Risk Factor And Predictive Score of the Intraoperative Hypothermia in Pediatric Patients

Worachet Saezhang

A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of
Master of Science in Health Sciences and Clinical Research
Prince of Songkla University
2024

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Major Program Health Sciences And Clinical Research

Academic Year 2023

ABSTRACT

Background: Inadvertent intraoperative hypothermia, defined as a decrease in core temperature of 35°C, is a common problem in patients undergoing anesthesia which can result in adverse consequences. Therefore, maintaining normothermia, especially in pediatric patients is a primary concern. This study aims to identify the incidence of intraoperative hypothermia and its risk factors for developing a risk prediction score.

Methods: A retrospective cohort study of 940 children under the age of 12 years underwent anesthesia in 2020 at Songklanagarind Hospital, Thailand, with one episode of body temperature <35°C indicated a mild and 35.1-35.9°C indicated a very mild hypothermia . Data, including patient demographics, clinical information, and perioperative data, were extracted from the hospital information system and were analyzed to identify the potential risk factors. The variables associated with intraoperative hypothermia at a p-value <0.2 then were included in the multivariate logistic regression analysis to establish a prediction model.

Results: Among 940 patients, 34 (3.62%) patients experienced intraoperative hypothermia. After multivariate logistic regression analysis, a final model demonstrated that intraoperative hypothermia with a body temperature of less than or equal to 35 °C was associated with ASA physical status > III (Adj OR 15.41 (7.13, 33.27), p<0.001), Preoperative body temperature > 37.2°C (Adj OR3.31 (1.47, 7.44), p=0.006), anesthetic time > 2 hours (Adj OR 3.14 (1.34, 7.37), p=0.006), and no active warming (Adj OR 9.25 (2.87, 29.82), p<0.001)

The risk prediction score with a cut-off point of 1 was chosen with sensitivity and specificity of 85.9% and 52.53% respectively. The final model showed good discrimination with an AUC of 0.775.

Conclusions: The risk prediction score for predicting intraoperative hypothermia with a cut-off point of 1, especially in patients who had a score more than 2.75 can help clinical physicians in early detection of intraoperative hypothermia and prevent adverse consequences caused by intraoperative hypothermia.

Keywords: Hypothermia; Pediatrics; Temperature; Perioperative; Risk factor; Score

ACKNOWLEDGEMENT

My grateful gratitude to the Department of Anesthesiology, Faculty of Medicine, Prince of Songkhla University for the invaluable opportunity to conduct this study.

I would like to express my sincere thanks to my thesis advisor, advisor, Associate Professor Maliwan Oofuvong M.D. for her invaluable help and constant encouragement throughout the course of this research. I am most grateful for her teaching and advice, not only the research methodologies but also statistical analysis. I would not have achieved this far and this thesis would not have been completed without her support.

Finally, I most gratefully acknowledge my parents and my friends for all their support.

Worachet Saezhang

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Chapter 1 Introduction

Inadvertent intraoperative hypothermia is a common problem in patients undergoing anesthesia. However, there is a controversy about the definition of intraoperative hypothermia found in various literatures. Several literatures defined intraoperative hypothermia as a core temperature below 36.0°C[1] while a few studies identified it as <35°C[2].

In adults, this incidence broadly occurs, ranging from four[1] to almost eighty percent[3]. Most of the anesthetic agents cause vasodilatation leading to a decrease in core body temperature, subsequent redistribution of temperature, and a decrease in shivering threshold[4]. In addition, The operative room environment influences body temperature as extremely ambient operative room temperature can lead to perioperative hypothermia from evaporation, convection, conduction, and radiation, especially in children[5].

There are many adverse consequences associated with perioperative hypothermia. Activating sympathetic activity in response to hypothermia with increasing norepinephrine levels leads to increased oxygen consumption, especially in the newborns[6].

The pediatric population is prone to developing hypothermia intraoperatively[7]. Physiologic change, as the immature thermoregulatory capacity, plays a major role in poor temperature control. In addition, A high surface area causes more heat loss affected by the operating room environment than in adults.

A literature review showed that there are few studies on pediatric perioperative hypothermia with limited risk factors and outcomes[8]. A study by Pearce B et al.[9] found that invasive procedures, older age, longer duration of anesthesia, greater blood loss, and blood transfusion are associated with intraoperative hypothermia. However, the population of the previous study consisted of wide ranges of ages from infants to young adolescents.

Additionally, in the previous cost-of-illness study, perioperative hypothermia is associated with a high burden on the healthcare welfare system with a cost of more than one thousand million Australian dollars a year[10].

However, the risk factors of pediatric hypothermia at temperature <36 °C were not well defined as well as the consequences after hypothermia. There was also no meta-analysis of intraoperative hypothermia in children. A recent meta-analysis in adults found that the cut-off point of 36°C was overestimated and not sensitive enough to distinguish associated adverse outcomes of intraoperative hypothermia[11,12]. Furthermore, body temperature of less than or equal to 35°C was correlated with a risk of bradycardia, low platelet count, and coagulopathy compared to 36°C cut-off[13]. Therefore, in our study, 35°C was used as a cut-off point for intraoperative hypothermia regarding the associated adverse outcomes of intraoperative hypothermia.

As a result, maintaining normothermia, especially in pediatric patients is a priority concern. This study thus aims to develop a risk prediction score to predict intraoperative hypothermia targeting the early detection of high-risk patients who might be confronted with adverse consequences associated with intraoperative hypothermia.

