Tampere University

SIRKKA-LIISA LAURONEN

New Insights Into Perioperative Thermal Management

Tampere University Dissertations 702

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ACADEMIC DISSERTATION
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ACADEMIC DISSERTATION
Tampere University, the Faculty of Medicine and Health Technology
Tampere University Hospital, Department of Anaesthesia
Finland

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PunaMusta Oy – Yliopistopaino
Joensuu 2022

To my family

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When I started my first study eleven years ago, I had no aim to graduate as a PhD. However, a few years later I found myself to be a doctoral candidate. This process has been laborious but gratifying. Though there have been tears, frustration, and exhaustion, I have still experienced satisfaction, happiness, and success during this instructive journey. I have learned a lot, mostly about myself, but also about writing, statistics, and time management, for example. I am proud of myself for having completed this entity; however, I have not completed it alone but have done so with the great help of many people.

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Tampere 24th October 2022

Sirkka-Liisa

ABSTRACT

Humans and other mammals are homeothermic species that can maintain constant core temperatures regardless of changes in environmental temperatures. The core temperature is kept within narrow limits at around 37 °C in humans by the thermoregulatory control of the hypothalamus. The physiological core temperature is referred to as *normothermia,* which is an important principle for survival.

Anesthesia-associated hypothermia has been recognized since soon after the first ether anesthesia. Changes in thermoregulation caused by anesthetics have been ascertained later. Anesthetics disrupt the normal function of the hypothalamus and cause vasodilatation of peripheral vessels, which then predisposes a patient to inadvertent hypothermia. Hypothermia has disadvantages, such as impaired coagulation, an increased risk of wound infections, decreased drug metabolism, an increased risk of cardiovascular incidences, and delayed recovery.

Intraoperative hypothermia has been defined as a core temperature below 36.0 °C. The normothermia of surgical patients is maintained by utilizing different passive and active warming methods, as well as by using preoperative warming and influencing of the ambient temperature. Despite the effective warming techniques currently in use, a great number of surgical patients still experience hypothermia.

Core temperature monitoring is standard in care. However, there is no ideal thermometer available so far. The most reliable core temperature measuring methods are invasive and thus unsuitable for conscious patients. Non-invasive methods that measure core temperature from the intact skin surface were introduced at the beginning of the twenty-first century.

The aim of this thesis was to study the effectiveness of using two new warming methods in attempts to prevent inadvertent intraoperative hypothermia. A thermal suit was studied in Studies I and II, and a self-warming (SW) blanket was studied in Study III. Further, two different non-invasive thermometers were evaluated in Study IV.

Study I was a randomized controlled trial in which 100 patients were recruited and allocated to wear either a thermal suit or cotton hospital clothes at a one-to-one ratio. There were neither differences in intraoperative core temperature drop nor the incidence of hypothermia between the groups.

Study II was a clinical device investigation for which 40 patients were recruited and allocated to wear either a thermal suit or cotton hospital clothes at a one-to-one ratio. All the patients had forced-air warming (FAW) set at 38 °C during surgery. Warm air was blown into the legs of a thermal suit. Patients wearing cotton clothes had a commercial lower-body FAW blanket and a warming mattress. The core temperature decreased in all the patients. However, the incidence of hypothermia was greater among the patients wearing cotton clothes than those wearing the thermal suit at a ratio of six to one. Two patients wearing a thermal suit were noticed to sweat.

Study III was a randomized controlled trial evaluating the efficacy of a SW blanket during prewarming and intraoperatively in patients scheduled for total knee arthroplasty (TKA) under spinal anesthesia. Altogether 150 patients were recruited and randomized to have either an SW blanket or an upper-body FAW blanket set at 38 °C at a one-to-one ratio. Both blankets were effective in preoperative warming. However, the incidence of intraoperative hypothermia was great and neither of the blankets was able to prevent the core temperature drop. However, the FAW set at 43 °C was able to raise the core temperature value of hypothermic patients during surgery.

Study IV was a prospective, observational method study in which two non-invasive core temperature monitoring methods, the zero heat flux (ZHF) method and the double sensor (DS) method, were evaluated perioperatively. Either two ZHF sensors or a ZHF sensor and a DS sensor were placed simultaneously on the forehead skin of a patient, with thirty patients in each group. Data was obtained from a subset of sixty patients recruited to Study III. Bilaterally placed ZHF sensors showed almost identical temperature values. The DS method mostly showed lower values than the ZHF method. The temperature difference between the ZHF and DS sensors increased when the core temperature decreased.

The conclusion of this thesis can be stated as follows. Surgical patients easily become hypothermic despite the active warming method used. However, FAW set at 43 °C is an effective method for restoring normothermia. The ZHF method seems to have a good internal validity. The temperature values measured with the DS method were usually lower than those obtained with the ZHF method.

TIIVISTELMÄ

Ihminen ja muut nisäkkäät ovat tasalämpöisiä, ja ne pystyvät pitämään elimistön ytimen lämpötilan vakaana ympäristön lämpötilasta riippumatta. Ihmisen ydinlämpötila on noin 37 astetta. Lämmönsäätelyn kontrollointi tapahtuu hypotalamuksessa. Muuttumaton ytimen lämpötila on välttämätöntä elimistön häiriöttömälle toiminnalle.

Anestesiaan liittyvä ytimen lämpötilan lasku on kuvattu jo noin 150-vuotta sitten. Myöhemmin on selvinnyt, että anestesia-aineet aiheuttavat muutoksia elimistön lämmönsäätelyssä. Anestesia-aineet häiritsevät hypotalamuksen toimintaa ja aiheuttavat lisäksi raajojen verisuonten laajenemista, mitkä altistavat tahattomalle jäähtymiselle. Jäähtyminen heikentää veren hyytymistä, lisää infektioita, pitkittää lääkevaikutusta, altistaa sydäntapahtumille sekä hidastaa toipumista.

Anestesian aikainen hypotermia on määritelty ydinlämpötilaksi alle 36.0°C. Leikkauspotilaan ydinlämpötilaa pyritään ylläpitämään pääsääntöisesti erilaisin passiivisin ja aktiivisin lämmityskeinoin, ennen anestesiaa tapahtuvalla lämmittämisellä, sekä ympäristön lämpötilaan vaikuttamalla. Käytössä olevista menetelmistä huolimatta iso osa leikkauspotilaista jäähtyy.

Ydinlämpötilan mittaaminen kuuluu leikkauspotilaan hoitoon. Ideaalista ydinlämpömittaria ei toistaiseksi ole saatavilla. Luotettavimmat käytössä olevat menetelmät ovat kajoavia ja täten soveltumattomia hereillä olevalle potilaalle. 2000-luvun alkupuolella kliiniseen käyttöön on tullut menetelmiä, jotka mittaavat ydinlämpötilaa ihon pinnalta.

Väitöskirjani tavoitteena oli tutkia kahden uuden lämmitysmenetelmän tehokkuutta leikkauksen aikaisen jäähtymisen ehkäisyssä. Lämpöhaalaria tutkin osatöissä I ja II sekä itselämpiävää aktiivipeitettä osatyössä III. Lisäksi arvioin kahta kajoamatonta ydinlämpömittaria osatyössä IV.

Osatyö I oli satunnaistettu, kontrolloitu tutkimus, johon osallistui yhteensä 100 potilasta. Puolet potilaista sai päälleen lämpöhaalarin ja puolet tavanomaiset sairaalavaatteet. Ryhmien välillä ei ollut eroa ydinlämpötilan laskussa eikä hypotermian esiintyvyydessä.

Osatyö II oli kliininen laitetutkimus, johon osallistui yhteensä 40 potilasta. Puolet tutkittavista satunnaistettiin lämpöhaalariryhmään ja puolet sairaalavaateryhmään.

Leikkauksen aikana haalarin lahkeisiin puhallettiin 38°C ilmaa. Sairaalavaateryhmän potilaita lämmitettiin alavartalolle asetettavalla lämpöpuhallinpeitolla, 38°C, ja lämpöpatjalla, 39°C. Ydinlämpötila laski yleisanestesian aikana molemmissa ryhmissä, mutta hypotermian esiintyvyys oli suurempaa sairaalavaateryhmässä, 6 vs. 1. Haittavaikutuksena kaksi haalariryhmän potilasta hikoili.

Osatyö III oli satunnaistettu, kontrolloitu tutkimus, jossa tutkittiin itselämpiävän peiton tehoa esilämmityksen ja leikkauksen aikana potilailla, joille tehtiin polven tekonivelleikkaus spinaalipuudutuksessa. Tutkimukseen otettiin yhteensä 150 potilasta, joista puolet satunnaistettiin saamaan itselämpiävä peitto ja puolet ylävartalolle asetettava lämpöpuhallinpeitto. Molemmat peitot olivat tehokkaita esilämmityksessä. Leikkauksen aikana puolet potilaista jäähtyi eikä kumpikaan peitto kyennyt ehkäisemään sitä. Lämpöpuhallinpeitto korkeimmalla asetetulla lämpötilalla kykeni nostamaan jäähtyneen potilaan ydinlämpötilaa leikkauksen aikana.

Osatyö IV oli etenevä, havainnoiva metodityö, jossa arvioitiin kahta kajoamatonta otsalta ydinlämpöä mittaavaa laitetta; zero heat flux -menetelmä (ZHF) ja double sensor -menetelmä (DS). Tutkimustiedot kerättiin 60 potilaalta, jotka oli rekrytoitu osatyöhön III. Potilaat saivat samanaikaisesti molemmille puolille otsaa joko kaksi ZHF-sensoria tai sekä ZHF- että DS-sensorin. Molemminpuoliset ZHF-sensorit antoivat lähes identtiset lämpötila-arvot. DS-menetelmä antoi pääsääntöisesti matalamman lämpötila-arvon kuin ZHF-menetelmä. Ero ZHF- ja DS-menetelmän välillä kasvoi ydinlämpötilan laskiessa.

Tutkimusten johtopäätöksenä voidaan esittää, että leikkauspotilaat jäähtyvät riippumatta käytetystä lämmitysmenetelmästä. Kuitenkin lämpöpuhallinpeitto 43 asteisena pystyy nostamaan potilaan ydinlämpötilan takaisin normotermiseksi. ZHF-menetelmän sisäinen tarkkuus vaikuttaa luotettavalta. DS-menetelmä näyttää yleensä matalampaa lämpötilalukemaa kuin ZHF-menetelmä.

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ABBREVIATIONS

ASA	American Society of Anesthesiologists
AV	arteriovenous
BA	Bland-Altman
BMI	body mass index, kg/m^2
°C	degrees Celsius
CI	confidence interval
CO_2	carbon dioxide
dB	decibel
DS	double sensor
FAW	forced-air warming
g	grams
GA	general anesthesia
h	hour
IPH	inadvertent perioperative hypothermia
IV	intravenous
kcal	kilocalorie
L	liters
LCCC	Lin`s concordance correlation coefficient
LoAs	limits of agreement
MAP	mean arterial pressure
MBT	mean body temperature
MH	malignant hyperthermia
MST	mean skin temperature
ml	milliliters
mmHg	millimeters of mercury
NA	neuraxial anesthesia
OR	operating room
RALP	robotic-assisted laparoscopic prostatectomy
RCT	randomized controlled trial
RR	recovery room

SD	standard deviation
SSI	surgical site infection
SW	self-warming
TKA	total knee arthroplasty
TRP	transient receptor potential (proteins)
TRPA	transient receptor potential ankyrin
TRPM	transient receptor potential menthol
TRPV	transient receptor potential vanilloid
ZHF	zero heat flux
W	watt

ORIGINAL PUBLICATIONS

Publication I Lauronen SL, Kalliomäki ML, Aho A, Kalliovalkama J, Riikonen J, Mäkinen MT, Leppikangas H, Yli-Hankala A (2017). Thermal suit in preventing unintentional intraoperative hypothermia during general anaesthesia: A randomized controlled trial. *Acta Anaesthesiologica Scandinavica* 61(9), 1133-1141

Publication II Lauronen SL, Mäkinen MT, Annila P, Huhtala H, Yli-Hankala A, Kalliomäki ML (2021). Thermal suit connected to a forced-air warming unit for preventing intraoperative hypothermia: A randomised controlled trial. *Acta Anaesthesiologica Scandinavica* 65(2), 176-181

Publication III Lauronen SL, Kalliovalkama J, Aho A, Mäkinen MT, Huhtala H, Yli-Hankala A, Kalliomäki ML. Self-warming blanket versus forced-air warming blanket during total knee arthroplasty under spinal anaesthesia: A randomised noninferiority trial. *Submitted.*

Publication IV Lauronen SL, Kalliomäki ML, Kalliovalkama J, Aho A, Huhtala H, Yli-Hankala A, Mäkinen MT (2022). Comparison of zero heat flux and double sensor thermometers during spinal anaesthesia: a prospective observational study. *Journal of Clinical Monitoring and Computing* 36(5), 1547-1555

AUTHOR'S CONTRIBUTIONS

Publication I The author took part in the study design. The author recruited and anesthetized the study patients and collected data with the help of co-authors. The author analyzed the data with the help of the supervisor and wrote the article with the help of co-authors. The author is the main author of this publication. The author submitted the article and acted as a corresponding author.

