



ORIGINAL INVESTIGATION

Forced-air warming and continuous core temperature monitoring with zero-heat-flux thermometry during cesarean section: a retrospective observational cohort study



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Abstract

Background: Over 30% of parturients undergoing spinal anesthesia for cesarean section become intraoperatively hypothermic. This study assessed the magnitude of hypothermic insult in parturients and newborns using continuous, high-resolution thermometry and evaluated the efficiency of intraoperative forced-air warming for prevention of hypothermia.

Methods: One hundred and eleven parturients admitted for elective or emergency cesarean section under spinal anesthesia with newborn bonding over a 5-month period were included in this retrospective observational cohort study. Patients were divided into two groups: the passive insulation group, who received no active warming, and the active warming group, who received convective warming through an underbody blanket. Core body temperature was continuously monitored by zero-heat-flux thermometry and automatically recorded by data-loggers. The primary outcome was the incidence of hypothermia in the operating and recovery room. Neonatal outcomes were also analyzed.

Results: The patients in the passive insulation group had significantly lower temperatures in the operating room compared to the actively warmed group (36.4°C vs. 36.6°C, $p = 0.005$), including temperature at skin closure (36.5°C vs. 36.7°C, $p = 0.017$). The temperature of the newborns after discharge from the postanesthetic care unit was lower in the passive insulation group (36.7°C vs. 37.0°C, $p = 0.002$); thirteen (15%) of the newborns were hypothermic, compared to three (4%) in the active warming group ($p < 0.01$).

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Conclusion: Forced-air warming decreases perioperative hypothermia in parturients undergoing cesarean section but does not entirely prevent hypothermia in newborns while bonding. Therefore, it can be effectively used for cesarean section, but special attention should be given to neonates.

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Introduction

Nowadays, cesarean sections account for about 7% of all surgical procedures worldwide¹ and over 85% of them are performed under neuraxial anesthesia.² Unintentional cooling of the patient's core temperature under 36.0°C is defined as inadvertent perioperative hypothermia.³ Hypothermia can increase the risk of complications such as surgical site infection, myocardial ischemia, coagulopathy, altered drug metabolism, and increased length of stay.⁴⁻⁶ The pathophysiological mechanism responsible for hypothermia after neuraxial blockades seems to be the core-to-peripheral redistribution of body heat through a lower body sympathectomy and altered thresholds for vasoconstriction and shivering.^{7,8}

Only 6% of the hypothermic patients undergoing a cesarean section under spinal anesthesia are symptomatic,^{7,9} and in clinical practice most of them will remain undetected if the core temperature is not properly monitored. Rates of perioperative hypothermia among this population have been estimated in a range from 32%⁹ to as high as 91%¹⁰ despite the use of intraoperative warming techniques.

Previous studies have demonstrated how maternal temperature at birth is also responsible for the temperature of newborns and have shown the impact on the neonatal umbilical vein, arterial pH and APGAR scores.^{11,12} Moreover, the concept of bonding implies an immediate and uninterrupted skin-to-skin contact between the newborn and the mother, and hypothermia rates of newborns during this procedure has proven to be as high as 80%.¹²

The thermal insult and the effect of forced-air warming on a broad heterogeneous parturient population including both elective and emergency cesarean sections, corresponding to the majority of the obstetric clinics, has yet to be studied by using modern high-resolution thermometry.

We hypothesize that the use of intraoperative forced-air warming could prevent maternal temperature loss during cesarean section under spinal anesthesia, lead to faster recovery to baseline temperature and prevent hypothermia in newborns while bonding on the mother's chest.

Methods

The corresponding Institutional Review Board - Ärztekammer Nordrhein, Düsseldorf, Germany - waived the requirement for written informed consent due to the retrospective study design and granted full approval for this trial on October 14, 2019 (Ethics Committee No. 236/2019). The study protocol was registered on www.ClinicalTrials.gov (registration number: NCT04132154; date of registration: October 18, 2019).

This analysis followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)

recommendations¹³ and was carried out in the anesthesia department of the St. Marien-Hospital in Düren, Germany. Over 1,500 deliveries, of which over 37% under cesarean section, were performed at our institution in 2018. Our standard anesthetic technique for cesarean sections is spinal anesthesia with hyperbaric bupivacaine supplemented with sufentanil and morphine.

