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REPORTS OF ORIGINAL INVESTIGATIONS

Development of local guidelines to prevent perioperative hypothermia in children: a prospective observational cohort study

Élaboration de nouvelles lignes directrices pour la prévention de l'hypothermie périopératoire chez les enfants : étude de cohorte observationnelle prospective

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Abstract

Purpose *Perioperative hypothermia (PH) is defined as core body temperature < 36°C during the perioperative period. The incidence of PH is not well established in children because of variations in perioperative temperature monitoring and control measures. We sought to 1) establish the incidence of pediatric PH, 2) assess its adverse outcomes, and 3) identify risk factors in our pediatric population to develop local guidelines for prevention of PH.*

Methods *We conducted a prospective observational cohort study at a single tertiary hospital (KK Women's and Children's Hospital, Singapore) from June 2017 to December 2017 based on existing institutional practice. We recruited patients aged ≤ 16 yr undergoing surgery and determined the incidence and adverse outcomes of hypothermia. We identified risk factors for PH using univariate and multiple logistic regression analysis and used these to develop local guidelines.*

Results *Of 1,766 patients analyzed, 213 (12.1%; 95% confidence interval, 10.6 to 13.7) developed PH. Among these cases of PH, only 4.5% would have been detected by a single measurement in the postanesthesia care unit (PACU). Adverse outcomes included a longer stay in the PACU (47 vs 39 min; P < 0.01), a higher incidence of shivering (7.1 vs 2.6%; P = 0.01), and more discomfort (3.8 vs 1.4%; P = 0.02) compared with normothermic patients. Risk factors for PH included preoperative temperature < 36°C, surgery duration > 60 min, ambient operating room temperature < 23.0°C, and several "high-risk" surgeries. Guidelines were developed based on these risk factors and customized according to clinical and workflow considerations.*

Conclusions *Perioperative hypothermia was a common problem in our pediatric population and was associated with significant adverse outcomes. Guidelines developed based on risk factors identified in the local context can facilitate workflow and implementation within the institution.*

Résumé

Objectif *L'hypothermie périopératoire (HP) est définie par une température corporelle centrale < 36 °C pendant la période périopératoire. L'incidence de l'HP chez les enfants n'est pas connue avec précision en raison des variations dans le suivi de la température périopératoire et des mesures de contrôle. Nous avons cherché à (1) déterminer l'incidence de l'HP pédiatrique, (2) évaluer ses effets préjudiciables et (3) identifier les facteurs de risque dans notre population pédiatrique afin d'élaborer des lignes directrices locales pour la prévention de l'HP.*

Méthodes *Nous avons mené une étude de cohorte observationnelle prospective dans un seul hôpital de niveau tertiaire (KK Women's and Children's Hospital, Singapour) de juin 2017 à décembre 2017 sur la base des*

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pratiques existantes dans l'établissement. Nous avons recruté des patients âgés de 16 ans ou moins subissant une intervention chirurgicale et nous avons déterminé l'incidence et les effets secondaires de l'hypothermie. Nous avons identifié les facteurs de risque de l'HP en utilisant des analyses de régression logistique monofactorielle et multifactorielle qui nous ont servi à élaborer ces lignes directrices locales.

Résultats *Parmi les 1 766 cas de patients analysés, 213 (12,1 %; intervalle de confiance à 95 % : 10,6 à 13,7) ont développé une HP. Parmi ceux-ci, seulement 4,5 % auraient été détectés par une mesure unique dans l'unité de soins post anesthésie (salle de réveil). Les événements indésirables ont inclus un séjour plus long en salle de réveil (47 contre 39 minutes; $P < 0,01$), une plus grande incidence de tremblements (7,1 % contre 2,6 %; $P = 0,01$) et plus d'inconfort (3,8 % contre 1,4 %; $P = 0,02$), comparativement aux patients normothermiques. Les facteurs de risque d'HP étaient, notamment, une température préopératoire < 36 °C, la durée de la chirurgie > 60 min, la température de la salle d'opération $< 23,0$°C et plusieurs chirurgies à « risque élevé ». Des lignes directrices ont été élaborées à partir de ces facteurs de risque et adaptées en tenant compte de considérations cliniques et des flux de travail.*

Conclusions *L'hypothermie périopératoire était un problème fréquent dans notre population pédiatrique et a été associée à des effets secondaires significatifs. Des lignes directrices élaborées en fonction de facteurs de risque dans un contexte local peuvent faciliter le flux de travail et leur mise en œuvre au sein d'un établissement.*

Keywords anesthesia · hypothermia · pediatric

Perioperative hypothermia (PH) is defined as the occurrence of core body temperature (CT) < 36°C in the perioperative period. Measures to prevent PH have been shown to improve patient experience and clinical outcomes and lower healthcare costs in adults.[1–4] The reported incidence of pediatric PH ranges from 20 to 86% in both adult and pediatric literature.[5–7] A diagnosis of PH depends on how and when the patient's CT is taken.[8] Perioperative hypothermia in children may be underdiagnosed because it is difficult to find a CT sensor that is well tolerated in the uncooperative child. While intraoperative hypothermia is more frequent, most pediatric studies report only the incidence of postoperative hypothermia.[9] Single-point prevalence of postoperative hypothermia measured during recovery may underestimate the real incidence and duration of PH.[10] A pediatric study reported 52% of patients developed hypothermia intraoperatively.[7]

Perioperative hypothermia in adults can lead to systemic effects resulting in cardiac events, coagulopathies, and wound infection. Similar effects may plausibly occur in pediatric patients, as hypothermia-induced thermogenesis increases metabolic rate, plasma catecholamine levels, and oxygen consumption, which may lead to acidosis and hypoxia.[11] Infants are at higher risk of PH because of reduced shivering thermogenesis, increased heat loss, thin skin, and little subcutaneous fat.[12–15] They are equally, if not more, susceptible to developing PH and experiencing its adverse effects.[9,11] Yet pediatric perioperative temperature management guidelines are often extrapolated from adult data. Resource-intensive recommendations may be costly, complicate workflow, and limit compliance. Against a background of existing but nonuniform temperature management practices, we sought to prospectively develop local guidelines that are relevant and easy to implement, to limit PH in our pediatric unit.

The primary aim of the study was to determine the incidence of pediatric PH in our hospital. The secondary aims were to determine adverse outcomes of PH and risk factors for PH to develop local guidelines for perioperative temperature management.

Materials and methods

Study design

This prospective observational cohort study was conducted at KK Women's and Children's Hospital, Singapore from June 2017 to December 2017. We recruited children aged ≤ 16 yr undergoing general anesthesia (GA) by consecutive sampling from daily elective and emergency operating lists. Patients with impaired temperature control (i.e., severe head injury, febrile illness), patients undergoing surgeries solely under local anesthesia, and critically ill patients directly admitted to the intensive care unit (ICU) postoperatively were excluded. This observational study was based on existing institutional practices regarding temperature management, which included continuous monitoring and active warming for children deemed at risk of hypothermia, as well as higher operating theater ambient temperatures of at least 24°C for infants less than one year of age. While zero heat flux (ZHF) sensors were made freely available for the duration of the study, the decision to monitor temperature intraoperatively, the choice of temperature measurement device, and the use of warming devices pre- or intraoperatively were left to the discretion of the attending anesthesiologists.

