BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

BMJ Open

A modified pediatric preoperative risk prediction score to predict postoperative ICU admission

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-036008
Article Type:	Original research
Date Submitted by the Author:	26-Nov-2019
Complete List of Authors:	Lian, Chunwei; The Second Affiliated Hospital & Yuying Children hospital of Wenzhou Medical University, Department of Anesthesiology Wang, Pei; The Second Affiliated Hospital & Yuying Children hospital of Wenzhou Medical University, Department of Anesthesiology Fu, Qingxia; The Second Affiliated Hospital & Yuying Children hospital of Wenzhou Medical University, Department of Anesthesiology Du, Xudong; The Second Affiliated Hospital & Yuying Children hospital of Wenzhou Medical University, Department of Medical Quality Management and Statistics Wu, Junzheng; Cincinnati Children Hospital Medical Center, Department of Anesthesia and Pediatrics Lian, Qingquan; The Second Affiliated Hospital & Yuying Children hospital of Wenzhou Medical University, Department of Anesthesiology ShangGuan, Wangning; The Second Affiliated Hospital & Yuying Children hospital of Wenzhou Medical University, Department of Anesthesiology
Keywords:	Paediatric anaesthesia < ANAESTHETICS, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Paediatric surgery < SURGERY, INTENSIVE & CRITICAL CARE

SCHOLARONE™
Manuscripts

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

A modified pediatric preoperative risk prediction score to predict postoperative ICU admission

Chunwei Lian[1], Pei Wang[1], Qingxia Fu[1], Xudong Du[2], Junzheng Wu[3], Qingquan Lian[1], WangNing Shangguan[1*]

1. Department of Anesthesiology and Perioperative Medicine, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, China

2. Department of Medical Quality Management and Statistics, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, China

3. Department of Anesthesia and Pediatrics, Cincinnati Children Hospital Medical Center, Cincinnati, OH, USA

*Corresponding author: Dr Wangning ShangGuan

Department of Anesthesiology and Perioperative Medicine, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, 109 West Xueyuan Road, Wenzhou 325027, China.

E-mail: sgwning@163.com.

Tel: 86-577-88002927.

For peer review only

ABSTRACT

Objective: To integrate intrinsic surgical risk into the Pediatric preoperative risk prediction score (PRPS) model to construct a more comprehensive risk scoring system (Modified preoperative risk prediction score, Modified PRPS) and improve predicting accuracy of postoperative ICU admission in pediatric patients.

Design: Retrospective study between 1st January to 30th December of 2016. The data of age, American Society of Anesthesiology physical status (ASA-PS), oxygen saturation (SpO_2), prematurity, non-fasted status, the severity of surgery, and whether transferred to ICU immediately after surgery were collected. A Modified PRPS was developed by Logistic regression in the derivation cohort, which was tested and compared with Pediatric PRPS and ASA-PS by Hosmer-Lemeshow test, the receiver operating characteristic curve (ROC) and Kappa analysis in the validation cohort.

Setting: Hospital-based study in China.

Particpants: Pediatric patients (≤14yrs) who received surgery under general anesthesia were included, and those who needed reoperation owing to surgery complications or stayed in ICU preoperatively were excluded.

Main outcome measure: ICU admission rate, defined as any patients' direct disposition from the operating room to ICU immediately after the surgery.

Results: 9261 pediatric patients were included in this study, with 418 patients were admitted into ICU. In the validation cohort, Modified PRPS model fitted the test data well (deciles of risk goodness-of-fit χ^2=6.84, P=0.077). The area under the ROC

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

(AUC) of Modified, Pediatric PRPS and ASA-PS were 0.963, 0.941 and 0.870 respectively (P <0.05); the values of Kappa were 0.620, 0.286 and 0.267 respectively. Analyses in the cohort indicated that Modified preoperative risk prediction score was superior to Pediatric preoperative risk prediction score and ASA-PS.

Conclusions: Modified PRPS integrated with intrinsic surgical risk shows a better predicting accuracy than the previous PRPS.

Key words: Pediatric surgery, Intensive critical care, Pediatric anesthesia, Risk management

ARTICLE SUMMARY

Strengths and limitations of this study

Use of the new simple intrinsic severity of surgery category, it would be easier to do preoperative risk assessment.

The Modified preoperative risk prediction score could only be applied to ICU admission (planned and unplanned ICU admission), because there was no information regarding unplanned ICU admission.

Limitations include the lack of information, such as adverse events and indicators to ICU, which may be more objective than decision made by the agreement of surgery and anesthesiology teams.

Word account: 2163

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

INTRODUCTION

Perioperative morbidity and mortality are higher in children, especially in neonates and infants.[1,2] Intensive care unit (ICU) admission offers a measure of additional safety and improves survival rate for high risk patients after operations.[3] In recent years, several risk stratification tools have been developed to predict the perioperative surgical risk to improve postoperative outcome and facilitate resource allocation in pediatric patients.[4,5]

In our previous publication,[4] we have established the pediatric preoperative risk prediction score (PRPS) to predict postoperative ICU admission and death. However, the intrinsic surgical risk factor was not applied to the Pediatric PRPS. Arvidsson et al reported that the procedure magnitude turned out to have a closest correlation with adverse events compared to other risk indicators.[6] Aaron et al constructed a 22-point Preoperative Complication Score Model for pediatrics undergoing any type of surgery.[7] Among the six predictors, surgery magnitude took one half ratio of score, with neurological surgery contributing the greatest to the overall score (5 points), followed by cardiovascular surgery (4 points), and orthopedic surgery (2 points). Nasr et al performed a retrospective analysis of 367065 surgical cases from Pediatric databases of the American College of Surgeons National Surgical Quality Improvement Program database, and found pediatric risk stratification is improved by integrating the intrinsic risk of individual pediatric surgical procedures.[8]

The aim of this study was to integrate intrinsic surgical risk into the Pediatric PRPS model to create a new and more comprehensive risk scoring system (Modified PRPS),

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

so as to improve the prediction accuracy of postoperative ICU admission in pediatric patients.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

METHODS

This study is developed in accordance with Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) reporting guidelines.[9]

Patients

A retrospective cohort study of pediatric patients underwent surgical procedures at the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University from January to December 2016 was performed by two independent examiners. The enrolled patients were ≤14 years old who received surgeries under general anesthesia after an informed written consent signed by parents. The exclusion criteria including patients who needed reoperation owing to surgery complications or those who had being stayed in ICU preoperatively.

Study design

In Pediatric PRPS, the data from five preoperative predictors including age, ASA-PS, prematurity, SpO_2 (before anesthesia induction), and non-fasted status were collected from electronic anesthesia records (variables defined as previously described).[4] For Modified PRPS, we integrated an additional variable, the intrinsic severity of surgeries, into the scoring system. The severity of surgeries was graded into minor, moderate and major three classes, and all surgical patients would fall into one of these categories based on a pre-set simplified criterion, as follow: Class I (minor surgery: extremities and body surface surgery): orthopedics surgery, arthroscopy, superficial tissue surgery, tonsillectomy/adenoidectomy,

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

grommet/cochlear prosthesis insertion, mastoidectomy, strabotomy, circumcision, anoplasty, urethroplasty, inguinal herniorrhaphy, resection of testicular hydrocele; Class II (moderate surgery: intraperitoneal surgery): open abdominal procedure (abdominal organ, exploratory laparotomy, diaphragmatic hernia) and laparoscopic surgery; Class III (major surgery: thoracic or intracranial surgery): open thoracic or intracranial procedure: craniotomy (intracranial hematoma, hydrocephalus and neoplasms), thoracotomy (cardiac, pulmonary, esophageal atresia, pericardiectomy, and pyothorax surgery) and thoracoscopy.

The primary outcome of the study, ICU admission, was defined as any patients' direct disposition from the operating room to ICU immediately after the surgery. The final decisions for patients' postoperative direct transfer to ICU were generally made together by the anesthesiologist and surgeon. The second outcome, perioperative mortality, was defined as death within 30 days after the surgery.

Statistical Analysis

The data set (9261 patients) was randomly divided into two cohorts: a derivation cohort of approximately two-thirds of the sample, and a validation cohort consisting of the remainder. Logistic regression was used to create the Modified PRPS model to predict ICU admission after surgery in the derivation cohort. Then, the Modified PRPS model was tested on the validation cohort. A risk score was derived from each patient by taking the sum of the model coefficients for risk factors present. Differences among groups were examined with Cochran-Armitage test for trend. The

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

accuracy of Modified PRPS model was assessed in the validation cohort by using the Hosmer-Lemeshow (H-L) test. The receiver operating characteristic (ROC) was used to measure discrimination; the cut-off point was determined by Youden's index. ROC curve and kappa statistic were used to compare the accuracy of the Modified PRPS with Pediatric PRPS and ASA-PS. A kappa value of 1 indicates perfect agreement, whereas a kappa of 0 indicates agreement equivalent to chance.

