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Original study

Evaluation of risk prediction model for perioperative respiratory adverse events in pediatric anesthesia

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Abstract

Background: **Perioperative respiratory adverse events are among the most common critical incidents in pediatric anesthesia. Three risk prediction models have been developed to predict occurrence of such adverse events in children. However, these tools were only internally validated, limiting generalization. The Perioperative Respiratory Adverse Events in Pediatric Ambulatory Anesthesia risk prediction tool developed by Subramanyam et al. consists of five predictors: age ≤ 3 years, ASA physical status II and III, morbid obesity, preexisting pulmonary disorder, and surgery.**
Aims and Methods: **We aimed to evaluate the suitability of Subramanyam's model in predicting the occurrence of perioperative respiratory adverse events in a more general tertiary care pediatric population, including anesthesia for both outpatient and inpatient procedures. Therefore we validated this scoring system in a tertiary care cohort of 204 children included in the APRICOT study at our hospital through retrospective analysis of this data. Secondarily, we aimed to study the incidence of perioperative respiratory adverse events in our hospital.**
Results: **Overall incidence of perioperative respiratory adverse events in our sample was 19,6%. Applying Subramanyam's prediction model to our cohort, we found no patients categorized as low risk, 76 patients as intermediate risk and 128 patients as high risk. Discriminatory ability of the risk scoring system was modest, with AUC of the simplified model 0,65 (95% CI 0,57-0,74) and AUC of the original logistic regression model 0,66 (95% CI 0,57-0,75). Calibration of the simplified model was rather poor, with Brier score 0,49. The original logistic regression model calibrated better, with Brier score 0,18. A subgroup analysis considering solely ambulant patients in Ghent-APRICOT yielded comparable results.**
Conclusions: **We conclude that the overall performance of Subramanyam's risk prediction tool in our cohort was moderate. Modest discrimination and calibration suggest that the risk score may not reliably predict perioperative respiratory adverse events in individual patients in our tertiary care pediatric population. Therefore the clinical relevance of the implementation of this scoring system in our tertiary hospital would be negligible, which leaves us with the lack of good scoring systems to predict perioperative respiratory adverse events in our population. In addition, we found the incidence of these adverse events in our hospital to be markedly higher as compared to the sample of Subramanyam.**

Keywords (MeSH terms): **Anesthesia/adverse effects, Respiratory system, Perioperative period, Child, Risk assessment, Validation study.**

This study was approved by HIRUZ, Ghent University Hospital medical ethics committee (Health, Innovation and Research Institute, Corneel Heymanslaan 10, 9000 Ghent, Belgium - head of department Prof. Dr. Van Der Straeten Catherine). The reference number of this study is BC-11752 and approval took place on February 9 2022. For all included patients a written informed consent was obtained as part of the APRICOT study.

Introduction

In the last decades significant advancements have been made in the safe delivery of pediatric anesthesia as a result of improvements in monitoring and equipment, the arrival of safe and more easily titratable anesthetic agents, and the practice of subspecialization[1,2]. Despite this progression, the perioperative period can still be fraught with risks for the pediatric patient. Perioperative respiratory adverse events (PRAEs) are challenging complications to most anesthesiologists as they are among the most common critical incidents in children, frequently demand quick escalation of care and can rapidly progress to a life-threatening situation if not handled adequately, especially in young children[1,3]. Since children naturally have less cardiorespiratory reserve, they are more vulnerable to promptly develop cyanosis, bradycardia and cardiac arrest[2]. PRAEs in pediatric anesthesia are associated with poor outcomes, such as increased morbidity, unanticipated ICU admission, and increased risk of in-hospital mortality[1,3,4,5]. Nevertheless, no standardized definitions of PRAEs have yet been formulated in pediatric literature. Accordingly, reported incidence of these critical events varies significantly from 0,1% to 27%[1,3-4,6-9].