For the purpose of this study, we defined PH as any episode of CT < 36°C from anesthesia induction in the intraoperative period until discharge from the postanesthesia care unit (PACU). Postoperative hypothermia was defined as a CT < 36°C measured within 15 min of arrival until discharge from PACU.

Core body temperature was measured preoperatively and postoperatively in all patients with tympanic or temporal artery infrared (TM/TA-IR)[16] thermo-scanners. When continuous temperature monitoring was used, intraoperative CT readings were monitored using either nasopharyngeal, esophageal, rectal, axillary, or ZHF (3M™ SpotOn™, 3M Healthcare, St. Paul, MN, USA) thermometry. Intraoperative temperature readings were recorded at five predetermined time points: immediately following anesthesia induction (first temperature recorded by the intraoperative thermometry employed), when the CT first dropped to < 36°C (if any), at the highest CT and lowest CT, and during recovery from anesthesia (first CT within 15 min upon arrival in PACU). If the CT dropped < 36°C, the duration of PH was recorded.

Patient demographic, surgical, and anesthetic details were prospectively recorded on a purpose-designed data collection form by the anesthesia team in charge. Surgeries were categorized as major (open body cavity, e.g., thoracotomy, laparotomy), minor (short, not breaching the body cavity), or intermediate (the rest). Temperature control measures for each patient were recorded. These included passive warming methods such as cotton blankets and plastic covers, and/or active warming methods including forced air warming (FAW), warm rapid fluid infuser (HOTLINE®, ICU Medical, Inc., San Clemente, CA, USA), heated humidifier, radiant warmer, circulating water, and heated coil mattress.

Additionally, any occurrence of shivering or discomfort, cardiac arrhythmias, or significant blood loss was documented. Long-term adverse outcomes such as length of PACU stay, hospital stay, and surgical site infection documented within three months from time of surgery were also collected.

Postanesthesia shivering (PAS) was defined by the presence and intensity of PAS recorded by the PACU nurse using the scale devised by Crossley and Mahajan:[17] grade 0—no shivering; grade 1—no visible muscle activity, but one or more of the following: piloerection, peripheral vasoconstriction, or peripheral cyanosis (other causes excluded); grade 2—muscular activity in only one muscle group; grade 3—moderate muscular activity in more than one muscle group; and grade 4—violent muscle activity that involves the entire body. Postanesthesia care unit discomfort was defined as any reports of discomfort due to cold, with or without shivering, as documented by the PACU nurse. Significant intraoperative blood loss was defined as blood loss > 10 $mL \cdot kg^{-1}$ body weight.

Data were entered into an anonymized indexed database by an independent research coordinator.

Patient and perioperative risk factors predisposing to PH were identified and clinical practice guidelines developed predicated on data analysis, clinical considerations, and feasibility.

The study was approved by SingHealth Central Institutional Review Board, and consent waiver was granted (IRB reference number: 2017/2298, approved 23 May 2017). The study was funded by a grant from the SingHealth Foundation and registered on ClinicalTrials.gov (NCT03770364).

Statistical analysis

Perioperative hypothermia status was coded as a binary outcome: "No" if no occurrence of PH and "Yes" for any occurrence of CT < 36°C from anesthesia induction until discharge from the PACU. Continuous variables are summarized as mean with standard deviation (SD) or median with interquartile range [IQR] as appropriate, and categorical variables as frequency with %. Group differences were assessed using a two-sample *t* test or Mann–Whitney U test as appropriate for continuous variables and a Fisher's exact test for categorical variables. The proportion of PH is reported as a percentage with Clopper–Pearson exact 95% confidence interval (CI). Age (< 1, 1 to < 5, and 5 to ≤ 16 yr) was analyzed as a categorical variable. Risk factors informing guideline development were systematically identified via a process incorporating both statistical significance and clinical relevance. Initially, univariate logistic regression analysis was used to identify variables associated with PH at $P < 0.15$. This subset comprised the candidate predictors obtained using both the stepwise and backward elimination multiple logistic regression analyses, with the stepwise algorithm producing the more clinically tenable model. Selected variables were evaluated and adopted into the proposed guidelines, ultimately contingent upon considerations of relevance and veracity of effect as a protective or a risk factor. Logistic regression results were summarized using odds ratios (ORs) with 95% CIs.

Multicollinearity among surgery duration, high-risk surgeries, and continuous temperature monitoring were checked via correlations and the variance inflation factor. All tests were two sided. Statistical significance was set at $P < 0.05$. SAS v9.4 (SAS/STAT 15.1; SAS Institute, Inc., Cary, NC, USA) software was used for analysis. In consideration of type I error inflation resulting from the multiple hypothesis tests associated with the six selected

model variables (six rejected hypotheses), the positive false discovery rate (pFDR) approach[18] was invoked. The *q* values obtained using the pFDR approach are directly related to the *P* values and allow control of the expected proportion of "false discoveries," i.e., incorrectly rejected null hypotheses among multiple hypotheses tested at a specified level. The "Exact Binomial" option was used in the SAS PROC FREQ procedure. The *q* values were computed using SAS PROC MULTTEST.

Accuracy of the Zero-Heat-Flux thermometer (SpotOn) in patients who had both SpotOn and TM/TA-IR temperature measurements in the PACU was assessed using Bland–Altman plots and the intraclass correlation coefficient (Fig. 1, Electronic Supplementary Figure, and eTable).

A pilot study of nearly 800 pediatric patients carried out from October to December 2016 indicated a PH rate of 12.5%. To estimate a low PH rate of 12% and achieve a 95% CI width of 0.035 (i.e., incidence of PH between 10.4% and 13.9%), 1,326 patients were required. To account for 20% missing data or absurd data, we aimed to recruit 1,700 patients. A rule of thumb is that a multivariable logistic regression model should have at least 20 events per predictor variable.[19] Therefore, because we had ten clinically meaningful variables to account for in the prognostic model, we needed to target at least 20 x 10 = 200 events in the cohort. Based on the following assumptions, our study of 1,700 patients was adequately powered at ≥ 80% to detect 12% PH with an OR of 1.84 (or reciprocal = 0.65) at an alpha of 5%. PASS© software (NCSS, LLC; Kaysville, UT, USA) was used to calculate the sample size.