Chapter 2 Review of Literature/Methodology

Intraoperative hypothermia in pediatric patients

Intraoperative hypothermia is defined as a core body temperature less than 36°C[1]. In adults, this incidence broadly occurs, ranging from four[1] to almost eighty percent[3]. However, there are only a few studies in pediatric population. The pediatric population is prone to developing hypothermia intraoperatively [7]. Physiologic change, as the immature thermoregulatory capacity, plays a major role in poor temperature control especially in newborn. A high surface area is a main cause of intraoperative hypothermia in pediatric differently from adults.

Table 1 : Risk factor of intraoperative hypothermia in pediatrics

First author	Design	Title	Subjects	Total patients	Results
Pearce, et al 2010[9]	Prospective cohort study	Perioperative Hypothermia in the Pediatric Population: Prevalence, Risk Factors and Outcomes	Pediatric patient < 18 years old	530 patients	Invasive procedures, older age, longer duration of anesthesia, greater blood loss and blood transfusion were associated with hypothermia
Okamura, et al 2021[14]	Retrospective cohort study	Incidence of Unintentional Intraoperative Hypothermia in Pediatric Scoliosis Surgery and Associated Preoperative Risk Factors	10–19 years old Scoliosis patient	103 patients	Lower BMI, and lower initial core body temperature were independent risk factors associated with intraoperative hypothermia
Lee, et al 2020[15]	Prospective cohort study	Perioperative Temperature Management in Children: What Matters?	Pediatric patient < 16 years old	869 patients	Active force air warming is protective factor for postoperative hypothermia
Zhao J, et all 2023[16]	Retrospective cohort study	Risk factors and outcomes of intraoperative hypothermia in			younger age, lower weight, longer surgery time, received more fluid, and no prewarming

		neonatal and infant patients undergoing general anesthesia and surgery			management were the common risk factors of intraoperative hypothermia

Chapter 3 Research Methodology

Study design

A single-center retrospective cohort study in children under the age of 12 years underwent anesthesia in 2020 at Songklanagarind Hospital, Thailand, were selected. The data from the cohort study included patient demographics, clinical information, and perioperative data extracted from the hospital information system. Furthermore, anesthetic records were collected and analyzed to identify the outcomes.

This retrospective observational study was approved by the institutional Ethics Committee of the Faculty of Medicine, Prince of Songkla University (REC 65-003-8-4)

Inclusion and Exclusion criteria

The inclusion criteria consists of children less than 12 years of age who underwent any surgical procedure under anesthesia from 1 January to 31 December 2020 with ASA classification of 1 to 4.

The exclusion criteria were intraoperative hyperthermia, defined as a rise in core temperature of 37.8°C at least one episode, as well as children who underwent cardiopulmonary bypass with deliberate intraoperative hypothermia, and cases where no temperature monitoring were being recorded.

Data collection

All the information including patient baseline characteristics and perioperative profiles were obtained from the hospital information system (HIS) and anesthetic record.

The outcome of the study

Intraoperative temperature ≥ 36°C was considered as normothermia. Intraoperative temperature between 35.1- 35.9 °C was considered as very mild hypothermia, while at least one episode of core temperature ≤ 35°C indicated mild hypothermia. The severity of intraoperative hypothermia was classified as mild hypothermia (35-32 °C), moderate hypothermia (32-28 °C), and severe hypothermia (28-20 °C)[4].

The explanatory variables

The following clinical variables that might be predictors associated with intraoperative hypothermia were recorded. Patient-related predictors included gender, age, body weight (kg), body height(cm), body surface area (BSA) calculated by using the Mosteller equation ($\sqrt{\frac{\text{Weight(kg)xHeight(cm)}}{3600}}$)[17], Weight-to-BSA ratio defined as a ratio of weight (kg) to a BSA, ASA physical status classification and baseline preoperative body temperature defined as the last temperature recorded at the ward before the operation.

Surgery-related risk factors included site of surgery, type of surgery (open and endoscopic surgery), and magnitude of surgery classified as major operation (surgery in which body cavities or major vessels are exposed to an ambient temperature such as major abdominal, thoracic, major vascular, thoracic spine surgery with instrumentation) medium (surgery in which body cavities are exposed to a lesser degree such as appendectomy, herniotomy), and minor surgery (superficial surgery)[18].

Anesthesia-related risk factors included anesthetic drugs, duration of operation, anesthetic time, estimated blood loss, blood transfusion, method of temperature monitor (i.e. nasopharyngeal, esophageal, rectal, or skin sensors), and active forced-air warming use.

The duration of the operation was defined as the duration between surgical wound incision and surgical wound closure. The duration of anesthesia was defined as the duration between an anesthetic drug given and extubation. The duration of anesthesia preparation was defined as the duration between induction drugs given and surgical wound incisions.

Temperatures were measured by nurse anesthetists with various routes and recorded in the anesthetic chart every 30 minutes. The temperature measured in the ear and skin (axillary route) is less accurate compared to the rectum monitor with a value of less than 0.5 °C[19], therefore, we added 0.5 °C to account for the error of the measurement.

Statistical analysis

Data were entered with Epidata (version 3.1) and analyzed in program R version 4.2.1. All categorical variables were presented with frequency and percentage. While continuous variables were presented with mean and standard deviation. The chi-square test or Fisher's exact test was used to compare categorical variables. The unpaired student t-test was used to compare parametric categorical variables, while the Wilcoxon rank sum test was used to analyze non-parametric categorical variables.

The variables associated with intraoperative hypothermia at a p-value <0.2 were included in the multinomial logistic regression analysis to identify the dose-response relation between 2 outcomes (Body temperature 35.1-35.9°C and ≤ 35°C) with backward stepwise selection. The final model had the lowest AIC. The continuous variables were converted into binary variables for a feasible final model. Predictors in the final multinomial logistic model would be included in multivariate logistic regression to find the association presented as an odd ratio (OR) and 95% confidence interval (CI). An ROC analysis was used to define an optimal cut-point using the closest top-left method.