Publication II The author took part in the study design. The author recruited and anesthetized the study patients and collected data. The author analyzed the data with the help of a statistician and wrote the article with the help of co-authors. The author is the main author of this publication. The author submitted the article and acted as a corresponding author.

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None of the publications appears in any other thesis.

1 INTRODUCTION

> The most effective means (of cooling a man) is to give an anaesthetic
>
> Pickering, 1958

The first description of perioperative hypothermia was introduced in 1847, only one year after the first general anesthesia with ether was performed (Bräuer, 2017). The core temperature decrease was found in anesthetized rabbits. Two decades later, the core temperature range of a human was declared and *normothermia* was defined. The first perioperative hypothermia in patients was described in 1880, and active warming with intravenous (IV) fluids was recommended one year later. Further, the dominant thermoregulatory site in mammals was found to be the hypothalamus in 1912.

The mechanisms behind the thermal perturbations caused by anesthesia and surgery were intensively studied in the last decades of the twentieth century. Hypothermia was found to be more contributed to by anesthetic-induced impairment of thermoregulatory control than by exposure to cold ambient temperature per se (Sessler et al., 1988). Further, the initial core temperature decrease after anesthesia induction was found to result from the redistribution of body heat

content (Holdcroft et al., 1979; Matsukawa et al., 1995). To prevent redistribution hypothermia, preinduction warming is utilized to increase the temperature of extremities (Hynson et al., 1993).

Inadvertent hypothermia was found to relate to distinct adverse effects, such as impaired coagulation (Reed et al., 1992), decreased drug metabolism (Leslie et al., 1995), an increased risk for wound infections (Kurz et al., 1996), and cardiac events (Frank et al., 1997), as well as delayed recovery (Lenhardt et al., 1997). It is thus recommended to keep patients normothermic perioperatively (Forbes et al., 2009; Hooper et al., 2009; National Institute for Health and Clinical Excellence & (NICE), 2016).

Despite the available passive and active warming methods, inadvertent hypothermia is common even today (John et al., 2016; Scholten et al., 2018; Alfonsi et al., 2019; Sari et al., 2021). Moreover, core temperature monitoring is often ignored, especially during neuraxial anesthesia (NA) (Torossian, 2007; Koh et al., 2021).

In this thesis, I study the effectiveness of two newly developed warming methods, a thermal suit and a SW blanket, in preventing inadvertent intraoperative hypothermia. The aim of the thesis is to find a warming method that is effective, easy to use, and cost-efficient. In addition, two non-invasive thermometers are evaluated in patients under spinal anesthesia.

2 REVIEW OF THE LITERATURE

2.1 Physiological thermoregulation

A human being is both an endotherm and a homeotherm as a person regulates his or her body temperature via metabolic processes and maintains a constant core temperature independent of the ambient temperature.

Body temperature is not evenly distributed. Hence, the body can be divided into the central core, which refers to the deep organs and tissues surrounding the central nervous system, and the peripheral thermal compartments, which refer to the skin and extremities (Burton, 1935). The core and the peripheral compartments have different meanings in thermoregulation.

The core is essentially the source of heat production. Heat is a principal by-product of metabolism, which involves all the cells of the body. Metabolism depends on the rate of energy consumption, and thus of O_2 consumption, and is therefore not constant. Heat is especially produced in the liver, brain, and heart and in skeletal muscles during physical activity or shivering. Extra metabolism and heat production are also caused by hormones, such as thyroxine and epinephrine, and by the thermogenic effect of food. (Hall & Hall, 2021)

A normal core temperature is approximately 37 °C and it is strictly controlled within a few tenths of a degree of the target temperature. Values less than 36°C or greater than 38 °C usually indicate a loss of thermal control or an ambient temperature so extreme that it overcomes thermoregulatory defenses. Core temperature has a circadian rhythm with at least 1°C oscillation between a daytime maximum (at 3:00 to 6:00 p.m.) and a nighttime minimum (at 3:00 to 6:00 a.m.). Besides this, female core temperature varies during the menstrual cycle, being 0.5 °C higher during the postovulatory phase. (Refinetti, 2010)

The peripheral compartments regulate heat loss from the body. Via the skin surface, the body also gains external heat. The temperature of the skin and extremities is variable and strongly dependent on the ambient temperature.

2.1.1 Body temperature control

Thermoregulation is based on negative and positive feedback in order to minimize perturbations from the targeted, normal value. The components of the thermoregulatory network are (1) afferent sensing, (2) central regulation, and (3) efferent responses (which include behavioral thermal control and autonomic responses) (see Fig. 1). (Tan & Knight, 2018)

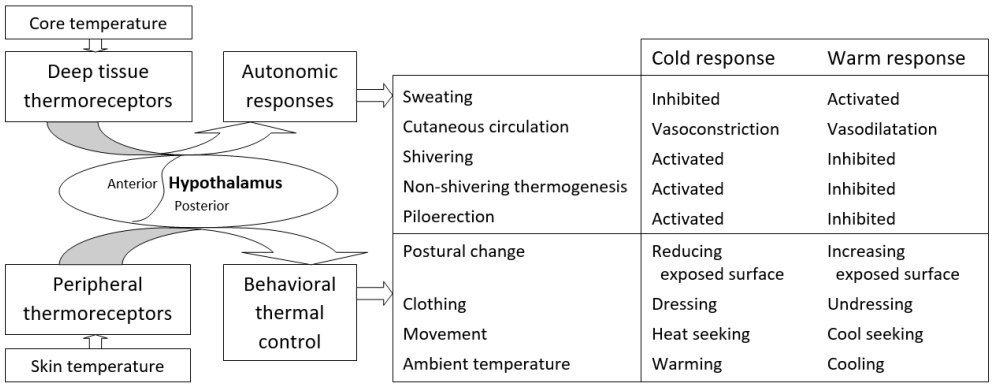

Figure 1. Thermoregulation. Figure modified from the article of Tan & Knight, 2018

Afferent sensing

Temperatures are sensed from thermoreceptors, which are free nerve endings containing the transient receptor potential (TRP) family of cation channels (Kashio, 2021). The vanilloid receptors (TRPV1–4) are activated by heat (Caterina et al., 1997; Benham et al., 2003) and the menthol receptors (TRPM8) and ankyrin receptors (TRPA1) are activated by cold (Peier et al., 2002; Story et al., 2003).

Thermally responsive neurons are located in the skin and in the deep tissues. Skin primarily senses environmental temperature and has ten times as many cold-sensing neurons as it has warmth-sensing neurons. The thermal neurons of deep tissues (such as abdominal and thoracic tissues, the spinal cord, the brain stem, and the preoptic area of the anterior hypothalamus) play a major role in detecting changes in core temperature and mainly sense warmth rather than cold. (Hall & Hall, 2021)

The information about changes in temperature is relayed to the hypothalamic thermoregulatory center. Cold afferent signals traverse Aδ nerve fibers and warm signals traverse unmyelinated C nerve fibers (Poulos, 1981).

Central control

The dominant thermal controller in mammals is the hypothalamus, in which thermal inputs from deep tissues and skin are integrated. The anterior hypothalamus receives eighty percent of its thermal information from deep tissues and mediates autonomic thermal control (Satinoff, 1978). Mean skin temperature (MST) only accounts for ten to twenty percent of the information informing autonomic thermal control. The posterior hypothalamus receives inputs from the skin (Frank et al., 1999), mediates subjective thermal sensation, and is responsible for behavioral thermal control (see Fig. 1).

The thermostatic core temperature control center is in the preoptic area of the anterior hypothalamus. Temperature sensory signals from the preoptic area and from tissues throughout the body are transmitted to the posterior hypothalamus. There, the thermal information is combined and integrated in order to control the reactions of the body undertaken for maintaining the core temperature within relatively narrow limits. (Hall & Hall, 2021)

Efferent responses

The body responds to thermal perturbations via effector mechanisms that promote heat loss, heat conservation, or heat production. Thermoeffectors are behavioral thermal control and autonomic responses, such as sweating, vasoconstriction and vasodilatation, and shivering and non-shivering thermogenesis (see Fig. 1). Autonomic responses are controlled by the sympathetic nervous system. Each response has its own threshold (a triggering core temperature), gain (the rate at which response intensity increases, once triggered), and maximum intensity. Moreover, each of them is activated in an efficient order in proportion to need. (Tan & Knight, 2018)

The interthreshold range is defined as the temperature range between the first autonomic warmth response (sweating) and the first autonomic cold response (vasoconstriction). The range only spans 0.2 °C (Lopez et al., 1994). A core

temperature within the range does not trigger autonomic thermoregulatory responses.

Behavior

Behavior is the first and most important thermoregulatory defense mechanism that responds to a change in ambient temperature (Hardy, 1971). Behavioral thermoregulation is approximately half mediated by skin temperature. It is triggered when thermal information is provided to the cerebral cortex for conscious perception. Behavioral adaptations involve postural changes, heat or cool seeking, dressing, or altering the ambient temperature (see Fig. 1).

Clothing reduces conductive and convective heat loss by enclosing air between the skin and the cloth. A dry layer of clothes decreases the rate of heat loss to about half of that of a nude body. In damp or wet clothes, the rate of heat transmission increases 20-fold or more and the effectiveness of clothing in maintaining body temperature is almost lost.

Heat radiates from the skin to the clothing. If the inside of clothing is coated with a thin layer of metal, heat is reflected back to the body. This phenomenon is utilized in reflective blankets, which are especially used in first aid.

Sweating

Sweating is a principal mechanism for heat loss. It is activated when the core temperature is increased but can be influenced by the temperature of the skin. Sweating elevates the partial pressure of water vapor on the skin surface and promotes increased evaporation up to 4 L/hr.

Cutaneous circulation

Skin blood flow is the most effective mechanism of heat exchange between the core and the environment. Cutaneous vasoconstriction is the first thermoregulatory response during exposure to cold. It decreases skin blood flow and prevents heat dissipation, leading to heat conservation, which is more efficient than heat production. Cutaneous vasodilatation increases skin blood flow and convective heat loss during passive heat stress or exercise.

Cutaneous circulation consists of continuous venous plexus, arteriovenous (AV) anastomoses, arterioles, and the skin capillaries found in hands, feet, and ears. Tonic vasoconstriction of arterioles and AV anastomoses is dominant in normothermic humans. The rate of blood flow to the venous plexus can raise from barely zero (in a fully vasoconstricted state) to up to 30% of the total cardiac output (in a fully vasodilatated state) corresponding to an eightfold increase in the conductance of heat from the core to the skin.

Shivering

Shivering is involuntary, rhythmic muscle contraction and relaxation, generated by cold stress. It is driven by the same α motor neurons that innervate skeletal muscle for movement and posture, but the underlying mechanism of shivering is unknown. For brief intervals, shivering can triple or quadruple the metabolic rate, and for extended periods (hours), the metabolic rate can be doubled before fatigue occurs.

Non-shivering thermogenesis

Non-shivering thermogenesis is metabolic heat production, and it supplements cutaneous vasoconstriction when cold stress increases. The primary organ for non-shivering thermogenesis is brown adipose tissue in which the subsequent oxidation of fatty acids is the source of heat. Non-shivering thermogenesis increases the basal metabolic rate from 25% to 40% in adult humans. This response is important in infants, unlike in adults.

Piloerection

Piloerection is the involuntary contraction of smooth muscles in the hair follicles, activated in response to cold stress. A still layer of warm air close to the skin is retained to reduce the rate of heat loss. The thermoregulatory benefit of piloerection is slight in humans.

2.2 The mechanisms of heat transfer

Heat can be transferred between different objects by radiation, conduction, and convection (see Table 1). Heat transfers from a high-temperature object to a lower-temperature object, leading to the temperature difference equilibrating over time according to the second law of thermodynamics (see Table 2).

Radiation is proportional to the temperature difference between objects. Conduction is proportional to the area involved, to the temperature difference, and to the thermal conduction coefficient of an object but inversely proportional to the thickness of an object. Convection is proportional to the temperature difference, but it also depends on the velocity of the medium.

Table 1. Mechanisms of heat transfer

Mechanism	Definition
Radiation	Heat transfer by the infrared portion of electromagnetic waves. Radiation is generated by moving molecules with a temperature above absolute zero. It happens in all directions through empty space.
Conduction	Heat transfer between two objects in contact or between different parts of a single object. Conductive heat transfer is generated by microscopic collisions between atoms or molecules. It occurs in solid, liquid, and gas but more easily in solids and liquids where particles are closer than in gases where particles are further apart.
Convection	Heat transfer by the mass motion of liquid or gas from one location to another. *Natural convection* is the spontaneous flow of molecules due to density and temperature variation. *Forced convection* is the movement of molecules generated by an external source.

