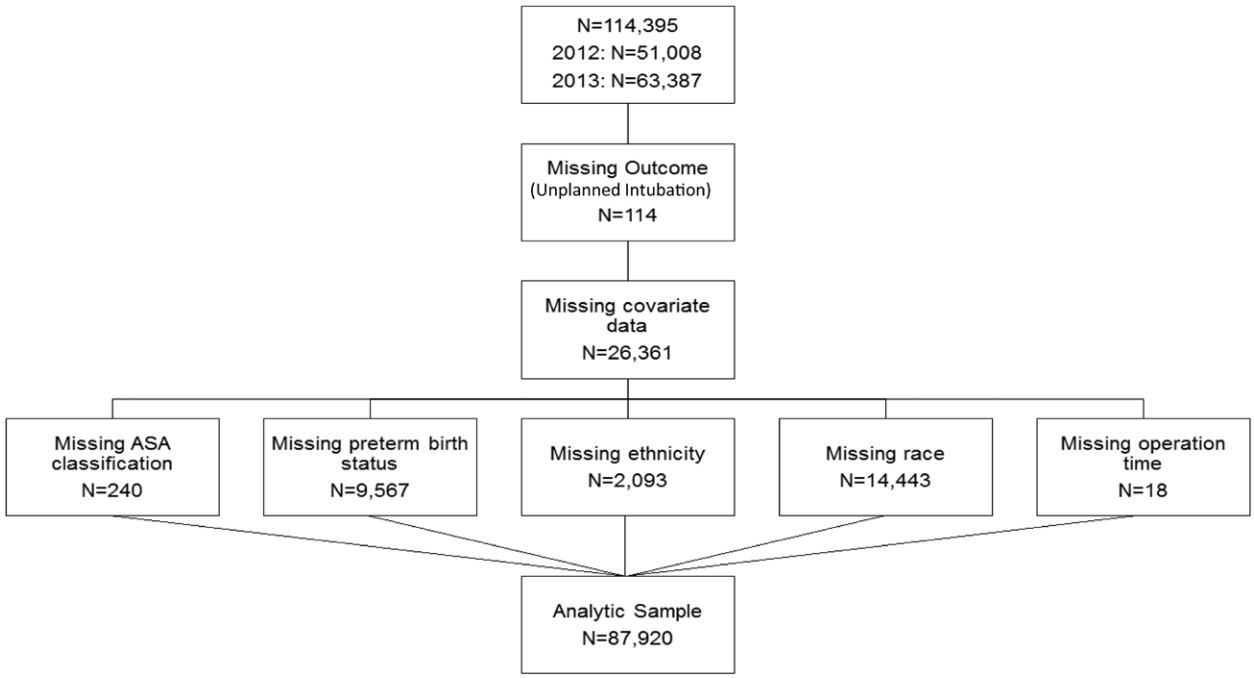

Fig. 1. Patient inclusion and exclusion criteria. The number of those cases excluded are listed below each respective criterion. ASA = American Society of Anesthesiologists physical status classification.

with all-cause, 30-day mortality ($P < 0.0001$; OR, 11.4; 95% CI, 5.8 to 22.4).

Missing data were present in our sample for ASA physical status classification, preterm birth status, ethnicity, race, and operation time. The proportion of missing data for each variable ranged from 0.02% (operation time) to 12.64% (race). There were 19,171 (16.78%) patients missing one variable, 5,254 (4.6%) missing two variables, and 1,936 (1.69%) patients missing three variables. The final multivariable model for our multiply imputed datasets indicated operation time (z-score), severe cardiac risk factors, ASA physical status classification greater than or equal to 2, tumor involving the CNS, developmental delay/impaired cognitive function, past or current malignancy, and neonate status as independent predictors of UPI, while structural pulmonary/airway abnormalities no longer met the inclusion criteria for the final model. Parameter

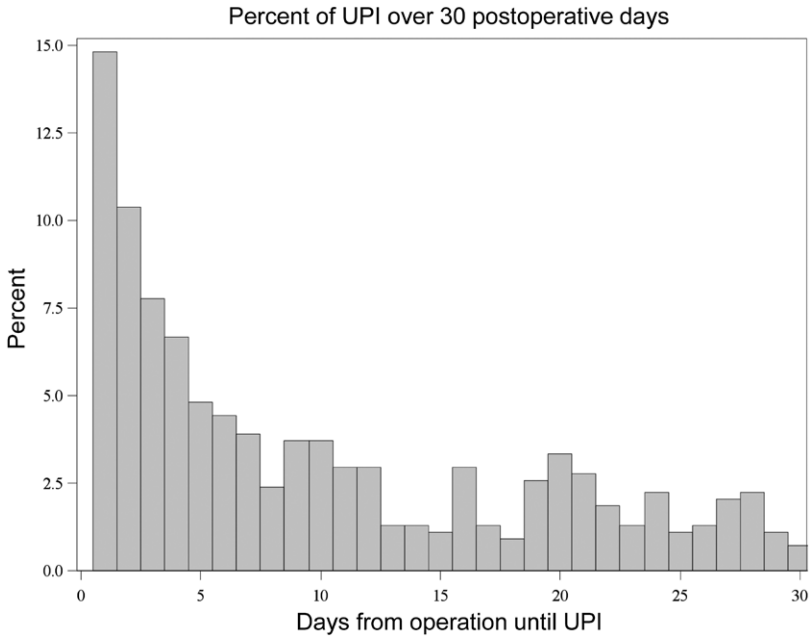

Fig. 2. Percent unplanned postoperative intubation (UPI) during 30 postoperative days. Histogram representation of UPI events as percent total by postoperative day.