All data were analyzed with SAS software (SAS 9.4; SAS Institute Inc., Cary, NC, USA). The data were presented as median (interquartile range), numbers, and percentages.

RESULTS

Initially, 9315 patients were enrolled into the data set and 54 patients were excluded because of missing information. Finally, two thirds of the 9261 patients were assigned to the derivation cohort (n=6174), while the other one third were used as validation cohort to examine the fit of the model (n=3087), as shown in Figure 1. The rates of ICU admission were 4.66% (288/6174) in the derivation cohort and 4.21% (130/3087) in the validation cohort. The perioperative mortality of the ICU admission patients was 12.15% (35/288) in the derivation cohort and 10% (13/130) in the validation cohort. No pediatric patients died in the operation room. The preoperative characteristics of enrolled patients were summarized (Table 1).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Table 1 The patient characteristics

Variables	Development data (n=6174)		Validation data (n=3087)	
	PACU n (%)	ICU n (%)	PACU n (%)	ICU n (%)
Age				
≥1y	356 (6.05%)	84 (29.17%)	182 (6.15%)	40 (30.77%)
1m-1y	5509 (93.59%)	116 (40.28%)	2752 (93.07%)	43 (33.08%)
<1m	21 (0.36%)	88 (30.56%)	23 (0.78%)	47 (36.15%)
ASA-PS				
I	5121 (87.00%)	44 (15.28%)	2519 (85.19%)	23 (17.69%)
II	715 (12.15%)	132 (45.83%)	418 (14.14%)	51 (39.23%)
III	49 (0.83%)	84 (29.17%)	15 (0.51%)	42 (32.31%)
IV/V	1 (0.02%)	28 (9.72%)	5 (0.17%)	14 (10.77%)
Premature				
no	5705 (6.92%)	232 (80.56%)	2850 (96.38%)	90 (69.23%)
yes	181 (3.08%)	56 (19.44%)	107 (3.62%)	40 (30.77%)
Non-fasted				
no	5806 (98.64%)	242 (84.03%)	2903 (98.17%)	112 (86.15%)
yes	80 (1.36%)	46 (15.97%)	54 (1.83%)	18 (13.85%)
SpO_2				
≥90%	5798 (98.50%)	251 (87.15%)	2895 (97.90%)	117 (90.00%)
<90%	88 (1.50%)	37 (12.85%)	62 (2.10%)	13 (10.00%)

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Table 1 Continued

Variables	Development data (n=6174)		Validation data (n=3087)	
	PACU n (%)	ICU n (%)	PACU n (%)	ICU n (%)
Severity of surgery				
Class I	3434 (58.34%)	26 (9.03%)	1728 (58.44%)	16 (12.31%)
Class II	2393 (40.66%)	128 (44.44%)	1193 (40.34%)	58 (44.62%)
Class III	59 (1.00%)	134 (46.53%)	36 (1.22%)	56 (43.08%)
30d mortality	-	35 (12.15%)	-	13 (10%)

(PACU= Post-Anesthesia Care Unit; ICU= intensive care unit; ASA-PS=American Society of Anesthesiology physical status).

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

The Modified PRPS model development and derivation:

The five variables (age, ASA-PS, SpO_2, prematurity, and non-fasted status) were recorded from the hospital information system as previously described in the Pediatric PRPS. For the Modified PRPS, the variable of intrinsic surgical risk was added and graded based on the increased risks associated with the location and range of the procedure. Therefore, this new model had six independent variables for predicting ICU admission, which was created by Binary logistic regression analysis (Table 2).

Table 2 Binary logistic regression analysis predicting the incidence of postoperative intensive care unit (ICU) admission

Variables	B	SE	Wald	OR（95%CI）	P value
Constant	-6.750	0.306	486.963	-	<.001
1m-1y	1.508	0.248	36.925	4.52(2.78,7.35)	<.001
<1m	4.736	0.354	178.604	113.97 (56.90,228.27)	<.001
ASA II	2.277	0.230	97.676	9.75 (6.20,15.31)	<.001
ASA III	2.741	0.355	59.640	15.50 (7.73,31.07)	<.001
ASA IV/V	7.092	1.273	31.044	1202.19 (99.21,14568.08)	<.001
Premature	1.038	0.331	9.819	2.82 (1.48,5.41)	0.002
Non-fasted	1.069	0.339	9.957	2.91 (1.50,5.65)	0.002
SpO_2<90%	0.963	0.467	4.247	2.62 (1.05,6.55)	0.040
Class III	4.836	0.334	210.182	126.00 (65.53,242.30)	<.001
Class II	1.761	0.292	36.263	5.82 (3.28,10.32)	<.001

(OR=odds ratio; SE=standard error; ASA=American Society of Anesthesiology).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

The model coefficients were used to develop a formula for a risk score as follows, where each variable was assigned a value of 1 if present and 0 if absent: Logit (P)=ln(P/1-P)= constant + risk score; risk score=[(1m-1y)*1.508] + (≤1m*4.736) + (ASA II*2.272) + (ASAIII*2.741) + (ASAIV/V*7.092) + (premature*1.038) + (non-fasted*1.069) + (SpO_2<90% *0.963) + (Class III *4.836) + (Class II *1.761). Predictor had its own control value, which was set as zero score (age ≥1year old, ASA I, SpO_2 ≥90%, full term, fasted, Class I). The sum of the highest values from each predictor was 50 points. A point value was assigned to each predictor by normalizing them consequently and converting them to integer scores. The Modified PRPS system was then constructed, as shown in Table 3.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Table 3 Risk score

Variables	Score	AUC
Age		0.963
≥1y	0	
1m-1y	4	
<1m	12	
ASA-PS		
I	0	
II	6	
III	7	
IV\V	18	
Premature	3	
Non-fasted	3	
SpO_2		
≥90%	0	
<90%	2	
Severity of surgery		
Class I	0	
Class II	4	
Class III	12	

(ASA-PS=American Society of Anesthesiology physical status; AUC= area under the ROC).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Comparison with the Pediatric PRPS and ASA-PS:

When these calculations were used to produce a percentage predicted ICU admission after surgery for each pediatric patient in the validation cohort, the area under the ROC (AUC) value for ICU admission rates was 0.963, indicating an excellent discrimination. It was calculated that the cut-off point for the risk predictor score was 10 points from the ROC curve. The P value for the H-L test was 0.077, indicated that the Modified PRPS model was well calibrated in the validation cohort.

Both the Pediatric PRPS and ASA-PS demonstrated moderately good discrimination when tested in the validation cohort, the AUC was 0.941 (95%CI, 0.932 to 0.949) and 0.870 (0.858 to 0.882) respectively (Figure 2A). However, among the pediatric patients who was admitted to ICU, the ROC curve for the discrimination between dead and survival pediatrics showed a similarly and relatively poor ability, where the AUC values of Modified PRPS, Pediatric PRPS and ASA-PS were 0.759 (95%CI, 0.676 to 0.830), 0.758 (0.675 to 0.829) and 0.762 (0.679 to 0.832) respectively (Figure 2B). The cut-off point for the risk predictor score was 19 points from the ROC curve in Modified PRPS model.

The accuracy was higher in Modified PRPS model compared with the Pediatric PRPS and ASA-PS (95.85%, 84.68% and 85.07%, respectively); and kappa statistics revealed 0.620, 0.286 and 0.267, respectively.

According to the results, the Modified PRPS was built, as shown in Table 4. Three risk categories (high/intermediate/low risk) were defined on the basis of the cut-off values. As the score of Modified PRPS increased, the incidence of propensity for ICU

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

admission was increased monotonically (P <0.0001).

Table 4 Outcomes for pediatric patients undergoing surgery in relation to Modified PRPS.

Risk level	Score	Patients (n)	Observed ICU admission n (%)	Predicted ICU admission n (%)	Prediction probability% Median (IQR)	P value
Low risk	<10	8283	37 (0.45%)	42 (0.51%)	0.40% (0.12%, 0.59%)	
Intermediate risk	10-18	690	138 (20%)	139 (20.14%)	8.63% (5.99%, 31.41%)	P<0.001
High risk	19-50	288	243 (84.3%)	259 (89.9%)	91.51% (87.89%, 98.12%)	

(ICU= intensive care unit; PRPS=Preoperative Risk Prediction Score; IQR=Interquartile Range).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

DISCUSSION

Principal findings

This study verified our previous Pediatric PRPS with an excellent AUC of 0.941 in the validation cohort. Then, with modification and update of the previous version, the new model, termed as Modified PRPS, offered better capability in prediction of ICU admission after surgery in children.