The data were acquired as part of an internal quality audit between April 1 and August 31, 2019, including all cesarean sections under spinal anesthesia at our facility (Fig. 1). For the first half of the study period, we did not change our standard passive warming protocol using cotton blankets in the operating room. During the second phase, our institution implemented the German S3 Guidelines on prevention of hypothermia,¹⁴ and in addition to passive warming, patients also received convective warming at 43°C through an underbody blanket. Only room temperature balanced full electrolyte solutions were used during our study. Detailed operating room temperature data were not available due to the retrospective design of this study. Patients were divided into two groups: the passive insulation (PI) group and the active warming (AW) group. Neither group received prewarming nor did they receive active warming following surgery.

The exclusion criteria were: different anesthetic procedures (e.g., intubation anesthesia, peridural anesthesia, etc.), BMI > 45 kg m⁻², patients with incomplete documentation, estimated perioperative blood loss > 500 mL, total infused fluid volume > 2,000 mL, and other perioperative complications (ex. insufficient analgesia and change in anesthesia procedure).

Temperature measurements

For this study, the same equipment was used in the operating and recovery rooms. Core temperature was continuously monitored using Zero-Heat-Flux (ZHF) technology (supplementary material) with the 3M™ Bair Hugger™ Temperature Monitoring System (former SpotON™, 3M™ USA, St. Paul, MN, USA, accuracy -0.23°C),¹⁵ and a 3M™ Temperature Hard Drive (3M™ Deutschland GmbH, Neuss, Germany) logging system was used to continuously and automatically record the data to ensure user-error free data acquisition from the induction of thermal insult to the recovery phase. The newborns' rectal temperature was measured using a standard hospital digital thermometer (AMPri Med-Comfort Modell 09801, Winsen, Germany, accuracy ± 0,05°C).

Anesthetic and temperature management

Preoperatively, all patients received 30 mL sodium citrate oral premedication and an infusion of 1,000 ml full balanced