Table 1. Univariable Analysis of the Derivation Cohort

	Mean ± SD/n (%)				
		UPI			
Risk Factor	Total Sample, n = 58,614	No, n = 58,495 (99.8%)	Yes, n = 119 (0.20%)	OR (95% CI)	*P* Value
Age at surgery, yr	6.88 ± 5.67	6.89 ± 5.67	4.81 ± 5.99	0.93 (0.9–0.97)	< 0.0001
Total operation time (z-score)	−0.01 ± 0.98	−0.01 ± 0.98	0.54 ± 1.18	1.35 (1.23–1.48)	< 0.0001
Gender, n (%)					
Female	24,751 (42.23)	24,703 (42.23)	48 (40.34)	[Ref]	
Male	33,863 (57.77)	33,792 (57.77)	71 (59.66)	1.08 (0.75–1.55)	0.6878
Race, n (%)					
White	47,598 (81.21)	47,514 (81.23)	84 (70.59)	[Ref]	
Black or African American	8,699 (14.84)	8,667 (14.82)	32 (26.89)	2.11 (1.41–3.16)	0.0965
Asian	1,858 (3.17)	1,855 (3.17)	3 (2.52)	1.06 (0.36–3.09)	0.9710
Other	459 (0.78)	459 (0.78)	0 (0)	0.61 (0.04–9.91)	0.5951
Ethnicity, n (%)					
Hispanic	6,509 (11.1)	6,500 (11.11)	9 (7.56)	0.69 (0.35–1.34)	0.2685
Not Hispanic	52,105 (88.9)	51,995 (88.89)	110 (92.44)	[Ref]	
Cardiac risk factors, n (%)					
No cardiac risk factors	53,022 (90.46)	52,948 (90.52)	74 (62.18)	[Ref]	
Minor cardiac risk factors	3,256 (5.55)	3,233 (5.53)	23 (19.33)	5.17 (3.24–8.22)	0.4165
Major cardiac risk factors	1,876 (3.2)	1,862 (3.18)	14 (11.76)	5.53 (3.15–9.73)	0.3157
Severe cardiac risk factors	460 (0.78)	452 (0.77)	8 (6.72)	13.35 (6.52–27.33)	< 0.0001
SIRS/sepsis/septic shock within 48 h, n (%)					
None	55,489 (94.67)	55,375 (94.67)	114 (95.8)	[Ref]	
SIRS	1,427 (2.43)	1,424 (2.43)	3 (2.52)	1.19 (0.41–3.45)	0.9857
Sepsis	1,593 (2.72)	1,591 (2.72)	2 (1.68)	0.76 (0.22–2.66)	0.4523
Septic shock	105 (0.18)	105 (0.18)	0 (0)	2.3 (0.14–37.56)	0.5498
ASA physical status classification, n (%)					
1	19,230 (32.81)	19,225 (32.87)	5 (4.2)	[Ref]	
2	24,678 (42.1)	24,657 (42.15)	21 (17.65)	3.05 (1.19–7.78)	<0.0001
3	12,941 (22.08)	12,869 (22)	72 (60.5)	19.69 (8.27–46.87)	< 0.0001
4/5	1,765 (3.01)	1,744 (2.98)	21 (17.65)	43.08 (16.86–110.05)	< 0.0001
Premature birth, n (%)	8,306 (14.17)	8,272 (14.14)	34 (28.57)	2.45 (1.65–3.64)	< 0.0001
Neonate, n (%)	2,749 (4.69)	2,724 (4.66)	25 (21.01)	5.52 (3.56–8.57)	< 0.0001
History of asthma, n (%)	3,655 (6.24)	3,647 (6.23)	8 (6.72)	1.15 (0.57–2.31)	0.7014
History of cystic fibrosis, n (%)	142 (0.24)	142 (0.24)	0 (0)	1.71 (0.11–27.96)	0.7055
Oxygen support, n (%)	2,117 (3.61)	2,091 (3.57)	26 (21.85)	7.64 (4.95–11.79)	< 0.0001
Structural pulmonary/airway abnormalities, n (%)	3,156 (5.38)	3,128 (5.35)	28 (23.53)	5.52 (3.62–8.41)	< 0.0001
Tumor involving CNS, n (%)	952 (1.62)	942 (1.61)	10 (8.4)	5.86 (3.1–11.07)	< 0.0001
Developmental delay/impaired cognitive function, n (%)	7,970 (13.6)	7,927 (13.55)	43 (36.13)	3.63 (2.5–5.27)	< 0.0001
Neuromuscular disorder, n (%)	3,073 (5.24)	3,056 (5.22)	17 (14.29)	3.1 (1.86–5.15)	< 0.0001
Weight loss or failure to thrive, n (%)	2,055 (3.51)	2,043 (3.49)	12 (10.08)	3.21 (1.79–5.78)	< 0.0001
Congenital malformation, n (%)	19,196 (32.75)	19,134 (32.71)	62 (52.1)	2.24 (1.56–3.2)	< 0.0001
Past or current cancer, n (%)	1,642 (2.8)	1,627 (2.78)	15 (12.61)	5.18 (3.03–8.86)	< 0.0001

Detailed definitions of each variable are listed in appendix 1.

ASA = American Society of Anesthesiologists; CNS = central nervous system; OR = odds ratio; [Ref] = referent group; SIRS = systemic inflammatory response syndrome; UPI = unplanned postoperative intubation.

estimates and corresponding ORs for each covariate of interest were within the 95% CIs presented in the initial complete case model. The AUC for the new final prediction model using the multiply imputed datasets ranged from 0.8768 to 0.8799; the AUC for the initial complete case model using the multiply imputed datasets ranged from 0.8782 to 0.8811.

