Queen's UNIVERSITY

DEPARTMENT OF ANESTHESIOLOGY

JOURNAL CLUB

Thursday September 28, 2017
1800 HOURS

LOCATION:
Aqua Terra Restaurant
1 Johnson Street

PRESENTING ARTICLES:
Dr. Tarit Saha & Dr. Sam Walsh

SPONSORED BY:
3M Canada – Ms. Marta McBurney &
Ms. Lynn Guthrie

SUGGESTED GUIDELINES FOR CRITICAL APPRAISAL OF PAPERS
ANESTHESIOLOGY JOURNAL CLUB
QUEEN'S UNIVERSITY

Two presenters will be assigned to choose and present summaries of their papers. Ideally the two papers will represent similar topics but contrasting research methodologies. The focus remains on critical appraisal of the research and manuscript, more than on the actual contents of the article. Each presenter will then lead an open discussion about the article, based around the guidelines below. The object is to open up the appraisal to wide discussion involving all participants, who will be expected to contribute pending suspension of bar privileges.

GENERAL

1. Title of paper: Does it seem like an important problem? Does it reflect the purpose/results?
2. Authors, institution and country of origin

INTRODUCTION

1. What is the problem being addressed?
2. What is the current state of knowledge of the problem studied?
3. What is the hypothesis being tested?
4. How does testing the hypothesis help solve the stated problem?

METHODOLOGY

1. Study design:
    a) Clinical trial vs. systematic review/meta-analysis
    b) Prospective vs. retrospective
    c) Observational vs. Experimental
    d) Randomized or not
    e) Blinded or not

2. Population studied:
    a) Human, animal, other
    b) Justification
    c) Control groups: experimental vs. historical
    d) Is the sample size/power calculated, and how?
    e) Is the population similar to your own practice?
    f) Single vs. multi-centre

3. Is the study ethically sound?
    a) Clinical equipoise
    b) Does treatment meet standard of care (esp controls)?
    c) Appropriate consent and institutional ethics approval

4. Exclusions: what groups are excluded and why?

5. Experimental protocol
    a) Is it designed to test the hypothesis?

b) Is it detailed enough to be reproducible?
c) Is the methodology validated?
d) Are the drugs/equipment used detailed?
e) How does the randomization take place?

6. What are the primary endpoints?
7. Is power sufficient to justify secondary endpoints?
8. Is the protocol clinically relevant?
9. Data collection and analysis
10. Statistical analysis: Is it appropriate? Are results

RESULTS

1. Are the groups comparable?
2. Were any subjects/data eliminated?
3. Analyzed by intent to treat?
4. Are adequate details of results provided? - data, graphs, tables

DISCUSSION

1. What is the main conclusion of the study?
2. Do the results support this conclusion?
3. Do the results address the stated purpose/hypothesis of the study?
4. How do the authors explain the results obtained?
5. Are there any alternative interpretations to the data?
6. Are the results clinically as well statistically relevant?
7. How do the results compare with those of previous studies?
8. What do the results add to the existing literature?
9. What are the limitations of the methods or analysis used?
10. What are the unanswered questions for future work?

APPLICABILITY OF THE PAPER

1. Have you learned something important from reading this paper?
2. Will the results of this study alter your clinical practice?
3. Was the food and wine up to the high standards expected by self-respecting anesthesiologists?

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Original Article

The effect of short time periods of pre-operative warming in the prevention of peri-operative hypothermia

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Summary

The aim of our study was to evaluate the performance of different durations of active pre-operative skin-surface warming (pre-warming) to prevent peri-operative hypothermia and postoperative shivering. We randomly assigned 200 patients, scheduled for surgery of 30–90 min under general anaesthesia, to receive passive insulation or forced-air skin surface warming for 10, 20 or 30 min. Body temperature was measured at the tympanic membrane. Shivering was graded by visual inspection. There were significant differences in changes of core temperature between the non-pre-warmed group and all the pre-warmed groups ($p < 0.00001$), but none between the three pre-warmed groups ($p = 0.54$). Without pre-warming, 38/55 (69%) patients became hypothermic (< 36 °C) at the end of anaesthesia, whereas only 7/52 (13%), 3/43 (7%) and 3/50 (6%) patients following 10, 20 or 30 min pre-warming, respectively, became hypothermic ($p < 0.001$ vs no pre-warming). Shivering was observed in 10 patients without, and in three, three and one patients with pre-warming in the respective groups ($p = 0.02$). Pre-warming of patients for only 10 or 20 min before general anaesthesia mostly prevents hypothermia and reduces shivering.

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Prevention of unintentional postoperative hypothermia has become standard treatment in the peri-operative management of patients undergoing general anaesthesia. New guidelines recommend specific measures to maintain patients' core temperature > 36 °C, postoperatively [1]. Measures to prevent hypothermia include continuous assessment of the patients' core temperature, adjustment of theatre temperature to > 21 °C, warming of intravenous fluids to 38–40 °C, and use of forced-air warming if core temperature is < 36 °C [1]. One guideline recommends active pre-operative warming (pre-warming) of patients in addition to intra-operative warming [2]. However, pre-anaesthetic cutaneous warming does not change core temperature, but instead, decreases heat redistribution following a core-to-peripheral-tissue temperature gradient after induction of anaesthesia [3].

In volunteers undergoing general anaesthesia, forced-air pre-warming was found to be effective when

applied for > 30 min by increasing peripheral tissue heat content [3]. In patients undergoing major surgery, pre-warming periods of 60 min were sufficient to avoid postoperative hypothermia [4]. However, both time periods may be impractical in daily clinical routine.