Identifying the odds of PRAEs occurring in the individual patient is thus a major area of concern for the (pediatric) anesthesiologist and individual risk stratification is crucial to help clinicians and parents with informed consent and medical decision-making[10]. It would allow for an optimized perioperative management strategy and improved allocation of clinical resources[1]. A comprehensive risk prediction model could be an attractive and practical instrument in this perspective. Whilst they are not intended to replace clinical judgement, studies have shown that prediction tools can supplement reasoning and decision-making of anesthesiologists by providing more objectively estimated risks[11]. Although there are plenty of published studies describing risk factors for PRAEs, only three risk prediction models are yet developed for the pediatric population: (1) Perioperative Respiratory Adverse Events in Pediatric Ambulatory Anesthesia Risk Prediction Tool3, (2) Snoring, Trouble Breathing, and Un-Refreshed (STBUR) score4, and (3) COLDS score[12]. Nonetheless, all three of these tools lack external validation. As external validation is essential for reassuring the generalizability and reproducibility of a prediction model in other settings[13], the aforementioned models, should be used cautiously in clinical practice. The primary aim of this study is to assess the utility of the risk prediction tool developed by Subramanyam and colleagues[3] in predicting the occurrence of PRAEs in a more general tertiary care pediatric population, including anesthesia for both outpatient and inpatient procedures. Therefore we validated this scoring system in patients included in the APRICOT study performed in our hospital, Ghent University Hospital. Secondarily, we aim to study the incidence of PRAEs in our tertiary care pediatric population.

Materials and Methods

This study was approved by HIRUZ, Ghent University Hospital medical ethics committee (Health, Innovation and Research Institute, Corneel Heymanslaan 10, 9000 Ghent, Belgium - head of department Prof. Dr. Van Der Straeten Catherine). The reference number of this study is BC-11752 and approval took place on February 9, 2022. It involves a retrospective analysis of prospectively collected APRICOT data at Ghent University Hospital in order to evaluate the usefulness of the risk prediction tool developed by Subramanyam et al.[3] in a general tertiary care pediatric population. For all included patients a written informed consent was obtained as part of the APRICOT study. This study was performed in accordance to the TRIPOD statement for the transparent reporting of studies developing, validating, or updating a prediction model[14].

Perioperative Respiratory Adverse Events in Pediatric Ambulatory Anesthesia Risk Prediction Tool[3]

In 2016 Subramanyam et al. developed and internally validated a risk score for the occurrence of PRAEs in children up to 18 years undergoing elective ambulatory anesthesia. This involved a retrospective study using prospectively collected data on 19.059 cases in their tertiary care hospital at Cincinnatti from 2007 to 2012. Patients were assigned to a development cohort (n = 8.904) if they underwent anesthesia between 2007 and 2009 and to a validation cohort (n = 10.155) between 2010 and 2012.

The overall incidence of PRAEs in the study was 2,8% (n = 520). Through stepwise multivariate logistic regression 5 predictors were included in the final risk prediction tool: age ≤ 3 years, ASA physical status II and III, morbid obesity, preexisting pulmonary disorder, and surgery (vs. radiology). For content of the category 'preexisting pulmonary disorder' we refer to supplement 1. To simplify the logistic regression model to an easy-to-use scoring system, a risk score was given to each predictor based on the ß regression coefficients. Table I gives an overview of the predictors and accompanying

risk scores. The composite score for an individual patient ranging from 0 to 11, is obtained by summing the risk scores from each predictor. The authors defined the simplified model to categorize the risk for PRAEs into 3 strata: low (score 0/11), intermediate (score 1 to 3/11) and high (score ≥ 4/11) risk. With a score of < 4/11, the chance of having a complication is < 1%.

APRICOT study[7]

The APRICOT study was a large prospective multicenter study of pediatric anesthesia cases, conducted in 261 centers across 33 European countries between 01/04/2014 and 31/01/2015. The primary endpoint of the APRICOT project was the occurrence of perioperative severe critical events. We have permission of the APRICOT Investigators from the European Society of Anaesthesiology Clinical Trial Network to use their data collected at Ghent University Hospital.

Patient population

The APRICOT data from Ghent University Hospital, hereafter referred to as Ghent-APRICOT cohort, comprises 238 consecutive pediatric procedures conducted between 23/06/2014 and 06/07/2014 in our tertiary care center. We studied the occurrence of PRAEs in children from birth up to 15 years of age undergoing elective or urgent anesthesia for a surgical or radiological procedure. We included inpatient and emergency procedures to study the applicability of Subramanyam's risk score[3] to a wider range of anesthetic cases, resembling daily practice in our tertiary hospital. As the risk prediction model was developed for purely elective ambulatory anesthesia, we assumed that application of the risk score to a more complex cohort would increase the likelihood of finding a lower predictive accuracy. To examine the value of the prediction model in our outpatient population, we will perform a subgroup analysis considering solely ambulant patients in Ghent-APRICOT.