Discussion

We demonstrate that UPI occurs with an incidence of 0.2% in pediatric patients after noncardiac surgery. Approximately one third of all postoperative intubations occurred within the first 72 h. We identified independent risk factors for noncardiac, pediatric UPI including operation time (z-score

Table 2. Independent Predictors for Unplanned Postoperative Intubation—Derivation Data

Risk Factor	OR (95% CI)	*P* Value
Total operation time (z-score)	1.27 (1.15–1.41)	< 0.0001
Race		
White	[Ref]	
Black or African American	1.88 (1.26–2.81)	0.1182
Asian	1.13 (0.4–3.25)	0.8349
Other	0.50 (0.03–7.68)	0.4978
Cardiac risk factors		
No cardiac risk factors	[Ref]	
Minor cardiac risk factors	1.99 (1.22–3.24)	0.7176
Major cardiac risk factors	1.49 (0.81–2.76)	0.3389
Severe cardiac risk factors	3.98 (1.85–8.54)	0.0064
ASA physical status classification		
1	[Ref]	
2	2.34 (0.92–5.95)	0.0311
3	7.6 (3.07–18.82)	< 0.0001
4/5	10.23 (3.69–28.39)	< 0.0001
Neonate	3.48 (2.08–5.8)	< 0.0001
Structural pulmonary/airway abnormalities	1.72 (1.1–2.7)	0.0170
Tumor involving CNS	2.26 (0.99–5.17)	0.0526
Developmental delay/impaired cognitive function	1.99 (1.32–2.99)	0.0010
Past or current cancer	2.69 (1.33–5.44)	0.0060

Detailed definitions of each variable are listed in appendix 1.

ASA = American Society of Anesthesiologists; CNS = central nervous system; OR = odds ratio; [Ref] = referent group.

more than 1), severe cardiac risk factors, ASA physical status classification greater than or equal to 2, tumor involving the CNS, developmental delay/impaired cognitive function, past or current malignancy, and neonate status. Using these risk factors, we created a valid model predictive of UPI with strong discriminant value. Finally, we report a more than 11-fold increased risk of unadjusted mortality when patients experienced a UPI.

UPI incidence in our study can be compared to that in the adult literature that similarly looked at intubation within three days of surgery. Ramachandran *et al.*[3] reported an intubation incidence of 0.83 to 0.9%, making UPI a rarer event in children as compared to adults. The same authors also demonstrated that approximately 50% of patients had an unplanned intubation by the third postoperative day,[3] whereas 33.0% of our pediatric patients were intubated during the same period. This reduction may be due to potentially different effects that surgery and anesthesia might have on the pediatric patient's oxygenation and sleep-associated breathing. Indeed, the original research that showed persistent hypoxemia through 72 h was performed in adults.[7–9,13] Instead, we found that 50% of patients were not intubated until approximately postoperative day 6 (data not shown), possibly suggesting a prolonged susceptibility to postanesthetic respiratory complications. However, another possible contributor to this finding is that a subset of higher risk patients may have been left intubated postoperatively, extubated at a later date, and reintubated outside the 72-h window, thus skewing the data. It should be pointed out that the adult NSQIP data regarding early unplanned intubation would have been susceptible to this potential skewing as well. Thus, this observed difference in percent intubated by 72 h remains an issue to be further investigated in the future.

The identification of independent predictors of pediatric UPI may provide clinicians a set of tangible perioperative variables that they can use in their risk assessment, preoperative counseling, and preemptive intervention to prevent a UPI. Not surprisingly, an ASA physical status classification 4 or greater produced the highest OR for UPI in our model. Ing *et al.*[2] found a high incidence of patients with an ASA physical status classification 3 among those reintubated. However, we demonstrate that even an ASA physical status classification 2 imparts an increased risk. A high incidence of cardiac comorbidity was also observed among reintubated children by Ing *et al.*[2] However, we established the presence of severe cardiac risk factors (uncorrected cyanotic heart disease) as a specific predictor of UPI, conceivably due to an impaired capacity for oxygen delivery. Similar to Ramachandran *et al.*,[3] we also found that a history of cancer was associated with an increased risk of UPI. Respiratory failure is one of the most common causes for admission to the pediatric ICU in children with cancer.[17–20] Among pediatric patients with leukemia, the most common childhood malignancy, respiratory failure is often secondary to a mediastinal mass, hyperleukocytosis, or infection.[21] The identification of both CNS tumor and developmental delay/

Table 3. Incidence of Unplanned Postoperative Intubation by the Number of Risk Factors

No. of Risk Factors	Derivation Cohort				Validation Cohort			
	No UPI, n (%)	UPI, n (%)	OR (95% CI)	*P* Value	No UPI, n (%)	UPI, n (%)	OR (95% CI)	*P* Value
0–1	40,108 (99.96)	15 (0.04)	[Ref]		20,202 (99.98)	5 (0.02)	[Ref]	
2	11,339 (99.68)	36 (0.32)	8.49 (4.65–15.51)	0.0152	5,597 (99.66)	19 (0.34)	13.72 (5.12–36.75)	0.2701
3	4,416 (99.33)	30 (0.67)	18.17 (9.77–33.79)	0.0753	2,120 (99.16)	18 (0.84)	34.31 (12.72–92.49)	0.0164
4–5	2,434 (98.66)	33 (1.34)	36.25 (19.66–66.83)	< 0.0001	1,236 (98.8)	15 (1.2)	49.03 (17.79–135.13)	0.0003
≥ 6	198 (97.54)	5 (2.46)	67.52 (24.31–187.57)	< 0.0001	92 (97.87)	2 (2.13)	87.83 (16.83–458.52)	0.0072

Risk factors included operation time (z-score), severe cardiac risk factors, American Society of Anesthesiologists physical status classification, tumor involving the central nervous system, developmental delay/impaired cognitive function, past or current malignancy, and neonate status. Detailed definitions of each variable are listed in appendix 1.