Score derivation and validation

The risk prediction score system was developed using the predictors derived from the multivariate logistic regression model. Based on the regression-coefficient model, the score of each predictor was derived from beta-coefficient and rounded to the nearest integer to make a maximum score of 10.

In the final model, each predictor score was summarized for predicting intraoperative hypothermia. Youden's index was used to evaluate the maximum specificity and sensitivity cutoff values of the prediction score. The performance of the final model was reported as an area under the receiver operating characteristic curve (AUC). An AUC value of more than 80 indicated a very good performance of the model. A Hosmer-Lemeshow test was used to assess the goodness-of-fit and calibration of the final risk prediction model.

Sample size calculation

We used the criteria as suggested by Riley et al.[20] and the package pmsampsize in program R to calculate a minimum sample size estimation required for developing a risk prediction model. Based on Riley et al. criteria, we used a parameter as a binary outcome to calculate sample size estimation.

The absolute margin of error $(\delta) = 1.96 \times \sqrt{\frac{\widehat{\phi}(1-\widehat{\phi})}{n}}$

Sample size estimation (n) $= (\frac{1.96}{\delta})^2 \widehat{\phi}(1 - \widehat{\phi})$

When $\widehat{\phi}$ = overall outcome proportion

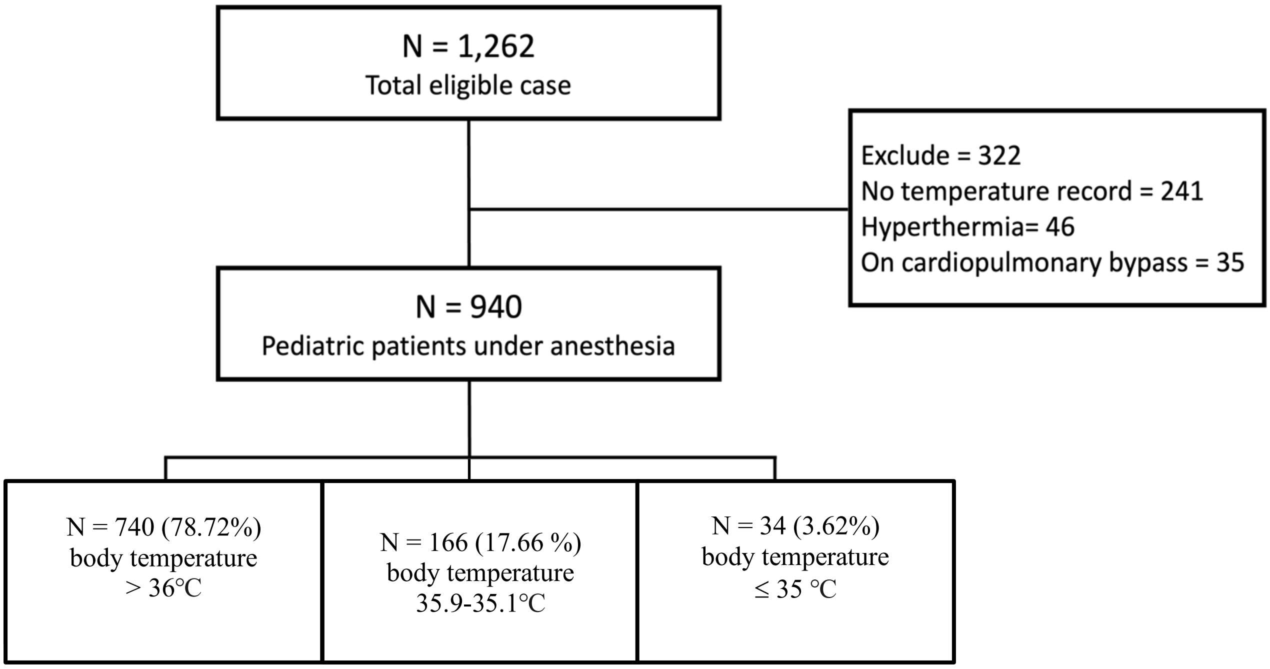
Sample size estimation in our study is based on the result from Hu Y's study about risk factors of intraoperative hyperthermia (defined as body temperature < 36°C)[21]. They reported an incidence of intraoperative hypothermia at 17.8% with an AUC of 0.758. In response, we expected 10 predictors in our risk prediction model, therefore the minimum sample size required for new model development, based on the Hu Y's study, was 689 patients with 118 events (assuming an outcome prevalence was 0.18 and an event per predictor was 11.71)

Chapter 4 Result

From January to December 2020, a total of 1,262 patients met the inclusion criteria, of these, 322 patients were excluded as the intraoperative temperature of 241 patients was not monitored, while 46 patients had intraoperative hyperthermia and 35 patients were on cardiopulmonary bypass with deliberate hypothermia intraoperatively. As a result, valid data from 940 patients were analyzed, as shown in Figure 1.

Among 940 patients, 34 patients (3.62%) experienced intraoperative hypothermia (Figure 1). The resulting sample of 940 patients and their baseline characteristics are presented in Table 1.