For 34 of 238 patients there were missing data on essential predictor variables. Therefore these individuals were excluded in the present study (n = 204). For all 204 included cases a written informed consent was obtained as part of the APRICOT study. Data entered into the Ghent-APRICOT database were derived from observation of routine care in the operating room and postanesthesia care unit (PACU), as well as from electronic medical records. In all cases, the observer was separate from and additional to the anesthesia care team. Induction of anesthesia included mostly inhalation induction with sevoflurane and oxygen. Anesthetic management was at the discretion of the attending anesthesiologist.

Predictors

Data from Ghent-APRICOT used in this study included age, sex, height, weight, ASA physical status, morbid obesity, current or recent (< 2 weeks preceding procedure) upper respiratory infection, wheezing in the last 12 months, snoring, any preexisting pulmonary disease, type of procedure (surgery or radiology) and patient type (inpatient or outpatient). For statistical analysis we converted the variable age to a binary variable with cutoff of 3 years, such as in the study of Subramanyam et al3. Morbid obesity was defined as a body mass index (BMI) above 97th percentile according to reference BMI-for-age growth charts from the World Health Organization for children less than 2 years of age (https://www.who.int/toolkits/child-growth-standards/standards/body-mass-index-for-age-bmi-for-age) and from the Centers for Disease Control for children aging 2 to 15 years (https://www.cdc.gov/healthyweight/bmi/calculator.html). Body mass

Table I. — Subramanyam's multivariable logistic regression model predicting occurrence of PRAEs and the risk scores. Adopted and adjusted from Subramanyam et al.[3].

Patient Characteristic	ß	OR (95% CI)	P value	Risk score
Age				
> 3y (reference)	0,00	1,00		0
≤ 3y	0,55	1,73 (1,36-2,21)	<0,0001	1
ASA physical status				
I	0,00	1,00		0
II	0,50	1,65 (1,24-2,21)	0,0006	1
III	0,79	2,20 (1,48-3,28)	<0,0001	2
Preexisting pulmonary disease	1,01	2,75 (2,06-3,66)	<0,0001	2
Morbid obesity	0,95	2,57 (1,36-4,87)	0,004	2
Type of procedure				
Radiology	0,00	1,00		0
Surgery	1,37	3,95 (2,56-6,08)	<0,0001	3

CI = confidence interval; OR = odds ratio.

index was calculated from the collected height and weight variables (BMI = kg/m²).

Outcome

Both in the study of Subramanyam et al.[3] and in our study PRAEs were defined as the occurrence of any 1 or combination of the following events from the onset of anesthesia induction until discharge from PACU: intraoperative or postoperative laryngospasm, intraoperative or postoperative bronchospasm, postoperative apnea/hypopnea, and postoperative prolonged oxygen requirement. The definition of each of these events was slightly different in our study as compared to Subramanyam's study[3]. In their study Subramanyam et al. defined laryngospasm as the requirement for positive pressure ventilation of > 20 cmH2O or administration of succinylcholine, bronchospasm as the use of albuterol, apnea/hypopnea as the need for bag mask ventilation, and prolonged oxygen requirement as a continued oxygen need 2 hours postoperatively to maintain SpO2 > 92%[3]. In our cohort laryngospasm was defined either as complete airway obstruction associated with rigidity of the abdominal and chest walls and leading to unsuccessful child's ventilation, or glottic closure associated with chest movement but silent unsuccessful child's respiratory efforts and assisted ventilation, unrelieved in both situations with jaw thrust and CPAP maneuvers and requiring the administration of medication (propofol, succinylcholine, etc.) and/or tracheal intubation. Bronchospasm was defined as an increased respiratory effort, especially during expiration, and wheeze on auscultation. Intraoperatively, if the patient was ventilated, bronchospasm was considered if a significant increase in peak inspiratory pressure (under volume controlled ventilation) or significant decrease in tidal volume (under pressure controlled ventilation) were observed. In all cases, any episode of airway constriction requiring the administration of a bronchodilator were also recorded as bronchospasm. A child was considered to have postoperative apnea/hypopnea when he/she needed additional bag mask ventilation or supplemental oxygen immediate after being extubated to keep SpO_2 > 92%. Prolonged postoperative oxygen requirement is the continued need of supplemental oxygen for more than one hour postoperatively to maintain SpO_2 > 92%7. As the definitions of PRAEs used in the APRICOT study are broader than those used in the study of Subramanyam et al.[3], it is expected that the incidence of PRAEs in the Ghent-APRICOT cohort can be slightly higher. Nevertheless we assume the difference cannot be as substantial to render the comparison of both cohorts worthless.