OR = odds ratio; [Ref] = referent group; UPI = unplanned postoperative intubation.

impaired cognitive function as risk factors may be related to the fact that patients with depressed mental status are at an increased risk of reintubation. A Glasgow Coma Scale score of less than 8 is an independent predictor of reintubation among adults.[22] Furthermore, in the ICU setting, many ventilator-weaning criteria fail to have discriminant value in predicting extubation success among patients with neurologic disease.[23] The maximal inspiratory and expiratory pressures, clinically reflected as the ability to cough and clear secretions, appear to be the most predictive of extubation success in these patients.[23] Interestingly, structural pulmonary/airway abnormalities dropped out of the final model after multiple imputation. While model diagnostics did not indicate substantial collinearity between our predictors of interest, it is possible that the parameter for structural pulmonary/airway abnormalities no longer met our threshold for inclusion in the final model after imputing missing data for ASA physical status classification such that prevalence of airway abnormalities increases as ASA physical status classification increases. We also note that the 95% CIs for the ORs were generally similar (complete case: OR, 1.72; 95% CI, 1.1 to 2.7 *vs.* multiple imputation: OR, 1.34; 95% CI, 0.88 to 2.04).

Among the identifiable risk factors, age and surgical duration were the only modifiable predictors. Younger patient age had previously been proposed to be a risk factor for reintubation, with an increased incidence of reintubation occurring in patients under 1 yr of age.[4,6] Consistent with these findings, age under 1 yr was significantly associated with increased unplanned intubation (data not shown). However, to avoid potential collinearity between neonate status and age under 1 yr, only neonate status was included in the multivariable model. Neonates possess multiple physiologic features that can predispose them to increased respiratory morbidity. For example, they are more prone to diaphragmatic fatigue due to fewer type I muscle fibers,[24] they have closing volumes greater than their functional residual capacity,[25] and they have a diminished hypercapnic ventilatory drive in the setting of hypoxia.[26] Furthermore, preterm infants have a risk of postanesthetic respiratory depression, which is inversely related to postconceptual age, thus placing preterm neonates at maximal susceptibility.[27] At the discretion of the clinician, consideration can therefore be given to the postponement of elective surgery in neonatal patients who, perhaps in the presence of other predictors, pose an unacceptable risk of UPI. This is the first demonstration of operative time as an independent predictor of UPI in children undergoing noncardiac surgery. Prolonged anesthesia may affect the airway and lungs in several ways, including atelectasis, airway edema from prolonged intraoperative intubation, and fluid overload. Another possible reason is the occurrence of venous thromboembolism. In adults, anesthesia duration has been implicated as a risk factor for the development of deep vein thrombosis and pulmonary embolism.[28,29] Similarly, in a cohort of pediatric patients undergoing repair of esophageal atresia, the number of paralytic episodes was the only independent predictor of symptomatic venous thromboembolism.[30] Indeed, we found that patients with longer operative times had an increased incidence of venous thrombosis requiring anticoagulation therapy. Similarly, those patients with UPI also had an increased incidence of venous thrombosis (appendixes 5 and 6). In those patients at risk, consideration could be given to the utilization of technical advancements to shorten procedure time, the opting out of bundling multiple procedures under one anesthetic, or even the decision not to proceed with a longer operation.[29] However, with data regarding the use of methods to shorten operative time being absent from our dataset, definitive conclusions must be left to future studies.

For the purpose of clinical applicability, we looked at the cumulative effect that our independent predictors had on the risk of UPI. As expected, the incidence of UPI increased as the number of risk factors increased. Those patients with six or more risk factors had a UPI OR of 67.52 (95% CI, 24.31 to 187.57) in the derivation cohort (table 3). So, while an ASA physical status classification of 2 may not provide predictive specificity to the clinician, in combination with one or more of the other listed predictors, this tool becomes useful in anticipating UPI in such a patient. While unadjusted, UPI was an independent predictor of death with an OR of 11.4 (95% CI, 5.8 to 22.4), which was also higher than that previously seen in the adult population (adjusted OR, 9.2; 95% CI, 5.6 to 15.0).[3] Taking the significant effect each predictor has on the risk of UPI and the associated predictive value UPI has for death, there is a clearer impetus to identify patients at high risk and treat them with the goal of preventing UPI. Measures include chest physiotherapy, which has been shown to improve oxygenation and pulmonary function in pediatric patients.[31,32] Another therapy is noninvasive ventilation, which has been shown by numerous studies to prevent intubation in the setting of respiratory distress/failure.[33–37] Furthermore, helium–oxygen has been shown to be a helpful adjuvant to noninvasive ventilation by decreasing the work of breathing and improving carbon dioxide elimination[38] and was found to improve postoperative pulmonary outcomes in infants.[39] There are also potential measures that remain to be explored. In adults identified to be at high risk of postoperative pulmonary complications, a low intraoperative tidal volume strategy resulted in fewer major postoperative pulmonary and extrapulmonary complications.[40] Whether this strategy would work in the pediatric population is yet to be studied, although the creation of this predictive tool can be the first step for such a trial.

Our study should only be interpreted within the context of its limitations. First, details regarding intraoperative anesthetic factors are not provided by NSQIP-P. Fluid management and respiratory complications such as pulmonary aspiration can affect all of the outcomes of this study but were not available. Second, our investigation was limited by a low mortality incidence. While an adjusted mortality risk is ideal, there was an insufficient number of events to perform a

multivariable logistic regression model for this outcome. This would be an ideal subject for future investigation. Third, our dataset contained 23% missing data on covariates. While a sensitivity analysis utilizing multiple imputation yielded few differences, the generalizability of our results may be limited. Finally, only ACS NSQIP-P–participating hospitals were included in this study (this database includes a higher number of academic medical centers and a smaller number of community hospitals); therefore, our findings may not be generalized to all hospital systems in the United States.

In conclusion, respiratory failure requiring unplanned intubation in the early postoperative period after noncardiac surgery occurred with an incidence of 0.2% in children. Of the total number of unplanned intubations, 33% occurred within the first 72 h after anesthesia. We identified operation time (z-score), severe cardiac risk factors, ASA greater than or equal to 2, tumor involving the CNS, developmental delay/impaired cognitive function, past or current malignancy, and neonate status as independent predictors of UPI. Knowledge of these predictors may allow for greater awareness of "at-risk" patients by clinicians before anesthesia and surgery.