Table 2. The laws of thermodynamics

	Definition	Scientist	Year
Zeroth law	**Thermal equilibrium** If two systems are each in thermal equilibrium with a third system, then they are in thermal equilibrium with each other.	Ralph Fowler	1931
First law	**Conservation of energy** The total energy of an isolated system is constant. Energy can neither be created nor destroyed, only altered in form.	Rudolf Clausius	1850
Second law	**The entropy of any isolated system always increases.** Heat does not spontaneously pass from a colder to a hotter body.	Nicolas Léonard Sadi Carnot Rudolf Clausius	1824 1854
Third law	The entropy of a system approaches a constant value as the temperature approaches absolute zero.	Walther Nernst	1905

In humans, heat is exchanged with these three mechanisms and is additionally lost with evaporation (see Fig. 2). There are two different evaporative heat loss mechanisms. First, insensible heat loss is derived from the uncontrolled, continuous diffusion of water from the skin and lungs. Second, sweating is controlled heat loss due to the production of fluids secreted by the sweat glands in the skin. The evaporative rate is proportional to the water vapor pressure gradient between the skin and environment but independent of the temperature gradient between them.

Heat loss and heat production are kept in balance so that core temperature remains constant. All heat dissipation occurs at the body surface. Two factors determine heat loss rate: (1) how rapidly heat is conducted from the body core to the skin and (2) how rapidly heat is then transferred to the surroundings. Heat transfer from the body surface is affected by insulators (which are skin, subcutaneous tissue, and fat). Fat only conducts heat one third as easily as other tissues.

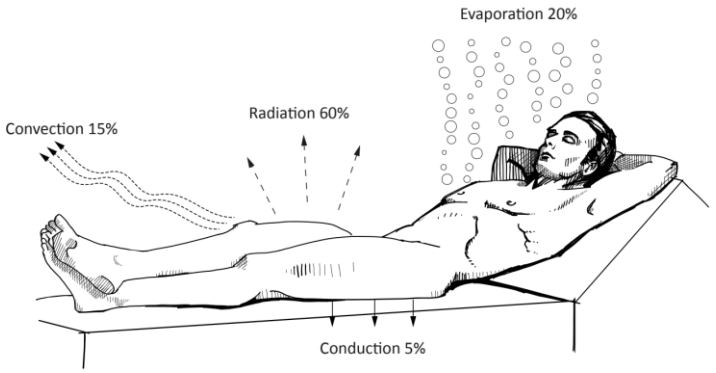

Figure 2. Heat exchange mechanisms. The proportions of different heat loss mechanisms depend on the ambient temperature, clothing, and the thermal balance of a person. Figure modified from the article of Sessler, 2000

2.3 Anesthesia and thermoregulation

Anesthesia and perioperative environments predispose patients to thermal disturbances. Anesthetics impair thermoregulation and cause vasodilatation, which leads to thermal redistribution and heat loss. Further, behavioral thermoregulation is mostly excluded in operating theatres.

2.3.1 General anesthesia

Anesthetics impair thermoregulatory control by decreasing vasoconstriction and shivering thresholds, and by elevating sweating thresholds. This impairment leads the strictly controlled interthreshold range of core temperature to broaden up to twenty-fold, from 0.2 °C to 4 °C (Lopez et al., 1994) (see Fig. 3). Thus, thermoregulatory responses are not triggered within the broadened limits. However, they will be activated when the core temperature outreaches the limits.

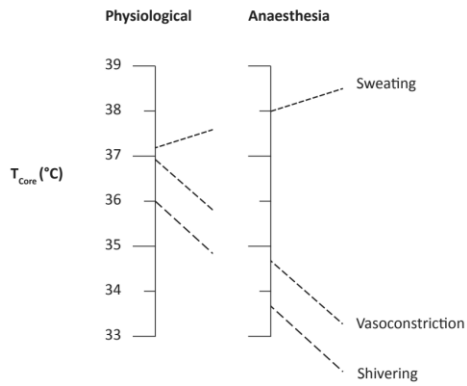

Figure 3. The anesthesia-induced broadening of the interthreshold range. Figure modified from the article of Matsukawa et al, 1995.

Anesthetics impair thermoregulation depending on their concentration. The iv anesthetics propofol (Leslie et al., 1994; Matsukawa et al., 1995) and dexmedetomidine (Talke et al., 1997), as well as opioid alfentanil (Kurz et al., 1995), have little effect on the sweating threshold whereas they linearly decrease the vasoconstriction and shivering thresholds. The volatile anesthetics halothane (Sessler et al., 1988), isoflurane (Støen & Sessler, 1990), enflurane (Washington et al., 1992), sevoflurane, and desflurane (Annadata et al., 1995; Ozaki et al., 1995) slightly increase the sweating threshold. Each of them greatly reduces the cold response thresholds and the reduction is more intense with higher concentrations of agents. The inhalation anesthetic nitrous oxide has a similar effect on response thresholds but to a lesser extent than equipotent concentrations of volatile anesthetics (Ozaki et al., 1995). Of the anesthetic agents tested thus far, midazolam impairs thermoregulatory control the least (Kurz et al., 1995).

Anesthetics, sedatives, and opioids have a different influence on the gain and maximum intensity of responses. Generally, sweating is largely preserved intact during general anesthesia (GA) (Washington et al., 1993; Lopez et al., 1994). The maximum intensity of vasoconstriction remains normal (Sessler et al., 1992) though the gain of vasoconstriction is reduced during desflurane anesthesia (Kurz et al., 1995). The maximum shivering intensity may be reduced (Ikeda et al., 1998). Nevertheless, the threshold reduction is far more important than the gain and intensity of the response when triggered in the thermoregulatory control.

The exact mechanism of how anesthetics impair thermoregulatory control remains unclear. A potential assumption may be the inhibitory effect of volatile anesthetics on TRPV1 receptors as they reduce the threshold for heat activation (Cornett et al., 2008). On the contrary, TRPV1 antagonists have been shown to dose-dependently prevent hypothermia in rats during GA (Garami et al., 2017).

2.3.2 Neuraxial anesthesia

Spinal and epidural anesthesia, termed *neuraxial anesthesia*, impair thermoregulation by preventing the most efferent neural input to the lower body. The inhibition of efferent neural input blocks vasoconstriction and shivering, or if they occur, the gain and maximum intensity are substantially reduced (Kim et al., 1998).

NA also impairs thermoregulatory control centrally, although local anesthetics used do not normally reach the brain. The exact mechanism for central impairment is unknown, but it has been shown that the effect is peripherally mediated (Joris et al., 1994). Afferent input is normally dominated by tonic cold signals (Pierau & Wurster, 1981) that are due to NA being interpreted as warmth in the brain (Doufas et al., 2008). This apparent but not actual increase in leg temperature causes the shivering threshold to decrease (Emerick et al., 1994; Ozaki et al., 1994). Further, patients under NA do not complain of feeling cold even when they are hypothermic (Glosten et al., 1992).

NA decreases the vasoconstriction thresholds (Kurz et al., 1993), causing the interthreshold range to broaden by up to 1 °C. The impairment of thermoregulatory control is proportional to the number of blocked dermatomes (Leslie & Sessler, 1996).

2.3.3 Thermal distribution and heat balance

Core temperature is usually 2 °C to 4 °C higher than the temperature of peripheral tissues. The core-to-peripheral tissue temperature gradient is maintained by the tonic thermoregulatory vasoconstriction of AV anastomoses. Anesthetics inhibit the vasoconstriction (Kurz et al., 1995; Robinson et al., 1997) and also directly influence to the smooth muscle cells of vessels (Akata & Warltier, 2007). The resulting vasodilatation leads to thermal redistribution (Holdcroft et al., 1979).

Thermal redistribution is the main cause for a rapid core temperature decrease during the first hour of GA (see Fig. 4). It corresponds to 81% of the initial core temperature decrease, which could even be 1.6 °C ± 0.3 °C (Matsukawa et al., 1995). According to the second law of thermodynamics, anesthesia-induced vasodilatation allows core heat to flow to legs and arms, which are warmed at the expense of the core. The extent of the core temperature decrease depends on the core-to-peripheral temperature gradient at the time of induction. This gradient, in turn, depends on the patient's thermoregulatory status and the prior thermal environment.

Thermal redistribution is also the main cause for the initial core hypothermia after the induction of NA. NA inhibits the afferent input from the blocked dermatomes, resulting in the dilatation of AV anastomoses. However, redistribution is limited to the lower body and the core temperature decreases by up to 1.0 °C that is less than under GA (Matsukawa et al., 1995).

Thermal redistribution is followed by a slow, linear reduction in core temperature for two to three hours. The reduction results from heat loss exceeding metabolic heat production. The metabolic rate and heat production are reduced by approximately 25% during GA (Stevens et al., 1971). They are better preserved during NA because shivering thermogenesis of upper body is maintained.

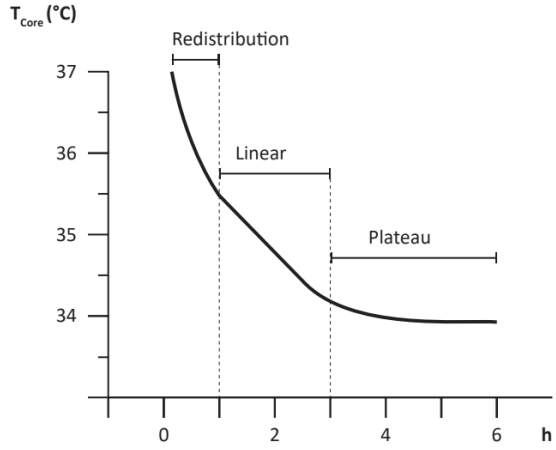

Figure 4. Thermal distribution and heat balance. Figure modified from the article of Kurz et al, 1995.

Three hours after anesthetic induction, the core temperature stabilizes and remains unchanged for the duration of the anesthesia (Sessler et al., 1988). At this core temperature plateau, heat production equals heat loss. The vasoconstriction threshold ranges from 33 °C to 35 °C, and when triggered, the intensity and gain remain normal, leading to heat being constrained to the core.

Patients under NA do not develop a core temperature plateau after several hours of anesthesia because the nerve block in the legs directly prevents vasoconstriction. Redistribution remains the major cause of core hypothermia, even after three hours of anesthesia (Matsukawa et al., 1995).

Combined GA and epidural anesthesia causes additive impairment in thermoregulation (Joris et al., 1994). Hypothermia is prolonged since metabolic heat production is reduced due to the GA, and heat loss through the skin is continued due to the epidural anesthesia.

It has been supposed that peripheral nerve blocks do not impair thermoregulation centrally (Sessler, 2016). Their effect is limited to the prevention of local thermoregulatory responses that are neurally mediated.

2.4 Inadvertent perioperative hypothermia

Inadvertent perioperative hypothermia (IPH) is defined as a core temperature below 36 °C (Vaughan et al., 1981; Sessler, 1997; National Institute for Health and Clinical Excellence & (NICE), 2016). IPH has been known for decades (Goldberg & Roe, 1967), and its incidence is still over 50% despite the use of passive and active warming (John et al., 2016; Alfonsi et al., 2019; Arkiliç et al., 2000; Scholten et al., 2018).

The anesthesia-induced impairment of thermoregulation is the most important reason for hypothermia. In addition, patient-related factors (as well as environmental- and surgery-related factors) contribute to hypothermia developing.

IPH has well-known disadvantages, many of which are potentially severe, and clinical guidelines recommend maintaining normothermia perioperatively (Forbes et al., 2009; Hooper et al., 2009; Torossian et al., 2015). In this thesis, the British guideline "The management of inadvertent perioperative hypothermia in adults having surgery" has been utilized (National Institute for Health and Clinical Excellence & (NICE), 2016). The guideline was published in 2008 and reviewed in

2016. It includes recommendations for patients' perioperative thermal management, such as assessing the risk of hypothermia, measuring and monitoring core temperature, and methods for keeping patients warm. Detailed recommendations for pre-, intra-, and postoperative phases are given in the guideline.

2.4.1 Patient-related risk factors

A patient's age influences the probability of IPH. Infants have a high surface-to-mass ratio that makes them more vulnerable to hypothermia or hyperthermia when exposed to a cold or hot environment, respectively. However, anesthetized infants and children have similar thermoregulatory response thresholds to those observed in adults (Bissonnette & Sessler, 1990). In elderly people, cold response thresholds are decreased by about 1 °C more than in younger adults (Kurz et al., 1993). Generally, elderly people have a reduced ability to sense cold and heat, as well as a reduced ability to generate or dissipate heat (Macmillan et al., 1967; Wagner et al., 1974).

Normal- and underweight patients have an increased risk for IPH compared with overweight patients (Fernandes et al., 2012). There is larger core-to-peripheral temperature gradient in thin patients than in overweight patients. Thus, thermal redistribution is more profound among thin patients (Kurz et al., 1995). Overweight patients, in contrast, have a high total body fat content that reduces heat loss (Anderson & Martin, 1994).

It has also been shown that peripheral (diabetic) neuropathy impairs thermoregulatory vasoconstriction, and a core temperature plateau may fail to develop (Kitamura et al., 2000). Further, female gender (Matos et al., 2018), and low preoperative systolic blood pressure and a decreased heart rate may increase the risk of intraoperative hypothermia (Kasai et al., 2001).