The Modified PRPS has six observing variables instead of five seen in Pediatric PRPS, and the total of combined risk scores are 50 points in both versions. Compared to Pediatric PRPS, Modified PRPS merged the categories of ASA IV and ASA V into one category. By considering the clinical gravities, slight plus or minus changes in the point distribution among the different categories were made, which allows the Modified PRPS more rational and clinically practical.

By using H-L test during validation process, the Modified PRPS displayed a better calibration, which suggested an improved discrimination when the ROC curve of the new model was compared with that of the Pediatric PRPS and ASA-PS scores. In addition, kappa statistic was used to compare the agreement of the observed and predicted ICU admission among the three score models. The Modified PRPS had a percentage accuracy of 95.85 percent with a kappa of 0.62, which was in the substantial agreement range, significantly higher than that of the other two models. After considering the severity of surgery, both of the AUC and kappa values were closer to 1, and the Modified PRPS was more accurate and closer to perfect.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Comparison with other studies

A variety of assessment score formulas for perioperative risk prediction have been published.[4,5,8,10-14] As a gold standard for evaluating a patient's general health and comorbidities preoperatively, the ASA-PS has been widely used to predict perioperative outcomes in children, even if it was not initially intended to be used in children for the reason of lacking objective.[10] The Pediatric Risk of Mortality Score[11] and pediatric index of mortality[12] were widely used to predict mortality for children, but the greatest limitation is that they are only used in intensive care unit. The Pediatric Risk Assessment score, including 13 preoperative variables had excellent accuracy in predicting perioperative mortality in children.[13] Stratified subgroup of surgeries was analyzed to be statistically significant on univariate analysis but not on multivariate regression analysis. However, stratified subgroups of surgeries are not equivalent to the severity of surgeries. The intrinsic risk of the surgical procedure was not included in the final model. Meanwhile, it was only applied to non-cardiac surgeries, but not all other types of surgeries. The American College of Surgeons National Surgical Quality Improvement Program Pediatric Surgical Risk Calculator was a tool to calculate the risk of complications and mortality for a variety of surgical procedures. However, it was never visible to the user and never validated in public.[14]

There is no uniform definition of what is considered "intrinsic severity of surgery" in current studies. Considering of the impact of surgery (type and complexity) on outcomes, some clinicians graded surgical severity according to their own criteria. In

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

1996, Arvidsson et al coded surgical interventions into 4-point scales ranging from minor interventions to extensive procedures, according to the official Swedish classification the interventions.[6] In 2002, the surgical risk score adopted the British United Provident Association operative grade category as one risk factor to predict the mortality in surgical patients.[15] In 2004, by modifying Johns Hopkins criteria, Donati et al simplified the surgical severity to three grades and developed their own new model for predicting operative risk.[16] Based on the Office of Population, Censuses and Surveys system codes, the Surgical Outcome Risk Tool graded the magnitude of surgical procedures into four severity categories in 2014.[17] And stratified subgroup analysis was also commonly applied for types of operation.[7,16] In this study, we classified the intrinsic severity of surgeries into minor, moderate and major three different levels, which was different from other surgical categories but easier to work with.

Limitations of the study

There were some limitations for the present study. Firstly, our primary endpoint includes both planned and unplanned ICU admission. However, maybe only the latter would be much more needed to be predicted. Secondly, the decision-making for ICU admission was mainly relied on clinical bias, and was also influenced by regional culture, economic factor and so on. Our result will be more objective and convincing, if it depends on a set of definable adverse event. Thirdly, A higher probability of dying was also at higher probability of being admitted to ICU, but it did not be treated both to be equivalent in our results. Finally, this is a single-center retrospective study,

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

some data (such as why the pediatric patients were transferred to ICU, how to distinct the planned and unplanned ICU admission) is difficult to collect.

CONCLUSION

In summary, with appropriate adjustment of ASA assessment and the integration of surgical severity into scoring model, the new Modified PRPS exhibits a more accurate prediction result and discriminates a better validation in ICU admission right after surgery in pediatric patients.

Acknowledgement The authors thank the support of Zhejiang provincial public welfare technology application research foundation of China.

Author Contributions

CL helped design the study, conduct the study, analyze the data, and write the manuscript.PW, MC and HD helped collect the data. XD helped analyze the data. JW helped revise the manuscript. QL helped design the study, conduct the study. WSG helped design the study, conduct the study, analyze the data, and revise the manuscript. All authors helped to conceptualise ideas, interpret findings and review drafts of the manuscript.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval

Ethics approval to collect the patients' data was obtained from the Ethics Committee of the Second Affiliated Hospital of Wenzhou Medical University (No. 2018-10), and

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

also the verbal informed consent from parents or guardians.

Funding This work was supported by Zhejiang provincial public welfare technology application research foundation of China grant number [2018ZD033].

Provenance and peer review Not commissioned; externally peer reviewed

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution 4.0 Unported (CC BY 4.0) license, which permits others to copy, redistribute, remix, transform and build upon this work for any purpose, provided the original work is properly cited, a link to the licence is given, and indication of whether changes were made. See: https:// creativecommons. org/ licenses/ by/ 4. 0

ORCID iD

Chunwei Lian https://orcid.org/0000-0003-4702-6147

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

REFERENCES

1. van der Griend BF, Lister NA, McKenzie IM, et al. Postoperative mortality in children after 101,885 anesthetics at a tertiary pediatric hospital. *Anesth Analg* 2011;**112**:1440-7.

2. de Bruin L, Pasma W, van der Werff DB, et al. Perioperative hospital mortality at a tertiary pediatric institution. *Br J Anaesth* 2015;**115**:608-15.

3. Jhanji S, Thomas B, Ely A, et al. Mortality and utilization of critical care resources amongst high-risk surgical patients in a large NHS trust. *Anaesthesia* 2008;**63**:695-700.

4. Lian C, Xie Z, Wang Z, et al. Pediatric preoperative risk factors to predict postoperative ICU admission and death from a multicenter retrospective study. *Paediatr Anaesth* 2016;**26**:637-43.

5. Goobie SM, Zurakowski D, Proctor MR, et al. Predictors of clinically significant postoperative events after open craniosynostosis surgery. *Anesthesiology* 2015;**122**:1021-32.

6. Arvidsson S, Ouchterlony J, Sjöstedt L, et al. Predicting postoperative adverse events. Clinical efficiency of four general classification systems. The project perioperative risk. *Acta Anaesthesiol Scand* 1996;**40**:783-91.

7. Weinberg AC, Huang L, Jiang H, et al. Perioperative risk factors for major complications in pediatric surgery: a study in surgical risk assessment for children. *J Am Coll Surg* 2011;**212**:768-78.

8. Nasr VG, Staffa SJ, Zurakowski D, et al. Pediatric Risk Stratification Is Improved

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

by Integrating Both Patient Comorbidities and Intrinsic Surgical Risk. *Anesthesiology* 2019;**130**:971-80.

9. Collins GS, Reitsma JB, Altman DG, et al. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement.

10. Saklad M. Grading of patients for surgical procedures. *Anesthesiology* 1941;**24**:281-4.

11. Pollack MM, Ruttimann UE, Getson PR. Pediatric risk of mortality (PRISM) score. *Crit Care Med* 1988;**16**:1110-6.

12. Shann F, Pearson G, Slater A, et al. Paediatric index of mortality (PIM): a mortality prediction model for children in intensive care. *Intensive Care Med* 1997;**23**:201-7.

13. Nasr VG, DiNardo JA, Faraoni D. Development of a Pediatric Risk Assessment Score to Predict Perioperative Mortality in Children Undergoing Noncardiac Surgery. *Anesth Analg* 2017;**124**:1514-9.

14. Faraoni D, Vo D, Nasr VG, et al. Development and Validation of a Risk Stratification Score for Children with Congenital Heart Disease Undergoing Noncardiac Surgery. *Anesth Analg* 2016;**123**:824-30.

15. Sutton R, Bann S, Brooks M, et al. The Surgical Risk Scale as an improved tool for risk-adjusted analysis in comparative surgical audit. *Br J Surg* 2002;**89**:763-8.

16. Protopapa KL, Simpson JC, Smith NC, et al. Development and validation of the Surgical Outcome Risk Tool (SORT). *Br J Surg* 2014;**101**:1774-83.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

17. Donati A, Ruzzi M, Adrario E, et al. A new and feasible model for predicting operative risk. *Br J Anaesth* 2004;**93**:393-9.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Figure captions:

Figure 1: Flowchart of the study.