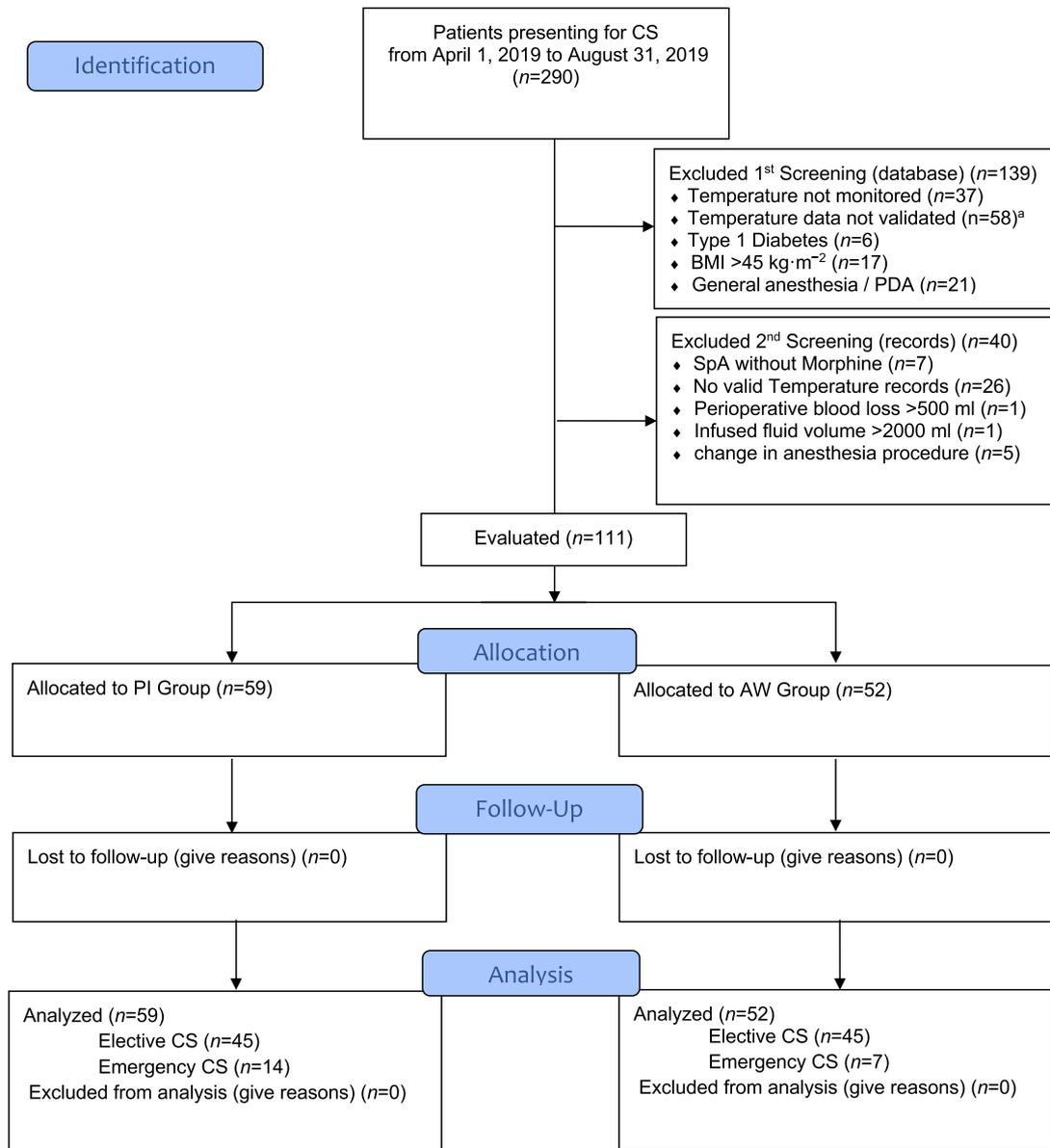


Figure 1 Flow Diagram of the study based on the STROBE Statement. Explanatory footnote: CS, cesarean section; PDA, peridural anesthesia; SpA, spinal anesthesia; PI, passive insulation; AW, active warming.

^a Data were considered valid if temperature monitoring was started prior to induction of anesthesia and the calibration of the ZHF sensor was completed.

electrolyte solution at room temperature. In the operating room standard monitoring – ECG (electrocardiogram), pulse oximeter, non-invasive blood pressure and ZHF temperature monitor sensor on the right side of the forehead – was applied on arrival. All parturients received a cotton blanket over their arms and upper torso, whereas the AW group patients additionally received active warming through an underbody blanket with forced-air flow at 43 °C (model 585, 3M™ Bair Hugger™ series) upon the application of the sterile sheets and until discharge from the operating room. Spinal anesthesia was induced by one of our randomly assigned anesthesiologists. The puncture site was first infiltrated with mepivacaine, and then dural puncture was performed at the L3/4 or L4/5 level with a 25G Whitacre spinal needle. As per our institutional standard practice, after confirmation of

free-flowing, clear cerebrospinal fluid, 0.05 mg·cm⁻¹ (patient's height) hyperbaric bupivacaine with 2.5 μg sufentanil and 1 μg·kg⁻¹ morphine (maximum dose of 80 μg) were injected into the subarachnoid space. Balanced electrolyte solutions at room temperature, vasoconstrictors (Akrinor™, ratiopharm GmbH, Ulm, Germany) and Atropine were used at the discretion of the primary anesthesiologist. In this setting, we were able to continuously monitor the core temperature of our patients before and during the induction of the spinal anesthesia, throughout the entire operative procedure, and also up to 3 hours postoperatively in the recovery room.

As per standard practice, newborn umbilical vein pH samples were collected at birth by the gynecologists and the rectal temperatures as well as the APGAR Scores were

recorded by the pediatricians. If the newborn was deemed stable, he/she was positioned naked on the mother's chest and secured with an elastic strap. The skin-to-skin contact was carried out in the operating room during surgery and in the postanesthetic care unit (PACU).

After the operating procedure, all parturients received passive insulation with cotton blankets in the maternity ward. Discharge from the maternity ward was at the disposition of the midwives; however, as per institutional practice, the patients could not be discharged while the level of spinal anesthesia remained above L1.

According to current guidelines and previous studies,^{3,14,16} maternal hypothermia was defined as a core body temperature lower than 36°C while hypothermia among newborns was recorded at a core temperature less than 36.5°C.

Baseline temperature was defined as the first recorded temperature validated after the calibration of the ZHF sensor while nadir temperature was defined as the lowest recorded temperature during the observation time.

The primary outcome was incidence of hypothermia during the peri- and postoperative phases. Neonatal outcomes (rectal temperature at birth and discharge from the recovery room, umbilical venous blood pH, base excess and APGAR score) were also reviewed in the context of the concept of bonding.