Results

A total of 2,320 patients were enrolled and 554 were excluded for reasons detailed in the CONSORT diagram (Fig. 2). Data from 1,766 patients were analyzed. The overall incidence of PH detected during the perioperative period was 12.1% (95% CI, 10.6 to 13.7), while the single-point incidence of postoperative hypothermia in the PACU was 4.5% (95% CI, 3.6 to 5.5). Of the included patients, 1,421/1,766 (80.5%) received intraoperative temperature monitoring, 1,342/1,421 (94.4%) of whom used SpotOn sensors, 10/1,421 (0.7%) esophageal methods, 33/1,421 (2.3%) naso-oropharyngeal methods, 22/1,421 (1.6%) rectal methods, 11/1,421 (0.8%) skin methods, and 3/1,421 (0.2%) intermittent tympanic methods. Temperature distribution of the five recorded time points from continuous temperature monitoring is shown in ESM eFig. 1. Duration of the PH episode was recorded in 78.4% (181/213) of all patients experiencing PH. The median [IQR] duration of hypothermia was 15 [0–30] min, and the median [IQR] % of case spent hypothermic was 11.32 [0–21.98]%.

The mean (SD) age of the children was 7.1 (4.6) yr, with higher proportions of male and Chinese ethnicity. Table 1 summarizes the demographic and clinical characteristics and the management practice by PH status.

Table 2 shows the effect of PH on immediate, short-term, and long-term clinical outcomes. Patients who developed PH had a statistically significantly higher incidence of shivering (7.1% *vs* 2.6%; $P = 0.01$) and discomfort (3.8% *vs* 1.4%; $P = 0.02$), a longer PACU stay (46.5 *vs* 39.0 min; $P < 0.01$), and greater intraoperative

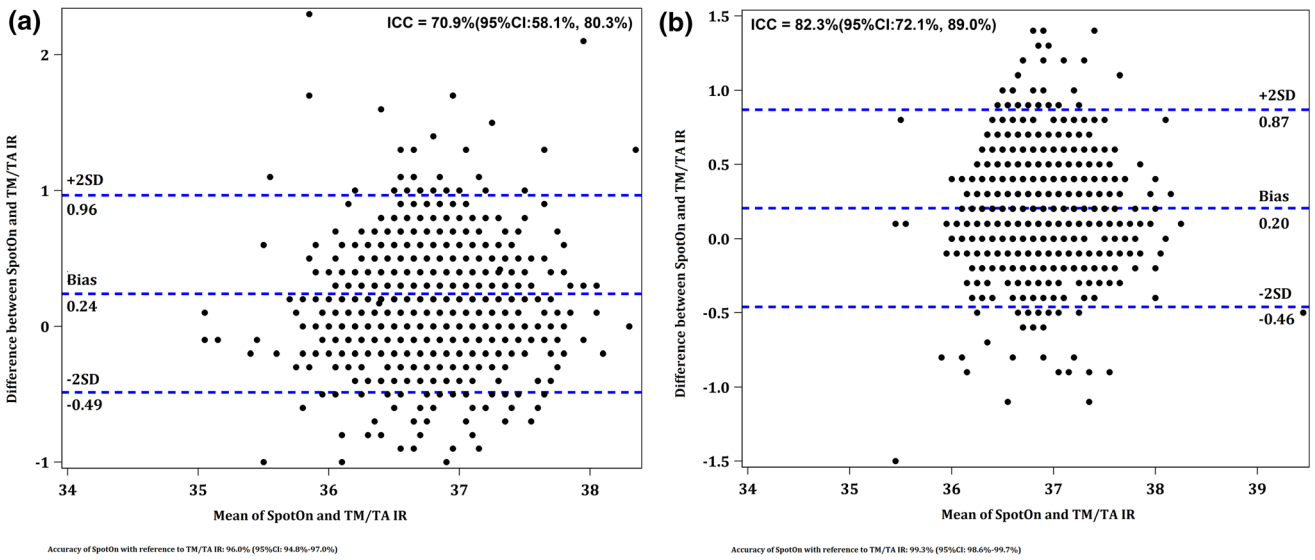

Fig. 1 Bland–Altman plot showing agreement between Zero-Heat-Flux thermometer (SpotOn) and TM/TA-IR temperature measurements at *a*) postanesthesia care unit arrival and *b*) postanesthesia care unit discharge.

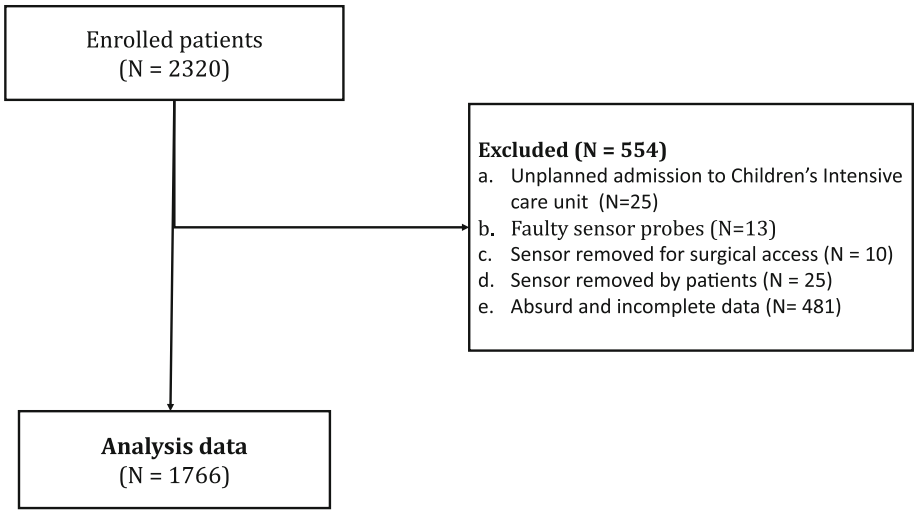

Fig. 2 Consort diagram of patient's recruitment

blood loss (> 10 mL·kg^{-1}) than normothermic patients did (1.0% *vs* 0.1%; $P = 0.04$).

Table 3 summarizes results of statistical analyses identifying perioperative factors associated with PH. Table 4 summarizes the multiple logistic regression analysis that includes all risk factors selected by the stepwise selection algorithm with the exception of sex. Among the six variables selected, the highest q value was 0.04, which means that the expected number of "false discoveries" (false positives) among the six predictors (rejected null hypotheses) in our guidelines model is $0.04 \times 6 = 0.024$. A statistical basis for excluding sex from the guidelines may be found in the Akaike's Information Criterion values of Tables 3 and 4 that show an information loss of only 4 (1218 – 1214 = 4) points. Area under the receiver operating characteristic (AUROC) curve after adding sex was not significantly improved ($P = 0.13$).