Statistical analysis

Two models from the original publication of Subramanyam et al.[3] were used to validate the risk score in our tertiary care pediatric population: the original logistic regression and the simplified point-based model3. Both methods are based on the same categorical predictors.

For both models, discrimination characteristics in the Ghent-APRICOT dataset were determined using ROC (Receiver Operating Characteristics) curve and its AUC (area under ROC curve). An AUC of 0,50 represents no predictive ability of the model beyond chance. An AUC of ≥ 0,70 is indicative of good discrimination, and a value ≥ 0,90 indicates excellent discrimination. Sensitivity and specificity for the optimal cutoff were calculated. To assess the accuracy of both prediction models, Brier score was calculated, and a calibration plot was constructed. For the Brier score a value closer to 0 is better, a value > 0,3 suggests poor calibration. For the original logistic regression, intercept and slope of the calibration plot were determined using a previously published method[15].

A subgroup analysis considering solely ambulant patients in Ghent-APRICOT was performed to assess the value of Subramanyam's model[3] for outpatient tertiary care pediatric procedures.

All analyses were done in R (4.2.0) using the tidyverse-package (1.3.1), rms-package (6.3-0) and the pROC-package (1.18.0) for analysis and visualization.

Results

Study cohort

Ghent-APRICOT comprises 238 pediatric cases. For 34 patients there were missing data on essential predictor variables, therefore these individuals were excluded in the present study (n = 204). All missing data concerned information on weight or height, and therefore BMI.

Demographic and clinical data on all patients are provided in Table II. To compare our study population with the cohorts of Subramanyam et al.[3], we included demographic and clinical data from their sample in Table II.

Of the 204 included patients, 129 underwent anesthesia for an ambulatory procedure and 75 for an inpatient procedure. All 129 ambulatory procedures were elective. 11 of 75 inpatient surgeries were of urgent nature.

The overall incidence of composite PRAEs in Ghent-APRICOT was 19,6% (n = 40). The incidence of PRAEs was 20% in neonates and infants (≤ 1 year), 30,6% in toddlers (> 1 years to ≤ 3 years), 16,3% in children (> 3 years to ≤ 13 years),

and 15,4% in teenagers (> 13 years to ≤ 15 years). Of the patients who experienced PRAEs, 50% was male. 36 children presented with an active or recent upper respiratory infection (URI), of whom 11 (30,6%) experienced PRAEs. Of 168 patients who had no recent history of URI, 29 (17,3%) developed PRAEs. The occurrence of PRAEs is shown in Table III.

Evaluation of risk prediction model

Applying the risk prediction tool of Subramanyam and colleagues[3] to our cohort, we found that there were no children with a risk score of 0/11. 76 patients were categorized as intermediate risk (risk score 1-3/11) and 128 patients as high risk (risk score ≥ 4/11). Table IV shows the proportion of PRAEs according to the risk categories.

To evaluate the utility of Subramanyam's prediction model[3] in a general tertiary pediatric population, we evaluated discrimination and calibration of both the simplified model and the original logistic regression in the Ghent-APRICOT cohort. For the simplified model, ROC curve is shown in Figure 1A. AUC is 0,65 (95% CI 0,57-0,74), sensitivity is 0,85 (95% CI 0,71-0,95), and specificity is 0,43 (95% CI 0,13-0,57). Model calibration was assessed through a calibration plot (Figure 2A) and Brier score is 0,49.