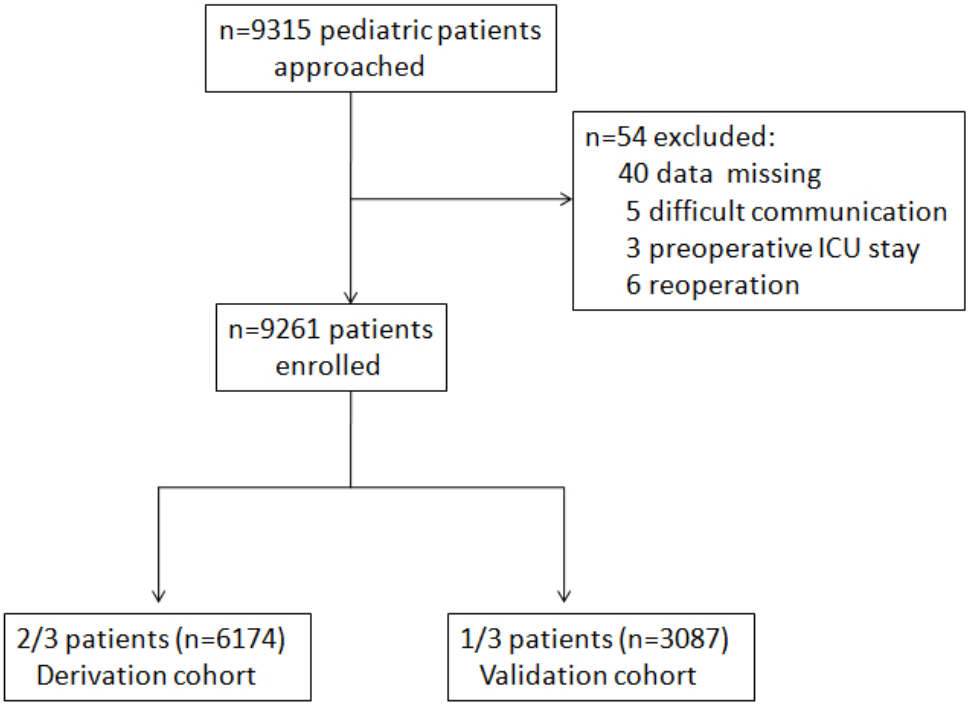
Figure 2:

(A)Receiver operating characteristic curve (ROC) curves for Modified preoperative risk prediction score (PRPS), PRPS, and ASA physical status (ASA-PS) for the validation cohort, a randomly selected individual who with intensive care unit (ICU) admission patients has an overall score higher than that of pediatrics who with post-anesthesia care unit (PACU) admission patients;

(B) Receiver operating characteristic curve (ROC) curves for Modified preoperative risk prediction score (PRPS), PRPS, and ASA physical status (ASA-PS) for the validation cohort, a randomly selected individual who died has an overall score higher than that of pediatrics who survived.

For peer review only

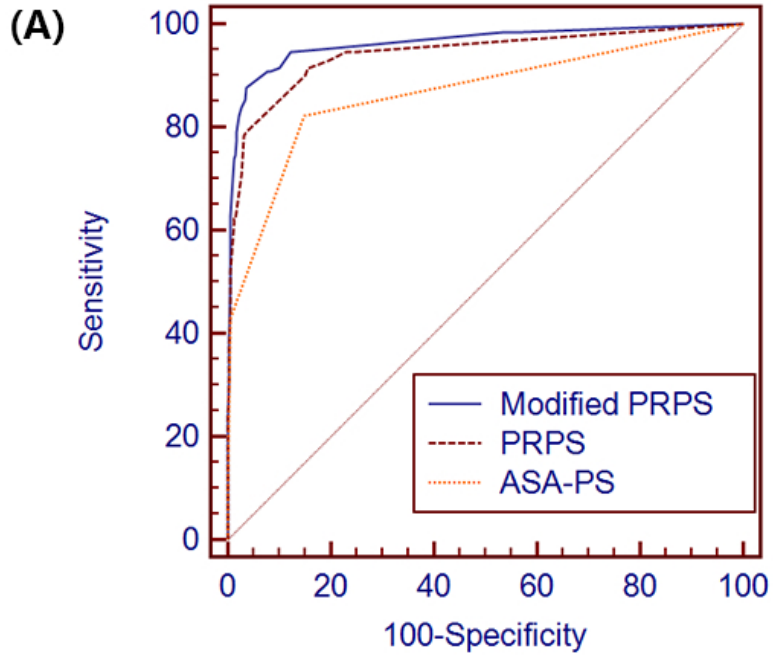
For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml



Flowchart of the study.

55x40mm (300 x 300 DPI)

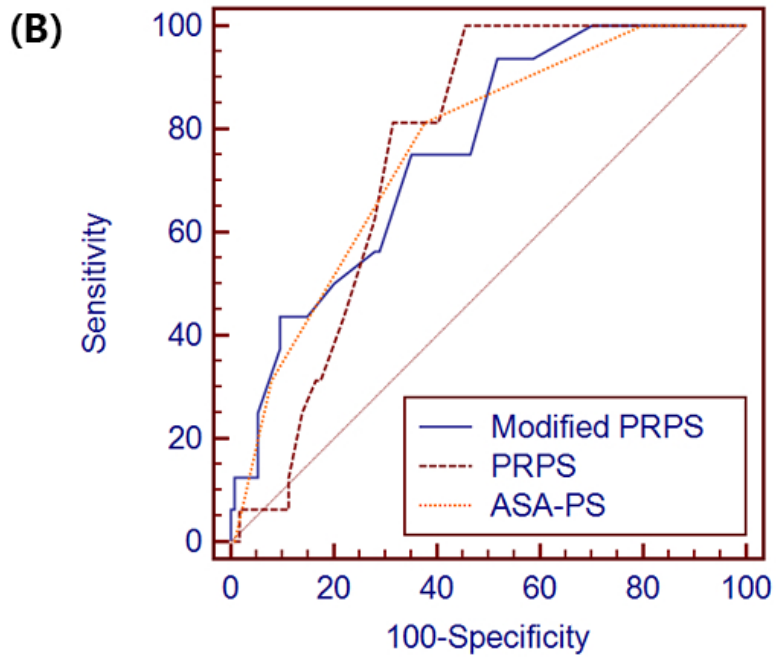
BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.



(A)Receiver operating characteristic curve (ROC) curves for Modified preoperative risk prediction score (PRPS), PRPS, and ASA physical status (ASA-PS) for the validation cohort, a randomly selected individual who with intensive care unit (ICU) admission patients has an overall score higher than that of pediatrics who with post-anesthesia care unit (PACU) admission patients;

55x40mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.



(B) Receiver operating characteristic curve (ROC) curves for Modified preoperative risk prediction score (PRPS), PRPS, and ASA physical status (ASA-PS) for the validation cohort, a randomly selected individual who died has an overall score higher than that of pediatrics who survived.

55x40mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

Reporting checklist for prediction model development and validation study.

Based on the TRIPOD guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the TRIPODreporting guidelines, and cite them as:

Collins GS, Reitsma JB, Altman DG, Moons KG. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement.

		Reporting Item	Page Number
Title			1
	#1	Identify the study as developing and / or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract			2-3

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

For peer review only

	#2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2-3
Introduction			4-5
	#3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	4
	#3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	4-5
Methods			6-7
Source of data	#4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6
Source of data	#4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
Participants	#5a	Specify key elements of the study setting (e.g., primary care, secondary care, general	6

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

		population) including number and location of centres.	
Participants	#5b	Describe eligibility criteria for participants.	6
Participants	#5c	Give details of treatments received, if relevant	n/a (no treatment)
Outcome	#6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	6
Outcome	#6b	Report any actions to blind assessment of the outcome to be predicted.	n/a (as a retrospective cohort study, no blind assessment)
Predictors	#7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured	6
Predictors	#7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	n/a (as a retrospective cohort study, no blind assessment)
Sample size	#8	Explain how the study size was arrived at.	n/a (only collect the sample for 1y)
Missing data	#9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	8
Statistical	#10a	If you are developing a prediction model	7

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

analysis methods		describe how predictors were handled in the analyses.	
Statistical analysis methods	#10b	If you are developing a prediction model, specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	7-8
Statistical analysis methods	#10c	If you are validating a prediction model, describe how the predictions were calculated.	7-8
Statistical analysis methods	#10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	7-8
Statistical analysis methods	#10e	If you are validating a prediction model, describe any model updating (e.g., recalibration) arising from the validation, if done	7-8
Risk groups	#11	Provide details on how risk groups were created, if done.	7
Development vs. validation	#12	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	7
Results			8-15
Participants	#13a	Describe the flow of participants through the study, including the number of participants with	8

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

For peer review only

		and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	
Participants	#13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	8-10
Participants	#13c	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	9-10
Model development	#14a	If developing a model, specify the number of participants and outcome events in each analysis.	8-10
Model development	#14b	If developing a model, report the unadjusted association, if calculated between each candidate predictor and outcome.	n/a(unadjusted)
Model specification	#15a	If developing a model, present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	11-12
Model specification	#15b	If developing a prediction model, explain how to the use it.	13,15