Data collection

The data from the data loggers were imported into the corresponding 3M™ Bair Hugger Temperature Intelligence™ software application (Version 1.0.3, 3M™ Deutschland GmbH, Neuss Germany). At this point the constructed database was visually processed and patients with incomplete data were excluded from further analysis. Data were considered valid if temperature monitoring was started prior to induction of anesthesia and the calibration of the ZHF sensor was completed. The remaining data were exported in a datasheet format and further handled and processed with Microsoft Excel (Mac 2019, Microsoft Inc, Redmond, WA). Raw core temperature data were processed to filter artefactual data before statistical analysis whereby all values under 30°C were removed, after which data points varying by 0.1°C or more in 10 seconds from the preceding value were removed on the basis of physiological implausibility. Through visual comparison of raw and processed temperature data, we confirmed that no critical information was accidentally deleted during

processing. It is plausible to assume that the excluded data were missing completely at random and no adjustments have been made in this regard. The datasets used during this study can be provided by the corresponding author on request.

Statistical analysis

Patient demographics, case characteristics, and temperature recordings were summarized using descriptive statistics. All statistical analyses were performed using SAS version 9.4 software (Windows x64, SAS Institute Inc. Cary, NC). Descriptive statistics were performed and distribution patterns of measures were observed by histograms, quantile-quantile plots and the Shapiro-Wilk test. We analyzed measures at single time points like temperature at time of skin closure or nadir of temperature by *t*-test or, if Gaussian distribution was not given, by one-way ANOVA. The χ^2 test was applied to test for differences in nominal or categorical variables. If the number of measures was five or lower, we applied Fisher's exact test.

For the analyses of repeated measurement between the two groups over time, we established generalized linear mixed models. We blocked patient ID, treated time as a random factor, and adjusted for multiple comparisons by a Tukey test. Heteroscedasticity was treated by Kenward-Roger approximation.

Nadir temperature and baseline temperature were used to calculate probability to recover from hypothermia. The time from nadir temperature to 30%, 50%, 70%, and 90% recovery to baseline temperature was obtained. SAS Proc Lifetest was used to conduct time-to-event analysis and generate Kaplan-Meier curves. Estimates of median recovery times were obtained. Homogeneity of time-to-event curves between treatments was tested using log-rank statistics. Data were right censored at the last available temperature measurement or 200 minutes post nadir temperature.

Results

Out of 290 reviewed records, we identified a total of 111 patients to be enrolled in the final analysis; 59 patients were included in the PI group, leaving 52 parturients for the AW group. There were no statistically significant differences between the two groups based on demographic, obstetric, or surgical data or based on treatment protocols.

Demographic data are summarized in Table 1; maternal and newborn outcomes are presented in Table 2.

Table 1 Demographic and perioperative data.

	PI group (n = 59)	AW group (n = 52)	<i>p</i> -value
Age (years)	31.6 ± 4.95	30.2 ± 6.79	0.21
BMI (kg·m ⁻²)	31.3 ± 6.40	30.9 ± 4.97	0.67
Gestational age (weeks)	38.7 ± 1.84	38.7 ± 1.67	0.88
Anesthesia to discharge OR (min)	57.2 ± 11.7	60.3 ± 16.1	0.24
Diabetes, n (%)	8 (13.6)	8 (15.4)	0.78
Thyroid disorder, n (%)	14 (23.7)	8 (15.4)	0.27
Primary CS, n (%)	45 (76.3)	45 (86.5)	0.168
Emergency CS, n (%)	14 (23.7)	7 (14.5)	0.168
Twin births, n (%)	3 (5.1)	2 (3.9)	0.75

Values are expressed as mean ± SD, and percentage as appropriate. There was no statistically significant difference between groups (*p* > 0.05 for all comparisons). PI, passive insulation; AW, active warming; OR, operating room; CS, cesarean section.

Table 2 Maternal and neonatal outcomes.

	PI group (n = 59)	AW group (n = 52)	p-value
Maternal outcomes			
T Baseline (°C)	37.6 ± 0.41	37.4 ± 0.33	0.048
T _{min} OR (°C)	36.4 ± 0.44	36.6 ± 0.42	0.08
T _{min} PACU (°C)	36.4 ± 0.46	36.6 ± 0.44	< 0.01
T Incision (°C)	37.3 ± 0.47	37.1 ± 0.39	0.06
T Partus (°C)	37.1 ± 0.44	37.0 ± 0.37	0.21
T Skin Closure (°C)	36.5 ± 0.44	36.7 ± 0.46	0.02
AUC 36 (°C*hr ⁻¹)	1.90 ± 5.37	0.52 ± 2.20	0.12
Hypothermia overall, n (%)	13 (22.0)	6 (11.5)	0.21
Hypothermia OR, n (%)	7 (11.9)	5 (9.6)	0.70
Neonatal outcomes			
T _{NB} OR (°C), (n)	37.4 ± 0.3 (29)	37.4 ± 0.4 (39)	0.67
T _{NB} PACU (°C), (n)	36.7 ± 0.5 (44)	37.0 ± 0.4 (42)	< 0.01
Hypothermia cases PACU ^a , (%)	13 (15.1)	3 (3.5)	0.016
Weight (g)	3236.7 ± 368.0	3243.5 ± 623.8	0.32
pH	7.30 ± 0.05	7.31 ± 0.05	0.96
BE (mmol*l ⁻¹)	-1.47 ± 2.29	-1.72 ± 1.76	0.52
APGAR1	8.7 ± 0.8	8.8 ± 0.6	0.59
AGPAR5	9.7 ± 0.7	9.8 ± 0.5	0.26
APGAR10	9.8 ± 0.5	9.9 ± 0.2	0.06