Therefore, the aim of our study was to evaluate whether shorter periods of 10, 20 or 30 min of forced-air pre-warming compared with passive insulation may be long enough to reduce the incidence of postoperative hypothermia and shivering.

Methods

This study was approved by the Institutional Review Board of the University Kiel. After written informed consent, we studied 200 healthy adult patients undergoing elective surgery under general anaesthesia: laparoscopic cholecystectomy; inguinal hernia repair; breast surgery; minor orthopaedic surgery; and ENT surgery with expected duration > 30 min, but < 90 min. Patients were not studied if they were < 18 years old, classified as ASA physical status 3 or higher or planned for combined general/regional anaesthesia.

Patients were premedicated with 3.75–7.5 mg oral midazolam at the discretion of the anaesthesiologist. About 60 min before the expected start of surgery, patients arrived at the pre-operative care unit where a venous cannula was inserted and an infusion of Hartmann's solution was started at 500 $ml.h^{-1}$ until the end of surgery. In concordance with our routine practice, all fluids were warmed to 39 °C; however, no active fluid warming device was used. Patients were randomly assigned to one of the four treatment groups: passive insulation (no active warming) or active pre-operative forced-air warming for 10, 20 or 30 min. Randomisation was performed by rolling a modified dice with four faces each representing one of the four treatment groups. Then, the forced-air cover (Level 1 Snuggle Warm® Upper Body Blanket; Smiths Medical, Rockland, MA, USA) was positioned over the whole body of the patients laying in their beds, covered by a cotton blanket. A Level 1 Equator® warmer (Smiths Medical) was set to 'high level' (44 °C) during the warming period determined by randomised study group. To guarantee correct duration of warming a countdown timer (Type 8G1HZ1A; EverFlourish Europe, Friedrichsthal, Germany) was used. During the warming procedure, patients were asked every 5 min about their thermal comfort; if they felt overheated the warmer was lowered to 40 °C. When active warming was stopped the blanket was left on the patient's skin without air-blow. Pre-, intra- and postoperative ambient temperatures were maintained near 23 °C.

After the pre-warming procedure, patients were transferred to theatre. General anaesthesia was induced with propofol/sufentanil and maintained with sevoflurane by an anaesthetist blinded to the pre-warming randomisation. A tracheal tube or laryngeal mask airway was inserted depending on the standard protocol for the surgical procedure. Atracurium was used for neuromuscular blockade. Postoperatively, patients were admitted to the postanaesthesia care unit (PACU).

In all groups, patients were covered with cotton blankets intra- and postoperatively. However, active warming of the upper body was started if core temperature decreased below 36 °C (Snuggle Warm Upper Body Blanket).

During the observation period, peripheral oxygen saturation, heart rate and mean arterial blood pressures (IntelliVue MP50; Philips, Boeblingen, Germany) were recorded. Core temperature was measured at the tympanic membrane continuously using a tympanic temperature sensor (YSI 400; Smiths Medical). The aural probes were inserted by the patients until they felt the thermocouple touch the tympanic membrane. Appropriate placement of the sensor was confirmed when patients easily detected a gentle rubbing of the attached wire. Then, the aural canal was occluded with cotton and taped in place. The first tympanic membrane temperature was assessed after an equilibrating period of 5 min. In accordance with the current guidelines, hypothermia was defined as a core temperature < 36 °C [1, 2, 5].

Postoperatively, shivering was graded by an investigator blinded to patients' core temperatures and group assignments using a four-point scale (0 = no shivering; 1 = intermittent, low-intensity shivering; 2 = moderate shivering; 3 = continuous, intense shivering). Thermal comfort was evaluated with a 100-mm visual analogue scale: 0 mm was defined as 'worst imaginable cold', 50 mm as 'thermally neutral', and 100 mm as 'insufferably hot'. A new unmarked scale was used for each evaluation. Haemodynamic variables, temperatures and

shivering were assessed in 5-min intervals, thermal comfort in 15-min intervals.

Sample size calculation for the study was based on an expected treatment effect of 0.5 °C on postoperative core temperature. A sample size of totally 200 patients, divided into four groups, was estimated to provide 80% power for detecting a statistically significant difference at an alpha level of 0.05.

Statistical analyses were performed using statistics software GraphPad Prism 5.0® (GraphPad Software, San Diego, CA, USA) and R 2.11.0 (R® Foundation for Statistical Computing, Vienna, Austria). Peripheral oxygen saturation, mean arterial blood pressure and heart rate were first averaged over time for each patient. These values were subsequently averaged among the patients in each group. Continuous, normally distributed variables were analysed using one-way ANOVA and Scheffé's F test. Differences between the groups were compared with paired or unpaired, two-tailed Tukey-Kramer's t-test and chi-squared tests. To determine the time × pre-warming interaction a repeated measures ANOVA was performed with 'time' as repeated measure and 'pre-warming' as factor followed by the Bonferroni correction. Then, this analysis was repeated without the non-pre-warmed control group to investigate possible differences between the three pre-warming periods [6]. A value of $p < 0.05$ was considered significant.

Results

Patients' characteristics, duration of surgery and room temperatures were not different between groups (Table 1). Intra-operative infusion volume and blood loss were comparable between groups.

All 200 included patients were investigated up to the end of the protocol. As a result of the randomisation procedure the number of patients between treatment groups was different (Table 1).