Determination of patient and ambient temperature thresholds for intervention in our guidelines

Among the 17 patients with preoperative temperatures < 36°C, 5 (29%) experienced PH, and among the 1,595 patients with temperatures ≥ 36.2°C, 180 (11.3%) experienced PH. Preoperative temperature cut-offs were chosen to strike a balance between negative predictive values (NPVs) at upper temperatures and positive predictive values (PPVs) at the lower temperatures—with a midrange interval of uncertainty. For preoperative patients with temperatures < 36°C, 5/17 (29%) experienced PH, corresponding to a PPV of 29%; among patients with temperatures ≥ 36.2°C, 1,415/1,595 (88.7%) didn't experience PH, corresponding to a NPV of 88.7%. Of the 154 patients in the midrange (≥ 36°C to ≤ 36.2°C), 28 (18%) experienced PH and 126 (82%) didn't. Therefore, the low-temperature threshold for high-risk of PH at < 36°C and the high-temperature threshold for low risk of PH at ≥ 36.2°C was set with a midrange uncertainty interval of 36°C to < 36.2°C.

The ambient operating room temperature cut-off of < 23°C versus ≥ 23°C was based on receiver operating characteristic curve analysis and the Youden J-statistic to identify a statistically optimal cut-off. Based on the risk factors identified in this study, we developed clinical guidelines for the prevention of PH.

Clinical guideline development

Guideline components are shown in Fig. 3.

A. Measuring preoperative baseline temperature with a view for prewarming

Mandatory measurement of patient preoperative baseline temperature identified those patients who would benefit from prewarming. We found that patients with baseline temperatures < 36.2°C had a significantly higher risk of PH ($P < 0.01$). Prior to guidelines, only 7.5% patients received prewarming based on the preference of the anesthesiologists, mostly in the form of cotton blankets (5.4%); only 0.8% received active FAW and 0.4% received prewarming from a radiant warmer. Consequently, prewarming with FAW was not associated with a reduced risk of PH ($P = 0.26$). Moreover, because FAW units are in limited supply, the difficulty of applying FAW in young awake children, and the potential danger of thermal injury, we recommend using FAW only for patients with a baseline temperature < 36°C and in the presence of a caregiver in the induction room.

Table 1 Demographic and clinical characteristics based on perioperative hypothermia status

Characteristic	Perioperative hypothermia		*P* value
	No *N* = 1,553	Yes *N* = 213	
Age (yr), *n*/total *N* (%)			0.64[a]
< 1	161/1,553 (10%)	20/213 (9%)	
1–< 5	418/1,553 (27%)	52/213 (24%)	
≥ 5	974/1,553 (63%)	141/213 (66%)	
Weight (kg), median [IQR]	22.0 [14.8–38.8]	25.2 [16.0–44.8]	**0.02**[c]
Height (m), median [IQR]	1.2 [1.0–1.4]	1.3 [1.1–1.5]	**< 0.01**[c]
BMI ($kg \cdot m^{-2}$), median [IQR]	16.5 [14.6–20.1]	17.4 [14.7–19.8]	0.57
Missing	636	124	
Sex, *n* (%)			**0.004**[a]
Female	464/1,553 (30%)	85/213 (40%)	
Male	1,089/1,553 (70%)	128/213 (60%)	
Race, *n*/total *N* (%)			0.45[a]
Chinese	811/1,553 (52%)	123/213 (58%)	
Indian	166/1,553 (11%)	22/213 (10%)	
Malay	393/1,553 (25%)	49/213 (23%)	
Others	182/1,553 (12%)	19/213 (9%)	
ASA, *n*/total *N* (%)			0.35[a]
I	983/1,553 (64%)	131/213 (62%)	
II	483/1,553 (32%)	66/213 (31%)	
III or higher	68/1,553 (4%)	14/213 (7%)	
Comorbidities, *n*/total *N* (%)			
Neurologic	56/1,553 (4%)	14/213 (7%)	0.06[a]
Endocrine	66/1,553 (4%)	6/213 (3%)	0.46[a]
Obese	28/1,553 (2%)	2/213 (1%)	0.57[a]
Syndrome	30/1,553 (2%)	5/213 (2%)	0.60[a]
Type of surgery, *n*/total *N* (%)			**0.05**[a]
Elective	1,378/1,553 (90%)	199/213 (94%)	
Emergency	153/1,553 (10%)	12/213 (6%)	
Surgery duration, mean (SD)	50.8 (57.3)	62.4 (61.7)	**0.01**[b]
Duration of surgery > 60 min, *n*/total *N* (%)	387/1,553 (25%)	76/213 (36%)	**0.001**[a]
Anesthesia duration, mean (SD)	78.0 (72.3)	93.9 (73.3)	**0.003**[b]
Nature of surgery, *n*/total *N* (%)			**0.01**[a]
Intermediate	418/1,553 (27%)	64/213 (31%)	
Major	42/1,553 (3%)	13/213 (6%)	
Minor	1,083/1,553 (70%)	132/213 (63%)	
Preoperative measures			
Preoperative baseline temperature (°C), mean (SD)	36.8 (0.4)	36.7 (0.5)	**0.001**[b]
Preoperative warming, *n*/total *N* (%)	110/1,553 (7%)	20/213 (9%)	0.26[c]
Intraoperative measures			
Continuous temp monitoring, *n*/total *N* (%)	1,232/1,553 (80%)	189/213 (89%)	**0.001**[a]
First temperature recorded (°C)			
Mean (SD)	36.9 (0.4)	36.3 (0.5)	**< 0.001**[b]
Median (range)	36.8 (35.7–39.0)	36.3 (34.7–37.8)	**< 0.001**[c]
Lowest temperature recorded (°C)			
Mean (SD)	36.6 (0.4)	35.8 (0.3)	**< 0.001**[b]
Median (range)	36.6 (34.4–39.0)	35.8 (34.7–37.0)	**< 0.001**[c]

Table 1 continued

Characteristic	Perioperative hypothermia		*P* value
	No *N* = 1,553	Yes *N* = 213	
Ambient operating room temperature (°C), mean (SD)	24.0 (1.5)	23.4 (1.7)	**< 0.001**[b]
Intraoperative FAW with disposable blanket, *n*/total *N* (%)	563/1,553 (38%)	96/213 (46%)	**0.01**[a]
Duration between induction to lowest intraoperative temperature (min), median [IQR]	25.0 [10.0–40.0]	35.0 [20.0–51.0]	**< 0.001**[c]
Duration between induction to highest intraoperative temperature (min), median [IQR]	20.0 [7.0–63.0]	25.0 [10.0–80.0]	**0.24**[c]

P values < 0.05 are in bold

[a] Fisher's exact test for categorical data

[b] Two-sample Student's *t* test for continuous normal data

[c] Mann–Whitney U test for continuous non-normal data

ASA = American Society of Anesthesiologists Physical Status score; BMI = body mass index; FAW = forced air warming; IQR = interquartile range; SD = standard deviation