$p < 0.05$ was considered statistically significant. T, temperature; AUC36, area under the time-temperature curve for a core temperature $< 36.0^{\circ}\text{C}$; PI, passive insulation; AW, active warming; PACU, postanesthetic care unit; T_{NB} OR, newborn's core temperature at birth; T_{NB} PACU, newborns core temperature at discharge from PACU; BE, base excess; APGAR1/5/10 APGAR score at 1, 5 and respectively 10 minutes after birth.

^a Newborn hypothermia was defined as a core body temperature lower than 36.5°C .

The changes in core temperature during the peri- and postoperative periods in the two groups are presented in [Figure 2](#). The baseline core temperature of the patients in the PI group was significantly higher than the baseline core temperature of the AW group ($37.6^{\circ}\text{C} \pm 0.41$ vs. $37.4 \pm 0.33^{\circ}\text{C}$, $p = 0.048$). A significantly lower temperature of $36.4^{\circ}\text{C} \pm 0.46$ ($p = 0.005$) was reached by the PI group in the operating room, compared to $36.6^{\circ}\text{C} \pm$

0.44 , ($p = 0.005$) reached by the AW group. Further, temperature at the time of skin closure was also significantly lower in the PI group ($36.5^{\circ}\text{C} \pm 0.43$ vs. $36.7^{\circ}\text{C} \pm 0.46$, $p = 0.017$). Thirteen patients (22%) in the PI group and six (11.5%) in the AW group were hypothermic during the entire observation period ($p = 0.207$).

A significant, faster recovery to baseline temperature was achieved if active warming was applied ([Fig. 3](#)). In all