Figure 1: Flow diagram



Patients baseline characteristics

In Table 1, the characteristics of 940 patients are presented. The median age of the normothermia group was 4.4 years (IQR 1.75-7.7) while the mild hypothermia group had a median age of 3.7 years (IQR 0.83, 7.7) and the very mild hypothermia group had a median age of 3.9 years (IQR 0.40, 10.3) . The median body weight in the normothermia group was 15.5 kilograms (IQR 10.0-22.6), 13.1 kilograms (IQR 8.00-21.7) in the very mild hypothermia group, and 16.6 kilograms (IQR 5-25). Most of the patients in the normothermia and very mild hypothermia groups were male (64.9% and 66.9% respectively) whereas the female gender was predominant (65.9%) in the mild hypothermia group.

Most of the patients in the normothermia group had an ASA physical status classification II (50.9%), but mild hypothermia patients, on average, had a higher ASA physical status (41.2% of which in Classification III and 38.2% in Classification IV). Baseline preoperative body temperature was a slightly higher in mild hypothermia group (37.2 [IQR36.6-37.9]).

Surgery-related risk factor

Considering the magnitude of the surgery, most of the patients in all groups underwent an intermediate operation. In the mild hypothermia group, 8 patients (23.5%) underwent a major operation compared to 55 patients (7.4%) in the normothermia group. The magnitude of the surgery and the site of the operation were shown in Table 2.

Table 2: Patient baseline characteristic

Characteristic	Normothermia (N=740)	Very mild hypothermia (N=166)	Mild hypothermia (N=34)	p-value
Male	480 (64.9%)	111(66.9%)	15 (44.1%)	**0.037**
Age (year)				0.10
median (IQR)	4.4 [1.75, 7.7]	3.7 [0.83, 7.7]	3.9 [0.40, 10.3]	
Body weight (kg)				**0.019**
median (IQR)	15.5 [10.00, 22.6]	13.1 [8.00, 21.7]	16.6 [5.05, 25.0]	
Body height (cm)				**0.035**
median (IQR)	102.0 [80.00, 122.0]	94.0 [70.00, 120.0]	101.5 [58.12, 145.0]	
Body surface area				**0.015**
median (IQR)	0.7 [0.47, 0.9]	0.6[0.38,0.8]	0.7 [0.34, 1.0]	
Weight to BSA ratio				**0.018**
median (IQR)	23.4 [21.0, 26.5]	22.9[19.27,25.6]	24.1 [16.58, 25.0]	
ASA classification				**<0.001**
I	158 (21.4%)	34 (20.5%)	5 (14.7%)	
II	377 (50.9%)	65 (39.2%)	2 (5.9%)	
III	188 (25.3%)	49 (30.1%)	14 (41.2%)	
IV	17 (2.3%)	18 (10.8%)	13 (38.2%)	
Emergency surgery	108 (14.6%)	30 (18.1%)	11 (32.4%)	**0.015**
Preoperative BT (C)				**0.010**
median (IQR)	36.8 [36.60, 37.0]	36.8[36.6-37]	37.2 [36.60, 37.9]	

Noted: BSA, body surface area; C, degree Celsius; SD, standard deviation; IQR, interquartile range; BT, body temperature

Table 3: Univariate regression analysis of surgery-related risk factors

Predictors	Normothermia (N=740)	Very mild hypothermia (N=166)	Mild hypothermia (N=34)	p-value
Magnitude of Surgery				**<0.001**
major	55 (7.4%)	36 (21.7%)	8 (23.5%)	
intermediate	521 (70.4%)	113 (68.1%)	25 (73.5%)	
minor	164 (22.2%)	17 (10.2%)	1 (2.9%)	
Laparoscopic and Endoscopic surgery	73 (9.9%)	13 (7.8%)	1 (2.9%)	0.4
Site of surgery				**<0.001**
superficial	120 (16.2%)	18 (11.0%)	4 (11.8%)	
eye, ENT	318 (43.0%)	47 (28.3%)	4 (11.8%)	
abdomen	127 (17.2%)	36 (21.7%)	4 (11.8%)	
extremities	136 (18.4%)	40 (24.1%)	13 (38.2%)	
intracranial	18 (2.4%)	9 (5.4%)	5 (14.7%)	
intrathoracic	22 (2.8%)	16 (9.6%)	4 (11.8%)	

Anesthesia-related risk factors

In Table 3, the anesthetic technique and intraoperative profiles of 940 patients were presented including anesthetic choice, airway management, regional anesthesia technique, anesthetic drugs, peripheral nerve block, anesthetic time, operation time, and time from induction to the starting of operation. Most of the patients underwent general anesthesia using endotracheal intubation (86.4%, 83.7% and 91.2% in the normothermia, very mild hypothermia, and mild hypothermia group, respectively). A longer duration of anesthetic time was found in the mild hypothermia group (a median of 157.5 minutes IQR 120-193.8) compared to the normothermia group (a median of 105 minutes IQR 80-146.2) and the very mild hypothermia group (a median of 140 minutes IQR 96.25-185). Likewise, the median operation time was longer in the mild hypothermia group as well.

The Forced-air warming system was routinely used in most cases (98% in both the normothermia and very mild hypothermia group and 73.5% in the mild hypothermia group). Intraoperative blood loss was higher in the mild hypothermia group, which also statistically significant required more blood transfusions.

The hypothermia group's characteristic

The intraoperative characteristics of 34 mild hypothermia and 166 very mild hypothermia patients were presented in Table 4. No patients experienced moderate and severe hypothermia. The median time of a hypothermic episode was 82.5 minutes (IQR 60-115) in the mild hypothermia group compared to 55 minutes (IQR 30-67.5) in the very mild hypothermia group.