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

Model performance	#16	Report performance measures (with CIs) for the prediction model.	14,15
Model-updating	#17	If validating a model, report the results from any model updating, if done (i.e., model specification, model performance).	14
Discussion			16-19
Limitations	#18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	18-19
Interpretation	#19a	For validation, discuss the results with reference to performance in the development data, and any other validation data	16
Interpretation	#19b	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	16
Implications	#20	Discuss the potential clinical use of the model and implications for future research	n/a(apply the model to identify three risk categories before surgery)
Other information			19-20
Supplementary information	#21	Provide information about the availability of supplementary resources, such as study	n/a (if needed,we would provide)

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

		protocol, Web calculator, and data sets.	
Funding	#22	Give the source of funding and the role of the funders for the present study.	20

None The TRIPOD checklist is distributed under the terms of the Creative Commons Attribution License CC-BY. This checklist can be completed online using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

BMJ Open

A modified paediatric preoperative risk prediction score to predict postoperative ICU admission in children: a retrospective cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-036008.R1
Article Type:	Original research
Date Submitted by the Author:	03-Feb-2020
Complete List of Authors:	Lian, Chunwei; The Second Affiliated Hospital & Yuying Children hospital of Wenzhou Medical University, Department of Anesthesiology Wang, Pei; The Second Affiliated Hospital & Yuying Children hospital of Wenzhou Medical University, Department of Anesthesiology Fu, Qingxia; The Second Affiliated Hospital & Yuying Children hospital of Wenzhou Medical University, Department of Anesthesiology Du, Xudong; The Second Affiliated Hospital & Yuying Children hospital of Wenzhou Medical University, Department of Medical Quality Management and Statistics Wu, Junzheng; Cincinnati Children Hospital Medical Center, Department of Anesthesia and Pediatrics Lian, Qingquan; The Second Affiliated Hospital & Yuying Children hospital of Wenzhou Medical University, Department of Anesthesiology ShangGuan, Wangning; The Second Affiliated Hospital & Yuying Children hospital of Wenzhou Medical University, Department of Anesthesiology
Primary Subject Heading:	Anaesthesia
Secondary Subject Heading:	Paediatrics, Surgery
Keywords:	Paediatric anaesthesia < ANAESTHETICS, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Paediatric surgery < SURGERY, INTENSIVE & CRITICAL CARE

SCHOLARONE™
Manuscripts

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

A modified paediatric preoperative risk prediction score to predict postoperative ICU admission in children: a retrospective cohort study

Chunwei Lian[1], Pei Wang[1], Qingxia Fu[1], Xudong Du[2], Junzheng Wu[3], Qingquan Lian[1], Wangning Shangguan[1*]

1. Department of Anaesthesiology and Perioperative Medicine, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, China

2. Department of Medical Quality Management and Statistics, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, China

3. Department of Anaesthesia and Paediatrics, Cincinnati Children Hospital Medical Center, Cincinnati, OH, USA

*Corresponding author: Dr. Wangning ShangGuan

Department of Anaesthesiology and Perioperative Medicine, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, 109 West Xueyuan Road, Wenzhou 325027, China.

E-mail: sgwning@163.com.

Tel: 86-577-88002927.

For peer review only

ABSTRACT

Objective: To integrate intrinsic surgical risk into the paediatric preoperative risk prediction score (PRPS) model to construct a more comprehensive risk scoring system (modified preoperative risk prediction score, modified PRPS) and improve the prediction accuracy of postoperative intensive care unit (ICU) admission in paediatric patients.

Design: This was a retrospective study conducted between January 1 and December 30, 2016. Data on age, American Society of Anaesthesiology physical status (ASA-PS), oxygen saturation (SpO_2), prematurity, non-fasted status, severity of surgery, and immediate transfer to the ICU after surgery were collected. The modified PRPS was developed by logistic regression in the derivation cohort; it was tested and compared with the paediatric PRPS and ASA-PS by the Hosmer-Lemeshow test, the receiver operating characteristic (ROC) curve and Kappa analysis in the validation cohort.

Setting: Hospital-based study in China.

Participants: Paediatric patients (≤14 years) who underwent surgery under general anaesthesia were included, and those who needed reoperation due to surgical complications or stayed in the ICU preoperatively were excluded.

Main outcome measure: ICU admission rate, defined as any patients' direct disposition from the operating room to the ICU immediately after the surgery.

Results: A total of 9261 paediatric patients were included in this study, with 418 patients admitted to the ICU. In the validation cohort, the modified PRPS model fit

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

the test data well (deciles of risk goodness-of-fit χ^2=6.84, P=0.077). The area under the ROC curve (AUC) of the modified PRPS, paediatric PRPS and ASA-PS were 0.963, 0.941 and 0.870, respectively (P <0.05), and the Kappa values were 0.620, 0.286 and 0.267. Analyses in the cohort indicated that the modified preoperative risk prediction score was superior to the paediatric PRPS and ASA-PS.

Conclusions: The modified PRPS integrating intrinsic surgical risk shows a better prediction accuracy than the previous PRPS.

Key words: Paediatric surgery, Intensive critical care, Paediatric anaesthesia, Risk management

ARTICLE SUMMARY

Strengths and limitations of this study

The new simple intrinsic severity of surgery category makes it easier to perform preoperative risk assessments.

The modified preoperative risk prediction score could only be applied to ICU admission (planned and unplanned ICU admission) because there was no information regarding unplanned ICU admission.

Limitation includes the shortage of the important information on indicators of transferring paediatric patients into ICU and reports of adverse events, which could help make more objective decisions than surgeons and anaesthesiology teams do.

Word account: 3494

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

INTRODUCTION

Perioperative morbidity and mortality are higher in children, especially in neonates and infants.[1,2] Intensive care unit (ICU) admission offers a measure of additional safety and improves the survival rate for high-risk patients after operations.[3] In recent years, several risk stratification tools have been developed to predict perioperative surgical risk to improve postoperative outcomes and facilitate resource allocation in paediatric patients.[4,5]

In our previous publication,[4] we established the paediatric preoperative risk prediction score (PRPS) to predict postoperative ICU admission and death. However, the intrinsic surgical risk factor was not applied to the paediatric PRPS. It is well known that surgeries themselves carry risks for adverse outcomes beyond the influence of anaesthesia and patient comorbidities. Jason and colleagues recently defined the intrinsic risk of surgical procedures for perioperative adverse cardiac events in adults.[6] To date, only one analysis of the intrinsic risk of surgical procedures in paediatric patients has been published. They performed a retrospective analysis of 367065 surgical cases of paediatric patients from the American College of Surgeons National Surgical Quality Improvement Program database and found that paediatric risk stratification was improved by integrating the intrinsic risk of individual paediatric surgical procedures.[7]

The aim of this study was to integrate intrinsic surgical risk into the paediatric PRPS model to create a new and more comprehensive risk scoring system (modified

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

PRPS) to improve the prediction accuracy of postoperative ICU admission in paediatric patients.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

METHODS

This study was developed in accordance with the Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) reporting guidelines.[8]

Patients

A retrospective cohort study of paediatric patients who underwent surgical procedures at the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University from January to December 2016 was performed by two independent examiners. The enrolled patients were ≤14 years old who underwent surgeries (both elective and non-elective surgeries) under general anaesthesia after informed written consent was signed by the parents. The exclusion criteria included patients who needed reoperation due to surgical complications or those who had stayed in the ICU preoperatively.

Study design

In the paediatric PRPS, the data of five preoperative predictors, including age, American Society of Anaesthesiology physical status (ASA-PS), prematurity, oxygen saturation (SpO_2, before anaesthesia induction), and non-fasted status, were collected from the electronic anaesthesia records (variables defined as previously described).[4] For the modified PRPS, we integrated a PRPS additional variable, the intrinsic severity of surgery, into the scoring system. The severity of surgery was graded into three classes: minor, moderate and major. All surgical patients fell into one of these categories based on a pre-set simplified criterion as follows: Class I

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

(minor surgeries: extremities and body surface surgeries): orthopaedic surgery, arthroscopy, superficial tissue surgery, tonsillectomy/adenoidectomy, grommet/cochlear prosthesis insertion, mastoidectomy, strabotomy, circumcision, anoplasty, urethroplasty, inguinal herniorrhaphy, and resection of testicular hydrocele; Class II (moderate surgeries: intraperitoneal surgeries): open abdominal procedure (abdominal organ, exploratory laparotomy, diaphragmatic hernia) and laparoscopic surgery; Class III (major surgeries: thoracic or intracranial surgeries): open thoracic or intracranial procedure: craniotomy (intracranial haematoma, hydrocephalus and neoplasms), thoracotomy (cardiac, pulmonary, oesophageal atresia, pericardiectomy, and pyothorax surgery) and thoracoscopy.