Acknowledgments

The authors thank Sarah Kennedy, M.S., M.S.N., R.N., National Surgical Quality Improvement Program Pediatric, Ann & Robert H. Lurie Children's Hospital, Chicago, Illinois, for her clarification of data collection processes and database variables.

Research Support

Support was provided solely from institutional and/or departmental sources.

Competing Interests

The authors declare no competing interests.

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Appendix 1: Variable and Outcome Definitions

Unplanned intubation: patient requiring the placement of an endotracheal tube or other similar breathing tube (laryngeal mask airway, nasotracheal tube, and orotracheal tube) and ventilatory support, which was not intended or planned at the time of the principal operative procedure, with the exception of when the patient is being intubated for additional surgical procedures.

Scenarios designated as unplanned: accidental self-extubation requiring reintubation; endotracheal tube replacement for mucous plug or concern for tube dislodgement; emergency tracheostomy; patients with a chronic/long-term tracheostomy who were not preoperatively mechanically ventilated and were postoperatively off mechanical ventilation but require resumption of mechanical ventilation due to cardiovascular or respiratory instability.

Scenarios *not* designated as unplanned: patients who undergo time off the ventilator, remain intubated, fail the trial, and were placed back on the ventilator without extubation; intubations for an unplanned return to the operating room; uneventful chronic tracheostomy replacement (planned or unplanned); intubation/reintubation while still in the operating room for the principal operative procedure; patients with tracheostomy who were on preoperative mechanical ventilator support.

Unplanned postoperative intubation: unplanned intubation (as defined above) within 72 h following surgery.

No cardiac risk factors: no preexisting cardiac conditions or compromise of cardiac function requiring medication.

Minor cardiac risk factors: (1) cardiac condition with or without medication and maintenance (*e.g.*, atrial septal defect, small to moderate ventricular septal defect with no symptoms or symptoms of well-controlled congestive heart failure, and patent ductus arteriosus); (2) status post repair of congenital heart defect with normal cardiovascular function and no medications (*e.g.*, atrial septal defect/patent foramen ovale, ventricular septal defect, patent ductus arteriosus, and coarctation of the aorta).

Major cardiac risk factors: (1) status post repair of congenital heart defect with residual hemodynamic abnormality with or without medications (*e.g.*, tetralogy of Fallot with wide open pulmonary insufficiency, aortic valve disease with aortic stenosis or aortic insufficiency based on the presence of echocardiographic gradient, and all single-ventricle patients [severe atrioventricular canal and hypoplastic left heart syndrome {including stage 1 repair}]).

Severe cardiac risk factors: (1) uncorrected cyanotic heart disease; (2) patients with any documented pulmonary hypertension; (3) patients with ventricular dysfunction requiring medication, may or may not be on heart transplant list (*e.g.*, hypertrophic cardiomyopathy).

Systemic inflammatory response syndrome: pediatric systemic inflammatory response. The presence of at least two of the following criteria, one of which must be abnormal temperature or leukocyte count.

- Temperature of more than 38.5°C or less than 36°C (axillary, temporal, tympanic, oral, rectal, bladder, or central catheter probe)
- Tachycardia in the absence of drugs, external or painful stimuli, which persists for more than 30 min. For children less than 1 yr of age: bradycardia in the absence of deep sedation, β blockers, or other cardioactive drugs, which persists for more than 30 min.
- Respiratory rate elevation in the absence of external or painful stimuli, which persists for more than 30 min, or mechanical ventilation not related to underlying neuromuscular disease.
- Leukocyte count elevated or depressed for age with leukopenia not secondary to chemotherapy.

Sepsis: to be assigned as sepsis, criteria from *both* pediatric systemic inflammatory response syndrome and suspected or proven infection must be met.

Suspected or proven infection: Infection caused by any pathogen or clinical syndrome associated with a high probability of infection. Must meet at least one of the following preoperative or intraoperative criteria:

Preoperative: positive blood culture, positive culture from any site thought to be causative, positive findings on clinical examination, such as purulent drainage at site, and imaging evidence of abscess

or

Intraoperative: confirmed tissue or organ infarction/devitalization requiring resection, purulence in the operative site, perforated bowel or other viscus (*e.g.*, ruptured appendix), and positive intraoperative cultures.

Septic shock: To be assigned as septic shock, criteria for sepsis must be met and the patient must have documented cardiovascular dysfunction.

Cardiovascular Dysfunction

The use of a vasoactive drug to maintain perfusion (dopamine, dobutamine, epinephrine, norepinephrine, vasopressin, isoproterenol, ephedrine, amrinone, and milrinone)

or

An increase in the dosage of a vasoactive drug or the addition of a second vasoactive drug in a patient receiving a vasoactive drug before the diagnosis of sepsis.

The ASA physical status classification: the patient's present physical condition on a scale from 1 to 5 as it appears on the anesthesia record. The classifications are as follows: ASA 1—normal healthy patient; ASA 2—patient with mild systemic disease; ASA 3—patient with severe systemic disease; ASA 4—patient with severe systemic disease that is a constant threat to life; and ASA 5—moribund patient who is not expected to survive without the operation.

Premature birth: birth occurred before 37 gestational weeks.

Neonate: patients up to the first 28 days of life.

History of asthma: A history of chronic reactive airway disease (RAD) resulting in functional disability in daily activities, chronic medication requirement, or hospitalization (not including emergency room visit or 23-h observation) for treatment of RAD within 1 yr before surgery. Also any patient who is on scheduled daily medications for asthma or RAD but does not have a formal diagnosis in the chart.

History of cystic fibrosis: A diagnosis of cystic fibrosis with or without respiratory compromise.

Oxygen support: patients who require supplemental oxygen support at the time of surgery. Oxygen can be delivered by any modality for any reason. Patients requiring supplemental oxygen at night are included. Patients who only receive oxygen in the operating room are not included.

Structural pulmonary/airway abnormalities: a structural pulmonary and/or airway abnormality is present with or without respiratory comprise.