Table 4: Univariate regression analysis of anesthesia-related risk factors

Predictors	Normothermia (N=740)	Very mild hypothermia (N=166)	Mild hypothermia (N=34)	p-value
Regional anesthesia	80 (10.8%)	24 (14.4%)	3 (8.8%)	0.4
Peripheral nerve block	52 (7.0%)	17 (10.2%)	1 (2.9%)	0.2
General anesthesia				0.5
Endotracheal tube	639 (86.4%)	139 (83.7%)	31 (91.2%)	
Laryngeal mask airway	101 (13.6%)	27 (16.3%)	3 (8.8%)	
Anesthetic time (minute)				**<0.001**
median (IQR)	105.0 [80.00, 146.2]	140.0[96.25,185.0]	157.5 [120.00, 193.8]	
Operation time (minute)				**<0.001**
median (IQR)	70.0 [50.00, 110.0]	100.0[60.00,135.0]	115.0 [86.25, 140.0]	
Anesthesia preparation time (minute)				**0.019**
median (IQR)	25.0 [20.00, 35.0]	30.0 [20.00,45.0]	30.0 [20.00, 55.0]	
TIVA	26 (3.5%)	1 (0.6%)	2 (5.9%)	**0.042**

Noted: SD, standard deviation; IQR, interquartile range; TIVA, total intravenous anesthesia

Table 4: Univariate regression analysis of anesthesia-related risk factors (Continue)

Predictors	Normothermia (N=740)	Very mild hypothermia (N=166)	Mild hypothermia (N=34)	p-value
Route of temperature monitor				0.01
rectal	72 (9.7%)	15 (9.1%)	3 (9.1%)	
nasal	163 (22.1%)	42 (25.5%)	9 (27.3%)	
oral	257 (34.8%)	56 (33.9%)	15 (45.5%)	
skin/axillary	246 (33.3%)	52 (31.5%)	6 (18.2%)	
Crystalloid (mL)				0.6
median (IQR)	170.0 [100.00, 300.0]	150.0 [60.25-307.5]	205.0 [73.00, 492.5]	
Colloid	7 (0.9%)	4 (2.5%)	0 (0%)	0.2
Blood loss (mL)				**< 0.001**
median (IQR)	5.0 [1.00, 15.0]	5.0 [2.00, 20.0]	35.0 [5.00, 137.5]	
Blood transfusion	40 (5.4%)	27 (16.3%)	14 (41.2%)	**< 0.001**
Active warming	725 (98.0%)	163 (98.2%)	25 (73.5%)	**< 0.001**

Noted: SD, standard deviation; IQR, interquartile range

Table 5: The hypothermia group's characteristic

	Very mild hypothermia body temperature 35.1-35.9°C (N=166)	Mild hypothermia body temperature ≤ 35°C (N=34)
Nadir temperature		
median (IQR)	35.6 [35.50-35.8]	34.9 [34.52, 35.0]
Duration of hypothermia		
median (IQR)	55.0 [30-67.5]	82.5 [60.00, 115.0]
Severity of hypothermia		
mild	163 (100%)	34 (100%)

Noted: SD, standard deviation; IQR, interquartile range

Multinomial logistic regression analysis of risk factors associated with intraoperative hypothermia

A cut-off point of 36°C was shown to be overestimated in adults[11]. Therefore, Predictors associated with intraoperative hypothermia were compared between a cut-off point of ≥36°C, 35.9-35.1 °C and ≤35°C using multinomial logistic regression analysis.

Patient-related predictors (gender, weight to body surface ratio [BSA] ratio, ASA physical status, baseline preoperative body temperature), surgery-related predictors (emergency surgery, magnitude of surgery, site of the operation, operation time), and anesthetic-related predictors (ASA classification, anesthetic duration, duration between induction to the starting of the operation, blood loss, blood transfusion) with a p-value less than 0.2 were initially included in the multivariate model.

The continuous variable predictors were modified into binary variables for a feasible final model. An ROC analysis was used to define an optimal cut-point using the highest Youden index. The optimal cut-points for preoperative body temperature, weight-to-BSA ratio, duration of surgery, duration of anesthesia, anesthetic time, and duration between induction to start the operation were 37.2°C, 24, 80 minutes, 130 minutes, , 120 minutes and 50 minutes respectively. Dose-response relationship between risk factors and the outcome were shown in Table 5.

Table 6: Multinomial logistic regression analysis of risk factors associated with intraoperative hypothermia (N=940)

	BT 35.1-35.9°C		**BT ≤ 35°C**		
Predictors	Beta coefficient	RRR (95%CI)	Beta coefficient	RRR(95%CI)	LR p-value
ASA classification > 3	1.73	5.62(2.51,12.56)	2.71	15.09(5.37,42.45)	<0.001
Preop BT > 37.2°C	-0.54	0.58(0.32,1.04)	2.69	2.69(1.17,6.17)	0.05
Major operation	0.67	1.96(1.17,3.26)	0.59	1.8(0.67,4.82)	0.033

Anesthetic time > 2 hours	0.99	2.68(1.85,3.88)	1.4	4.04(1.7,9.6)	<0.001
TIVA	-2.18	0.11(0.01,1.04)	0.14	1.15(0.17,7.86)	0.02
No active warming	0.12	1.13(0.3,4.26)	2.32	(2.98,34.6)	0.002

Noted: BT, Body temperature; RRR, Risk reduction ratio; TIVA, total intravenous anesthesia; CI, confidence interval

Multivariate logistic regression analysis of risk factors associated with intraoperative hypothermia