Table 2 Clinical adverse outcomes in hypothermic and normothermic groups

Variable	Perioperative hypothermia		*P* value
	No *N* = 1,553	Yes *N* = 213	
Shivering grade,[1] *n*/total *N* (%)			**0.005**[a]
0	1,511/1,553 (97.4%)	197/213 (92.9%)	
1	22/1,553 (1.5%)	9/213 (4.3%)	
2	12/1,553 (0.8%)	4/213 (1.9%)	
3	6/1,553 (0.5%)	2/213 (0.9%)	
PACU discomfort[2], *n*/total *N* (%)	22/1,553 (1.5%)	8/213 (3.8%)	**0.02**[a]
Short-term adverse outcomes, *n*/total *N* (%)			
Intraoperative blood loss > 10 $mL \cdot kg^{-1}$	1/1,553 (0.1%)	2/213 (0.9%)	**0.04**[a]
Arrhythmia	-	-	-
Long-term adverse outcomes			
Length of PACU stay[3] (min), median [IQR]	39 [25–55]	47 [35–62]	**< 0.001**[b]
Length of hospital stay (hr), median [IQR]	24.5 [15.0–34.6]	25.3 [8.5–44.7]	0.94[b]
Surgical site infection, *n*/total *N* (%)	1/1,553 (0.1%)	0/213 (0%)	1.00[a]

P values < 0.05 are in bold

[a] Fisher's exact test for categorical data

[b] Two-sample Student's *t* test for continuous normal data

[c] Mann–Whitney U test for continuous non-normal data

[1] PAS was defined by presence and intensity of PAS recorded by the PACU nurse using the scale devised by Crossley and Mahajan:[8] Grade 0—no shivering; Grade 1—no visible muscle activity, but one or more of the following: piloerection, peripheral vasoconstriction, or peripheral cyanosis (other causes excluded); Grade2—muscular activity in only one muscle group; Grade 3—moderate muscular activity in more than one muscle group

[2] One missing data value in each category

[3] Lack of shivering and PACU discomfort are both criteria for PACU discharge—hence affecting length of PACU stay

IQR = interquartile range; PACU = postanesthesia care unit; PAS = postanesthesia shivering

Table 3 Univariate and stepwise multiple logistic regression analyses to identify perioperative hypothermia risk factors

Characteristic	Univariate analysis		Stepwise multiple regression analysis[a]	
	Unadjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value (*q* value)[b]
Age (yr) (Ref ≤ 1)		0.61*		
1–5	1.00 (0.58 to 1.73)	1.00		
> 5	1.17 (0.71 to 1.92)	0.54		
Weight (kg)	1.01 (1.00 to 1.02)	**0.04**		
Height (m)	2.55 (1.31 to 4.94)	**0.006**		
BMI ($kg \cdot m^{-2}$)	1.00 (0.99 to 1.01)	0.85		
Female sex	1.56 (1.16 to 2.09)	**0.003**	1.49 (1.10 to 2.02)	**0.01** (0.015)
Ethnicity (Ref = Chinese)		0.43*		
Indian	0.87 (0.54 to 1.42)	0.58		
Malay	0.82 (0.58 to 1.17)	0.28		
Others	0.69 (0.41 to 1.15)	0.15		
ASA (Ref = I)		0.37+		
II	1.03 (0.75 to 1.41)	0.88		
III or higher	1.55 (0.84 to 2.83)	0.16		
Comorbidities				
Neurologic (Ref = No)	1.87 (1.03 to 3.43)	**0.04**		
Endocrine (Ref = No)	0.65 (0.28 to 1.52)	0.32		
Obese (Ref = No)	0.52 (0.12 to 2.18)	0.37		
Syndrome (Ref = No)	1.22 (0.47 to 3.17)	0.69		
Nature of surgery (Ref = Minor)		**0.01***		
Intermediate	1.26 (0.91 to 1.73)	0.16		
Major	2.54 (1.33 to 4.85)	**0.005**		
Emergency surgery (Ref = No)	0.54 (0.30 to 1.00)	**0.05**		
Surgery duration > 60 min	1.00 (1.001 to 1.01)	**0.01**	1.51 (1.10 to 2.07)	**0.01** (0.015)
High-risk surgery (Ref = No)	2.69 (1.91 to 3.79)	**< 0.001**	2.24 (1.56. 3.22)	**< 0.001** (< 0.006)
Preoperative temperature (Ref > 36.2°C)		**< 0.01***		**0.04+** (0.04)
< 36.0°C	3.28 (1.14 to 9.41)	**0.03**	2.99 (0.90 to 9.94)	0.07
36.0 to ≤ 36.2°C	1.75 (1.13 to 2.71)	**0.01**	1.59 (0.99 to 2.55)	0.05
Continuous temp monitoring (Ref = No)	2.03 (1.31 to 3.16)	**0.002**	1.63 (1.02 to 2.59)	**0.04** (0.04)
Ambient operating room temp ≥ 23°C (Ref < 23°C)	0.57 (0.41 to 0.78)	**0.001**	0.64 (0.46 to 0.89)	**0.01** (0.015)
Intraoperative forced air warming with disposable blanket (Ref = No)	1.41 (1.08 to 1.93)	**0.01**		
AIC			1,214	

P values < 0.05 are in bold

[a] Stepwise selection significance levels to enter and stay were both 0.15

[b] The pFDR was calculated for the six selected model variables (corresponding to six rejected hypotheses). The *q* value associated with each *P* value is the expected proportion of false positives consistent with that *P* value. Among the six variables selected the highest q value is 0.04, which means that the expected number of false positives among the six predictors in the guidelines model is 0.04 × 6 = 0.024.

* Omnibus *P* value.

ASA = American Society of Anaesthesiologists Physical Status score; AIC = Akaike's information criterion; BMI = body mass index; pFDR = positive false discovery rate

Table 4 Multiple logistic regression analyses incorporating selected risk factors for perioperative hypothermia (sex excluded)

Characteristic	Adjusted OR (95% CI)	*P* value
Surgery duration > 60 min (Ref ≤ 60min)	1.52 (1.11 to 2.09)	**0.01**
High-risk surgery (Ref = No)	2.33 (1.63 to 3.33)	**< 0.001**
Preoperative temperature (Ref > 36.2°C)		**0.04**[*]
< 36.0°C	2.94 (0.89 to 9.75)	0.08
36.0 to ≤ 36.2°C	1.57 (0.98 to 2.51)	0.06
Continuous temp monitoring (Ref = No)	1.64 (1.03 to 2.61)	**0.04**
Ambient operating room temp ≥ 23°C (Ref < 23°C)	0.63 (0.45 to 0.88)	**0.01**
AIC	1,218	

P values < 0.05 are in bold. No significant interaction (*P* = 0.66) was observed between high-risk surgeries and surgery duration in this multivariable model when interaction term was included. This suggested that high-risk surgeries and surgery durations were independent risk factors