Discrimination characteristics of the original logistic regression model in the Ghent-APRICOT dataset were similar, with ROC curve shown in Figure 1B and AUC of 0,66 (95% CI 0,57-0,75). Calibration characteristics are displayed by a calibration plot (Figure 2B), with intercept 1,33 and slope 0,78. This figure shows that calibration is moderate, with substantial deviation from the 45-degree line of perfect fit. The Brier score is 0,18.

The subgroup analysis considering only outpatient procedures yielded comparable results. For the simplified model the AUC is 0,61 (95% CI 0,45-0,76) and Brier score is 0,46. For the original model the AUC is 0,61 (95% CI 0,46-0,76) and Brier score is 0,12.

Discussion

Overall performance of Subramanyam's model[3] in our general tertiary care pediatric population is modest. Moderate AUC of both the simplified and the original model indicate the discriminatory ability of this tool to distinguish between those children who will and will not develop PRAEs is rather weak. Additionally, Brier scores and calibration plots show us there is poor consistency between predicted and observed probabilities. With both moderate discrimination and calibration characteristics, we question this risk score is an effective tool to predict PRAEs in individual patients in our hospital or in other tertiary care populations. Application of a prediction model developed in ambulatory setting to a more complex cohort that comprises a wider range of anesthetic cases, including inpatient and emergency surgery, is certainly a reason of finding a low predictive accuracy. However, even when only ambulant patients in our tertiary care hospital were taken into account, we found similar results for discrimination and calibration of the model as for the complete Ghent-APRICOT cohort.

As in previous studies evaluating published prediction models, we noted that the study of

Table II. — Demographic and clinical characteristics of the development and validation cohort from Subramanyam et al.3 and of the Ghent-APRICOT cohort.

Characteristics	Subramanyam et al. Development cohort (n = 8.904)	Subramanyam et al. Validation cohort (n = 10.155	Ghent-APRICOT (n = 204)
Age (y), (median; IQR)	†	†	5; 7,75
≤ 3 y	3.408 (38,3)	3.767 (37,1)	86 (42,2)
> 3 y	5.496 (61,7)	6.388 (62,9)	118 (57,8)
Sex			
Male	5.165 (58,1)	5.852 (57,6)	112 (54,9)
Female	3.720 (41,9)	4.302 (42,4)	92 (45,1)
ASA physical status			
I	4.497 (51,7)	4.132 (41,8)	106 (52)
II	3.328 (38,2)	3.942 (39,9)	57 (27,9)
III	878 (10,1)	1.810 (18,3)	39 (19,1)
Preexisting pulmonary disease	1.168 (14,7)	1.304 (13,5)	11 (5,4)
Morbid obesity	119 (1,5)	160 (1,7)	17 (8,3)
Type of procedure			
Surgery	6.801 (76,4)	6.999 (69,2)	187 (91,7)
Radiology	2.013 (23,6)	3.118 (30,8)	17 (8,3)

Data are presented as n (%). IQR: interquartile range.
† Subramanyam et al. reported age as mean ± SD. Development cohort: 5,6 ± 4,6. Validation cohort: 5,7 ± 4,6.

Table III. — Perioperative Respiratory Adverse Events in Ghent-APRICOT.

Characteristics	Overall (n = 204)
Intraoperative laryngospasm	6 (2,9)
Intraoperative bronchospasm	1 (0,5)
Postoperative hypopnea/apnea	17 (8,3)
Postoperative laryngospasm	7 (3,4)
Postoperative bronchospasm	5 (2,5)
Postoperative prolonged oxygen requirement	22 (10,8)
Composite PRAEs	40 (19,6)
Data are presented as n (%). PRAEs: perioperative respiratory adverse events.	

Table IV. — Number and proportion of perioperative adverse events in Ghent-APRICOT according to the risk categories.

Risk category	PRAEs	No PRAEs
Intermediate	6 (7,89)	70 (92,11)
High	34 (26,56)	94 (73,44)
Data are presented as n (%). PRAEs: perioperative respiratory adverse events.		

Subramanyam et al.[3] has some drawbacks. First, reporting of development and model presentation are incomplete. Subramanyam and colleagues presented their prediction tool as a simplified scoring system, whereby the regression coefficients for each predictor in the model were rounded to integers and then summed to obtain an overall integer score for a particular individual. However, they didn't report a method to equate the overall integer score to a predicted risk. The risk for PRAEs was categorized into three strata, that were labelled low, intermediate and high risk, with no indication of the range or mean of the predicted risk corresponding to each category. Therefore, users of their prediction model are unable to provide an exact estimate of PRAEs probability for a patient. Instead, it is recommended to present the final prediction model in the form of its original regression equation to limit loss of information[16]. In times of widespread use of digital applications, the use of a more complex original regression equation should not be an obstacle anymore.