The primary outcome of the study, ICU admission, including both planned and unplanned admission, was defined as all patients' direct disposition from the operating room to the ICU for any reason immediately after the surgery. The final decisions for patients' postoperative direct transfer to the ICU were generally made together by the anaesthesiologist and surgeon. The second outcome, perioperative mortality, was defined as death within 30 days after the surgery.

Statistical Analysis

The data set (9261 patients) was randomly divided into two cohorts: a derivation cohort (consisting of approximately two-thirds of the sample) and a validation cohort (consisting of the remainder). Logistic regression was used to create the modified PRPS model to predict ICU admission after surgery in the derivation cohort. Then,

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

the modified PRPS model was tested on the validation cohort. A risk score was derived for each patient by taking the sum of the model coefficients for the risk factors present. Differences among groups were examined with the Cochran-Armitage test for trend. The accuracy of the modified PRPS model was assessed in the validation cohort by using the Hosmer-Lemeshow (H-L) test.[9] The receiver operating characteristic (ROC) curve was used to measure discrimination; the cut-off point was determined by Youden's index. ROC curves and kappa statistics were used to compare the accuracy of the modified PRPS with those of the paediatric PRPS and ASA-PS. A kappa value of 1 indicates perfect agreement, whereas a kappa value of 0 indicates agreement equivalent to chance.

All data were analysed with SAS software (SAS 9.4; SAS Institute Inc., Cary, NC, USA). The data are presented as the median (interquartile range), numbers, and percentages.

Patient and Public Involvement

The project was approved by the Ethics Committee of the Second Affiliated Hospital of Wenzhou Medical University (No. 2018-10). Because it is an observational and retrospective study, there is no additional risk or burden on paediatric patients. It has nothing to do with the patients' priorities, experience, and preferences. We searched all paediatric patients who underwent surgical procedures in our hospital from January to December 2016. We will put our study results (or the published article link) on our hospital website.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

RESULTS

Initially, 9315 patients were enrolled in the data set, and 54 patients were excluded because of missing information. Finally, two-thirds of the 9261 patients were assigned to the derivation cohort (n=6174), while the other one-third was used as the validation cohort to examine the fit of the model (n=3087), as shown in Figure 1. The rates of ICU admission were 4.66% (288/6174) in the derivation cohort and 4.21% (130/3087) in the validation cohort. The perioperative mortality of the ICU admission patients was 12.15% (35/288) in the derivation cohort and 10% (13/130) in the validation cohort. No paediatric patients died in the operating room. The preoperative characteristics of the enrolled patients are summarized in Table 1.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Table 1 Patient characteristics

Variables	Development data (n=6174)		Validation data (n=3087)	
	PACU n (%)	ICU n (%)	PACU n (%)	ICU n (%)
Age				
≥1 y	356 (6.05%)	84 (29.17%)	182 (6.15%)	40 (30.77%)
1 m-1 y	5509 (93.59%)	116 (40.28%)	2752 (93.07%)	43 (33.08%)
<1 m	21 (0.36%)	88 (30.56%)	23 (0.78%)	47 (36.15%)
ASA-PS				
I	5121 (87.00%)	44 (15.28%)	2519 (85.19%)	23 (17.69%)
II	715 (12.15%)	132 (45.83%)	418 (14.14%)	51 (39.23%)
III	49 (0.83%)	84 (29.17%)	15 (0.51%)	42 (32.31%)
IV/V	1 (0.02%)	28 (9.72%)	5 (0.17%)	14 (10.77%)
Premature				
no	5705 (6.92%)	232 (80.56%)	2850 (96.38%)	90 (69.23%)
yes	181 (3.08%)	56 (19.44%)	107 (3.62%)	40 (30.77%)
Non-fasted				
no	5806 (98.64%)	242 (84.03%)	2903 (98.17%)	112 (86.15%)
yes	80 (1.36%)	46 (15.97%)	54 (1.83%)	18 (13.85%)
SpO_2				
≥90%	5798 (98.50%)	251 (87.15%)	2895 (97.90%)	117 (90.00%)
<90%	88 (1.50%)	37 (12.85%)	62 (2.10%)	13 (10.00%)

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Table 1, continued

Variables	Development data (n=6174)		Validation data (n=3087)	
	PACU n (%)	ICU n (%)	PACU n (%)	ICU n (%)
Severity of surgery				
Class I	3434 (58.34%)	26 (9.03%)	1728 (58.44%)	16 (12.31%)
Class II	2393 (40.66%)	128 (44.44%)	1193 (40.34%)	58 (44.62%)
Class III	59 (1.00%)	134 (46.53%)	36 (1.22%)	56 (43.08%)
30-d mortality	-	35 (12.15%)	-	13 (10%)

(PACU= Post-Anaesthesia Care Unit; ICU= intensive care unit; ASA-PS=American Society of Anaesthesiology physical status).

The modified PRPS model development and derivation

The five variables (age, ASA-PS, SpO_2, prematurity, and non-fasted status) were recorded from the hospital information system as previously described in the paediatric PRPS. For the modified PRPS, the variable of intrinsic surgical risk was added and graded based on the increased risks associated with the location and range of the procedure. Therefore, this new model had six independent variables for predicting ICU admission, which was created by binary logistic regression analysis (Table 2).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Table 2 Binary logistic regression analysis predicting the incidence of postoperative intensive care unit (ICU) admission

Variables	B	SE	Wald	OR (95% CI)	P value
Constant	-6.750	0.306	486.963	-	<0.001
1 m-1 y	1.508	0.248	36.925	4.52(2.78,7.35)	<0.001
<1 m	4.736	0.354	178.604	113.97 (56.90,228.27)	<0.001
ASA II	2.277	0.230	97.676	9.75 (6.20,15.31)	<0.001
ASA III	2.741	0.355	59.640	15.50 (7.73,31.07)	<0.001
ASA IV/V	7.092	1.273	31.044	1202.19 (99.21,14568.08)	<0.001
Premature	1.038	0.331	9.819	2.82 (1.48,5.41)	0.002
Non-fasted	1.069	0.339	9.957	2.91 (1.50,5.65)	0.002
SpO_2<90%	0.963	0.467	4.247	2.62 (1.05,6.55)	0.040
Class III	4.836	0.334	210.182	126.00 (65.53,242.30)	<0.001
Class II	1.761	0.292	36.263	5.82 (3.28,10.32)	<0.001

(OR=odds ratio; SE=standard error; ASA=American Society of Anaesthesiology).

The model coefficients were used to develop a formula for a risk score as follows, where each variable was assigned a value of 1 if present and 0 if absent: Logit (P)=ln(P/1-P)= constant + risk score; risk score=[(1 m-1 y)*1.508] + (≤1 m*4.736) + (ASA II*2.272) + (ASA III*2.741) + (ASA IV/V*7.092) + (premature*1.038) + (non-fasted*1.069) + (SpO_2<90% *0.963) + (Class III *4.836) + (Class II *1.761). The predictor had its own control value, which was set as a score of zero (age ≥1 year

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

old, ASA I, SpO_2 ≥90%, full term, fasted, Class I). The sum of the highest values from each predictor was 50 points. A point value was assigned to each predictor by consequently normalizing them and converting them to integer scores. The modified PRPS system was then constructed, as shown in Table 3.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Table 3 Risk score

Variables	Score	AUC
Age		0.963
≥1 y	0	
1 m-1 y	4	
<1 m	12	
ASA-PS		
I	0	
II	6	
III	7	
IV/V	18	
Premature	3	
Non-fasted	3	
SpO_2		
≥90%	0	
<90%	2	
Severity of surgery		
Class I	0	
Class II	4	
Class III	12	

(ASA-PS=American Society of Anaesthesiology physical status; AUC= area under the ROC curve).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

For peer review only

Comparison with the paediatric PRPS and ASA-PS

When these calculations were used to produce a percentage of predicted ICU admission after surgery for each paediatric patient in the validation cohort, the area under the ROC curve (AUC) value for ICU admission rates was 0.963, indicating excellent discrimination. From the ROC curve, it was calculated that the cut-off point for the risk predictor score was 10 points. The P value for the H-L test was 0.077, indicating that the modified PRPS model was well calibrated in the validation cohort.

Both the paediatric PRPS and ASA-PS demonstrated moderately good discrimination when tested in the validation cohort, with AUCs of 0.941 (95% CI, 0.932 to 0.949) and 0.870 (0.858 to 0.882), respectively (Figure 2A). However, among the paediatric patients who were admitted to the ICU, the ROC curve for the discrimination between dead and surviving paediatrics showed a similarly and relatively poor ability, where the AUC values of the modified PRPS, paediatric PRPS and ASA-PS were 0.759 (95% CI, 0.676 to 0.830), 0.758 (0.675 to 0.829) and 0.762 (0.679 to 0.832), respectively (Figure 2B). The cut-off point for the risk predictor score was 19 points according to the ROC curve for the modified PRPS model.