[*] Global *P* value

AIC = Akaike's Information Criterion

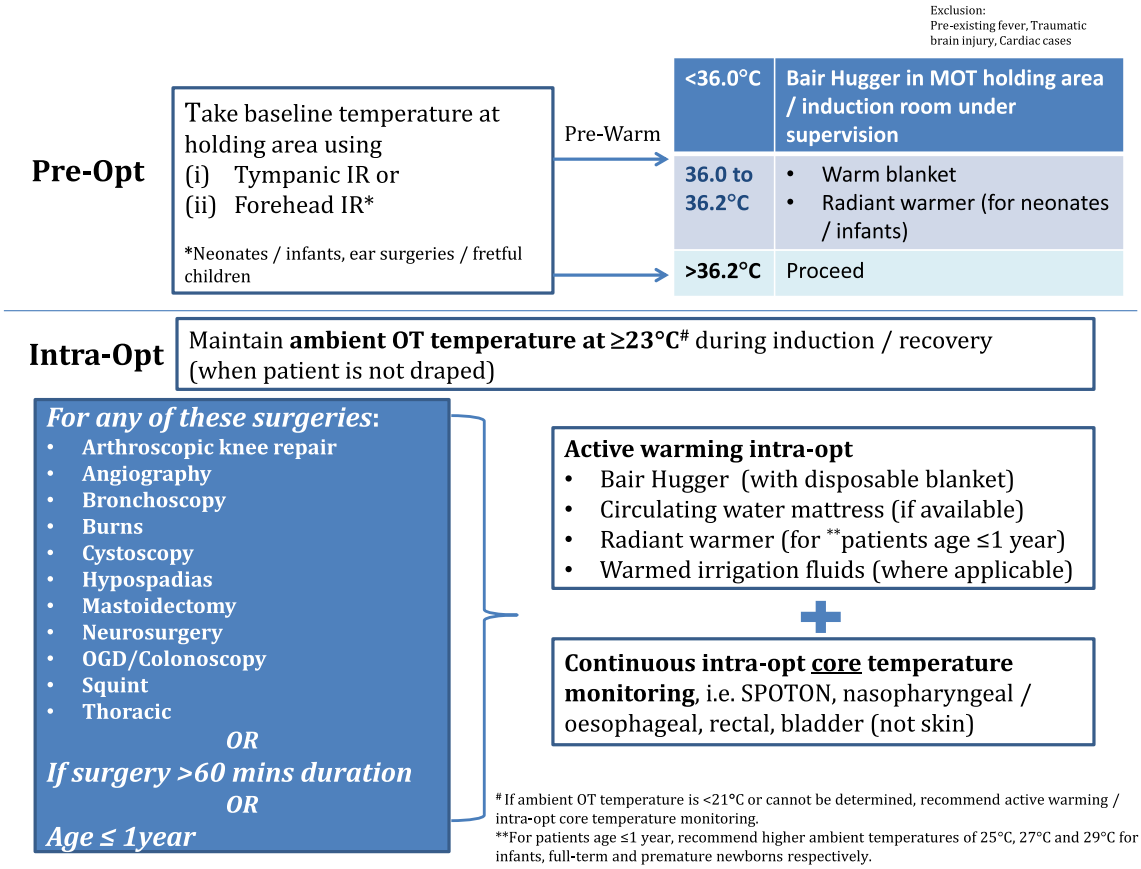

Fig. 3 KK pediatric anesthesia guidelines to prevent perioperative hypothermia in children

B. Maintain ambient operating room temperature ≥ 23°C during anesthesia induction and recovery

We chose 23°C as the ambient operating room temperature cut-off as a balance between statistical optimality and clinical feasibility. At the Youden index ambient operating room temperature cut-off of 23.9°C, the PPV was 90.9% (95% CI, 89.4 to 92.1) and the NPV was 15.9% (95% CI, 14.2 to 17.8). Area under the receiver operating characteristic analysis showed no significant differences at 23.0°C, 23.5°C, and 24°C with respective AUROCs of 0.55 (95% CI, 0.52 to 0.59), 0.57 (95% CI, 0.53 to 0.60),

and 0.58 (95% CI, 0.54 to 0.61). This suggests the operating room temperature should be maintained between 23°C and 24°C during induction and recovery when the patient is not draped. If the operating room is colder than 21°C at patient arrival, active warming should be considered with continuous temperature monitoring. Mean (SD) ambient operating room temperature of patients experiencing hypothermia was 23.4 (1.7)°C. At 23.0 °C, the PPV was 89.4% (95% CI, 88.5 to 90.3) and the and NPV was 17.3% (95% CI, 14.3 to 20.7), with little variation over the 23.0–23.9°C temperature range. Therefore, we recommend that operating room ambient temperature be maintained above 23.0°C to balance staff comfort with prevention of patient PH.

C. Identification of high-risk surgeries

Several types of surgeries were found to be associated with ≥ 20% risk of PH. These were angiography, arthroscopic knee repair, anterior cruciate ligament (ACL) reconstruction, bronchoscopy, burn surgery, cystoscopy, hypospadias, mastoidectomy, neurosurgery, thoracic, squint surgery, esophagoduodenoscopy, and colonoscopy, and were designated high-risk surgeries (ESM eFig 2). No significant interaction ($P = 0.66$) was observed between high-risk surgeries and surgery duration in this multivariable model when the interaction term was included. This suggested that high-risk surgeries and surgery durations were independent risk factors.

D. Surgeries > 60 min duration put patients at risk of pH

For patients receiving continuous CT monitoring, 20.0% needed additional interventions, such as adjusting the temperature settings of warming devices and ambient operating room temperature. These occurred in 53% of patients undergoing surgery for > 60 min, and were mostly related to the use of FAW.

The incidence of intraoperative iatrogenic hyperthermia was 1.8%. Of 25 patients who became hyperthermic (> 38°C) during surgery, 22 (88%) had received FAW. The mean anesthesia duration in these patients was 84 min. Continuous monitoring enabled interventions, e.g., stopping/decreasing FAW settings in 17 patients, such that only four remained hyperthermic on PACU arrival. Hence, continuous temperature monitoring was recommended in surgeries > 60 min, especially when active warming is used, to prevent iatrogenic hyperthermia.

E. Age

In our institution, it is already routine practice that all neonates and infants receive active warming and continuous intraoperative temperature monitoring, even though this is not a formal clinical guideline. Hence, it is not surprising that this age group did not emerge as risk factor in our statistical model. Nevertheless, in our clinical guidelines, we recommend that children younger than one year receive continuous monitoring and active warming; we also recommend higher ambient operating room temperatures of 25.0°C for infants, 27.0°C for full-term newborns, and 29.0°C for premature newborns.[20]

Guidelines resulting from our analysis and rationale are presented in Fig. 3 and apply to pediatric patients undergoing GA—except for those with pre-existing fever, those with traumatic brain injury, or those undergoing cardiopulmonary bypass surgeries.

Preoperatively, baseline temperatures should be taken in all patients. Those with a temperature of 36°C to ≤ 36.2°C should receive a warm cotton blanket and those with a temperature of < 36°C should receive FAW. Surgery should proceed only if the baseline temperature is > 36.2°C. The ambient operating room temperature should be set as ≥ 23°C during induction or recovery of anesthesia.

Patients undergoing the high-risk surgeries identified above or surgery expected to last > 60 min[21,22] must undergo active warming and continuous CT monitoring after GA induction. In surgeries with identifiable mechanisms of heat loss (e.g., cold irrigation fluids causing heat loss in cystoscopy and arthroscopy cases), active logistic measures were taken to prevent PH such as warming irrigation fluids.