Current/Unrepaired/Unresected/Recurrent

Upper airway —mass effect or lesion/structural abnormality of pharynx/larynx

- Neck tumors with airway compression (*e.g.*, teratoma and cystic hygroma/lymphangioma), laryngeal cleft, cricoid stenosis, subglottic stenosis, papillomas/intraluminal tumors, and Pierre-Robin/hypoplastic mandible
- Obstructive sleep apnea—must have abnormal sleep study (polysomnography) or nocturnal pulse oximetry within 1 yr or prescribed treatment (*e.g.*, continuous positive airway pressure) at the time of surgery
- Note: cleft palate is *not* included

Lower airway—mass effect or lesion/structural abnormality of trachea/bronchus

- Neck or mediastinal tumor/mass compressing trachea/bronchus (*e.g.*, lymphangioma, anterior mediastinal mass, and bronchogenic cyst), tracheal/bronchial stenosis, bronchial atresia, and papillomas/intraluminal tumors
- Pulmonary/parenchymal—mass effect or lesion/structural abnormality/disease of lung parenchyma
- Mass effect—bronchogenic/foregut duplication cyst, congenital or acquired diaphragmatic hernia, and diaphragmatic eventration/paralysis
- Intrathoracic lesion—congenital cystic adenomatoid malformation/congenital pulmonary airway malformation, pneumatocele, blebs/bullae, pulmonary abscess/cavitation, and intrathoracic pulmonary sequestration
- Pulmonary disease—congenital lobar emphysema and bronchiectasis

Acute

Pulmonary/parenchymal: mass effect—pneumothorax and pleural effusion (including empyema, hemothorax, and chylothorax) present within 7 days of surgery (treated or to be treated)

Chronic

Upper airway—mass effect or lesion/structural abnormality of pharynx/larynx (laryngomalacia and vocal cord paralysis)

Lower airway—mass effect or lesion/structural abnormality of trachea/bronchus (tracheomalacia and bronchomalacia)

Pulmonary/parenchymal—mass effect or lesion/structural abnormality/disease of lung parenchyma (pulmonary disease—pulmonary hypoplasia [*e.g.*, congenital diaphragmatic hernia and cystic–dysplastic kidneys]; previous pulmonary resection—pneumonectomy and lobectomy [two or more])

Tumor involving CNS: patient has a space-occupying tumor of the brain or spinal cord, which may be benign (*e.g.*, meningiomas, ependymoma, and oligodendroglioma) or primary (*e.g.*, astrocytoma, glioma, and glioblastoma multiforme) or secondary malignancies (*e.g.*, metastatic lung, breast, and malignant melanoma). Other tumors that may involve the CNS include lymphomas and sarcomas. Included whether the tumor was not treated or if the tumor was removed.

Developmental delay/impaired cognitive status: patient's medical record documentation states that the patient is not appropriate for developmental age. Includes patients who are blind and/or deaf. Patients with attention deficit disorder, attention deficit hyperactivity disorder, or psychiatric disorders are not included. Developmental status and/or cognitive ability impairment is defined when a child does not reach his/her developmental milestones at the expected times. It is an ongoing delay in the process of development. Delays can occur in one or many areas, such as gross or fine motor, language, and social or thinking skills. Delays may result from any etiology, including congenital malformations, acquired structural lesions, traumatic injury, birth asphyxia, and metabolic or unknown causes.

Neuromuscular disorder: if a patient has a congenital or acquired degenerative neuromuscular disorder that resulted in a slow, progressive deterioration in motor function. If there is documentation in the medical record, radiologic studies are not required to verify the presence of a neuromuscular disorder. Patients with decreased muscle tone or significant contractures that affect motor function are included. Patients with neuromuscular scoliosis are included.

Weight loss or failure to thrive: patients with a greater than 10% decrease in body weight in the 6-month interval immediately preceding surgery as manifested by serial weight loss documented in the chart. Patients with a current diagnosis in the medical record of failure to thrive are included. Patients who have intentionally lost weight as part of a weight reduction program do not qualify.

Congenital malformation: A congenital defect is present in a neonate at the time of surgery or if an infant, child, or teenager has a history of congenital defect at the time of surgery. Congenital malformations recorded under another preoperative risk factor are not included. Congenital malformations may include syndromes, chromosomal disorders, metabolic disorders, and skeletal and organ system disorders. These malformations can involve many different or multiple organ systems including the brain, heart, lungs, liver, bones, endocrine, and intestinal tract. Malformations may be caused by genetic factors or by prenatal events that are not genetic. These defects occur for many reasons including inherited (genetic) conditions, toxic exposure of the fetus, and birth injury or for unknown reasons.

Past or current history of cancer: past—patient has a history of malignancy but no evidence of active disease. The patient has a history of childhood malignancy treated with surgery, chemotherapy, and/or radiotherapy, but there is no current evidence of active disease documented in the medical record, and there is no plan for ongoing treatment. Current—patient has a childhood malignancy that is currently present and documented in the medical record. Patients for whom this is the diagnostic/definitive cancer surgery. Patients with a current cancer diagnosis who are actively undergoing treatment and also those who have not yet begun treatment are included.

Appendix 2: Statistical Analysis Outline

Primary Objective

To evaluate the association between presumed risk factors and postoperative reintubation in pediatric surgical patients.

Analytic Sample

To be determined: data from the National Surgical Quality Improvement Program Pediatric database.

Primary Outcomes

Postoperative Reintubation less than or equal to 72 h (3 days).