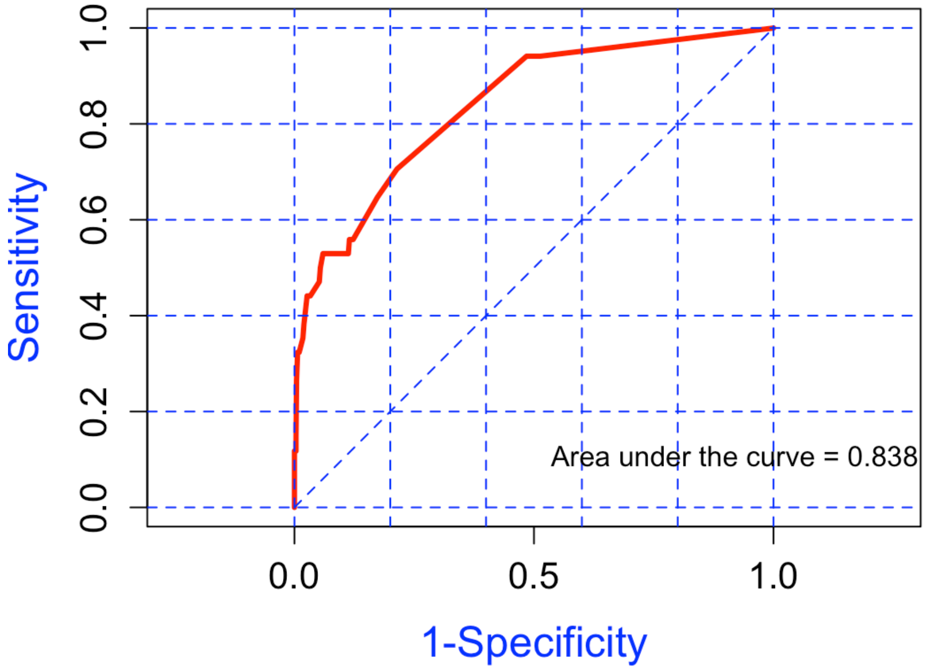
After multinomial logistic regression analysis, predictors in the final model were included in a multivariate logistic regression model to identify the association. Mild hypothermia was associated with ASA physical status > III (AdjOR 15.41(7.13,33.27), p<0.001), preoperative body temperature > 37.2°C (AdjOR3.31 (1.47,7.44),p=0.006), anesthetic time > 2 hours (AdjOR 3.14 (1.34,7.37),p=0.006), and no active warming (AdjOR 9.25 (2.87,29.82), p<0.001).

Table 7: Multivariate logistic regression analysis of risk factors associated with mild hypothermia compared to normal and very mild hypothermia (N=940)

Predictors	**Crude OR (95%CI)**	**Adjusted OR (95%CI)**	**p-value**
ASA Classification > III	15.41 (7.13,33.27)	8.01 (3.13,20.46)	**< 0.001**
Ref: ASA classification ≤ III			
Preoperative body temperature > 37.2 ℃	6.57 (3.25,13.26)	3.31 (1.47,7.44)	**0.006**
Ref: Preoperative body temperature ≤ 37.2 ℃			
Anesthetic time > 120 minutes	3.54 (1.67,7.49)	3.14 (1.34,7.37)	**0.006**
Ref: operative time ≤ 120 minutes			
Major operation	2.76 (1.21,6.27)	1.4 (0.53,3.73)	0.003
TIVA	2.03 (0.46,8.93)	1.7 (0.32,8.98)	0.552
No active warming	17.76 (7.27,43.4)	9.25 (2.87,29.82)	**<0.001**

Noted: OR, odd ratio; SD, standard deviation; IQR, interquartile range; TIVA,total intravenous anesthesia

Figure 2: Receiver operating characteristic (ROC) curves based on the risk factors associated with intraoperative hypothermia and respective areas under the ROC curves (AUCs).



Development of risk prediction score for predicting intraoperative mild hypothermia

Predictors derived from the multivariate logistic analysis model were included in the regression coefficient-based model.

Table 7 presents the final model of risk prediction score comprised of the ASA physical status classification > III, preoperative body temperature > 37.2 °C, anesthetic time > 120 minutes, major operation, TIVA, and No active force-air warming used during the operation.

Table 8: Risk prediction score using the regression coefficient-based model

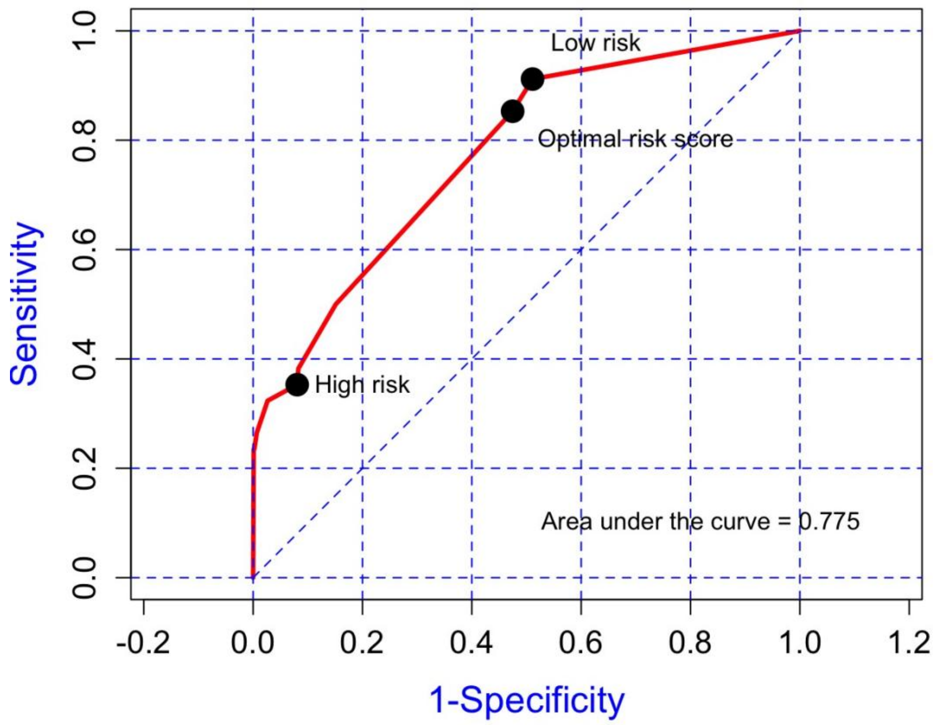
Predictors	Regression coefficient	Score
ASA Classification > III	2.0806	3
Preoperative body temperature > 37.2 °C	1.1965	1.5
Anesthetic time > 120 minutes	1.1445	1.5
Major operation	0.3374	0.5
TIVA	0.5286	0.5
No active warming	2.2246	3