Discussion

The reported incidence of hypothermia in pediatric surgical patients is wide-ranging and depends on how and when temperature is measured in the perioperative period.[9] Failing to measure intraoperative hypothermia may result in a falsely low incidence of perceived PH. This is shown in our study where the incidence of postoperative hypothermia (4.5%), taken at one postoperative time point, is much lower than the incidence of PH (12.1%) when temperature was monitored throughout the perioperative period, as 11% had intraoperative hypothermia. To avoid false assurance of the quality of care, we developed our guidelines based on PH as our primary outcome.

Our incidence of PH is much lower than that reported by Pearce *et al.,*[7] who found that 52% (278/530) of the pediatric population had intraoperative hypothermia (defined as < 36°C for more than five minutes). Nevertheless, a significant limitation of Pearce's study was that in approximately 30% of patients with intraoperative temperatures < 36°C, the temperature was

recorded by skin monitoring, a modality which consistently underestimates core temperatures. As such, the incidence of PH may have been overestimated. The reported incidence of PH varies with the method of detection. We used SpotOn monitoring, a reliable method of CT monitoring,[23] for the vast majority of our patients. Thus, our methodology may have detected PH more accurately.

Clinical implications of perioperative hypothermia in children

There is a paucity of evidence regarding adverse clinical outcomes of hypothermia in the pediatric population.[9] Expert opinion had established that hypothermia contributes to several surgical complications including blood loss, surgical site infection, and delayed postanesthesia recovery.[24] Similar to a study on 3,132 patients undergoing GA,[25] our study found that hypothermic patients had a longer PACU stay, but no difference in surgical site infection (Table 2). Nevertheless, a difference in PACU stay of 7.5 min may be of limited clinical significance, as PACU stay may be influenced by various other factors other than PH. We found a higher incidence of significant blood loss (> 10 mL·kg^{-1}) among hypothermic patients in our study, as was previously reported by Sun *et al.* in 58,814 patients.[26] Nevertheless, the number of patients with significant blood loss in our study is very small, which limits the interpretation of the clinical significance of our findings.

Guideline components

Although infants and children differ in thermoregulatory capabilities from adults, most reported adverse outcomes and published hypothermia guidelines are derived from adult data. A recent comprehensive review by Nemeth *et al.*[9] provided detailed management recommendations to limit hypothermia in children. Our study aims to show how selected practices may be employed efficaciously in at-risk populations within each institution, by the development of local guidelines.

Indications for active preoperative and intraoperative warming

Unlike the National Institute for Health and Care Excellence guidelines,[27] we do not recommend prewarming with FAW on all patients, but only patients who are hypothermic (TMIR/TA-IR < 36°C) preoperatively. As children have a smaller limb-to-torso/head ratio, core heat redistribution is lower. Perhaps due to our warm climate—the mean (SD) preoperative TM/TA-IR temperature was 36.8 (0.42)°C, and only 5.0% of patients had temperatures < 36.2°C at baseline. Thus, we do not think that it is necessary to prewarm every patient in our unit. Moreover, prewarming with FAW in awake young children who do not keep still is challenging and has potential risks of injury. Hence, we recommend prewarming with FAW only in patients with TMIR/TA-IR < 36°C preoperatively, aiming to simplify the logistics and reduce manpower and consumable costs.

Nevertheless, the well-documented practice of prewarming may still be relevant to prevent cooling before induction, especially in a unit situated in a cooler climate.[9]

The National Institute for Health and Care Excellence guidelines[27] recommends intraoperative FAW for all "at-risk" patients, or those having anesthesia for > 30 min. This recommendation holds true for our pediatric population, as we found that the mean time from induction of anesthesia to onset of hypothermia is approximately 36 min (Table 1). Nevertheless, we found no significant difference in PH incidence for surgeries with duration < 30 min compared with those between 30 to 60 min ($P = 0.13$). Thus, for reasons of simplicity, practicality and cost—reasons previously cited by others[28–30]—we decided to implement active warming for high-risk surgeries lasting 60 min or longer. We found a cut-off of 60 min to be more practical in ensuring compliance to workflow and cost-effectiveness.

Ambient operating room temperature

A warm ambient operating room temperature reduces the temperature gradient between the patient and the environment, thereby reducing the rate of core heat redistribution and heat loss via radiation. An increase of 1°C in the operating room temperature reduces heat loss by approximately 10%.[11] This is especially useful in a situation where preoperative warming of the active child is logistically challenging. Cassey *et al.* established significant thermal advantages in preoperative environmental warming in children when comparing an ambient operating room temperature of 26°C *vs* 21°C in a randomized trial.[31] Based on our results, we chose an ambient operating room temperature target of ≥ 23°C to minimize the ambient-body temperature gradient that contributes to heat loss after induction of GA. This ambient operating room temperature setting is only enforced when the child is undraped during induction and recovery to preserve comfort for the surgical team. With regards to concerns of high ambient operating room temperatures compromising infection control, unidirectional ventilation at a flow rate of 0.65–0.80 m·sec^{-1} should be maintained. The air exchange rate should be 25 times/hr for systems relying on recirculated air, and approximately 15 times the operating room

volume/hr for systems solely using outdoor air.[11] A relative air humidity of 40–60% is ensured in our operating complex.

High-risk surgeries

Patients undergoing major or intermediate surgeries are at risk of PH.[27] It is well known that neonates and infants are at high risk;[32] hence, extra care and continuous temperature monitoring are already routine for patients in this age group in our unit. Based on routine practice, we recommend that all patients aged one year or less should receive continuous monitoring and active warming, and higher ambient temperatures of 25°C for infants, 27°C for full-term newborns, and 29°C for premature newborns.[20]

In addition, we took a different approach and identified a list of surgeries where ≥ 20% of our patients developed PH (ESM eFig. 2). We deemed these surgeries "high risk" and our guidelines recommend that patients undergoing these surgeries receive both monitoring and active warming. Through this analysis, we identified several short surgeries lasting < 60 min, such as esophagoscopy/colonoscopy, bronchoscopy, and cystoscopy, which predispose patients to PH. We postulate the use of cold irrigation fluids and insufflation gases as the cause of hypothermia in cystoscopy/arthroscopy and endoscopy/bronchoscopy. Other likely causes of heat loss are excessive exposure due to surgical access (burns cases). Our univariate analysis (Table 3) found that taller children are at risk of hypothermia (unadjusted OR, 2.6; 95% CI, 1.3 to 5.0; $P < 0.01$). We postulate that core heat redistribution is more significant in larger/taller children, as older children have relatively larger and cooler extremities to which core heat can be redistributed, leading to a steeper phase 1 exponential drop in core temperature. Less attention paid to temperature control measures in older children may also be a contributory reason.