At the beginning of ('baseline') and during pre-operative care, tympanic membrane temperatures were comparable between the four groups. Eight of the 200 patients (4%) were already hypothermic on arrival at the pre-operative care unit, one in the group without pre-warming and 3, 1 and 3 in the respective 10-, 20- and 30-min pre-warming groups. At the start of surgery, hypothermia remained in the non-pre-warmed patient; the other seven patients became normothermic during the pre-warming procedure. Pre-operative warming was well tolerated by the patients. Only 2 of 50 patients (4%) in the 30-min group asked for the warming device temperature to be lowered to 40 °C for the last 10 min of warming.

Fifteen minutes after the start of surgery core temperatures of non-pre-warmed patients decreased significantly in contrast with the pre-warmed patients (Fig. 1). Core temperatures of the pre-warmed patients

Table 1 Characteristics of patients, duration of surgery, room temperatures, airway management and type of surgery in patients receiving no pre-warming and those pre-warmed for 10, 20 or 30 min. Values are mean (SD), number, median (IQR [range]) or proportion (%).

		Pre-warming		
	No pre-warming (n = 55)	10 min (n = 52)	20 min (n = 43)	30 min (n = 50)
Age; years	49 (14)	55 (16)	52 (13)	54 (11)
Sex; (female/male)	38/17	36/16	27/16	35/15
Weight; kg	78 (16)	75 (15)	80 (17)	78 (15)
Body mass index; $kg.m^{-2}$	26.7 (5.3)	26.1 (4.4)	27.1 (5.2)	26.9 (4.2)
Duration of surgery; min	65 (35–95 [30–165])	60 (30–90 [30–140])	60 (40–95 [30–155])	65 (35–100 [30–165])
Room temperature; °C				
Pre-operative	23.1 (0.9)	23.0 (0.8)	23.3 (1.2)	23.3 (1.0)
During surgery	23.0 (0.8)	22.9 (0.7)	22.9 (0.9)	22.8 (1.0)
In recovery unit	23.3 (1.0)	23.3 (0.8)	23.3 (1.2)	23.3 (1.0)
Tracheal intubation	36 (65%)	28 (54%)	32 (74%)	32 (64%)
Type of surgery				
Laparoscopic	21 (38%)	20 (38%)	26 (60%)	28 (56%)
Breast	8 (15%)	8 (15%)	8 (19%)	10 (20%)
Orthopaedic	10 (18%)	3 (6%)	1 (2%)	4 (8%)
Other	16 (29%)	21 (40%)	8 (19%)	8 (16%)

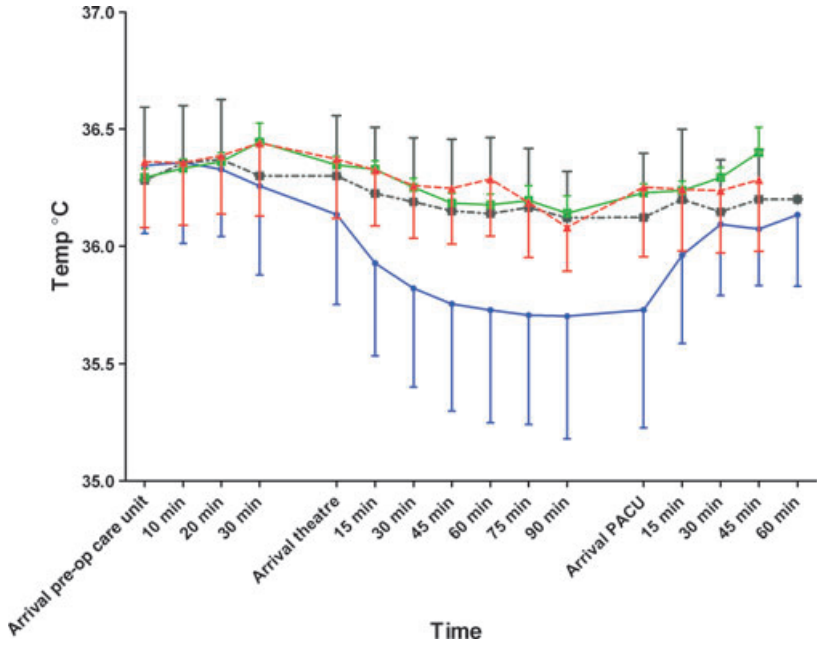

Figure 1 Mean tympanic membrane temperatures in patients receiving no pre-warming (blue) or 10 min (grey), 20 min (green) or 30 min (red) of active pre-warming. The patients not pre-warmed were significantly colder at all times from 15 min after arrival in theatre to 15 min after arrival in the post-anaesthesia care unit (PACU). Error bars are SD.

were not different between the three groups (Fig. 1). At start of PACU 38 out of 55 patients (69%) in the non-pre-warmed group were hypothermic, whereas after 10 min pre-warming 7 out of 52 patients (13%), and after 20 and 30 min pre-warming only 3 out of 43 patients (7%) and 3 out of 50 patients (6%) were hypothermic, respectively. A repeated measures ANOVA for determination of time × pre-warming interaction across the four treatment groups revealed significant differences. However, there were no significant differences between the three pre-warmed groups ($p = 0.54$) so we conclude that there were no differences between the 10, 20 and 30 min pre-warming periods.

The period between the end of pre-warming and the start of anaesthesia was 25–30 min and comparable between groups (Table 2). In the pre-warmed groups, the necessity for intra- and postoperative warming was lower, and the duration was shorter, than in the patients who were not pre-warmed (Table 2).

Shivering was observed as intermittent, low-intense shivering (grade 1) in 10 out of 55 of the non-pre-warmed patients (18%). The incidence of, shivering was significantly less in the pre-warmed groups compared with the non-pre-warmed group (Table 2). Postoperative thermal comfort scores were not different between groups.