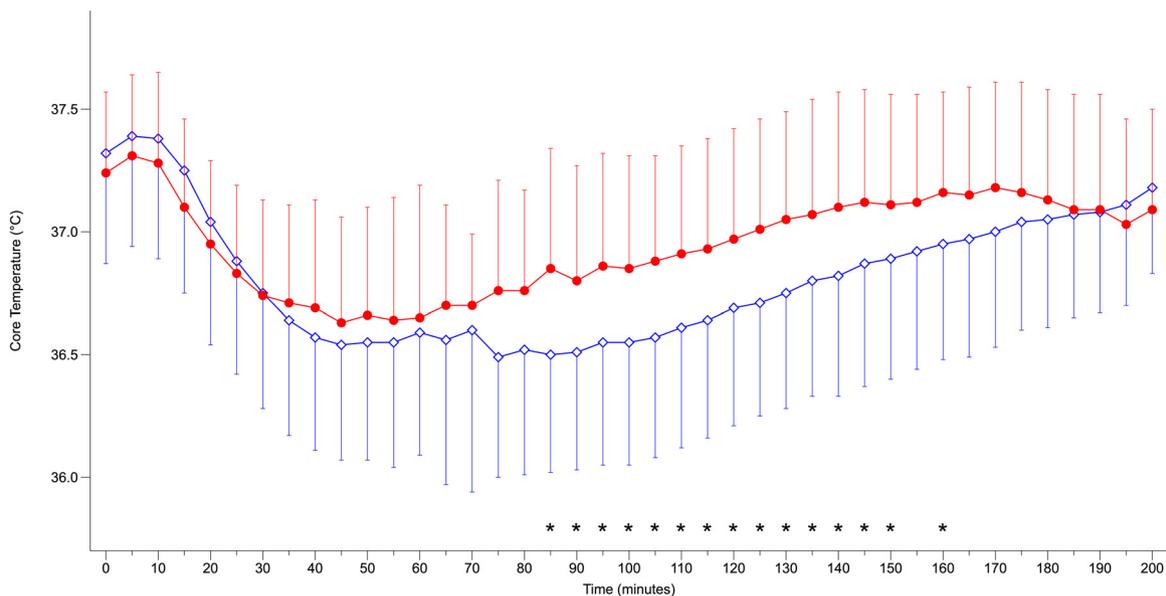


Figure 2 Maternal core temperature. Explanatory footnote: Values are presented as the mean and the whiskers are SD. Time 0 represents onset of spinal anesthesia; continuous red line: active warming (AW) group; continuous blue line: passive insulation (PI) group; *: statistically significant differences AW group vs. PI group ($p < 0.05$).

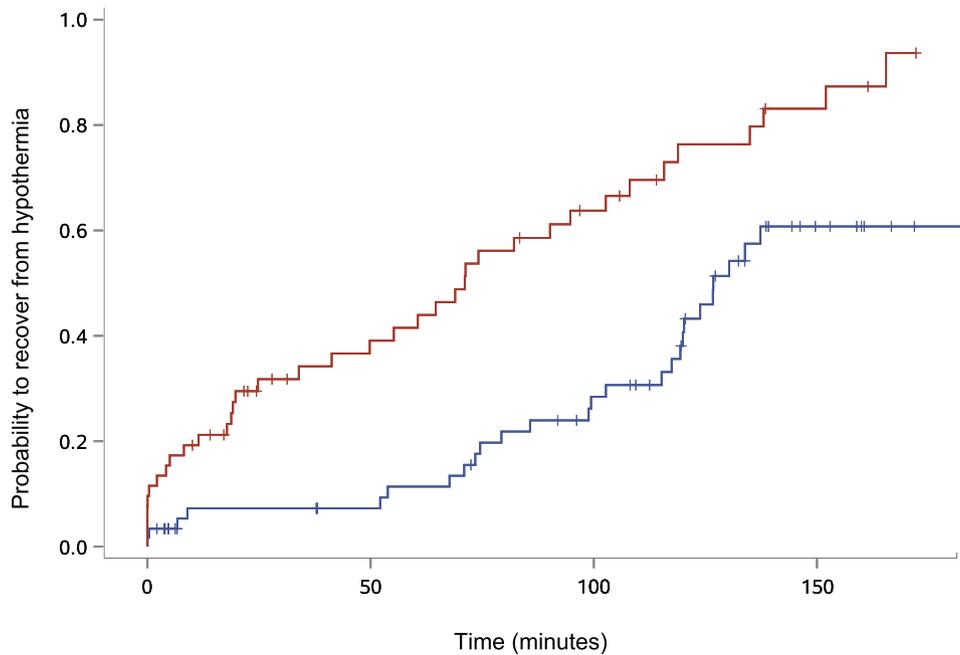


Figure 3 Probability to recover from hypothermia. Explanatory footnote: Kaplan-Meier curve showing the probability to recover from hypothermia to 90% of the baseline temperature. Differences are statistically significant ($p < 0.001$). Time 0: nadir of temperature, defined as the lowest recorded temperature during the observation time; continuous red line: active warming (AW) group; continuous blue line: passive insulation (PI) group; right censored data represented by “|”.

time-to-event analyses, the difference between groups was statistically significant; actively warmed patients reached the percent temperature recovery milestones faster than did the patients in the PI group (Table 3).

Neonatal temperatures at birth were similar between the two groups; however, as shown in Figure 4, newborns' temperature after discharge from PACU was significantly lower in the PI group ($36.7^{\circ}\text{C} \pm 0.5$ vs. $37.0^{\circ}\text{C} \pm 0.4$, $p = 0.002$). Thirteen (15.1%) of the newborns in the PI group were hypothermic at discharge from PACU, compared to three (3.5%, $p = 0.016$) in the AW group. No statistically significant difference between the groups was found based on neonate pH, BE or APGAR scores.

Table 3 Recovery from hypothermia based on time-to-event analysis.

Recovery milestone	PI group (n = 59)	AW group (n = 52)	p-value
30%	56 (46-70)	13 (5-44)	< 0.001
50%	78 (65-86)	44 (11-50)	< 0.001
70%	104 (98-112)	59 (25-77)	< 0.001
90%	127 (117-182)	71 (41-102)	< 0.001
Censored (n =)			
30%	10	7	
50%	13	9	
70%	25	10	
90%	32	15	

Values are expressed in minutes with 95% CI. $p < 0.05$ was considered statistically significant. The time median is the estimate of how long it would take patients in the group to recover from the lowest recorded temperature to a specific percent milestone of baseline temperature. PI, passive insulation; AW, active warming.