Predictors

Primary

Surgical specialty
Premature birth
Oxygen support
Structural pulmonary/airway abnormalities
Neuromuscular disorder
Neonate (yes/no)
ASA physical status classification
Total operation time
Body mass index
Surgical procedure risk

Secondary

History of asthma
History of cystic fibrosis
Cardiac risk factors
Tumor involving the CNS
Developmental delay/impaired cognitive function
Weight loss or failure to thrive
Systemic inflammatory response syndrome/sepsis/septic shock within 48 h
Congenital malformation
Childhood malignancy

Analysis Outline

- Run descriptive statistics
  - Mean/SD or median (interquartile range) for continuous variables
  - Frequencies/percentages for categorical variables
- Cross-validation analysis
  - Divide sample into a training dataset (66.7%) and test dataset (33.3%)
  - Evaluate unadjusted/bivariate relationships in train dataset using logistic regression
    - PROC LOGISTIC
  - Develop a multivariable logistic regression model to best explain the relationship between risk factors and postoperative reintubation
    - Obtain AUC and examine (more than 0.80 considered good prediction)
    - Output predicted probabilities
    - Use predicted probabilities to model reintubation
    - Examine coefficient of determination (R-sq) option for train dataset
    - Evaluate Hosmer–Lemeshow goodness-of-fit test
  - Use β estimates from training output to estimate predicted probabilities for test data
    - Model test data outcome (reintubation) *versus* predicted probabilities
    - Examine R-sq and Hosmer–Lemeshow goodness-of-fit test
      - Evaluate shrinkage of R-sq (less than 0.10 considered good)
    - Examine β from test dataset and compare to β from training dataset
      - Evaluate relative percent change in β

Appendix 3: Distribution Comparison of Development and Validation Data

Variable	Mean ± SD/n (%)		
	Derivation, n = 58,614	Validation, n = 29,306	*P* Value
Reintubation, < 72 h, n (%)	119 (0.20)	59 (0.20)	0.9579
Age of surgery, yr	6.88 ± 5.67	6.83 ± 5.64	0.1537
Total operation time (z-score)	−0.01 ± 0.98	−0.01 ± 1.02	0.6193
Gender, n (%)			0.6857
Female	24,751 (42.23)	12,417 (42.37)	
Male	33,863 (57.77)	16,889 (57.63)	
Race, n (%)			0.7035
White	47,598 (81.21)	23,807 (81.24)	
Black or African American	8,699 (14.84)	4,361 (14.88)	
Asian	1,858 (3.17)	930 (3.17)	
Other	459 (0.78)	208 (0.71)	
Ethnicity, n (%)			0.1401
Hispanic	6,509 (11.1)	3,352 (11.44)	
Not Hispanic	52,105 (88.9)	25,954 (88.56)	
Cardiac risk factors			0.8585
No cardiac risk factors	53,022 (90.46)	26,526 (90.51)	
Minor cardiac risk factors	32,56 (5.55)	1,630 (5.56)	
Major cardiac risk factors	1,876 (3.2)	911 (3.11)	
Severe cardiac risk factors	460 (0.78)	239 (0.82)	
SIRS/sepsis/septic shock within 48 h, n (%)			0.9530
None	55,489 (94.67)	27,760 (94.72)	
SIRS	1,427 (2.43)	700 (2.39)	
Sepsis	1,593 (2.72)	797 (2.72)	
Septic shock	105 (0.18)	49 (0.17)	
ASA physical status classification			0.5861
1—no disturb	19,230 (32.81)	9,641 (32.9)	
2—mild disturb	24,678 (42.1)	12,382 (42.25)	
3—severe disturb	12,941 (22.08)	6,448 (22)	
4—life threat/5—moribund	1,765 (3.01)	835 (2.85)	
Premature birth, n (%)	8,306 (14.17)	4,134 (14.11)	0.7964
History of asthma, n (%)	3,655 (6.24)	1,800 (6.14)	0.5875
History of cystic fibrosis, n (%)	142 (0.24)	65 (0.22)	0.5550
Oxygen support, n (%)	2,117 (3.61)	1,090 (3.72)	0.4224
Structural pulmonary/airway abnormalities, n (%)	3,156 (5.38)	1,549 (5.29)	0.5396
Tumor involving CNS, n (%)	952 (1.62)	479 (1.63)	0.9095
Developmental delay/impaired cognitive function, n (%)	7,970 (13.6)	3,922 (13.38)	0.3806
Neuromuscular disorder, n (%)	3,073 (5.24)	1,488 (5.08)	0.2975
Weight loss or failure to thrive, n (%)	2,055 (3.51)	996 (3.40)	0.4122
Congenital malformation, n (%)	19,196 (32.75)	9,634 (32.87)	0.7121
Past or current cancer, n (%)	1,642 (2.8)	805 (2.75)	0.6433
Neonate, n (%)	2,749 (4.69)	1,318 (4.5)	0.1999

ASA = American Society of Anesthesiologists; CNS = central nervous system; SIRS = systemic inflammatory response syndrome.

Appendix 4: Model Estimate Regression Coefficients for Final Prediction Model

Parameter	Derivation β	Validation β	Relative % Difference
Intercept	−6.3869	−6.2928	
Total operation time (z-score)	0.2418	0.2204	−0.1
Race			
White		Ref	
Black or African American	0.6183	0.1757	−0.7
Asian	0.1103	−0.1414	−2.3
Other	−0.7149	0.5168	−1.7
Cardiac risk factors			
No cardiac risk factors		Ref	
Minor cardiac risk factors	0.0695	0.2765	3.0
Major cardiac risk factors	−0.2165	−0.4442	1.1
Severe cardiac risk factors	0.7641	0.9101	0.2
ASA physical status classification			
1—no disturb		Ref	
2—mild disturb	−0.4502	−0.0292	−0.9
3—severe disturb	0.7271	1.2062	0.7
4—life threat/5—moribund	1.0244	1.3204	0.3
Structural pulmonary/airway abnormalities	0.5444	0.0551	−0.9
Tumor involving CNS	0.8173	1.5007	0.8
Developmental delay/impaired cognitive function	0.6857	0.6347	−0.1
Past or current cancer	0.9889	−0.3869	−1.4
Neonate	1.2455	2.2048	0.8

ASA = American Society of Anesthesiologists; CNS = central nervous system; Ref = referent group.