Second, we observed that the model is set up rather stringent, demonstrated by the small fraction of patients classified as low risk in both their and our studies. Hardly any child had a risk score of 0/11. Additionally, one should critically appraise the clinical relevance of the distinction between the low and intermediate risk category, as Subramanyam et al. reported that for both categories (i.e. risk score < 4/11) the chance of developing a complication is < 1%[3].

With this study, we would like to highlight that clinicians in search of an adequate method to estimate the perioperative risk of respiratory complications in their patients, should be mindful of pitfalls in the use of published risk prediction tools. All three published models to date lack external validation, implicating their usefulness and performance in settings different from those in which they were developed, has not been evaluated. We assessed the suitability of Subramanyam's risk score[3] in a general tertiary care pediatric population, including both ambulatory and inpatient anesthesia, and found that its performance in our cohort was modest. As this risk score was designed in the context of purely ambulatory procedures, we acknowledge this could have affected the results of low predictive

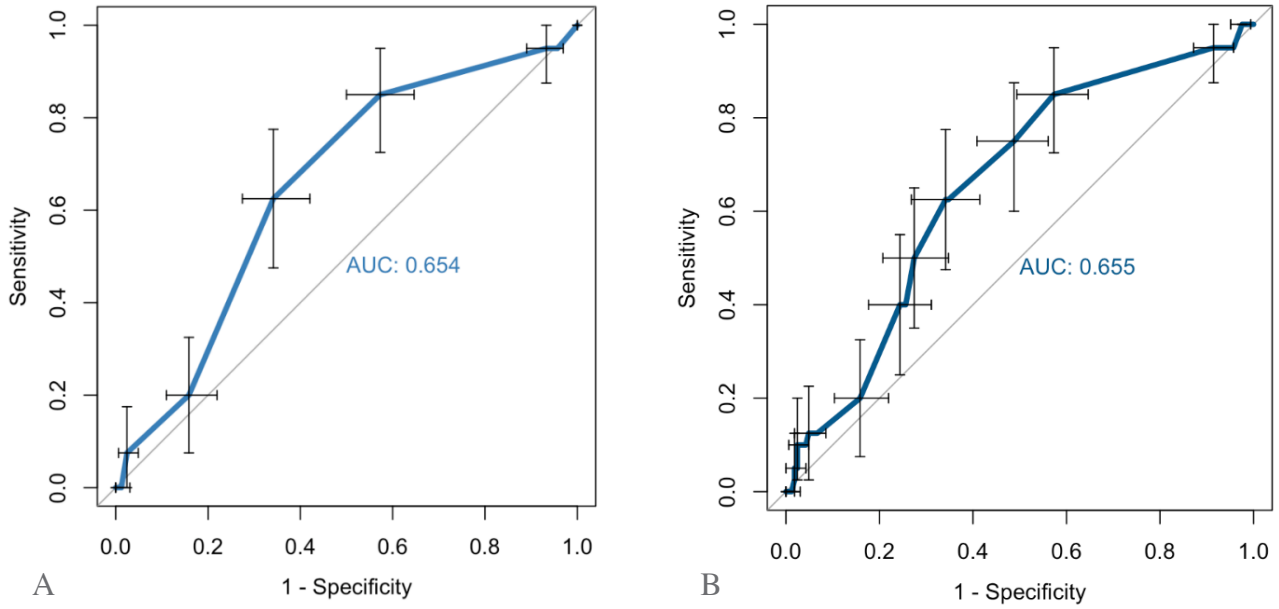

Fig. 1 — Receiver operating characteristic curves showing the discriminative value of the simplified point-based risk prediction model (1A) and the original logistic regression model (1B) in Ghent-APRICOT.

accuracy. However, we emphasize that a subgroup analysis considering only ambulant patients in our tertiary care population, yielded similar results. We therefore conclude the risk prediction model created by Subramanyam and colleagues[3] is not a very effective tool to predict PRAEs in our tertiary care pediatric population.