Discussion

The main findings of our study were that the core temperature of patients who were not pre-warmed declined more than with pre-warming, despite active warming during the surgical procedure. Even 10 min of pre-warming was sufficient to prevent hypothermia. Longer periods of 20 or 30 min of pre-warming did not change the absolute core temperature profile, nor did it significantly reduce the proportion of postoperatively hypothermic patients (from 13% to 7% and 6% in the respective groups).

Our results also demonstrate that starting active warming intra-operatively for the first time, when core temperature has already decreased below 36 °C, does not reverse or prevent further hypothermia. These findings were consistent with the incidence of postoperative shivering, which was significantly reduced in the three pre-warmed groups compared with the non-pre-warmed patients.

Table 2 Time between the end of pre-operative warming and the start of anaesthesia, duration of active warming during surgery and in the postoperative care unit, and incidence of shivering. Values are median (IQR [range]) or number (proportion).

		Pre-warmed		
	No pre-warming (n = 55)	10 min (n = 52)	20 min (n = 43)	30 min (n = 50)
Time between end of pre-operative warming and start of anaesthesia; min	–	20 (10–34 [0–85])	20 (10–50 [5–160])	20 (10–36 [5–110])
Active warming required during surgery	37 (67%)	16 (31%)*	1 (2%)*†	3 (6%)*†
Duration of active warming during surgery; min	45 (0–75 [0–120])	0 (0–15 [0–75]) *	0 (0–0 [0–60]) *†	0 (0–0 [0–90]) *†
Active warming required in PACU	36 (65%)	7 (13%)*	1 (2%)*†	4 (8%)*†
Duration of active warming in PACU; min	25 (0–35 [0–110])	0 (0–0 [0–55]) *	0 (0–0 [0–30])*	0 (0–0 [0–35]) *
Shivering in PACU	10 (18%)	3 (6%)*	3 (7%)*	1 (2%)*

PACU, postoperative care unit.
*$p < 0.05$ vs 0 min warming.
†$p < 0.05$ vs 10 min warming.

Avoiding peri-operative hypothermia still remains challenging. From the first studies describing the beneficial effects of pre-warming in 1993 [7–9] there was a period of 16 years until pre-operative warming was implemented as a standard procedure in clinical guidelines. In 2009, Forbes et al. advocated a multidisciplinary team approach of surgeons, anaesthesiologists and nurses, and recommended using forced-air and intravenous fluid warming systems and raising room temperature to 22 °C [2], for surgical procedures with expected duration > 30 min. However, clinical acceptance of these measures was limited as early studies demonstrated beneficial effects of 60–120 min pre-warming, which was impractical for routine use [8–10].

Later, Sessler et al. performed a controlled study in volunteers investigating the necessary time for effective pre-warming [3] and found that 30 min of forced-air warming increased tissue heat content more than previously demonstrated [11]. Unfortunately, in that study 50% of the volunteers suffered from uncomfortable sweating after 1 h of pre-warming, so Sessler recommended a pre-warming period between 30 and 60 min [3].

Our results echo the suggestion of Bräuer et al. who speculated that pre-warming periods < 30 min could be sufficient [12]. It may be surprising that only 10 min of pre-warming appears necessary, but modern warming systems cover a wide area of skin and ensure efficient heat transfer to tissues. Our study might be criticised as patients did not undergo open surgery, but (in the main) laparoscopy. On the other hand, the incidence of peri-operative hypothermia in laparoscopic surgery has been found to be comparable with patients undergoing open abdominal surgery [13]. Our other results relating to 20 and 30 min warming are in agreement with Cooper et al.'s review of different pre-warming studies [14]. We might have investigated the relationship of warming to the duration of stay in PACU, but interpretation would have been complex as many other factors determine PACU length of stay.

It is notable that 4% of our patients were already hypothermic on arrival in the pre-operative care unit, and they were at increased risk of peri-operative hypothermia [2]. Midazolam premedication may have been responsible [15]. Yet, all bar one of these patients became normothermic after pre-warming.

The interpretation of our findings may be limited because we did not measure the actual 'heat content' of the patients. However, core temperature is the main outcome measure in clinical practice. In our study, patients were not blinded and were aware of the warming period, but it is unlikely that this would have

influenced the results. Moreover, the distribution of surgery types across groups was not completely equal, with laparoscopic surgery more common in the 20- and 30-min pre-warming groups, and this may have influenced our results. However, blood loss (in the range 30–500 ml) and infusion volumes (300–1300 ml) – perhaps surrogates for the overall 'invasiveness' of surgery – were comparable between groups.

In summary, forced-air pre-warming of 10, 20 or 30 min considerably reduced the risk of peri-operative hypothermia and postoperative shivering in comparison with passive insulation. With respect to the incidence of postoperative hypothermia, no significant differences between 10, 20 and 30 min of pre-warming were detected. However, the need for intra- and postoperative active warming following 20 and 30 min of pre-warming was lower than after 10 min of pre-warming. As a result, we recommend a standardised pre-warming period of 10 min, or if possible 20 min, before surgery under general anaesthesia.

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Competing interests

No funding or competing interests declared.