2.4.2 Environmental and surgery-related factors

Many environmental and surgery-related factors affect the incidence of IPH. A cool operating room (OR) predisposes patients to hypothermia (Morris & Wilkey, 1970), especially if a patient is not actively warmed (Frank et al., 1992; Pei et al., 2018). Air conditioning and undressing a patient for surgery both increase heat loss by

convection and radiation. Wide operative fields (Roe, 1971) and surgical skin preparation with alcohol-based solutions (Sessler et al., 1993) both increase the incidence of hypothermia.

The temperature of insufflation gas has no effect on core temperature changes (Farley et al., 2004; Davis et al., 2006). The effect of irrigation solutions on core temperature depends on the temperature and volume of solutions (Campbell et al., 2015; Steelman et al., 2018).

2.4.3 The consequences of mild intraoperative hypothermia

Impaired coagulation

Hypothermia has been shown to increase blood loss and transfusion requirements (Schmied et al., 1996; Hofer et al., 2005; Sun et al., 2015; Yi et al., 2018). Even mild hypothermia (35.5 °C) increases blood loss by about 20% (Rajagopalan et al., 2008).

Hypothermia-induced coagulopathy is well documented. Coagulopathy mostly results from the impairment of platelet aggregation due to the reduced release of thromboxane A3 (Valeri et al., 1992; Michelson et al., 1994). Hypothermia also inhibits the enzymatic reactions of the coagulation cascade, which reduces clot formation (Rohrer & Natale, 1992). Coagulopathy becomes apparent when coagulation screening tests are performed at hypothermic temperatures instead of at 37 °C (Reed et al., 1992; Staab et al., 1994).

An increased risk of wound infection

Patients having final intraoperative core temperature value of 34.7 °C have been shown to be three times more prone to developing a surgical site infection (SSI) than normothermic patients (Kurz et al., 1996). Hypothermia contributes to SSI by a few mechanisms. First, hypothermia decreases tissue oxygenation via postoperative vasoconstriction (Sheffield et al., 1996). Tissue oxygen is required for oxidative killing by neutrophils. Second, hypothermia directly impairs the immune function (VanOss et al., 1980; Wenisch et al., 1996). Third, hypothermia reduces wound healing, which predisposes patients to recontamination.

Decreased drug metabolism

Enzymatic reactions are thermal-based reactions. A core temperature value of approximately 34 °C has been shown to decrease drug metabolism and, thus, to prolong the action of drugs. The solubility of volatile anesthetics is increased (Han & Helrich, 1966) as well as a propofol plasma concentration is increased (Leslie et al., 1995). The duration of the action of muscle relaxants is also prolonged (Heier et al., 1991; Leslie et al., 1995).

Shivering

Shivering rarely occurs intraoperatively since vasoconstriction is effective even during anesthesia and the core temperature seldom decreases the additional 1 °C required to reach the shivering threshold (De Witte & Sessler, 2002). Further, the use of a muscle relaxant or NA excludes or diminishes the possibility of shivering.

Postoperative shivering is more common in hypothermic patients than in normothermic patients and occurs in approximately 20% of patients with a core temperature value between 34 °C and 35.5 °C on admission to the recovery room (RR) (Vaughan et al., 1981; Yi et al., 2017). Shivering increases oxygen consumption (Just et al., 1992), intraocular and intracranial pressure (Mahajan et al., 1987; Rosa et al., 1995), and aggravates wound pain by stretching surgical incisions.

An increased risk of myocardial injury

Mild hypothermia, indicated by a temperature from 35 °C to 35.5 °C, has been shown to cause adverse myocardial effects (Frank et al., 1995, 1997; Nesher et al., 2003). However, in these studies, these were found in patients who already had coronary artery disease or were at high risk of it. The extent to which hypothermia contributes to myocardial outcomes remains unclear. Nearly normothermic final intraoperative core temperatures were not associated with myocardial injury in a recent retrospective cohort study of noncardiac patients (Schacham et al., 2018).

Mild hypothermia has been shown to provoke an adrenergic response that includes an increased norepinephrine concentration, vasoconstriction, and hypertension (Frank et al., 1995). These may lead to myocardial ischemia and arrhythmia. Hypothermic patients have been shown to have a threefold increase in

morbid cardiac events (Frank et al., 1997) and elevated troponin I levels compared with normothermic patients (Nesher et al., 2003).

Prolonged recovery and an increased risk of mortality

The duration of postanesthetic recovery and hospitalization were found to be prolonged in patients who had a final intraoperative core temperature value below 35 °C (Lenhardt et al., 1997; Kurz et al., 1996). A core temperature over 35 °C has not been shown to lengthen hospitalization with clinical significance (Sun et al., 2015).

A core temperature below 36 °C in postoperative intensive care unit patients has been shown to be associated with in-hospital mortality (Karalapillai et al., 2009). However, the hypothermic patients who died in this study were sicker and older than the patients who survived.

2.5 Hyperthermia and fever

Hyperthermia is a core temperature exceeding normal values due to failed thermoregulation. In hyperthermia, more heat is produced or absorbed by the body than can be dissipated. Hyperthermia can result from prolonged exposure to heat or a high ambient temperature, and the risk is increased with simultaneous dehydration or hypovolemia. Hyperthermia may also be caused by drugs and narcotics (Eyer & Zilker, 2007), including drug interactions (such as serotonin syndrome and neuroleptic malignant syndrome) (Tormoehlen & Rusyniak, 2018), and stress (Oka, 2015).

Passive intraoperative hyperthermia may result from excessive patient insulation and heating, especially when adequate temperature monitoring is not used. This kind of hyperthermia does not result from failed thermoregulation and can be treated by removing excessive insulation and discontinuing active warming.

Hyperthermia is rarer than hypothermia perioperatively, but it is more dangerous compared with a similar degree of hypothermia. Excessive hyperthermia leads to disseminated intravascular coagulation, rhabdomyolysis, and myocardial necrosis and may cause acute hepatic insufficiency and pancreatitis (Bouchama & Knochel, 2002).

Malignant hyperthermia (MH) is an inherited anesthetic-related complication that is uncommon but potentially life-threatening (Larach et al., 2014). The MH condition is caused by the abnormal function of the skeletal muscle ryanodine receptor and atypical intracellular calcium handling. It may be triggered by volatile anesthetics or succinylcholine. MH is seen as a rapidly increasing core temperature, acidosis, tachycardia, increased end-tidal carbon dioxide, and muscle rigidity. The only medication for reversing the symptoms is dantrolene, which attenuates myoplasmic calcium concentrations (Gupta & Hopkins, 2017).

A fever is a regulated elevation of the core temperature, induced by the central thermoregulatory system itself. It is a response to endogenous pyrogens (Dinarello et al., 1986; Davatelis et al., 1989), which are activated by a variety of inflammatory and infectious stimuli. Infection is thus by far the most common cause of fever perioperatively. Other causes may be mismatched blood transfusions, allergic reactions, and blood in the fourth ventricle. The treatment of fever involves the administration of antipyretic medication and possibly also involves active cooling.

2.6 Perioperative thermal management

Perioperative hypothermia results from the combined action of anesthetic-induced impairment in thermoregulation, surgery-related factors, and ambient temperature. However, most thermal managements are based on limiting cutaneous heat loss and active skin surface warming. Other methods—such as deep-body warming, and pharmacological and nutritional methods—are seldom used. Various approaches have different efficacy.

2.6.1 Passive insulation

Passive insulation is the easiest way to decrease cutaneous heat loss. There are several options for insulation, such as blankets (including reflective blankets), surgical drapes, and plastic and cloth sheets. A single layer of an insulator reduces heat loss by approximately 30% regardless of the type of insulator (Sessler et al., 1991). The insulation effect of covers is based on air being trapped between the skin and the cover. Hence, increasing the number of covers does not proportionally increase the insulation effect (Sessler & Schroeder, 1993). Moreover, warming the blankets is

momentary and relatively ineffective (Sessler & Schroeder, 1993). More important than the material or number of covers is the amount of the body that is covered by the cover since cutaneous heat loss is roughly comparable to the exposed area throughout the body.

The thermal suit

The T-Balance® thermal jumpsuit (Telespro Finland Ltd.) is designed to prevent thermal loss via skin, especially during the perioperative period (see Fig. 5). It is worn preoperatively instead of cotton hospital clothes and can be used for various surgical procedures due to having multiple zippers. The suit is made of a three-layer laminated fabric composed of an outer layer of smooth woven microfiber, a waterproof middle layer of breathable fabric, and an inner layer of microfleece. It is reusable and can be washed up to 80 times (or until 180 weeks of use if the number of washes cannot be calculated).

The T-Balance® thermal suit has been studied in two randomized controlled trials so far. In one trial, the suit has been shown to be effective in preventing intraoperative hypothermia (Hirvonen & Niskanen, 2011), but in the other trial, the suit did not have any effect in the prevention of inadvertent hypothermia (Brodshaug et al., 2019).

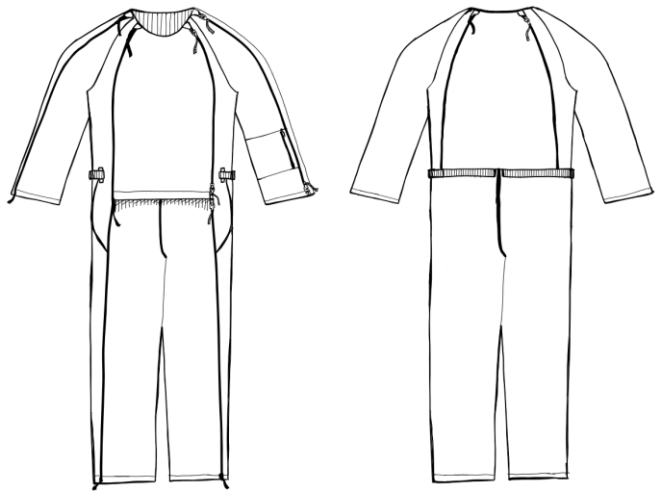

Figure 5. The thermal suit (T-Balance®). The front view (on the left) and the back view (on the right). Figure modified from the article of Hirvonen & Niskanen, 2011.

2.6.2 Active cutaneous warming methods

Cutaneous warming is an efficient way to transfer heat via the skin into the body core. Cutaneous methods include forced-air warming (FAW), circulating water, and electric and chemical warming technologies. FAW is the most studied and the most used method (Madrid et al., 2016). Heat transfer with all these technologies depends on the available skin surface area and its circulatory convection, temperature, and tissue insulation.

Forced air

The function of the FAW method is based on using convective heat transfer to move warm air across the skin. The FAW system consists of a power unit (as a heat source), a hose with a nozzle and a filter, and a disposable blanket. Warm forced air is produced by an electrical heater and a blower, and is led through the hose inside a blanket. The blanket is made of plastic bonded into tubular channels with a series of micro-perforations on the underside. Through these perforations, the heated air exits directly to the patient's body surface.

The FAW method has diverse options to choose between. The temperature of the heater can typically be set to 32 °C, 38 °C, or 43 °C. Moreover, some power units have an ambient air temperature setting that can be used to cool patients. The power of the blower can be set to *low* or *high* in most devices. Further, the blankets are available in different shapes and sizes in order to best suit the surgery.

The shape and size of a blanket is known to be associated with heat distribution (Bräuer & Quintel, 2009). In small FAW blankets, heat is distributed more evenly, and therefore, they are more efficient than larger blankets (Bräuer et al., 2009). On the other hand, the larger the area of skin that is covered under the blanket, the better the efficacy of the FAW. The method not only transfers heat to the body but reduces convective and radiant heat loss from exposed skin. The heat transfer capacity differs between FAW devices, but this has little clinical relevance (Giesbrecht et al., 1994).

FAW is a well-tolerated method but has some shortcomings. Noise is generated by the power unit with a level ranging from 46 dB to 58 dB, which may be disturbing (Cleves et al., 2010). Burns have been reported despite proper use (Stewart & Harban, 2012; Kafrouni & Fadel, 2016). Moreover, the risk of SSIs associated with the use of FAW has been discussed (Avidan et al., 1997). The current evidence is

that FAW devices do not increase SSIs (Wood et al., 2014; Haeberle et al., 2017; Poveda et al., 2020).

Circulating water

Water has great heat capacity and thermal conductivity (Wadhwa et al., 2007; Rein et al., 2007). Circulating water is utilized as a conductive heating method in mattresses and garments. The efficacy of mattresses is only modest since a mattress covers a relatively small fraction of the body's surface area. Moreover, a person`s back is poorly perfused because of the compression of cutaneous capillaries when one is lying on one`s back. Further, more heat is lost via radiation and convection from the anterior surface than via conduction into the operating table. It has been shown that a circulating water mattress is not as effective as FAW in maintaining intraoperative normothermia (Kurz et al., 1993). However, a segmented circulating water garment that covered the entire torso and extremities has been shown to transfer more heat to the patient than a full-body FAW blanket (Taguchi et al., 2004).