Discussion

The objective of this retrospective cohort study was to assess the magnitude of hypothermia in the parturient population undergoing cesarean section under spinal anesthesia and to investigate the implication of hypothermia in newborns while bonding on the mother's chest. We found that intraoperative forced-air warming for cesarean section could be effective in decreasing the incidence of hypothermia in parturients; however, warming the patients while bonding did not completely prevent hypothermia in the newborns after discharge from PACU.

Our research could provide new insight in regard to the necessity of standardizing temperature monitoring and forced-air warming during cesarean section with skin-to-skin bonding immediately after birth. Furthermore, it could derive practical implications for the standard clinical routine.

Proper core temperature monitoring and the use of active warming are strongly supported by current published guidelines for intraoperative care in cesarean delivery.¹⁷ Yet, core temperature in parturient patients under spinal anesthesia is poorly monitored due to practical difficulties,^{17,18} and studies in this area have produced mixed results.^{8,10,12,19-22} An optimum approach for clinicians on monitoring patients' core temperature and preventing hypothermia during cesarean sections remains to be determined.^{17,23}

The positive impact of our intraoperative warming strategy on inadvertent hypothermia in obstetric patients can be visualized in Figure 2. Reliable and regular intervals of core temperature measurements should be used, since after induction of anesthesia, the decline in core temperature is rapid and can be seen in both actively warmed and passively insulated patients. After approximately 45 minutes of

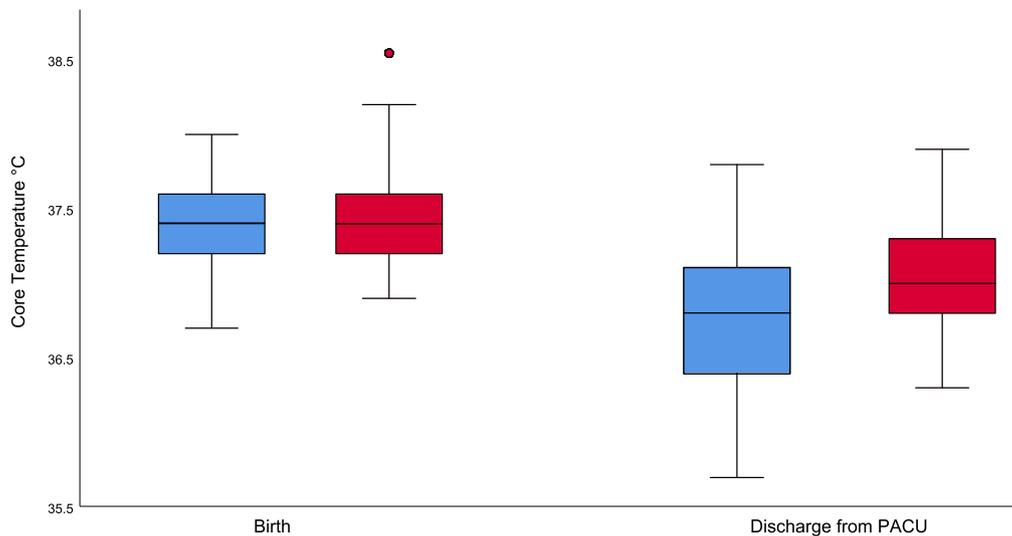


Figure 4 Newborn core temperature. Explanatory footnote: Box and whisker plot of newborns core temperature. No statistically significant difference at birth ($p = 0.67$); statistically significant difference ($p = 0.002$) at discharge from the postanesthetic care unit (PACU). Boxes indicate the lower and upper quartile. Horizontal line in each box represents the median temperature. Vertical lines represent the minimum and maximum recorded temperatures. The dot outside the boxes represents mean temperature outside the expected distribution. Red boxes: active warming group; blue boxes: passive insulation group.

intraoperative active warming, the temperature of the AW group started an uptrend while the temperature of the PI group continued to decline for another 30 minutes. In the PACU, the core temperature increased in both groups; however, the AW group exhibited a statistically significant higher mean core temperature than the control group (Table 2), and patients recovered significantly faster from hypothermia (Fig. 3). The hypothermia rate (22%; $p = 0.207$) in the PI group was slightly lower compared to previous studies.^{9,10}

Our warming strategy was selected based on a practical approach in the context of bonding newborns to their mothers' chest. Prewarming was not available due to logistical reasons and this could be seen as a limitation. A similar intraoperative warming strategy was used by Hoefnagel and her team, but they also warmed the patients before surgery.²² While they concluded that prewarming did not result in higher initial core temperatures in the OR, active warming was associated with higher intra- and postoperative temperature measurements.