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Unintentional perioperative hypothermia is associated with severe complications and high mortality in elective operations

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Introduction. *Hypothermia occurs in as many as 7% of elective colorectal operations and is an underestimated risk factor for complications and death. Rewarming of hypothermic patients alone is not sufficient to prevent such adverse events. We investigated the outcomes of patients who became hypothermic (<35°C) after elective operations and compared them with closely matched, nonhypothermic operative patients to better define the impact of hypothermia on surgical outcomes, as well as to identify independent risk factors for hypothermia.*

Methods. *We queried the University HealthSystem Consortium (UHC) database for elective operative patients who became unintentionally hypothermic from October 2008 to March 2012, and identified 707 patients. Exclusion criteria were deliberate hypothermia, age <18 years, or death on day of admission. Separately, to validate the accuracy of hypothermia coding, we reviewed the hospital charts of all University of Louisville Hospital patients with hypothermia whose data were submitted to UHC.*

Results. *All patients from UHC with a code for hypothermia were indeed unintentionally hypothermic. Hypothermic patients undergoing elective operations experienced a 4-fold increase in mortality (17.0% vs 4.0%; P < .001) and a doubled complication rate (26.3% vs 13.9%; P < .001), in which sepsis and stroke increased the most. Several independent risk factors for hypothermia were amenable to preoperative improvement: anemia, chronic renal impairment, and unintended weight loss. Severity of illness on admission, age >65 years, male sex, and neurologic disorders also were risk factors.*

Conclusion. *Hypothermia is associated with an increased rate of mortality and complications. Preventive treatment of these risk factors before operation and aggressive warming measures in the "at risk" population may decrease hypothermia-related morbidity and mortality in elective operations. Randomized-controlled trials should be conducted to evaluate the impact of aggressive warming measures in the at-risk population. (Surgery 2014;156:1245-52.)*

From the Hiram C. Polk Jr. MD Department of Surgery,[a] University of Louisville School of Medicine, Louisville, KY; University of Louisville Hospital,[b] Louisville, KY; and University HealthSystem Consortium,[c] Chicago, IL

Improving quality and safety while decreasing costs are major concerns in contemporary health care. Several process parameters have been delineated to enhance the quality and safety of operative care. The Surgical Care Improvement Project has (among other issues) focused on reducing wound infection rates.[1] Seven process measures address wound infection prophylaxis and include the appropriate choice, timely administration, and discontinuation of prophylactic antibiotics, as well as blood glucose control and atraumatic hair-removal. Body temperature monitoring and the avoidance of hypothermia also are recommended for the prevention of wound infection. Further recommended process measures include venous thromboemboli prophylaxis and continuation of beta-blockade in patients with pre-existing cardiac diseases.

The majority of these Surgical Care Improvement Project measures aiming to decrease wound infections are not new. The successful use of

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prophylactic antibiotics was described in elective surgery as early as 1969.[2] More recent publications focused on the use of prophylactic antibiotics in low-risk operations and the time point of prophylaxis termination.[3-5] Hypothermia was described as a risk factor for wound infections in elective colorectal surgery by Kurz et al[6] and others.[3,7] Still, some authors have questioned the association between hypothermia and wound infections in elective operative patients.[8,9] Surprisingly, the frequency of hypothermia coincidental to elective operation remains poorly defined. In colorectal operations, perioperative hypothermia has been described as occurring in 7–74% of cases. Patients who required postoperative admission to the intensive care unit were hypothermic as often as 30% of the time.[10-12] In addition to wound infection, perioperative hypothermia has also been implicated causally in increased postoperative cardiac complications.[13]

Thus far, most studies evaluating the impact of hypothermia have been conducted in colorectal surgery with a relatively narrow focus on wound infections. The purpose of this study is two-fold. First, we aimed to examine the impact of hypothermia in a broader group of operative patients on outcome parameters to include cardiac complications and death. Second, we aimed to identify risk factors that may be used to identify patients at risk for perioperative hypothermia that are amenable to specific preventive measures.

METHODS

This study was approved by the Institutional Review Board of the University of Louisville. We used the database of the University HealthSystem Consortium (UHC) to identify patients who became hypothermic coincident with an elective operation. UHC started as a purchasing entity for University hospitals but became a data aggregator for the constituents and the Centers for Medicare & Medicaid Services. Participating hospitals transmit data through UHC and receive risk-adjusted benchmark values for their performances from UHC. Currently, >200 University and University-affiliated hospitals submit their data to the UHC database. UHC receives data on patient demographics, diagnoses, and comorbid conditions based on *International Classification of Diseases*, 9th Revision (ICD-9) codes and procedures as well as information on complications, reoperations, death, and readmission to the same hospital, from all contributing hospitals. In addition, some hospitals provide more granular data such as billing information and laboratory values.

Patients. A number of surgical reports have used the UHC database and have been queried regarding the accuracy of coding,[14] but we wished to validate and confirm the accuracy of UHC coding for hypothermia, so we reviewed manually the charts of all hypothermic patients who were treated at and reported by the University of Louisville Hospital (ULH). Thirty-nine of the 5,512 hypothermic patients of the initial study cohort were treated at ULH. All 39 patients were hypothermic, with a body temperature <35°C; however, 14 (35.9%) were deemed unsuitable for our study because of their disease process. Two patients were neonates and an additional seven patients became hypothermic after admission to ULH associated with exsanguinating trauma and died the same day. On the basis of these findings, we added the additional exclusion criteria of age <18 years, trauma as cause for admission, and death on the day of admission. In total, 2,138 patients were examined.

We queried the entire UHC database for patients who became hypothermic during or after an elective operation from October 1, 2008, to March 31, 2012. There are several ICD-9 codes for hypothermia that are recorded in the UHC dataset. UHC registers ICD-9 codes related to hypothermia but not how many events or actual body temperature. Therefore, the following inclusion and exclusion criteria were chosen and are outlined in Table I. Importantly, the included patients were not hypothermic on admission. 24,194 patients were identified using the codes in Table I. Of these, 16,379 patients were hypothermic on admission and were therefore excluded from this study. In 2,345 cases, data on the time point at which hypothermia occurred (at admission or during the hospital stay) were missing, so these patients were also excluded. After application of these exclusion criteria, 2,138 operative patients were then studied in more detail.