The accuracy was higher in the modified PRPS model than in the paediatric PRPS and ASA-PS (95.85%, 84.68% and 85.07%, respectively), with kappa statistics of 0.620, 0.286 and 0.267.

According to the results, the modified PRPS was built, as shown in Table 4. Three risk categories (high/intermediate/low risk) were defined based on the cut-off values. As the score of the modified PRPS increased, the incidence of propensity for ICU

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

admission increased monotonically (P <0.0001).

Table 4 Outcomes for paediatric patients undergoing surgery in relation to the modified PRPS.

Risk level	Score	Patients (n)	Observed ICU admission n (%)	Predicted ICU admission n (%)	Prediction probability % Median (IQR)	P value
Low risk	<10	8283	37 (0.45%)	42 (0.51%)	0.40% (0.12%, 0.59%)	
Intermediate risk	10-18	690	138 (20%)	139 (20.14%)	8.63% (5.99%, 31.41%)	P<0.001
High risk	19-50	288	243 (84.3%)	259 (89.9%)	91.51% (87.89%, 98.12%)	

(ICU= intensive care unit; PRPS=Preoperative Risk Prediction Score; IQR=interquartile range).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

DISCUSSION

Principal findings

This study verified our previous paediatric PRPS with an excellent AUC of 0.941 in the validation cohort. Then, with the modification and update of the previous version, the new model, termed modified PRPS, offered better capability in the prediction of ICU admission after surgery in children.

The modified PRPS had six observing variables instead of the five seen in the paediatric PRPS, and the total of combined risk scores are 50 points in both versions. Compared to the paediatric PRPS, the modified PRPS merged the categories of ASA IV and ASA V into one category. By considering the clinical gravities, slight plus or minus changes in the point distribution among the different categories were made, which allowed the modified PRPS to be more rational and clinically practical.

By using the H-L test during the validation process, the modified PRPS displayed a better calibration, which suggested an improved discrimination when the ROC curve of the new model was compared with that of the paediatric PRPS and ASA-PS scores. In addition, the kappa statistic was used to compare the agreement of the observed and predicted ICU admission rates among the three scoring models. The modified PRPS had an accuracy of 95.85% with a kappa value of 0.62, which was in the substantial agreement range and significantly higher than that of the other two models. After considering the severity of surgery, both the AUC and kappa values were closer to 1, and the modified PRPS was more accurate and closer to perfect.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Comparison with other studies

A variety of assessment score formulas for perioperative risk prediction have been published.[4,5,8,10-14] As a gold standard for evaluating a patient's general health and comorbidities preoperatively, the ASA-PS has been widely used to predict perioperative outcomes in children, even if it was not initially intended to be used in children for the reason of lacking objective.[10] The Paediatric Risk of Mortality Score[11] and Paediatric Index of Mortality[12] have been widely used to predict mortality for children, but the greatest limitation is that they are only used in intensive care units. The Paediatric Risk Assessment score, including 13 preoperative variables, had excellent accuracy in predicting perioperative mortality in children.[13] Statistically significant differences of stratified surgical subgroups were found in univariate analysis, but not in multivariate regression analysis. However, stratified subgroups of surgeries are not equivalent to the severity of surgery. The intrinsic risk of the surgical procedure was not included in the final model. Moreover, it was only applied to non-cardiac surgeries, not all types of surgeries. The American College of Surgeons National Surgical Quality Improvement Program Paediatric Surgical Risk Calculator is a tool to calculate the risk of complications and mortality for a variety of surgical procedures. However, it requires a fill-in of CPT code (current procedural terminology), which is not easily accessible for health care-givers in other countries outside of United States. [14]

There is no uniform definition of what is considered "intrinsic severity of surgery" in current studies. Considering the impact of surgery (type and complexity) on

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

outcomes, some clinicians graded surgical severity according to their own criteria. In 1996, Arvidsson et al coded surgical interventions into a 4-point scale ranging from minor interventions to extensive procedures, according to the official Swedish classification of the interventions.[15] In 2002, the surgical risk score adopted the British United Provident Association operative grade category as one risk factor to predict mortality in surgical patients.[16] In 2004, by modifying the Johns Hopkins criteria, Donati et al simplified surgical severity to three grades and developed their own new model for predicting operative risk.[17] Based on the Office of Population, Censuses and Surveys system codes, the Surgical Outcome Risk Tool graded the magnitude of surgical procedures into four severity categories in 2014.[18] Stratified subgroup analysis was also commonly applied for the types of operation.[17,19] In this study, we classified the intrinsic severity of surgeries into three different levels (minor, moderate and major levels), which was different from other surgical categories but easier to work with.

Limitations of the study

There were some limitations to the present study. First, our primary endpoint includes both planned and unplanned ICU admissions. Second, the decision-making for ICU admission mainly relied on clinical bias and was also influenced by regional culture, economic factors and so on. Third, a higher probability of dying was also associated with a higher probability of being admitted to the ICU, but they were not treated as equivalent in our results.

CONCLUSION

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

In summary, with an appropriate adjustment of the ASA assessment and the integration of surgical severity into the scoring model, the new modified PRPS exhibits a more accurate prediction result and better discriminates ICU admission immediately after surgery in paediatric patients.

Acknowledgements The authors thank the support of Zhejiang Provincial Public Welfare Technology Application Research Foundation of China and the involved paediatric patients and their guardians.

Author Contributions

CL helped design the study, conduct the study, analyse the data, and write the manuscript. PW and QF helped collect the data. XD helped analyse the data. JW helped revise the manuscript. QL helped design the study and conduct the study. WSG helped design the study, conduct the study, analyse the data, and revise the manuscript. All authors helped to conceptualize ideas and interpret findings and reviewed drafts of the manuscript.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval

Ethics approval to collect the patients' data was obtained from the Ethics Committee of the Second Affiliated Hospital of Wenzhou Medical University (No. 2018-10).

Funding This work was supported by Zhejiang Provincial Public Welfare Technology Application Research Foundation of China, grant number 2018ZD033.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

For peer review only

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution 4.0 Unported (CC BY 4.0) license, which permits others to copy, redistribute, remix, transform and build upon this work for any purpose, provided the original work is properly cited, a link to the license is given, and an indication of whether changes were made is provided. See: https:// creativecommons. org/ licenses/ by/ 4. 0

ORCID iD

Chunwei Lian: https://orcid.org/0000-0003-4702-6147

For peer review only

REFERENCES

1. van der Griend BF, Lister NA, McKenzie IM, et al. Postoperative mortality in children after 101,885 anaesthetics at a tertiary pediatric hospital. *Anesth Analg* 2011; 112:1440-7.

2. de Bruin L, Pasma W, van der Werff DB, et al. Perioperative hospital mortality at a tertiary pediatric institution. *Br J Anaesth* 2015; 115:608-15.

3. Jhanji S, Thomas B, Ely A, et al. Mortality and utilization of critical care resources amongst high-risk surgical patients in a large NHS trust. *Anaesthesia* 2008; 63:695-700.

4. Lian C, Xie Z, Wang Z, et al. Pediatric preoperative risk factors to predict postoperative ICU admission and death from a multicenter retrospective study. *Paediatr Anaesth* 2016;26:637-43.

5. Goobie SM, Zurakowski D, Proctor MR, et al. Predictors of clinically significant postoperative events after open craniosynostosis surgery. *Anesthesiology* 2015; 122:1021-32.

6. Liu JB, Liu Y, Cohen ME, et al. Defining the Intrinsic Cardiac Risks of Operations to Improve Preoperative Cardiac Risk Assessments. *Anesthesiology,* 2018;128:283-92.

7. Nasr VG, Staffa SJ, Zurakowski D, et al. Pediatric Risk Stratification Is Improved by Integrating Both Patient Comorbidities and Intrinsic Surgical Risk. *Anesthesiology* 2019; 130:971-80.

8. Collins GS, Reitsma JB, Altman DG, et al. Transparent reporting of a multivariable

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement.

9. Hosmer DW, Lemeshow S: Assessing the Fit of the Model in Applied Logistic Regression, 2nd edition. New York, John Wiley & Sons, 2005:143 – 202

10. Saklad M. Grading of patients for surgical procedures. *Anesthesiology* 1941; 24:281-4.

11. Pollack MM, Ruttimann UE, Getson PR. Pediatric risk of mortality (PRISM) score. *Crit Care Med* 1988;16:1110-6.

12. Shann F, Pearson G, Slater A, et al. Pediatric index of mortality (PIM): a mortality prediction model for children in intensive care. *Intensive Care Med* 1997;23:201-7.

13. Nasr VG, DiNardo JA, Faraoni D. Development of a Pediatric Risk Assessment Score to Predict Perioperative Mortality in Children Undergoing Noncardiac Surgery. *Anesth Analg* 2017; 124:1514-9.