The risk prediction score value ranged from 0-6. The final risk prediction model showed a good discriminative ability to distinguish patients with intraoperative hypothermia, with an AUC of 0.775.

A cut-off point of 1 was chosen, which was closest to the top-left part of the ROC analysis. The sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) of the prediction score were 85.29, 52.53, 80.57, 11.67, and 98.47%, respectively. (Figure 3)

The degree of risk of intraoperative mild hypothermia was classified into high-risk patients who had a risk score of more than 2.75 (sensitivity 35.29% and specificity 91.95%), intermediate risk patients who had a risk score of 0.25-2.75, and low-risk patients who had a risk score of less than 0.25 (sensitivity 91.18% and specificity 48.89%) as shown in Figure 3. The chi-square value of the Hosmer-Lemeshow test was 1.5742 (p = 0.455), corresponding to good model calibration.

Figure 3: Receiver operating characteristic (ROC) curves based on the risk prediction score for predicting intraoperative hypothermia, an optimal cut-off point, and respective areas under the ROC curves (AUCs)



Chapter 5 Conclusion and Discussion

Body temperature is one of the most important standards used for patient-monitoring as disruption of body thermoregulation occurs occasionally during either general or neuraxial anesthesia. In this study, children with the age of <12 years old were used as a sample in order to reduce the variety of age groups as found in the previous study on body surface area in the pediatric age group by Boniol et al.[22]. The incidence of intraoperative hypothermia in our setting was only 3.62% since the definition of mild hypothermia in our study was ≤ 35 °C. Despite a controversy in the definition of intraoperative hypothermia, the awareness of the adverse consequences of intraoperative hypothermia has been increasing. Although the cut-off point of 36°C was broadly accepted in many literatures, a recent meta-analysis of RCTs nevertheless showed that the cut-off point of 36°C was not an adequately sensitive criterion for intraoperative hypothermia. The detrimental effects of intraoperative hypothermia were predisposed to be overestimated[11].

All of the patients in our research experienced only mild hypothermia (defined as a body temperature of 35-32°C[12]) because, at Songklanagarind hospital, the forced-air warming system is routinely used in most of pediatric surgery, at the rate of up to 98.4% (98% in very mild hypothermia group and 73.5% in mildhypothermia group). Thus, there was no moderate or severe hypothermia observed in this study.

After multivariate logistic analysis, Potential risk factors associated with intraoperative hypothermia were ASA physical status classification > III, Preoperative body temperature > 37.2 °C, Anesthetic time > 120 minutes, and no active air warming used. Active force air warming was a preventable predictor in our study.

In the adult population, several studies were conducted to determine the risk factor of hypothermia. A systematic review and meta-analysis of risk factors by Pu J et al. found that older age, low BMI, ambient operative room temperature, preoperative heart rate, duration of anesthesia > 2 hours, and intravenous fluid administration >1,000 mL were associated with intraoperative hypothermia[23]. Meanwhile, Wongyingsinn M.'s study revealed that ASA physical status III-IV and preoperative hypothermia were associated with intraoperative hypothermia as well[24].

Due to the dissimilarity of the physiology in age groups, Risk factors of intraoperative hypothermia in adult studies may not be applicable to pediatric patients. Unfortunately, there are only a few studies about risk factors in the pediatric population. Our study was the first to date in the study of risk prediction scores for predicting intraoperative hypothermia in pediatric patients.

ASA Physical status classification

ASA physical status classification was used to categorize the patient based on the severity of co-existing diseases. Wongyingsinn M. et al.[23] demonstrated that ASA physical status III-IV had a higher incidence of intraoperative hypothermia in adults. The result was similar to the studies of Belayneh[25] and Monzón et al.[26]. In the pediatric population, J Zhao's et al[16] illustrated the association between higher ASA physical status and intraoperative hypothermia in neonates and infants as well. Patients with a higher ASA physical status had poor thermoregulatory control and were prone to develop vasodilatation from co-existing medical diseases resulting in intraoperative hypothermia.

Pediatric patients who had an ASA physical status classification of more than III would receive a risk prediction score of 3 indicating a high-risk patient. Temperature monitoring should be vigorously considered along with preoperative active warming application, and intraoperative warming protocol including active-forced air warming, and intravenous fluid warming device use.