Demographics of hypothermic patients within the UHC database such as age, sex, and race were registered. The data in the UHC database are coded by professional coders based on physician notes in patients' medical charts. Twenty-one comorbid conditions were analyzed and counted as defined by the Agency for Healthcare Research and Quality.[15] Also, the clinical service that cared for the patients was collected using 3M MS-DRG (Medicare Severity and Diagnosis Related Groups) software and Major Diagnostic Categories.[16] Outcome parameters such as duration of stay, death, complications, such as sepsis and wound infections, as well as cardiovascular complications,

Table I. Inclusion and exclusion criteria

Inclusion criteria
ICD-9 codes not present upon admission
995.89 Hypothermia following anesthesia
991.6 Hypothermia
780.65 Hypothermia not associated with low environmental temperature
Exclusion criteria
ICD-9 codes
99.81 Therapeutic hypothermia
39.62 Hypothermia incidental to open heart surgery
Age <18 y
Death on day of admission or operation
Heart surgery
Trauma surgery

ICD-9, International Classification of Diseases, 9th Revision.

Table II. Matching criteria

Sex
Age
Race
Type of operation
MS-DRG *after* discharge
Severity of illness at admission
Number of comorbid conditions
Blood transfusion

MS-DRG, Medicare Severity and Diagnosis-Related Group.

such as strokes and myocardial infarctions were analyzed. Complications were defined according to the Agency for Healthcare Research and Quality.[17,18] In addition, wound infections were defined by the ICD-9 code 998.5x indicating any postoperative infection. To exclude patients presenting with wound infections after a previous operation, patients with the ICD-9 code 998.5x present on admission were excluded.

Total actual hospital costs, not hospital charges, were noted by hospitals that submit the information. To assess the impact of hypothermia on patients' outcomes, the hypothermic patients were matched very closely (1:1) for type of procedure, Medicare Severity and Diagnosis Related Groups (MS-DRG), demographics, severity of illness at admission, preexisting comorbid conditions at admission, and blood transfusions (Table II). MS-DRG data are calculated after hospital discharge based on the in-hospital course. Hence, using MS-DRG data allow for accurate matching of patients, because the course of the hospital stay influences the MS-DRG grouping. Similarly, the severity of illness was determined from administrative data with use of the 3M MS-DRG software, which allowed us to match for severity of the disease process at admission. The only difference between the two groups was the presence of hypothermia in the study group. Therefore, we focused on a group of patients who underwent elective procedures, because these procedures offer the most promising opportunities to improve operative care by preventing hypothermia.

In the next step, we identified risk factors for hypothermia. Clinical parameters that demonstrated a difference between hypothermic and normothermic patients at the time of hospital admission were entered into a logistic regression model. We purposely focused on preexisting comorbid conditions and other conditions present on admission, which are potentially amenable to correction or preventive treatment. Odds ratios were calculated, and a receiver operator characteristics curve was generated to assess the quality of the predictive model.

Statistical analysis. Nominal data, such as the existence of certain conditions or the absence of a condition, were analyzed with the Fisher exact test. Continuous data were analyzed with the Mann-Whitney *U* test, when two groups were compared. Significant differences with regard to comorbid conditions and patient demographics were entered into a stepwise logistic regression model. Odds ratios and 95% confidence intervals were calculated. Data are stated as mean ± SD. Statistical analysis was conducted with a current version of the SAS software package (SAS Inc., Cary, NC).

RESULTS

Validation of hypothermic events in ULH patients as coded by UHC. Thirty-seven hypothermic patients were treated at ULH. After excluding 12 patients with trauma or exsanguinating injuries, 25 patients were analyzed further. Sixteen of the remaining cases were on the medical service, and nine were on the surgical service. The hypothermic operative patients underwent a wide variety of operations, including general, gynecologic, and head and neck operations. Seven of these nine patients had a body temperature between 34 and 34.9°C; the other two had a temperature of <34°C. Five of the seven patients had a single episode of hypothermia, with an average duration of 181 minutes, either during the operation or shortly thereafter. The other two patients had several episodes of hypothermia during the operation, as well as afterward, in the surgical intensive care unit. Surviving patients were hypothermic for a mean of 167 minutes, whereas nonsurvivors were hypothermic for a mean of 208 minutes ($P = .17$).

The mortality of the hypothermic surgical patients was 33.3%. Two of these patients died due to sepsis, whereas the other patient died of recurrent intracranial bleeding due to a ruptured aneurysm. The predicted mortality according to the UHC risk-adjustment model for patient-specific procedures and their comorbid conditions was 20%, whereas the observed mortality was 33%. The ULH patients in UHC had been precisely coded by UHC.

Overview of hypothermic patients in the UHC database. An overview of the elective operative patients included in this study is shown in Table III. The age of patients who became hypothermic ranged from 18 to >90 years, although 70% were between 30 and 75 years. These patients were relatively sick, with an average of 2.5 preexisting comorbid conditions at admission. In addition, 48.3% of elective operative patients who became hypothermic had major or extreme severity of illness at admission. Still, 16.5% of elective operative patients who became hypothermic had mild severity of illness upon admission. The included patients were treated for many reasons. Most were treated by the general surgery service (25%) for gastrointestinal diseases, including bowel, pancreatic, and hepato-biliary surgery and the orthopedic service (27%) for joint replacements and spine surgery. Other services with hypothermic patients included neurosurgery (7%), vascular surgery (7%), thoracic surgery (7%), obstetrics and gynecology (7%), and urology (4%). Procedures in all these specialties in which therapeutic hypothermia was used were excluded.