Interestingly, Pearce *et al.*[7] also found a lack of association of intraoperative hypothermia with weight (OR, 0.065), and a positive association of older age (mean [SD]: 7.2 [5.6] *vs* 6.4 [5.2] yr; OR, 0.064) with hypothermia. We concur with their postulation that this finding may simply reflect differences in types of procedures conducted in the various age groups (e.g., adolescents had longer orthopedic procedures such as spinal fusion), and that temperature was more carefully managed in younger patients than in older children in those settings. Likewise, in our study, some procedures associated with a higher risk of PH, e.g., ACL reconstruction and endoscopy, tended to be done in older children who may have received less attention to temperature control from clinicians.

This phenomenon does seem to reflect that hypothermia depends more on the actual warming strategy and less on patient factors, such as age, as postulated by Nemeth *et al.*[9]

Monitoring

Some guidelines recommend temperature monitoring in patients who have surgeries longer than 30 min,[31] whereas others recommend monitoring in most surgical patients.[33] The National Institute for Health and Care Excellence (NICE) guidelines recommend patient temperature be taken before induction of anesthesia and then every 30 min until the end of surgery.[27] Nevertheless, temperature sensors are expensive, so to maintain cost-effectiveness, we recommend taking the baseline TMIR/TA-IR temperature before GA induction and after surgery in the PACU for all patients. We only recommend continuous CT monitoring in "high-risk" surgeries and/or when surgery lasts > 60 min. Nevertheless, clinicians are encouraged to monitor CT more frequently at their discretion, even if the surgery lasts < 60 min.

In this study, 3M SpotOn[23] sensors were purchased with grant funds and made available at no cost. This was a strategic decision to facilitate a reliable and consistent mode of noninvasive continuous core monitoring—even in cases where nasopharyngeal/rectal temperature could not be used—to establish the baseline incidence of PH. SpotOn, a ZHF thermometry system, measures core temperature noninvasively. First described in the early 1970s,[34,35] ZHF thermometry measures tissue temperature approximately 1 to 2 cm below well-perfused skin surfaces, approximating the core temperature. The cutaneous sensor consists of two thermistors separated by an insulator and covered by a servo-controlled electric heater, creating an isothermal tunnel.[36]

Studies have validated SpotOn against the pulmonary artery,[36] nasopharyngeal,[37,38] distal esophageal,[39,40] and bladder[41] temperature sensors, which are considered the "gold standard." As invasive core thermometers are rarely tolerated by the awake child, SpotOn sensors provide a noninvasive alternative approach to measuring core temperature in the perioperative period. SpotOn has been shown to be as safe and accurate as esophageal probes for intraoperative monitoring in children.[23]

We emphasize that continuous intraoperative temperature monitoring is vital not only to detect hypothermia but also to detect and prevent iatrogenic hyperthermia, especially in surgeries exceeding 60 min. Our results suggest that, in addition to warming measures, intraoperative cooling measures are also important, and the decision whether to warm or to cool can only be guided by intraoperative temperature monitoring.

Limitations

First, due to the lack of automated electronic charting, temperature was not continuously captured in the anesthetic charting even when it was continuously monitored. This led to a significant number of cases being excluded because of incomplete data collection (see Fig. 2). As a result, a time-weighted average outcome could not be measured. Second, female sex as a risk factor in our study reflects an inherent sex selection bias owing to the large number of boys undergoing day-surgery circumcision lasting < 30 min (23.8% of all boys undergoing GA) who tend not to become hypothermic. Third, we excluded patients with impaired temperature control (such as those with severe head injury, febrile illness, or critical illness) as their temperature outcomes may have been confounded by factors other than the temperature control interventions. In the same way, major surgeries such as laparotomies and thoracotomies requiring ICU admission may be excluded, causing these potentially "high-risk" surgeries to be under-represented. This may have excluded patients who were most vulnerable to PH. Fourth, the number of patients with adverse events in our study was relatively small, which limits the clinical relevance of our findings. In addition, reports of shivering and complaints of discomfort may be less reliable in younger children, which may limit the interpretation of this outcome. The long-term clinical significance of these findings remains uncertain. Two compared with one patient in the hypothermic group had significant blood loss. Only one patient in the whole cohort developed surgical site infection. Due to the overall low complication rates, future larger studies powered for these outcomes will be needed. Fifth, although stepwise multiple regression is widely used as a variable selection technique for building predictive models, the inherent biases and limitations of the approach are well documented.[42] The principal drawbacks of stepwise multiple regression include potential bias in parameter estimation and possible inconsistencies among model selection algorithms. This is an inherent problem of multiple hypothesis testing and reliance on a single best model. We have attempted to ameliorate the biases and limitations of the approach, as well as type I errors due to multiple hypothesis tests by researching and selecting candidate predictors that are well established in the literature[6,7,12,22,32,43–45] as clinically relevant and statistically verified risk factors associated with PH, using both stepwise and backward variable selection approaches and by addressing the false positive rate due to multiple hypothesis tests by reporting the pFDR q value, and developing a predictive model with an eye toward balancing parsimony with clinical relevance supported by statistical significance. Finally, postoperative hypothermia was captured using TM/TA-IR in our study. This method may be inconsistent if the sensor fits poorly into the aural canal and underestimates the core temperature by measuring the skin temperature instead.[16] Though this may lead to a less consistent measurement of core temperature, it would likely be no less sensitive in picking up hypothermia and identifying at-risk groups.

Conclusions

Continuous monitoring of core temperature detects a higher incidence of hypothermia than a single measurement in the PACU does (12.1% compared with 4.5% in our unit). As such, PH is a more accurate reflection of incidence of hypothermia in the perioperative period than postoperative hypothermia is.

Perioperative hypothermia is common in children and is associated with adverse outcomes such as increased discomfort and increased length of stay in the PACU. The more concerning longer term adverse effects of hypothermia on coagulation, wound healing, surgical site infection, and hospital length of stay that have been documented in adults should be investigated in children.

We report an approach to developing site-specific guidelines on limiting PH in children. This approach is based on risk factors identified when routine temperature management practices are followed and access to a noninvasive thermography sensor is freely available. Of significance, we found older children undergoing short duration, peripheral procedures such as arthroscopic knee repair, bronchoscopy, cystoscopy, esophagoduodenoscopy, and colonoscopy may also develop PH.

Temperature monitoring and perioperative temperature management is not standardized between centers; therefore, the PH rates, risk factors, and high-risk procedures we report here might be institution specific. Nevertheless, our approach could be used to develop local guidelines to mitigate the incidence of PH in pediatric patients. Such customized guidelines may ensure better physician compliance and concentrate resources to at-risk groups.

Author contributions *Rehena Sultana* contributed to data analysis and writing and reviewing the manuscript. *John C. Allen* contributed to designing the trial and reviewing the manuscript. *Yew Nam Siow* contributed to designing the trial and data collection. *Choon Looi Bong* and *Shu Ying Lee* contributed to designing the trial, data collection, and writing and reviewing the manuscript.

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