Preoperative baseline temperature

In our study, preoperative baseline temperature > 37.2 °C was associated with intraoperative hypothermia. On the contrary, previous studies showed the opposite result. Research by Yi J, conducted in adults, showed that high baseline core temperature before anesthesia was a protective factor for intraoperative hypothermia[27]. However, infectious causes of preoperative hyperthermia were excluded in their study. Moreover, a study by Cho Ck et al.[28], completed in adults who underwent orthopedic surgery, revealed that lower baseline core temperature before anesthesia was a protective factor as well. The median baseline temperature was 36.8 °C [36.6-36.9] which was lower compared to our study (37.2°C [36.60, 37.9]). Hyperthermia is the thermoregulatory response to systemic inflammation[29]. During the perioperative period, vasodilation from systemic inflammatory response may be exaggerated, and thermoregulatory capacity was also suppressed by various anesthetic agents leading to sub-temperature.

Pediatric patients who had a preoperative high body temperature would be addressed with a risk prediction score of 1.5 indicating an intermediate-risk patient. A decrease in preoperative temperature methods such as a tepid sponge, oral paracetamol, or postponing elective surgery might be considered to minimize the risk of intraoperative hypothermia.

Duration of the anesthesia

Our results showed that the duration of anesthesia was independently associated with intraoperative hypothermia. This result is similar to recent research by Yan L's who emphasized their study on adults who underwent colorectal surgery indicated that a longer duration of surgery was associated with intraoperative hypothermia[30]. In addition, a study by J Zhao, in infants and neonates, revealed that the duration of surgery longer than 60 minutes two times increased the risk of intraoperative hypothermia[16]. Likewise, A systematic review and meta-analysis in Pu J et al's study found the duration of anesthesia > 2 hours increasing the risk of intraoperative hypothermia[23] similar to our result. A prolonged duration of anesthesia may lead to longer exposure to ambient operating room temperature and necessitate the administration of additional unwarm intravenous fluid as well.

Pediatric patients who had undergone a long duration of operation prediction would receive a risk score of 1.5 indicating an intermediate-risk patient. A preoperative active warming protocol might be used. Additionally, the intraoperative hypothermia prevention methods include warming intravenous fluid, active-forced air warming use, warm operating room temperature, and warming fluid irrigation to mitigate the risk of prolonged duration associated with intraoperative hypothermia.

Active forced-air warming

In various studies found in the literature, active forced-air warming was considered as a strong protective predictor against intraoperative hypothermia. Using an active convention warming method, active forced-air warming transmits heat by blowing warm air through a blanket aiming to prevent heat loss during the operation. Lee SY et al. reported that the use of forced-air warming reduced the incidence of intraoperative hypothermia in pediatric patients (age less than 16 years old)[15]. In addition, Su et al. found that forced-air warming was more effective than passive insulation in preventing adverse consequences regarding intraoperative hypothermia[31]. Corresponding to previous studies, our data showed that if no active forced-air warming was used, the risk of intraoperative hypothermia increased more than nine times.

No use of an active forced-air warming system indicates a high risk of developing intraoperative hypothermia in pediatric patients. An active forced-air warming system must be used in all children for both preoperative and intraoperative periods to diminish adverse consequences regarding intraoperative hypothermia.

This risk prediction score in our study was feasible to use and could be easily adopted in the perioperative period. In consequence, intraoperative hypothermia is commonly preventable. Observations of high-risk patients using our risk prediction scores may help in early detection of intraoperative hypothermia and prevent further adverse consequences causing by hypothermia. Due to the source-limited country, additional interventions may not be possible to facilitate in all cases. The most effective prevention is early recognition and awareness. Several areas for improvement including pre-warming implementation, and increased vigilance especially in patients with a risk score of more than 1.

The implication of the study

Since active forced-air warming and high preoperative body temperature > 37.2 ℃ were modifiable predictors of intraoperative hypothermia in our study, early warming intervention, will decrease the risk of intraoperative hypothermia. This could be supplemented by an active force air warming implementation.

An attempt to decrease preoperative body temperature such as a tepid sponge, oral paracetamol administration, and postponing an elective operation might be considered to minimize the risk of developing intraoperative hypothermia.

In our study, A risk prediction score value of more than 1 increased the risk of intraoperative hypothermia in pediatric patients. Therefore, Only one risk factor from ASA physical status > III, anesthetic time > 2 hours, preoperative body temperature > 37.2 ℃, or no active warming use might lead to intraoperative hypothermia. Patients with a risk score of more than 1 should be vigorously temperature monitored and maintain a normothermia. Especially in high-risk patients who had a risk score of more than 2.75.

Strength and Limitation

There are some limitations in our study. As our study is retrospective cohort, some data couldn't be collected such as the precise ambient temperature of an operating room (approximately 22-24℃), the amount of fluid irrigation, the temperature of the fluid, and the waiting time before the operation. Moreover, almost 20% of missing temperature monitoring data was recorded, especially in short-duration operations like esophagoscopy or colonoscopy. In addition, some data could not be gathered accurately, for instance, the body temperature was recorded in 30 minute-intervals in which the temperature change in the record was too rough to observe changes. Further prospective studies are thus encouraged to evaluate other risk factors.

Due to the small number of patients in the hypothermia group, an odd ratio from the multivariate model might be overestimated. The implication of this study should be used with caution. A larger sample size might be required to obtain a precise association.

Finally, due to the lack of external validation of the prediction scoring system, further multicenter studies might be performed on this risk prediction score to validate this model.

Conclusion

Our study found that potential risk factors associated with intraoperative hypothermia with a body temperature of less than or equal to 35 °C, ASA physical status classification > III, preoperative body temperature > 37.2 ℃, anesthetic time > 120 minutes, and no active warming. Active forced-air warming and preoperative body temperature> 37.2 ℃ were preventable predictors in our study. The risk prediction score with a cut-off point of 1 can help clinical physicians in the early detection of intraoperative and decrease adverse outcomes regarding intraoperative hypothermia.

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