Effect of hypothermia on outcomes in elective patients and independent predictors of hypothermia. Elective operative patients who became hypothermic were matched very closely with patients who did not become hypothermic for age, sex, race, MS-DRG (adjusting for hospital course), preexisting comorbid conditions, blood transfusions, admission status, and severity of illness at admission (Table II). This close matching allows for an accurate investigation of the impact of hypothermia on operative patients. Hypothermia had a profound impact on mortality in elective patients. Although the rate of mortality of nonhypothermic patients was only 4%, the death rate of elective operative patients who became hypothermic was 17% ($P < .001$.) Furthermore, the complication rate in elective operative patients who became hypothermic doubled (26.3% vs 13.9%; $P < .001$). The leading complication was sepsis. Cardiovascular complications, such as stroke and myocardial infarctions, were both more frequent in hypothermic patients. Wound infections, however, did not increase in hypothermic patients. The greatest increase of any complication between hypothermic and nonhypothermic patients was the sixfold increase in strokes (6.5% vs 1.0%, respectively). Also, the increase in number of early deaths among hypothermic patients is more pronounced in elective operative patients. Not surprisingly, elective operative patients who became hypothermic spent more time both in the intensive care unit and in the hospital overall.

Table III. Overview of UHC patient demographics

	Elective operative patients with unintentional hypothermia
Number of patients	707
Age (mean years ± SD)	61.3 ± 16.8
Sex (% male)	41.3
Race, %	
White	68.5
Black	20.1
Other	11.5
Admission status, %	
Emergency	0
Urgent	0
Elective	100
Comorbid conditions	
≥1 at admission	85.9%
Mean (±SD)	2.5 ± 2.0
Severity of illness at admission, %	
Mild	16.5
Moderate	33.1
Severe	37.6
Extreme	12.7
Blood transfused during hospital stay, %	44.8

Admission status: Emergency: operation within 12 hours; urgent operation within 24 hours.
UHC, University HealthSystem Consortium.

Severity of illness at admission was the strongest predictor for hypothermia in elective operative patients (Table V). Unintentional weight loss, chronic renal failure, and anemia were among the other independent predictors for hypothermia in elective patients. All these conditions can be treated and/or improved before an operation in elective patients. Neurologic disorders include a broad group of diseases, such as Alzheimer, seizures, and other neurodegenerative disorders. Men older than 65 are also at a greater risk for hypothermia. Diabetes mellitus without end organ damage, however, was found to be protective. All

Table IV. Outcomes in elective hypothermic operative patients compared with closely matched controls

	Elective patients with unintentional hypothermia	*Elective patients without unintentional hypothermia*	P *value*
Number of patients	707	698	n.s.
Age (mean years ± SD)	61.3 ± 16.8	60.7 ± 16.3	n.s.
Sex (% male)	41.3%	41.3%	n.s.
Comorbid conditions			
≥ 1 at admission	85.9%	85.7%	n.s.
Mean (±SD)	2.5 ± 2.0	2.4 ± 1.9	n.s.
Mortality	17.0%	4.0%	<.001
Deaths <72 h after admission	6.9%	0.3%	<.001
Complications	26.3%	13.9%	<.001
Myocardial infarction	3.3%	1.1%	.01
Stroke	6.5%	1.0%	.001
Sepsis	7.5%	2.6%	<.001
Wound infection	5.0%	3.3%	.14
Pneumonia	5.1%	1.3%	<.001
Duration of stay, d			
Overall hospital stay	17.3 ± 23.4	11.8 ± 22.6	<.001
ICU stay	8.5 ± 18.3	4.4 ± 10.8	<.001
Total hospital costs (±SD)	$77,313 ±103,838	$47,014 ± 94,370	<.001

ICU, Intensive care unit; *n.s.*, not significant.

these risk factors together outline the patients at high risk for hypothermia: elderly, diabetic men with anemia, chronic renal failure, unintended weight loss, and Alzheimer disease. The receiver operator characteristics curve for this prediction model had an area under the curve of 0.69.

DISCUSSION

Hypothermia is a well-described risk factor for mortality and complications, such as wound infections, sepsis, multiple organ failure, and cardiovascular incidents, including strokes and myocardial infarctions.[3,6,7,10,19,13] Most previous studies, however, have investigated the effects of hypothermia in a select group of patients: those undergoing elective colon resections. The purpose of our study was to investigate the impact of hypothermia in a larger and broader cohort of elective operative patients. We excluded trauma and cardiac operations because of their use of therapeutic hypothermia. We believed that our data source was unable to uniformly differentiate between patients who became hypothermic unintentionally and those who were treated with intentional hypothermia. Furthermore, to ensure the reliability of this dataset, we manually reviewed the charts of hypothermic patients treated at ULH to confirm that these patients were indeed hypothermic.