14. Faraoni D, Vo D, Nasr VG, et al. Development and Validation of a Risk Stratification Score for Children with Congenital Heart Disease Undergoing Noncardiac Surgery. *Anesth Analg* 2016;123:824-30.

15. Arvidsson S, Ouchterlony J, Sjöstedt L, et al. Predicting postoperative adverse events. Clinical efficiency of four general classification systems. The project perioperative risk. *Acta Anaesthesiol Scand* 1996;40:783-91.

16. Sutton R, Bann S, Brooks M, et al. The Surgical Risk Scale as an improved tool for risk-adjusted analysis in comparative surgical audit. *Br J Surg* 2002;89:763-8.

17. Donati A, Ruzzi M, Adrario E, et al. A new and feasible model for predicting

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

operative risk. *Br J Anaesth* 2004; 93:393-9.

18. Protopapa KL, Simpson JC, Smith NC, et al. Development and validation of the Surgical Outcome Risk Tool (SORT). *Br J Surg* 2014; 101:1774-83.

19. Weinberg AC, Huang L, Jiang H, et al. Perioperative risk factors for major complications in pediatric surgery: a study in surgical risk assessment for children. *J Am Coll Surg* 2011;212:768-78.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Figure captions:

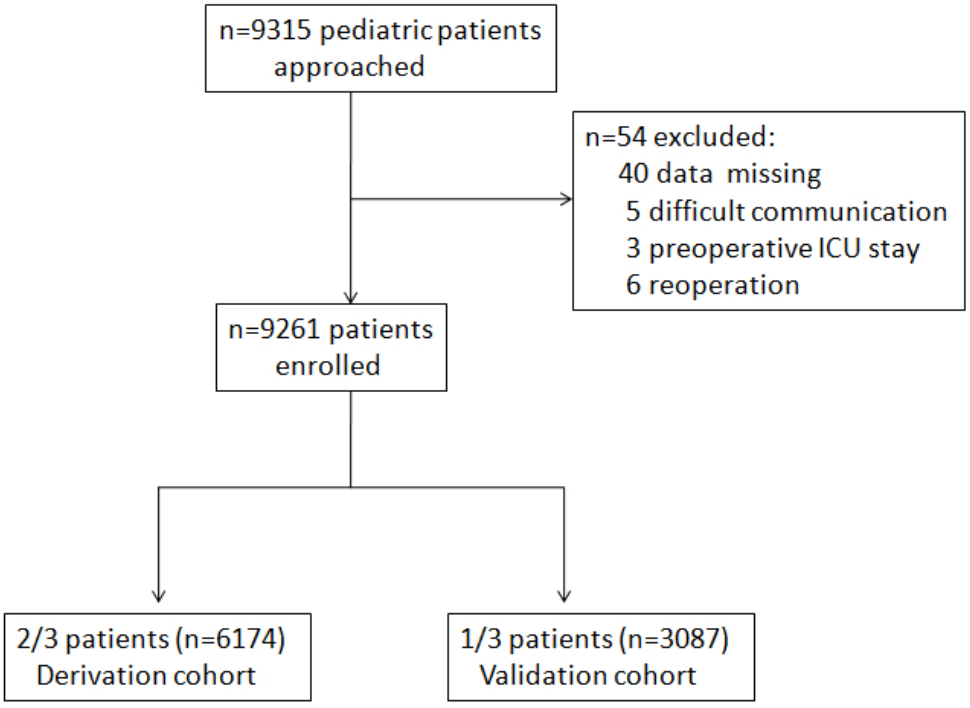
Figure 1: Flowchart of the study.

Figure 2:

Receiver operating characteristic (ROC) curves for the modified preoperative risk prediction score (PRPS), PRPS, and ASA physical status (ASA-PS) for the validation cohort: (A) a randomly selected individual who had intensive care unit (ICU) admission had an overall score higher than that of paediatric patients who had post-anaesthesia care unit (PACU) admission; (B) a randomly selected individual who died had an overall score higher than that of paediatric patients who survived.

For peer review only

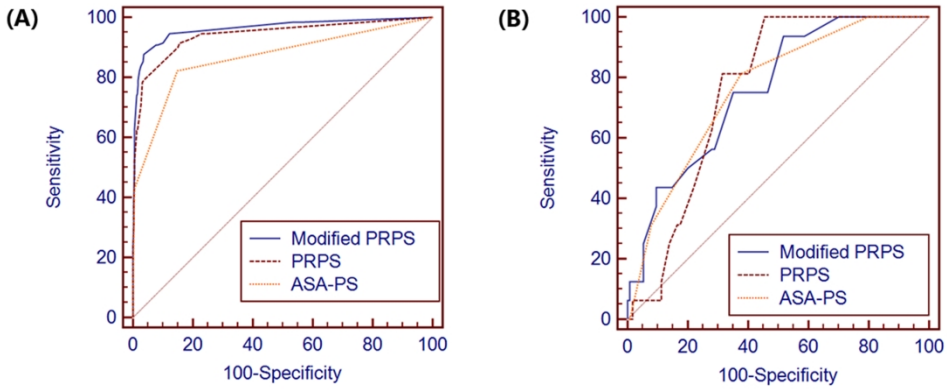
For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml



Flowchart of the study.

55x40mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.



Receiver operating characteristic (ROC) curves for the modified preoperative risk prediction score (PRPS), PRPS, and ASA physical status (ASA-PS) for the validation cohort: (A) a randomly selected individual who had intensive care unit (ICU) admission had an overall score higher than that of paediatric patients who had post-anaesthesia care unit (PACU) admission; (B) a randomly selected individual who died had an overall score higher than that of paediatric patients who survived.

300x150mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

Reporting checklist for prediction model development and validation study.

Based on the TRIPOD guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the TRIPODreporting guidelines, and cite them as:

Collins GS, Reitsma JB, Altman DG, Moons KG. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement.

		Reporting Item	Page Number
Title			1
	#1	Identify the study as developing and / or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract			2-3
	#2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2-3
Introduction			4-5
	#3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to	4

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

For peer review only

		existing models.	
	#3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	4-5
Methods			6-8
Source of data	#4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6
Source of data	#4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
Participants	#5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	6
Participants	#5b	Describe eligibility criteria for participants.	6
Participants	#5c	Give details of treatments received, if relevant	n/a (no treatment)
Outcome	#6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	6
Outcome	#6b	Report any actions to blind assessment of the outcome to be predicted.	n/a (as a retrospective cohort study, no blind assessment)
Predictors	#7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured	6
Predictors	#7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	n/a (as a retrospective cohort study, no blind assessment)
Sample size	#8	Explain how the study size was arrived at.	n/a (only collect the sample for 1y)

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

Missing data	#9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	8
Statistical analysis methods	#10a	If you are developing a prediction model describe how predictors were handled in the analyses.	7
Statistical analysis methods	#10b	If you are developing a prediction model, specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	7-8
Statistical analysis methods	#10c	If you are validating a prediction model, describe how the predictions were calculated.	7-8
Statistical analysis methods	#10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	7-8
Statistical analysis methods	#10e	If you are validating a prediction model, describe any model updating (e.g., recalibration) arising from the validation, if done	7-8
Risk groups	#11	Provide details on how risk groups were created, if done.	7
Development vs. validation	#12	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	7
Results			9-16
Participants	#13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	9-11
Participants	#13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants	9-11

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

For peer review only

		with missing data for predictors and outcome.	
Participants	#13c	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	9-11
Model development	#14a	If developing a model, specify the number of participants and outcome events in each analysis.	12-13
Model development	#14b	If developing a model, report the unadjusted association, if calculated between each candidate predictor and outcome.	n/a(unadjusted)
Model specification	#15a	If developing a model, present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	12-13
Model specification	#15b	If developing a prediction model, explain how to the use it.	14,16
Model performance	#16	Report performance measures (with CIs) for the prediction model.	12
Model-updating	#17	If validating a model, report the results from any model updating, if done (i.e., model specification, model performance).	15-16
Discussion			17-20
Limitations	#18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	19
Interpretation	#19a	For validation, discuss the results with reference to performance in the development data, and any other validation data	18
Interpretation	#19b	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	18-19
Implications	#20	Discuss the potential clinical use of the model	n/a(apply the model to

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.

For peer review only

		and implications for future research	identify three risk categories before surgery)
Other information			20-21
Supplementary information	#21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	n/a (if needed,we would provide)
Funding	#22	Give the source of funding and the role of the funders for the present study.	20

None The TRIPOD checklist is distributed under the terms of the Creative Commons Attribution License CC-BY. This checklist can be completed online using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2019-036008 on 18 March 2020. Downloaded from http://bmjopen.bmj.com/ on April 23, 2024 by guest. Protected by copyright.