To our knowledge, this is the first study evaluating the PRAEs risk prediction tool of Subramanyam et al.[3] in a population outside the cohort it was developed in. The present report has many strengths including use of prospectively collected data, examination of composite PRAEs as a comprehensive, patient oriented outcome and evaluation of the prediction model by independent investigators, not involved in the original development study. However, also the limitations of this report should be noted.

First, this study was conducted in a referred population at a tertiary care center. We included children with complex pathologies requiring inpatient and urgent surgical procedures. This implies the cohort being studied may be too deviating from the cohort in which the risk model was designed. Through performing a subgroup analysis considering only outpatient tertiary care procedures, we sought to address this shortcoming. Our findings, however, remain pertinent to anesthesiologists treating children in other tertiary care institutions.

In addition, there is the rather small effective sample size of our database and the exclusion of 34 children due to missing data. With 204 included children and only 40 cases of PRAEs, our cohort was meaningfully smaller than the sample of Subramanyam et al[3]. Moreover, we had less than 10 PRAEs cases for each predictor variable in the model, as the common rule of thumb for effective sample size dictates[13].

At last, the definitions of PRAEs used in our cohort differ slightly from those applied in the study of Subramanyam et al.[3], which could have impacted the incidence of PRAEs and our finding of lower performance measures of the risk score in our Ghent-APRICOT cohort.

The secondary purpose of our study was to analyze the incidence of PRAEs at our tertiary care institution. We found a remarkably higher rate of

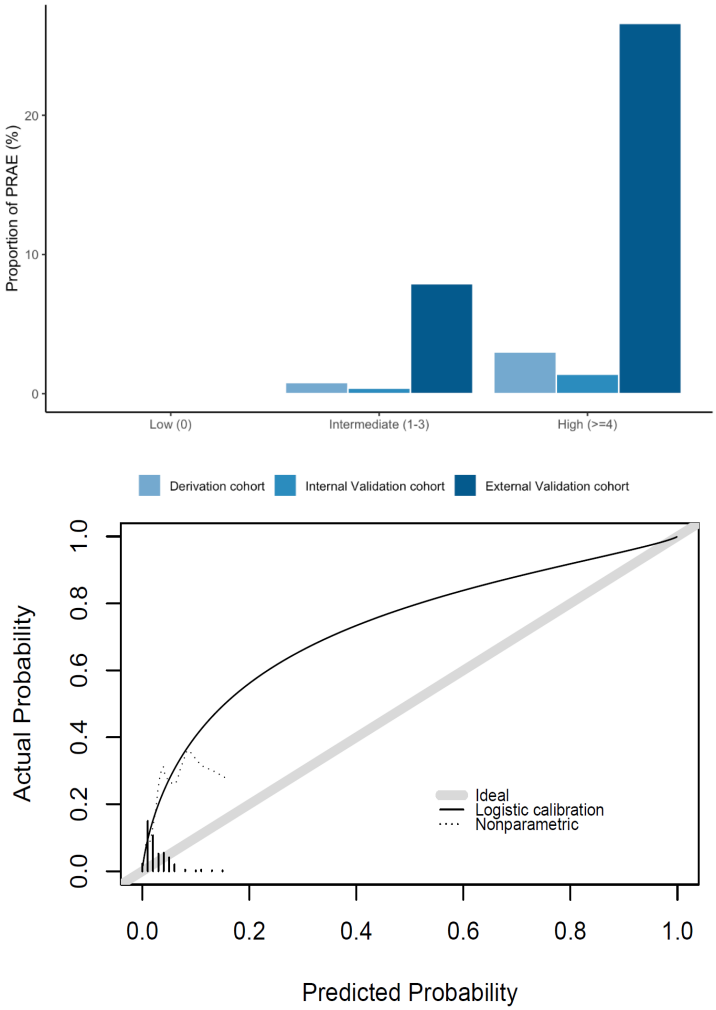

Fig. 2 — Plots showing calibration of the simplified point-based model (2A) and the original logistic regression model (2B) in the Ghent-APRICOT cohort.