Using the large UHC database, we found that hypothermia has a major detrimental impact on operative patients. Hypothermia was associated with a 4-fold increase in mortality and doubled the complication rate in elective operative patients (Table IV). Sepsis was the most frequent complication in hypothermic, elective operative patients. Strokes and myocardial infarctions also were much more frequent in hypothermic patients. These results confirmed previous studies investigating the effects of hypothermia on operative patients[3,6,7,13]; in contrast, wound infections were not more common in hypothermic patients, a finding confirmed by a recent study.[20]

To prevent hypothermia, it is of clinical importance to identify risk factors accurately. Hypothermia prevention is pivotal because, thus far, no specific treatment except rapid rewarming exists.[21-23] We identified specific risk factors for hypothermia in elective operative patients. The strongest predictor of hypothermia was the severity of illness on admission, a risk factor that is generally not amenable to correction (Table V). Other noncorrectable risk factors include age >65 years and male sex. Several risk factors for hypothermia, however, can be corrected rather easily or at least modified before a procedure even in nonelective cases.

Anemia and preexisting neurologic disorders, such as Alzheimer disease, were independent predictors of hypothermia in elective patients. Anemia can be easily corrected with blood transfusions, but neurologic disorders are not amenable to treatment. Unintended weight loss and chronic

Table V. Independent predictors of hypothermia in elective operative patients

Variables present on admission	*Odds ratio*	*95% CI*
High severity of illness at admission	2.82	2.28–3.47
Neurologic disorder (Alzheimer, etc.)	1.71	1.06–2.78
Male sex	1.65	1.36–2.01
Age >65 y	1.61	1.33–1.96
Weight loss	1.6	1.04–2.48
Anemia	1.49	1.12–1.98
Renal failure	1.43	1.07–1.92
Diabetes mellitus without end organ damage	0.58	0.44–0.75
Area under the curve for the regression model	0.69	

CI, Confidence interval.

renal failure were also risk factors for hypothermia in elective patients. These conditions can either be altered preoperatively, or the procedure may be delayed to maximally improve conditions before the operation. Surprisingly, we found that diabetic patients without end organ damage who undergo elective operations were less likely to become hypothermic. Recent work indicates that diabetic patients undergoing elective operations have results similar to nondiabetic patients.[24,25] We believe that the additional alertness due to the patients' diabetes may improve medical practice, and quality improvement protocols may be followed more closely in these patients, as a result.

Intraoperative prevention of hypothermia is the most promising strategy to decrease the complications and mortality related to hypothermia. A recent study clearly demonstrates that targeted measures can decrease the frequency of hypothermia.[26] Our results define a group of patients at a particular risk for hypothermia: elderly men with chronic renal failure, anemia, weight loss, and Alzheimer disease. Dedicated warming measures must be used in these patients. Thus far, no advantage of forced-air warming compared to resistive-polymer systems has been shown.[27-29] Warm water wraps and water mattresses, however, seem to be superior at maintaining the body temperature of patients undergoing abdominal operations.[30] Also, local insufflation of warm and humidified CO_2 into the wound increases wound temperature and core temperature.[31] Combining these newer methods with traditional forced-air warming and resistive systems may prevent hypothermia, especially in the high-risk group of patients we identified in this study. Warming of the operating room does not appear to influence patients' body temperatures.[32] The rigorous application of established, standardized process to all patients is important to the prevention hypothermia regardless of procedure type. Andersson et al[33] demonstrated that processes established to decrease wound infections are not followed equally stringently for patients undergoing operations for fracture fixation as they are for patients undergoing joint replacement. To determine whether aggressive warming measures and the prevention of hypothermia improve operative outcomes in the at-risk population we defined, randomized-controlled should be conducted in several operative specialties.

Prevention of hypothermia is pivotal, because there are no established treatments besides rapid rewarming.[21,22] The lack of treatment options is supported by the effects of hypothermia on the immune system as well as other body systems that are poorly understood. It has been shown that hypothermia increases the production of tumor necrosis factor-α in whole blood and monocytic cell lines, whereas interleukin-10 production is suppressed.[34-36] In addition, hypothermia decreases neutrophil function and monocyte antigen presenting capacity, as measured by human leukocyte antigen (HLA-DR) expression on monocytes. Monocyte HLA-DR is a well-established biological marker for monitoring susceptibility to infections and sepsis.[37-42] Further studies must investigate the mechanisms of hypothermia-related immune dysfunction, and the relationship of hypothermia and cardiovascular complications. It is clear, however, that the local and systemic application of heat decreases wound infections.[43]

Our study has several limitations. First, the data are based on a widely used and reputable administrative database, and the accuracy of coding is critical to producing clinically meaningful results and the subsequent interpretation of findings. Further, we do not have actual temperature measurements for the patients in this study. We addressed these inherent limitations by manually reviewing all hypothermic patients who were treated at ULH. We found very accurate coding, as others did,[14] and all patients with a code for hypothermia had established core temperatures <35°C in close temporal association to an operation. Thus, we are confident that all patients in this study were indeed hypothermic. Patients with very mild hypothermia, however, were unlikely to be coded as hypothermic. Our study likely includes only patients who had moderate to severe hypothermia, explaining the much more profound impact of hypothermia on mortality and complications in this report than in

previous studies. Furthermore, we tried to eliminate as many confounding factors as possible by matching the hypothermic patients for the procedure type (based on ICD-9 procedures codes) as well as for blood transfusions to account for intraoperative complications such as major bleeding. It is still possible, however, that hypothermic patients had intraoperative complications that were not addressed by a database study such as this one.

Nonetheless, our findings herein are relevant and of clinical importance. Our results highlight the detrimental effects of hypothermia on patients' outcomes, as well as costs of health care. Of note, severe complications such as sepsis, stroke, and myocardial infarction, are affected by hypothermia much more strongly than less severe complications such as wound infections. Hypothermia can easily and inexpensively be avoided by strict adherence to established quality measures and standardized procedures for the at-risk patients we defined previously.

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