Appendix 5: Venous Thrombosis

Occurrences of venous thrombosis: new diagnosis of blood clot or thrombus within the venous system, which may be coupled with inflammation and requires treatment. Must be noted within 30 days after the principal operative procedure and one of the following A or B below:

(A) New diagnosis of a (new) venous thrombosis, confirmed by a duplex, venogram, computed tomographic scan, or any other definitive imaging modality (including direct pathology examination such as autopsy) and the patient must be treated with anticoagulation therapy and/or placement of a vena cava filter or clipping of the vena cava, or the record indicates that treatment was warranted, but there was no additional appropriate treatment option available.

(B) As per (A) above, but the patient or decision maker has refused treatment. There must be documentation in the medical record of the (patient's) refusal of treatment.

Appendix 5a: Operative Time and Venous Thrombosis Requiring Therapy

Analysis Variable: OPTIME Total Operation Time								
Occurrences VT	N	Mean	SD	Median	Lower Quartile	Upper Quartile	Minimum	Maximum
No complication	87,828	−0.01	0.99	−0.25	−0.63	0.37	−2.31	25.77
VT requiring therapy	92	0.42	1.31	0.12	−0.47	1.03	−1.64	5.98

Wilcoxon Two-sample Test	
Statistic	4,892,718.0000
Normal approximation	
Z	3.4867
One-sided $P_r > Z$	0.0002
Two-sided $P_r > \|Z\|$	0.0005
Z includes a continuity correction of 0.5	

OPTIME = operative time; VT = venous thrombosis.

Appendix 5b: Venous Thrombosis among Patients with Unplanned Postoperative Intubation

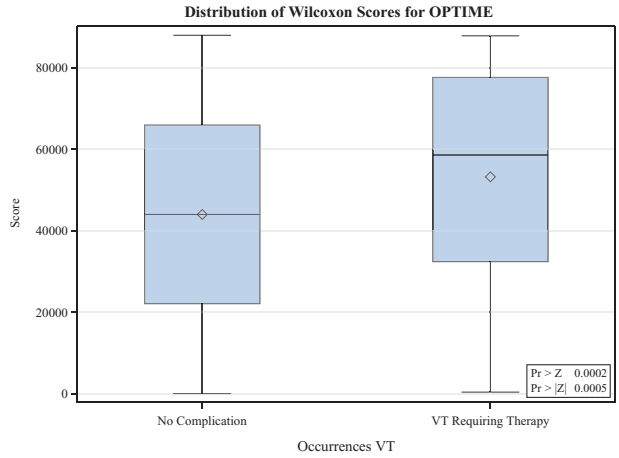
Analysis of Maximum Likelihood Estimates					
Parameter	DF	Estimate	SE	Wald Chi-Square	P_r > ChiSq
Intercept	1	–6.2454	0.0768	6,618.0183	< 0.0001
VT requiring therapy	1	3.8940	0.3779	106.1887	< 0.0001

DF = degrees of freedom.

Odds Ratio Estimates			
Effect	Point Estimate	95% Wald Confidence Limits	
VT requiring therapy	49.109	23.415	102.994

VT = venous thrombosis.

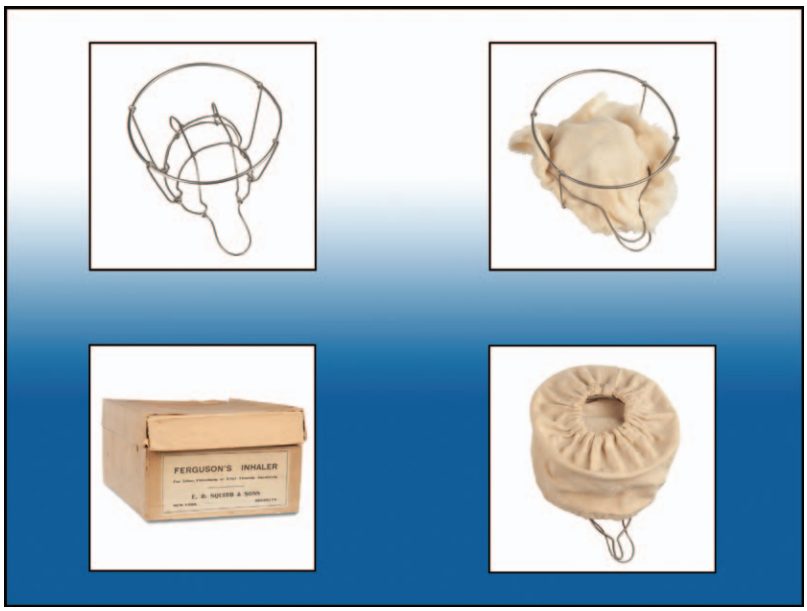
Appendix 6: Distribution of Wilcoxon Scores for Operative Time



OPTIME = operative time; VT = venous thrombosis.

ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

Squibb's Ferguson Inhaler for Open Drop Administration of Anesthesia



Before moving to the New York and New Jersey area, Robert H. Ferguson, M.D. (1857 to 1945), published from Boston about his double-chambered inhaler for ether, chloroform, or ethyl bromide, "but not for" ethyl chloride. Ferguson noted in 1905's final issue of the *Journal of the American Medical Association* that the wireframe (*high left*) of the Ferguson Inhaler could be "fitted accurately to the face of the patient by bending slightly the flexible face wire." Ohio's F. H. McMechan, M.D., observed that the wireframe "when covered with layers of gauze held in position by a wire spring [*high right*], formed the vaporizing chamber. This was surrounded and overtopped by a wire superstructure with a flannelette cover, perforated by the drop hole [*low right*] and forming a warming or rebreathing chamber." The inventor's employer, E. R. Squibb & Sons, mass produced the double-chambered device in a box (*low left*) labeled "Ferguson's Inhaler for Ether, Chloroform or Ethyl Chloride Anesthesia." (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

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