PRAEs in our hospital compared to the study of Subramanyam et al. (19,6% vs. 2,8% respectively)[3]. This lower incidence of PRAEs in the study of Subramanyam et al. may be partially explained by the inclusion of purely elective ambulatory anesthesia. It is plausible that inclusion of certain unmeasured comorbidities that foreclose ambulatory anesthesia in our study, increased the risk of the population as a whole. Medical conditions such as chronic lung disease, congenital heart disease and neuromuscular disorder, which hold a high potential for the development of PRAEs[2,9,17], were not excluded in our database. Moreover, the inclusion of urgent and high-risk surgical procedures, which are independent risk factors for PRAEs, is a plausible cause of the higher incidence in our population[5,18,19]. It should be noted that the frequency of PRAEs in our population was much greater than that observed in the cohort of healthy children of Subramanyam and colleagues[3], but similar to that of other large studies in pediatric tertiary centers[9,20-22].

In addition, we established higher occurrence of risk factors for PRAEs in our population as opposed to the cohort of Subramanyam and colleagues[3], as shown in Table II. First and foremost, we have a marked higher rate of surgical procedures. It is likely that surgical procedures are associated with a higher occurrence of PRAEs compared with radiology, because of differences in requirement of opioids and airway management between both groups. Secondarily, we have proportionally more children with ASA physical status III. Previous studies have demonstrated that a higher ASA score is strongly associated with higher odds of PRAEs in children[3,6,19]. The same applies for the proportion of children with morbid obesity. Obesity is a known risk factor of PRAEs[3,8,9,19]. Both the number and severity of comorbidities (i.e. asthma, sleep disordered breathing) that contribute to PRAEs are increased in obese children, possibly through presence of systemic and/or subclinical airway inflammation[3,8].

Another issue that deserves discussion in perspective of the higher rate of PRAEs in our hospital, is the substantial number of children presenting with active or recent upper respiratory infection (URI). The association between URI and PRAEs has been documented and it is known that airway hyperreactivity and increased risk for PRAEs continues a few weeks after resolution of acute URI symptoms[2,8,17]. However, to date there are no standardized rules with regard to cancellation of procedures when children present with active or recent URI. In our hospital most anesthesiologists would reschedule surgery if a patient has signs of active lower respiratory infection, such as wheezing, and/or preoperative hypoxemia, as well as presence of systemic illness (fever), because evidence shows that these children are at highest risk for PRAEs[2,12]. However, the majority of children with mild URI symptoms would proceed to undergo anesthesia, as opposed to a more extensive cancellation policy in other institutes.

At last, the remarkable difference in incidence of PRAEs between our study and that of Subramanyam et al.[3] could be related to differences in routine care. For example, the administration of a loading dose piritramide or morphine before the end of anesthesia and low-threshold use of supplemental oxygen for transportation of a child to the PACU are part of routine care in our center. However, both of these measures could affect occurrence of postoperative hypopnea[9].

As this study points out various reasons for persistent high incidence of perioperative respiratory adverse events in children, especially in tertiary care populations, and fails to identify the prediction model created by Subramanyam et al.[3] as an adequate tool to estimate the risk of these adverse events in individual patients of a general population, this leaves us with the lack of a comprehensive scoring system to further tackle this relevant problem in pediatric (tertiary care) anesthesia. In the future it would be valuable to evaluate the applicability of the remaining two prediction models in our cohort or to develop a new prediction tool specifically designed for a tertiary care pediatric population suffering from a high incidence of perioperative adverse events.

Conclusions

The development of a comprehensive risk prediction tool for perioperative respiratory adverse events, thoroughly validated and with established evidence of excellent discrimination and calibration, would be an important next step in providing safe anesthesia to all children, especially in tertiary care cohorts where the incidence of these adverse events remains remarkably high. It would allow us to have a maximal preoperative optimization of comorbidities in children with a high risk of PRAEs, to guide allocation of clinical resources, and to optimize our perioperative management strategy. We evaluated the suitability of the risk prediction model created by Subramanyam et al.[3] in our general tertiary care pediatric population and concluded its overall performance in our cohort is moderate. Modest discrimination and calibration suggest that the risk score may not reliably predict perioperative respiratory adverse events in individual children treated in our tertiary care institution. Therefore

the clinical relevance of the implementation of this scoring system in our hospital would be negligible, which leaves us with the lack of good scoring systems to predict perioperative respiratory adverse events.

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