A significant limitation of many studies in the area is the lack of automatic continuous core temperature measurement and of a high accuracy device to avoid user error and provide high-resolution data on thermal insult and recovery. Furthermore, there is limited research on the parturient population undergoing cesarean section that investigates recovery from hypothermia in the postoperative period. Our data compare with high-resolution data on thermal insult and thermal recovery associated with spinal anesthesia for cesarean section provided by duToit and his colleagues¹⁸; however, for this descriptive study, the authors used an ingestible telemetric sensor and no active warming. Cobb and his team used the 3M™ ZHF thermometer to compare the possibility of combining warmed IV fluid and lower body forced-air warmer against no warming and concluded that multimodal active warming for the parturient population is difficult and has only modest benefits.¹⁰

We did not use fluid warming and excluded from the final analysis the cases with a total infused volume $>2,000$ ml. A Cochrane Review showed that the efficacy of fluid warming along with other warming strategies may not be clear.²⁴ In a randomized controlled trial, Cantürk and his team demonstrated that isotherm warmed fluids could attenuate the incidence of perioperative hypothermia in parturients and improve APGAR Scores.²⁵

Intrathecal hyperbaric bupivacaine supplemented with sufentanil and morphine, for a prolonged analgesic effect, was the standard anesthesia technique in this study. Despite findings suggesting that perioperative hypothermia may be exacerbated by intrathecal opioids, the pathophysiological mechanism on how opioids influence thermoregulation is still not clear.¹⁹ A recent retrospective case-controlled study failed to prove this hypothesis.²⁶

Besides applying active warming and measuring core temperature, room temperature conditions also play an important role. In fact, increasing operating room temperature during cesarean sections may reduce the rate of neonatal and maternal hypothermia.²⁷

Our study also tried to address the hypothesis that maternal temperature and lack of proper thermal management during the operative procedure could influence neonatal outcomes. In our clinic, bonding during cesarean section is a standard procedure for healthy neonates. Better thermal stability was previously mentioned among the numerous benefits of this procedure.²⁸ Comparably to previous trials,²³ neonatal outcomes at birth were similar between the two groups (Table 2). Yet, our data shows how insufficient thermal management during cesarean section could drive hypothermia in newborns (Fig. 4).

At this point, it should be mentioned that the interpretation of neonatal outcomes could be difficult since several factors during the postoperative period could influence those outcomes.

There are some limitations to our study. The retrospective design and lack of randomization and blinding may have influenced the results. Since our primary goal was to investigate hypothermic insult based on our current hospital treatment protocol, we did not discard the patients with metabolic disorders such as hypothyroidism or diabetes from the analysis, as in most previous studies. Such conditions could impair thermoregulation and this could also be considered a bias of our research.^{29,30} We excluded the patients diagnosed with type 1 diabetes from the final analysis, but we maintained those diagnosed with gestational diabetes.

We were not able to consider other parameters such as the incidence of shivering and maternal comfort, or detailed room temperature measurements, and our report does not provide equivalent data to be compared with previous studies. We could also criticize a selection bias since a total of 179 patients were excluded from the final analysis based on our previously defined inclusion criteria (Fig. 1).

Published Guidelines for prevention of hypothermia support ZHF thermometry for perioperative core temperature monitoring^{3,14} and previous studies have successfully implemented it on parturients.¹⁰ Still, there is evidence suggesting that this method might not be adequate for monitoring rapid changes in core temperature.³¹

Conclusions

To conclude, we were able to show that forced-air warming alone for cesarean section is effective in decreasing the incidence of perioperative hypothermia in parturients, and could be used as a standalone warming solution. However, special attention should be given to neonates, since active warming during the skin-to-skin bonding period did not prevent hypothermia in the newborns after their discharge from PACU.

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Conflicts of interest

LM has received payments for lectures from 3M. JH has received payments for lectures from 3M, The Surgical Company and Abbvie. The other authors have no conflicts of interest to declare. The Bair Hugger™ temperature sensors and warming blankets were provided by 3M™ Deutschland GmbH, Neuss Germany; the company has played no role in this research nor in the decision to submit the article for publication.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.bjane.2021.10.007.

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