Potential complications of water warming devices are burns (Gali et al., 2003). A supine patient's posterior surface skin is vulnerable to pressure-heat necrosis due to reduced perfusion. Pressure-heat necrosis is difficult to prevent as the posterior surface cannot easily be observed during surgery.

Resistive heating

The resistive heating method is based on carbon fiber technology that is powered from electrical mains. Heat is generated when a converted low-voltage direct current passes through semiconductive carbon fiber fabric strips.

Resistive heating is utilized in covers as a conductive method. Covers are available in many configurations and the temperature can be set, ranging from 37 °C to 42 °C. The resistive heating system is reusable, silent, and fully isolated, it does not interfere with other OR electronics. Resistive heating maintains core body temperature as effectively as FAW (Matsuzaki et al., 2003).

The self-warming blanket

The principle of the single-use, conductive SW blanket (BARRIER® EasyWarm®, Mölnlycke Health Care AB, Gothenburg, Sweden) is based on a chemical reaction. The Barrier® EasyWarm SW blanket has twelve warming pads containing iron powder. Each pad is 13 cm x 10 cm in size and enclosed into pocket on the outer surface of the blanket. Heat is generated when the iron powder exothermically reacts with ambient oxygen when the blanket is unwrapped and exposed to air. The pads reach a maximum temperature of between 40 °C and 42 °C within 30 minutes and maintain the achieved temperature for up to 10 hours.

The SW blanket has advantages over other active cutaneous warming methods but also some disadvantages. The SW blanket is simple to use and does not need a power supply to function, and therefore, it can easily be used perioperatively. It does not cause air turbulence and is silent. However, the temperature of the pads cannot be regulated, and heat is not evenly distributed in the blanket. The blanket can be placed directly onto the skin, but to avoid burns, the blanket may not be covered.

The superiority of the SW blanket over standard hospital clothes has been shown (Torossian et al., 2016). However, other randomized controlled trials that compare the perioperative use of the SW blanket to a FAW blanket under NA or GA have conflicting results (Verra et al., 2018; Thapa et al., 2019; Tyvold, 2019).

2.6.3 Active deep-body warming

Airway heating

Evaporative heat loss via a respiratory tract only represents a small fraction of total heat loss during anesthesia (Bickler & Sessler, 1990). Heated humidifiers and heat and moisture exchangers that warm and moisten inspired gases have not been shown to have any advantage in preserving core body temperature (Goldberg et al., 1992).

Warming IV fluid

For infusions over 500 ml per hour in adults, IV fluid warming is recommended (National Institute for Health and Clinical Excellence & (NICE), 2016). One liter of IV fluid at 21 °C decreases core temperature by 0.25 °C (Gentilello et al., 1990).

Fluids are usually delivered between 37 °C and 41 °C, and there are several in-line fluid-warming devices available. Different devices have distinct heating methods that affect the heat-delivering capacity of a device. Heat-delivering capacity is also influenced by the flow rate and the length of tubing between a warmer and a patient (Presson et al., 1993). It has been shown that warmed iv fluids keep core temperature about half a degree warmer than fluids given at room temperature (Campbell et al., 2015).

Another option to using warm iv fluids is using a warming cabinet where fluids are pre-warmed and then administered to a patient through conventional giving sets. The prewarming of fluids to the targeted temperature of between 37 °C and 41 °C takes over eight hours. In short surgical procedures, a warming cabinet is comparable to a commercial in-line warming device at preventing IPH (Andrzejowski et al., 2010).

Irrigation fluid or insufflated gas warming

Irrigation fluids are primarily used in different endoscopies. Warmed irrigation fluid at 39 °C can decrease, but not eliminate, the drop in core temperature (Moore et al., 1997). The benefit of warmed irrigation fluids is especially seen in hip and shoulder arthroscopies (Steelman et al., 2018). However, multiple factors (such as the duration of endoscopy, ambient temperature, and the amount of irrigation fluid) may have a greater impact on the core temperature than the irrigation fluid temperature per se (Jaffe et al., 2001).

Insufflated carbon dioxide (CO_2) is used to create pneumoperitoneum in laparoscopic surgery. Insufflated CO_2 is usually at room temperature and dry. However, warming and humidifying 100 L of CO_2 to 37 °C and to 100% humidity would result in a heat transfer of 3.2 kcal, which equals a decrease of temperature of 0.06 °C in a 70 kg patient (Roth & Sea, 2014). Warming and humidifying insufflated CO_2 has a minimal effect on core temperature and does not prevent a decrease in body temperature (Nelskylä et al., 1999).

An esophageal heat exchanger

An esophageal heat exchanger is a single use, orogastric tube that can be used to warm or cool the body. It consists of three integrated tubes the with external ports

that are connected to a circulating water system and a central lumen that is for gastric drainage. Circulating water can be warmed to a maximum of 41 °C or cooled to a minimum of 3 °C. Heat transfer depends on the temperature difference between the esophagus and the circulating fluid (Kalasbail et al., 2018), as well as the flow rate of fluid, the thickness and thermal insulation of exchange element, and the ability of the esophagus to absorb or relinquish heat. An esophageal heat exchanger has been shown to be ineffective in preventing hypothermia during hip arthroplasty and laparotomy (Kulkarni et al., 1993).

Endovascular and extracorporeal methods

Endovascular and extracorporeal heat exchange techniques are effective but very invasive methods, and the latter requires expertise and equipment not found in every hospital. Endovascular warming or cooling is implemented by a heat-exchanging catheter that is inserted into the inferior vena cava via the femoral vein. Extracorporeal methods need venous–venous or arterio–venous access and a connection to a device that directly warms blood. The method includes hemofiltration, hemodialysis, a cardiopulmonary bypass, and extracorporeal membrane oxygenation. These methods are mainly utilized to warm accidentally hypothermic patients.

Pharmacological and nutritional methods

Pharmacological methods may restrict the initial thermal redistribution. The narcotics selection in anesthetic induction—such as using sevoflurane instead of propofol (Ikeda et al., 1999) or ketamine (Ikeda et al., 2001), as well as using an intraoperative phenylephrine infusion (Ikeda et al., 1999)—reduces the magnitude of redistribution hypothermia.

Anesthetics do not impair the mechanisms for nutrient-induced thermogenesis (Sellden et al., 1994). The preoperatively started infusion of amino acid has been shown to raise patients' preanesthetic core temperatures but not to prevent initial thermal redistribution (Sellden et al., 1996).

2.6.4 Preoperative skin surface warming

The decrease in core temperature is fastest during the first hour of anesthesia and largely results from the redistribution of heat from the warm core compartment to cold peripheral tissues due to anesthesia-induced vasodilatation (Holdcroft et al., 1979). Redistribution equals the heat flow of 46 kcal during the first hour of GA and 20 kcal during the first hour of epidural anesthesia (Matsukawa et al., 1995; Matsukawa et al., 1995). Redistribution hypothermia is difficult to treat when it occurs because there are no effective means of increasing body heat content rapidly (Hynson & Sessler, 1992). Heat applied to the skin surface requires considerable time to reach the core thermal compartment.

Redistribution hypothermia can be diminished by preoperative skin surface warming (Moayeri et al., 1991). Prewarming increases body heat content by elevating the temperature of legs and arms. The temperature gradient between the core and peripheral tissues is decreased and, thus, the initial core temperature drop is reduced and normothermia is maintained better (Just et al., 1993). Prewarming seldom changes core temperature, which remains well regulated (Sessler & Moayeri, 1990). Thirty minutes of prewarming with a whole-body FAW blanket and a blower set to *high* increases peripheral tissue heat content by 69 kcal, which is more than the amount typically redistributed (Sessler et al., 1995). Only 10 min of prewarming with an upper-body FAW blanket has been shown to reduce the risk of perioperative hypothermia (Horn et al., 2012).

Prewarming can be performed in wards, in holding areas, and in the OR. However, if a patient is exposed to a cold ambient temperature after prewarming, the body loses heat and the benefit of prewarming is not preserved. Moreover, it has been shown that hypothermia commonly occurs when the interruption time between pre- and intraoperative warming exceeds over 20 minutes (Grote et al., 2019).

Sweating and thermal discomfort may limit the benefits of prewarming. Sweating is an effective thermoregulatory response and is provoked by high or rapidly increasing skin temperature (Libert et al., 1978). Aggressive cutaneous warming causes thermal discomfort and sweating that easily dissipate more heat than is provided by the prewarming. To avoid sweating, the temperature of a heater can be set to *medium* instead of *high* since it has been shown that the increase of tissue heat content is nearly equal with these two settings (Sessler et al., 1995).

2.7 Temperature monitoring

Since body temperature is not evenly distributed, monitoring core temperature is normally a sufficient indicator of thermal status. Skin temperatures vary from region to region, and their measurement may be used to evaluate vasomotion (Rubinstein & Sessler, 1990). Both core temperature and MST are required to estimate mean body temperature (MBT) and body heat content.

Core temperature monitoring is recommended by several guidelines in order to observe hypothermia or fever, to prevent overheating, and to detect malignant hyperthermia (Forbes et al., 2009; Hooper et al., 2009; National Institute for Health and Clinical Excellence & (NICE), 2016). Core temperature should be measured one hour before anesthetic induction, during anesthesia exceeding 30 minutes, and postoperatively until a patient is normothermic. The same measuring method is preferred pre-, intra-, and postoperatively, and continuous monitoring is more favorable than taking single measurements.

Objective core temperature monitoring is needed since the anesthetized patient's thermal status cannot be estimated without an adequate thermometer being used by an anesthesiologist (Frank et al., 1999; Arkiliç et al., 2000). Further, patients under epidural anesthesia are frequently unaware that they are hypothermic (Glosten et al., 1992; Sessler & Ponte, 1990)

The accuracy of temperature monitoring depends on the thermometer and the measurement site. The thermometers currently available in clinical practice have a relatively comparable performance and accuracy within 0.2 °C (Childs & Machin, 2009). The possible measurement inaccuracy is commonly caused by the measurement site, which may not correctly reflect the true core temperature value.

2.7.1 Thermometers

Thermometers were conceptualized by Galileo at the end of the sixteenth century, and currently, there are several different types of thermometer that can be used perioperatively. Still, none of them has met the ideal standards of a temperature measurement system. The characteristics of an ideal thermometer are being a small size, easy to use, comfortable, fast (for spot checks), continuous, accurate, non-invasive, low in energy consumption, and affordable (Wartzek et al., 2011).

A thermometer is considered sufficiently accurate if it is accurate to within ±0.5 °C (i.e., there is a range of 1 °C) because normal circadian fluctuations are within this range (Sessler et al., 1991). Further, 0.5 °C is the smallest difference that has been shown to be associated with hypothermia-induced complications (Winkler et al., 2000).

A mercury thermometer

A mercury-in-glass thermometer was the first accurate, practical, and widely used thermometer, invented by physicist Daniel Fahrenheit at the beginning of the eighteenth century. The thermometer has a glass tube filled with mercury and a standard temperature scale marked on the tube. The mercury expands and contracts with changes in temperature, which can then be read on the scale. Mercury thermometers are slow and cumbersome and have been replaced by digital thermometers. In addition, mercury is poisonous and a biohazard when spilled.

Electronic thermometers

The most common electronic thermometers are thermocouples and thermistors, discovered at the beginning of the nineteenth century by Thomas Seebeck and Michael Faraday, respectively. A thermocouple is a transducer consisting of a junction of dissimilar metals in which an electric current is generated in direct proportion to temperature changes. One of the metals is held at a known temperature. Thermistors are temperature sensitive semiconductors, thus, small resistors. Their resistance is strongly dependent on temperature, and temperature can be defined by measuring the resistance. Thermocouples and thermistors are sufficiently accurate for clinical use and inexpensive enough to be disposable.

Infrared thermometers

Infrared thermometers estimate temperature via thermal radiation from the tympanic membrane or the temporal artery. Tympanic infrared thermometers are accurate when infrared signals are actually obtained from the tympanic membrane (Matsukawa et al., 1993). However, the aural canal is long and not straight, and most infrared thermometers are too large to optimally fit into it. Hence, instead of measuring tympanic temperature they usually measure the skin temperature of the

external auditory canal. Temporal artery thermometers measure skin surface temperature across the forehead, including the region of the temporal artery that is supposed to approximate core temperature. Altogether, the accuracy of infrared thermometers is too inconsistent for clinical use (Imamura et al., 1998; Greenes & Fleisher, 2001).

2.7.2 Non-invasive deep-body thermometers

Non-invasive deep-body thermometers measure core temperature from the skin surface, commonly from the forehead. The measurement method is based on vertical heat flow from deep tissue to the skin. Two commercial devices are currently available and in clinical use. Both include a sensor that contains the technique for temperature measurement. However, the principle of temperature measurement differs between the devices (see Fig. 6).

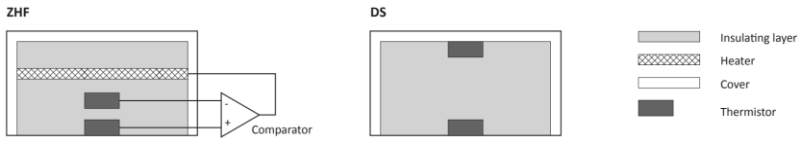

Figure 6. The schematic structure of non-invasive devices. ZHF = zero heat flux; DS = double sensor. Figure modified from the article of Sim et al, 2015.

The zero heat flux method

A zero heat flux (ZHF) method was invented by Fox and Solman at the beginning of the 1970s (Fox, 1971; Fox et al., 1973). The method was subsequently further developed in Japan (Kobayashi et al., 1975; Nemoto & Togawa, 1988; Yamakage & Namiki, 2003), and it was utilized in clinical circumstances (Matsukawa et al., 1997; Langham et al., 2009).

The current, improved commercial ZHF device (3M™ BairHugger™) was introduced in 2013, having a disposable sensor and a short equilibrium time (Eshraghi et al., 2014). The ZHF system also includes a reusable control unit that is compatible with existing monitors. Other features of the system are the need of an

electrical current, an equilibrium time of three minutes, and a measurement accuracy of ±0.2 °C for a range of 25–43 °C (see Table 3) (3M™ Bair Hugger™ temperature monitoring system, 2013)

The temperature measurement technique is based on an electric heater and two thermistors, separated by insulating foam and a cover, all of which are incorporated into a sensor (see Fig. 6). The heater eliminates heat loss to the environment, creating a zone of perfect insulation. At the same time, the lateral convection of heat by blood is ignored to avoid the accumulation of heat. The result is the formation of an isothermal tunnel between the subcutaneous tissue and the skin. Hence, the tissue temperature from the depth of 1 to 2 cm can be measured from the skin surface, which is regarded to approximate core temperature in a well-perfused area of the body (Eshraghi et al., 2014).

The ZHF method has been compared to conventional core temperature monitoring methods in various clinical circumstances in recent years. It has been shown to be accurate and precise enough for clinical use as long as the core temperature perturbations are relatively slow (Iden et al., 2015; Mäkinen et al., 2016; DahyotFizelier et al., 2017; Boisson et al., 2018; Pesonen et al., 2019; West et al., 2020; Verheyden et al., 2021).

The double sensor method

A double sensor (DS) method was released by Dräger in 2006. The latest-generation DS system includes a disposable, self-adhesive sensor and a battery-powered adapter (which, however, is only compatible with Dräger monitors). The equilibrium time of the system is approximately ten minutes (see Table 3) (Kimberger et al., 2009).

Temperature measurement is based on two thermistors, with an insulator placed between them (see Fig. 6) and it uses the formula $T_d = T_1 + K_{insul}/K_{tis}$ x $(T_1 - T_2)$. Heat from deep tissue to the sensor is measured at each point of the thermistors (T_1 and T_2). Deep tissue temperature (T_d) is estimated from T_1 and T_2 and from the ratio of the thermal conduction coefficient of the insulator (K_{insul}) to that of human tissue (K_{tis}) (Gunga et al., 2008).

The DS method has been compared to conventional core temperature monitoring methods in a few clinical and experimental studies. However, there are conflicting results concerning the accuracy of the method (Gunga et al., 2008, 2009; Kimberger et al., 2013; Sastre et al., 2019; Soehle et al., 2019).

Table 3. Descriptions of the ZHF method and the DS method

	ZHF method[1]	**DS method[2]**
Disposable sensor	Yes	Yes
Height (mm)	41	49
Width (mm)	41	58
Thickness (mm)	5	5
Reusable control unit* or adapter‡	Yes*	Yes‡
Battery option	No	Yes
Compatible with existing monitors	Yes[3]	No[4]
Temperature measuring method	Servo-controlled heater creates a zone of perfect insulation that enables deep body temperature to be measured from the skin surface	Formula $T_d = T_1 + K_{insul}/K_{tis} \times (T_1 - T_2)$
Number of thermistors	2	2
Equilibrium time (min)	3	10
Laboratory accuracy within 25–45 °C	±0.2 °C	±0.1 °C

1. ZHF = zero heat flux, 3M™BairHugger™ (3M™ Bair Hugger™ temperature monitoring system, 2013)
2. DS = double sensor, Dräger Tcore™ (Kimberger & Quast, 2015)
3. The control unit is compatible with all patient monitors that accept YSI-400 type inputs.
4. A battery-powered adapter is only compatible with Dräger monitors.

2.7.3 Temperature monitoring sites

Core temperature monitoring sites

Core temperature can be measured from a site that is well perfused, such as the pulmonary artery, distal esophagus, nasopharynx, and tympanic membrane. The temperatures of these sites remain reliable even during rapid thermal perturbations and are largely interchangeable. Temperature monitoring requires invasive methods

(e.g., a catheter or a probe), the placement of which may cause disadvantages, such as bleeding. Moreover, these sites are seldom suitable for patients who are awake.

The pulmonary artery is the most accurate site for measuring core temperature and is regarded as providing the golden standard (Launey et al., 2016). Temperature is measured by a thermistor in a pulmonary artery catheter, lying 4 cm proximal to the tip of catheter. This method is very invasive and rarely available since it is only used when the benefits exceed the risks.

Esophageal and nasopharyngeal temperatures are the most obvious temperature monitoring sites during GA because they are easily available. Esophageal temperature is measured by a probe inserted via the mouth or nostril to a position of maximal heart sounds or inserted more distally to avoid cooling by respiratory gases (Kaufman, 1987). If esophageal monitoring is precluded for instance with a supraglottic airway device, nasopharyngeal temperature monitoring is preferred. A nasopharyngeal probe is inserted to the depth of approximately 10 cm from nares to represent true core temperature (Lee et al., 2014). The temperatures of a malpositioned probe may be influenced by ambient temperature or respiratory gases. Both esophageal and nasopharyngeal probes can be used in patients who are awake, though the use of them may cause discomfort and anxiety for the patients.

Tympanic membrane is a reliable core temperature monitoring site when well-insulated probes containing thermocouples or thermistors are carefully positioned adjacent to the membrane itself (Sato et al., 1996). The insertion of a flexible tympanic probe may be difficult since the aural canal is long and not straight. Further, the tympanic membrane is sensitive, and the insertion of a probe may be uncomfortable. Hence, the probe may not be inserted far enough to reach the membrane itself, which results in an inaccurate temperature estimate. However, the risk of puncturing the tympanic membrane is negligible since commercial probes are soft and pliable.

Near core monitoring sites

Core temperature can be estimated with reasonable accuracy using oral, axillary, bladder, and rectal temperatures. These sites are non-invasive or minimally invasive and are mostly easily available. However, they may be affected by artifacts that need to be known before use.

Sublingual and axillary temperatures are good estimates of core temperature (Langham et al., 2009; Lodha et al., 2000). Oral temperature may be influenced by liquids that have recently been ingested and by breathing through the mouth. Axillary temperature is more reliable when the probe is placed over the axillary artery and the arm is adducted. Arm position and ambient temperature are compensated for by using a more sophisticated axillary thermometer (Pei et al., 2017).

The temperatures of the urinary bladder and rectum are less reliable because both sites are poorly perfused and thus temperature changes occur slowly. Bladder temperature lags behind core temperature when urine flow is low (Sato et al., 2008). Rectal temperature detects fever and rapid thermal perturbations poorly (Ash et al., 1992).

Skin

Skin temperature varies considerably as a function of ambient temperature, air speed, and peripheral perfusion. Forehead skin temperature is less variable but it still poorly approximates core temperature (Ikeda et al., 1997).

MST is the area-weighted average temperature of the skin surface. Though the accuracy of MST improves with the increasing number of measurement sites, MST can be calculated by using a formula and only four sites: $\text{MST} = 0.3 \times (T_{\text{chest}} + T_{\text{arm}}) + 0.2 \times (T_{\text{thigh}} + T_{\text{leg}})$ (Ramanathan, 1964), where T is temperature (°C). MST contributes to the rate of cutaneous heat loss as well as to central thermoregulatory control. The combination of MST and core temperature can be used to estimate MBT and, therefore, body heat content. MBT can be calculated from the formula: $\text{MBT} = 0.64 \times T_{\text{core}} + 0.36 \times T_{\text{MST}}$ (Burton, 1935).

3 THE AIMS OF THE STUDY

The objectives of this thesis were to investigate two new warming methods related to preventing intraoperative hypothermia. Furthermore, two non-invasive thermometers were evaluated.

The specific aims of Studies I–IV were as follows:

I To study if the use of a thermal suit, instead of cotton hospital clothes, is beneficial in preventing hypothermia in patients during robotic-assisted laparoscopic prostatectomy (RALP).

II To assess the effectiveness and convenience of using a thermal suit connected to a FAW unit in maintaining normothermia in patients during GA.

III To compare the efficacy and suitability of an SW blanket with the efficacy and suitability of an upper-body FAW blanket in patients who were scheduled for elective unilateral TKA under spinal anesthesia.

IV To evaluate and compare non-invasive ZHF and DS temperature monitoring methods perioperatively in patients under spinal anesthesia.

4 PATIENTS AND METHODS

4.1 Designs

To investigate the benefit and efficacy of the thermal suit and the SW blanket in relation to preventing intraoperative hypothermia, three separate, prospective, randomized trials were conducted in perioperative settings. The fourth observational study of non-invasive thermometers was carried out with the patients of the third study. All the studies were single-center studies, performed in Tampere University Hospital. A summary of Studies I–IV is presented in Table 4.

4.2 Data collection

4.2.1 Study I

The study population consisted of men scheduled for RALP under GA. Inclusion criteria were patients needing to be aged from 18 to 90 and being in American Society of Anesthesiologists (ASA) Classes I to III. Exclusion criteria were decreased mental status, neuromuscular disorders, Raynaud's phenomenon, and unstable coronary artery disease. One hundred patients were recruited and randomized to wear either a thermal suit or cotton hospital clothes at a one-to-one ratio.

Intraoperative warming and anesthesia management were similar in each group. An upper-body FAW blanket set at 38 °C and a warming mattress set at 38.5 °C were used. In-line warming was used to warm IV fluids to approximately 41 °C. Patients wearing cotton clothes also had leg stockings added in the OR. GA was induced and maintained with target-controlled infusions of propofol and remifentanil. Rocuronium was used to facilitate endotracheal intubation.

Table 4. A summary of Studies I–IV

	Study I	**Study II**	**Study III**	**Study IV**
Study period	November 2012 to April 2013	February to July 2018	November 2018 to May 2020	May to November 2019
Design of the study	Prospective randomized controlled trial	Prospective randomized controlled trial	Prospective randomized non-inferiority trial	Prospective observational study
Allocation	1:1	1:1	1:1	1:1
Study group Control group	Thermal suit Hospital clothes	Thermal suit Hospital clothes	SW blanket FAW blanket	DS method ZHF method
Number of patients	100	40	150	60
Study population	Men undergoing RALP due to prostate cancer	Women undergoing breast surgery due to breast cancer	Patients undergoing unilateral total knee arthroplasty	Patients undergoing unilateral total knee arthroplasty
Anesthesia	General anesthesia	General anesthesia	Spinal anesthesia	Spinal anesthesia
Method of data collection	Saving electronically and manually to the data collection file	Saving manually to the data collection file	Saving electronically and manually to the data collection file	Saving electronically and manually to the data collection file
Main outcome measure	Core temperature difference intraoperatively	Core temperature difference on admission to the recovery room	Core temperature difference on admission to the recovery room	Agreement between temperature measurement methods
The objective of the study	To study the benefit of the Thermal suit in preventing intraoperative hypothermia	To investigate the usability and the effectiveness of the Thermal suit connected to the FAW unit	To compare the perioperative use of the SW blanket and the upper-body FAW blanket	To evaluate the non-invasive core temperature measurements methods

SW = self-warming; FAW = forced-air warming; DS = double sensor; ZHF = zero heat flux;
RALP = robotic-assisted laparoscopic prostatectomy

Baseline temperature was measured with an infrared tympanic thermometer before the patient dressed to study clothes. Intraoperatively, core temperature was measured with an esophageal probe, inserted at anesthetic induction. Skin temperatures were measured from axilla, the middle finger, and the dorsum of the foot, and sensors were placed on a patient after he had moved onto the operating table. Postoperatively, temperature recordings continued until the patient was transferred to the ward or for up to 3 h. The temperature and humidity of the OR were measured.

4.2.2 Study II

Study II was a clinical device investigation into a new warming method where warm air was blown inside a thermal suit via a Y-piece adapter connected between the legs of the suit and the nozzle of an FAW unit. Valvira (the National Supervisory Authority for Welfare and Health in Finland) was informed about the study in advance.

The study population consisted of females undergoing a unilateral mastectomy because of breast cancer. Inclusion criteria were being aged from 20 to 90, being in ASA Classes I to III, and having a body mass index (BMI) in the range from 25 to 40. An exclusion criterion was the inability to give informed consent. Forty women were recruited and randomized to wear either a thermal suit or cotton hospital clothes at a one-to-one ratio.

All the patients had FAW. The new method was used in patients wearing the thermal suit. Patients wearing cotton clothes had a commercial lower-body FAW blanket and a warming mattress set at 37 °C. FAW was turned on at 38 °C after surgical draping for all patients. Warmed IV fluids were taken from the warming cabinet, but the fluids were not actively warmed perioperatively.

GA was induced and maintained with target-controlled infusions of propofol and remifentanil. A laryngeal mask was used to secure the airway.

Baseline temperature was measured once with an infrared tympanic thermometer before a patient dressed to study clothes. Core temperature was measured with a ZHF sensor and a nasopharyngeal probe that was inserted to the depth of the distance between the nostril and the auditory canal after anesthetic induction. Peripheral temperatures were measured from chest, upper arm, thigh, and leg contralateral to the site of the surgery. A ZHF sensor and skin sensors were placed

on after a patient had moved onto the operating table (see Fig. 7). Temperatures were recorded continuously and saved at 10-minute intervals intraoperatively and for up to one hour postoperatively (except for nasopharyngeal temperature, which was only recorded during anesthesia). The temperatures of the preoperative holding area and OR were measured.

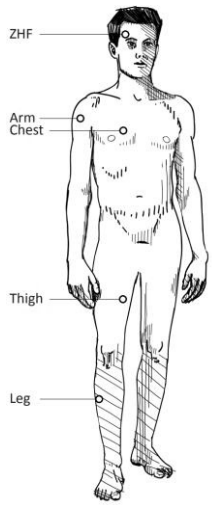

Figure 7. The skin temperature measuring sites of Studies II and III. ZHF = zero heat flux.

4.2.3 Study III

The study population consisted of patients scheduled for unilateral TKA under spinal anesthesia. Inclusion criteria were being aged from 40 to 90, being in the ASA Classes I–III, and having BMI in the range from 25 to 40. Exclusion criteria were an unstable coronary artery disease, revision or bilateral surgery, GA, or the inability to give written consent. One hundred and fifty patients were recruited and randomized to have either an SW blanket or an upper-body FAW blanket at a one-to-one ratio.

Before the induction of spinal anesthesia, patients were prewarmed with an allocated blanket for a thirty-minute period in the preoperative holding area. Active

warming was discontinued during anesthetic induction and during transfer to the OR or to the RR. After arriving at the OR, active warming with the SW blanket was continued immediately, but the FAW was turned on at 38 °C after surgical draping. Warmed IV fluids were taken from the warming cabinet, but they were not actively warmed perioperatively.

Baseline temperature was measured with an infrared tympanic thermometer after a patient had dressed in cotton hospital clothes. Core temperature was measured with a ZHF sensor placed on the right side of the forehead. Peripheral temperatures were measured from the chest and upper arm on the right side, and from the thigh and leg on the contralateral side to the surgery (see Fig. 7). Temperature recordings started just before prewarming and continued for up to one hour postoperatively. Temperatures were saved at 10-minute intervals, except preoperatively, when they were only saved at the start and the finish of prewarming. The temperatures of the preoperative holding area and OR were measured.

4.2.4 Study IV

Two non-invasive core temperature monitoring methods, the ZHF method and the DS method, were evaluated from the beginning of prewarming to up to one hour postoperatively. Data was obtained from sixty patients recruited for Study III. All the patients had a ZHF sensor on the right side of their forehead to take a reference temperature. The comparative temperature was obtained either by a ZHF or DS sensor placed on the left side of the forehead, with thirty patients in each group.

The temperature data of the bilateral ZHF sensors was collected electronically at ten-second intervals and retrieved for statistical analysis at five-minute intervals. The temperature data of the ZHF and DS sensors was collected manually. The temperatures were saved at one-minute intervals for the first ten minutes and, thereafter, at five-minute intervals. The data collection was interrupted during the transmission of a patient to the OR or to the RR.

4.2.5 Temperature management

Hypothermia was noted when the core temperature decreased below 35.0 °C (in Study I) or below 36.0 °C (in Studies II–IV). When hypothermia occurred, active

warming was enhanced. The temperature of the FAW was raised to 43 °C (except for the patients wearing the thermal suit in Study II). The temperature of the warming mattress was set to 39 °C or 40 °C and IV fluids were actively warmed to 38 °C. If the core temperature exceeded 38 °C, active warming was discontinued.

4.3 Ethical considerations

The Regional Ethics Committee of the Expert Responsibility area of Tampere University Hospital, Tampere, Finland, granted approval for Studies I–III. For Study IV, the ethics committee was notified with an amendment to Study III. The studies were registered at ClinicalTrials.gov prior to the patients' enrolment. A written informed consent was obtained from all the patients before study measurements. The studies were conducted according to the rules and regulations of the Declaration of Helsinki. Personal data were processed in accordance with the European Union's General Data Protection Regulation requirements.

All the studies originated from the researchers. Departmental funding was utilized for materials, except for the Tcore™ adapter and a transport monitor (Infinity M540) that were lent by OneMed Finland. Otherwise, the studies were financially supported by competitive research funding from Tampere University Hospital, the Doctoral Programme of Tampere University, the Scientific Foundation of the City of Tampere, the Paulo Foundation, and the Finnish Society of Anaesthesiologists.

4.4 Statistics

Continuous data was reported as a mean with standard deviation (SD) for parametric data or as a median and quartiles (Q1–Q3) for non-parametric data. The categorical variables were presented as a number (*n*) and a percentage (%).

A t-test was used for parametric comparisons and the Mann-Whitney U test was used for non-parametric data. A paired t-test was applied for analyzing the statistical difference in paired samples. The categorical values were analyzed with chi-square test or Fisher's exact test. A multivariate logistic regression model was used to predict

the categorical dependent variable. Spearman's correlation was calculated to determine the statistical relationship.

MST was calculated for evaluating thermal redistribution and Ramanathan's formula was applied: $MST_R = 0.3 \times (T_{chest} + T_{arm}) + 0.2 \times (T_{thigh} + T_{leg})$ (Ramanathan, 1964), where T is temperature (°C). MBT was calculated for assessing body heat content using Burton's formula: $MBT_B = 0.64 \times T_{core} + 0.36 \times T_{MST}$ (Burton, 1935). Heat transfer was computed using the standard calorimetric calculation: $Q = m \times C \times (T_{final} - T_{initial})$, where Q is the heat flow (kcal), m is the mass (kg), C is the specific heat of human (0.83 kcal/kg/°C) (1 kcal = 1.163 W/h), and T is temperature (°C).

To assess the relationship between two paired variables, a Bland-Altman (BA) plot was performed (Bland & Altman, 2007). The mean difference and 95% limits of agreement (LoAs; ±1.96 SD around the mean difference) were calculated. In addition, in Study IV, 95% confidence intervals (CIs) for the LoAs were calculated (Zou, 2013). Lin's concordance correlation coefficient (LCCC) was calculated in order to quantify the agreement between the two measures of the same variable (Lin, 1989).

When $p < 0.05$, p was considered statistically significant.

5 RESULTS

5.1 Core temperature

In general, core temperature changed similarly in all the patients perioperatively. There were no statistically significant differences in the core temperature values between the groups in each study. Core temperature decreased after anesthetic induction but tended to rise at the end of surgery, and the increase of core temperature continued postoperatively. The perioperative changes of core temperature are presented in Table 5.

5.2 Skin temperatures

In Study I, the measurement sites of peripheral temperatures differed from those using in the formula of Ramanathan and, hence, MST was not calculated. Peripheral skin temperatures did not differ between groups except for the foot dorsum temperatures, which were statistically significantly lower in patients wearing the thermal suit than in patients wearing hospital clothes from anesthetic induction to up to 30 minutes after induction and at the time point of 120 minutes after induction.

The MST changes were similar in the patients of Studies II and III. MST raised intra- and postoperatively when active warming was used and decreased during transfer when active warming was discontinued. The perioperative MST values are shown in Table 6.

In Study II, the MST was statistically significantly higher in patients wearing the thermal suit than in patients wearing cotton hospital clothes on admission to the OR ($p = 0.002$). The preoperative suit time did not correlate to the first measured MST ($r_S = -0.208$). The highest intraoperative skin temperature value of 38.0 °C was measured from the thigh and leg of patients wearing hospital clothes. Arm temperatures, in turn, were statistically significantly higher in patients wearing the thermal suit ($p < 0.001$).

Table 5. Perioperative core and ambient temperature values

	Study I				**Study II**				**Study III**			
	Esophageal probe				ZHF method				ZHF method			
	TS		HC		TS		HC		SW		FAW	
	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD
Core temperature °C												
After arriving at the hospital[1]	36.5	0.4	36.6	0.4	36.5	0.3	36.3	0.4	36.2	0.4	36.3	0.3
Start of prewarming	-		-		-		-		36.6	0.4	36.6	0.4
On admission to the OR	-		-		36.9	0.3	36.8	0.4	36.6	0.3	36.6	0.4
At the induction of anesthesia	36.3	0.6	36.3	0.6	37.0	0.3	36.9	0.4	36.7	0.3	36.7	0.3
Drop in the OR	0.6	0.3	0.7	0.4	0.8	0.2	0.9	0.3	0.7	0.3	0.7	0.3
Lowest in the OR	36.0	0.7	36.0	0.8	36.2	0.3	36.1	0.4	35.9	0.4	35.9	0.5
On admission to the RR	36.2	0.6	36.3	0.9	36.5	0.4	36.7	0.3	36.1	0.3	36.1	0.4
At 1 hour postoperatively	36.4	0.8	36.4	0.9	36.7	0.4	36.8	0.3	36.4	0.3	36.4	0.3
Temperature °C												
Holding area	-		-		23.0	0.4	23.1	0.4	23.3	0.7	23.3	0.7
OR	21.4	0.4	21.3	0.4	21.9	1.0	21.8	0.9	18.9*	0.8	19.2*	0.7

ZHF = zero heat flux; TS = thermal suit; HC = hospital clothes; SW = self-warming blanket; FAW = forced-air warming blanket; OR = operating room; RR = recovery room

[1] Measured with an infrared tympanic thermometer; * Statistically significant difference, p-value = 0.011

Table 6. Perioperative mean skin temperatures

	Study II					Study III				
	TS		HC			SW		FAW		
	mean	SD	mean	SD	p-value	mean	SD	mean	SD	p-value
Prewarming										
Beginning	-		-			33.5	0.8	33.0	0.7	< 0.001
End	-		-			34.5	0.7	34.9	0.7	< 0.001
Operating room										
Admission	33.7	0.6	33.0	0.6	0.002	33.8	0.7	33.8	0.7	0.702
End	35.4	0.4	35.1	0.9	0.138	34.6	0.7	34.8	0.8	0.337
Recovery room										
Admission	34.7	0.4	34.3	0.7	0.080	33.8	0.6	33.8	0.6	0.969
One hour	34.9	0.6	35.0	0.8	0.587	34.8	1.0	35.0	1.2	0.290

TS = thermal suit; HC = hospital clothes; SW = self-warming; FAW = forced-air warming

5.3 Prewarming, Study III

Core temperature changed minimally, rising from 36.6 °C (0.4) to 36.7 °C (0.3) in the patients of each group during prewarming (see Table 5). Six of the seven initially hypothermic patients gained normothermia during prewarming (see Table 7).

MST rose statistically significantly during prewarming in all patients, but the rise was even more pronounced in patients with the upper-body FAW blanket (see Table 6). MBT increased by 0.4 °C (0.3) and 0.8 °C (0.3) in patients with an SW blanket and an upper-body FAW blanket, respectively ($p < 0.001$). Heat flow (Q) to the patient equaled 29 kcal/h (≈ 34 W) with the SW blanket and 54 kcal/h (≈ 63 W) with the FAW blanket.

Nine patients who were allocated to have the SW blanket and thirteen patients who were allocated to have the FAW blanket felt cold before prewarming. One with the FAW blanket even felt cold after prewarming, though the patient's measured core temperature had been at least 37 °C preoperatively. All the other patients who initially felt cold felt comfortable by the end of prewarming.

Table 7. The incidence of hypothermia

	Study I				**Study II**				**Study III**			
	Esophageal probe				ZHF method				ZHF method			
	TS, n = 50		HC, n = 46		TS, n = 20		HC, n = 19		SW, n = 74		FAW, n = 73	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Hypothermia												
Before prewarming	-		-		-		-		3	4.1	4	5.8
On admission to the OR	-		-		0	-	0	-	1	1.5	3	4.3
At the induction of anesthesia	10	20.0	7	15.2	0	-	0	-	0	-	1	1.4
Incidence in the OR	19	38.0	16	34.8	1*	5.0	6*	31.6	45	60.8	36	49.3
On admission to the RR	9/39	23.1	7/41	17.1	1	5.0	0	-	32	43.8	25	34.2
At 1 hour postoperatively	6/37	16.2	5/39	12.8	2	10.0	0	-	4	5.4	4	5.5

ZHF = zero heat flux; TS = thermal suit; HC = hospital clothes; SW = self-warming; FAW = forced-air warming; OR = operating room; RR = recovery room; * Statistically significant difference, p-value = 0.04

5.4 Intraoperative hypothermia

Intraoperative hypothermia occurred frequently and often persisted until the postoperative period. Eighteen patients were hypothermic upon anesthetic induction, and all but one of them were included Study I. Hypothermia had appeared by the 30- to 42-minute time point after arriving at the OR. Perioperative incidences of hypothermia are shown in Table 7.

In Study II, the number of hypothermic patients was statistically significantly lower in patients wearing the thermal suit connected to the FAW unit when compared with the patients wearing hospital clothes and using a lower-body FAW blanket and a warming mattress (one patient versus six patients, respectively; p = 0.04; see Fig. 8). All the hypothermic patients with the commercial lower-body FAW blanket regained normothermia by the end of anesthesia. One hypothermic patient wearing the thermal suit was hypothermic at the end of anesthesia and until one hour postoperatively.

In Studies I and III, the incidence of hypothermia was high in both study groups. However, the patients were only slightly hypothermic. The lowest mean core temperature was 36.0 °C (0.7) and 36.0 °C (0.8) in the patients wearing the thermal suit and hospital clothes, respectively (Study I), and 35.9 °C (0.4) and 35.9 °C (0.5) in the patients having the SW blanket and the FAW blanket, respectively (Study III).

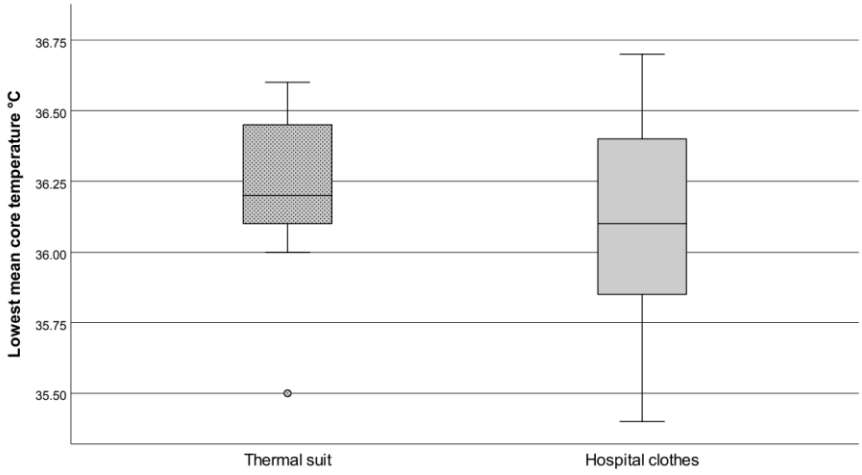

Figure 8. The lowest mean core temperatures of patients wearing either the thermal suit or hospital clothes

A great number of the hypothermic patients were still hypothermic when admitted to the RR. Nevertheless, normothermia was gained by most of the patients postoperatively, during the first postoperative hour (see Table 7).

In Study III, multivariate logistic regression analysis revealed that propofol sedation (which was used in 126 patients out of 147 patients) statistically significantly increases the risk of hypothermia. In contrast, other variables (such as age, gender, BMI, and ASA class) were insignificant. Ambient temperature was excluded from the analysis since it was equal in all patients.

Incidences of hypothermia-related complications (such as blood loss, infections, and postoperative shivering) did not statistically significantly differ between intraoperative hypothermic and normothermic patients. Estimated blood loss was minimal in all studies and varied between 18 ml and 165 ml. Postoperative infection was diagnosed in 1/96 patients of Study I and in 3/147 patients of Study III. In Study II, the patients were not followed up in regard to postoperative infections. Shivering was observed in three normothermic patients of Study III.

5.5 The disadvantages and costs of the warming methods

Some disadvantages of the warming methods were noted perioperatively. In Study II, two patients wearing the thermal suit were sweating. This was noticed by the surgeon in the OR for one of the patients, and the other was noted to be sweating in the RR.

In Study III, active warming was found to be uncomfortable by a few patients. Seven patients in each group sensed prewarming to be excessively warm. Two patients with the SW blanket already felt too warm at the beginning of prewarming. One of those and another patient, too, sweated at the end of prewarming. Intraoperatively, seven patients felt uncomfortably warm under the upper-body FAW blanket.

Tissue irritation or burns were not reported by the patients or the personnel in any of the studies.

The operating costs of the warming methods used are presented in Table 8.

Table 8. The costs of the warming methods

Method			Value per wear (€)
Thermal suit	Acquisition cost	€ 150	1.90
	Laundry cost		12.65
			14.55
SW blanket			12.60
Lower-body FAW			7.85
Upper-body FAW			8.10

SW = self-warming; FAW = forced-air warming

5.6 Non-invasive deep-body temperature monitoring, Studies II and IV

In Study II, temperatures obtained with nasopharyngeal probes paralleled those obtained with ZHF sensors thirty minutes after anesthetic induction. Divergent data was excluded from the BA analysis between ZHF and nasopharyngeal temperatures. A total of 324 measurement pairs were obtained intraoperatively. The mean difference between the methods with 95% LoAs was 0.15 °C ± 0.36 °C. The proportion of temperature difference within 0.5 °C was 98.5% and LCCC was 0.75 (95% CI ± 0.04). The chronological temperature changes and BA plot are illustrated in Fig. 9 and Fig. 10, respectively.

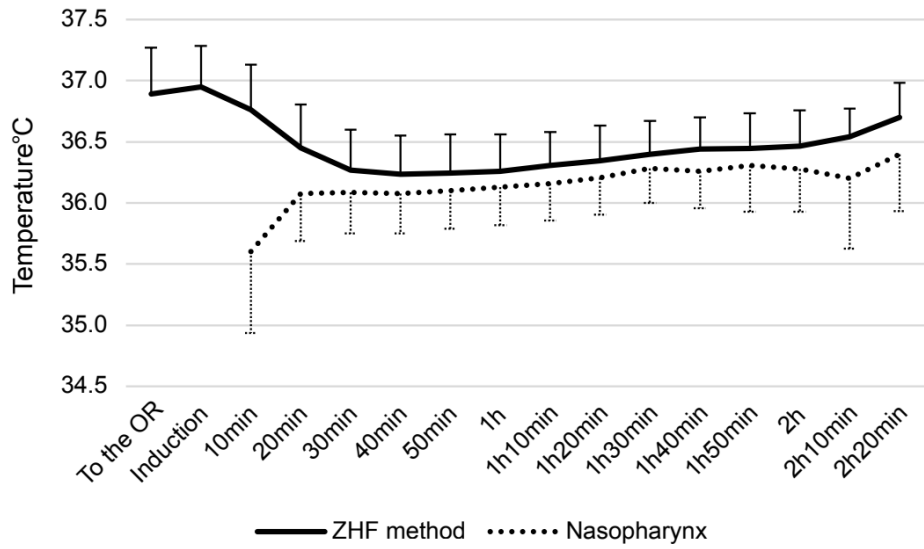

Figure 9. The temperatures of the ZHF method and the nasopharyngeal probe intraoperatively, mean (SD)

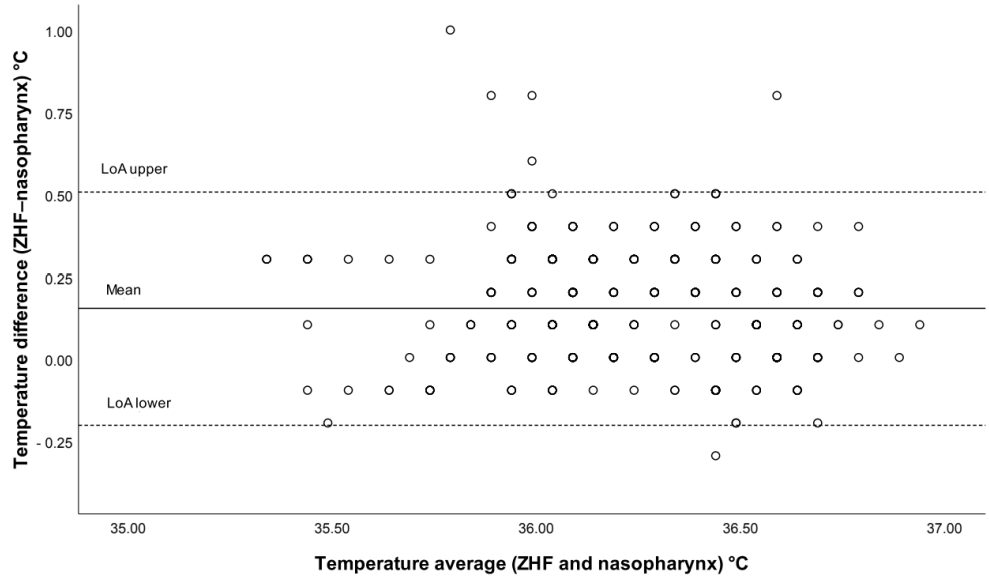

Figure 10. A Bland-Altman plot of the temperature values obtained with the ZHF method and the nasopharyngeal probe

In Study IV, a total of 1,261 measurement pairs were obtained perioperatively at five-minute intervals between two ZHF sensors and 1,129 pairs were obtained perioperatively at five-minute intervals between ZHF and DS sensors. The temperature values measured with the ZHF sensor stabilized within four minutes, and with the DS sensor, values stabilized within ten minutes. Unstable temperature data were excluded from the statistical analyses.

The mean perioperative difference between two ZHF sensors with 95% LoAs was 0.05 °C ± 0.42 °C (95% CI ± 0.08 °C). The proportion of temperature differences within 0.5 °C was 99% and LCCC was 0.88 (95% CI ± 0.01). The side of the forehead did not influence the temperature reading.

The mean perioperative difference between ZHF and DS sensors with 95% LoAs was 0.33 °C ± 0.88 °C (95% CI ± 0.20 °C). The proportion of temperature differences within 0.5 °C was 66% and LCCC was 0.59 (95% CI ± 0.03).

6 DISCUSSION

The thesis reveals that it is difficult to prevent intraoperative hypothermia with a thermal suit or an SW blanket. Moreover, these warming methods do not seem to have such advantages that the use of them should be preferred to the conventional FAW method. The FAW method also could not prevent the initial core temperature decrease, but it was effective in raising core temperature with the maximum set heating temperature.

The findings of the study of non-invasive temperature monitoring methods show that the forehead side does not influence the temperature recordings of the ZHF method. Also, the internal validity of the ZHF method is determined to be good. The DS method seems to express lower temperature values than the ZHF method.

6.1 The thermal suit

The thermal suit has been developed to prevent hypothermia by reducing heat loss via skin, and its action is based on passive insulation. Patients wearing the thermal suit had higher MST values on admission to the OR compared with patients having cotton hospital clothes. However, the preoperative suit time did not correlate to the MST value. The actual preoperative increase of MST (if there even was an increase) remains unknown since peripheral temperatures were only measured in the OR.

Intraoperative hypothermia was more seldom in patients wearing the suit connected to the FAW unit than in patients wearing hospital clothes. Reasons for that might be: first, the peripheral temperatures were higher at anesthetic induction, which might result in a minor initial redistribution of body heat. Second, the zippers of the suit allowed the exposed area to be kept no larger than necessary for anesthesia and surgery, which further diminished heat dissipation. Last, forced air spread inside the suit and warmed the entire anterior surface of the body, which might be more effective than only using lower-body warming.

Despite theoretical advantages, it has been shown that the thermal suit cannot prevent the initial core temperature drop after GA induction. Core temperature decreased equally in the patients wearing the suit as in the patients wearing cotton clothes, which has also been seen in a previous study (Brodshaug et al., 2019). However, the benefit of the suit has been shown in a study of patients scheduled for transurethral resection of the prostate under spinal anesthesia where the core temperature decrease was statistically significantly lower in patients wearing the suit (Hirvonen & Niskanen, 2011).

Hypothermic patients wearing the suit have been shown to be slower to regain normothermia than patients wearing cotton clothes when commercial active warming methods were used (Brodshaug et al., 2019). The reason for this persistent hypothermia might be the insulation effect of the suit. The three-layered fabric of the suit prevents the heat of external warming devices from reaching the patient. This thermos phenomenon was also seen in two of the studies of this thesis as hypothermia persisted longer in patients wearing the thermal suit (Study I, Study II).

The three-layered fabric may be responsible for the poor breathability of the suit, too. This was apparent when forced air was blown inside the suit, resulting in two patients sweating (Study II). In contrast, sweating was not noticed in patients wearing the thermal suit undergoing RALP. However, they had a commercial upper-body FAW blanket over the suit rather than having warm air blown inside the suit.

The operating costs of a suit are higher than of using hospital clothes together with a conventional FAW blanket. The economic benefit of the suit is achieved when the suit is worn from preoperative time to up to the first postoperative day since the laundry costs create most of the operating costs. However, it is unlikely that wearing the suit is desirable as some women wearing the suit changed into cotton clothes after entering the ward. This may have been caused by the impracticality of the suit.

The ecological aspect of the suit is uncertain. Waste is not produced with a single use since the suit is washable. However, the inner layer of the suit is made of fleece that has been shown to be harmful for the water system when washed (Carney et al., 2018).

In general, passive insulation is less effective than active warming in preventing inadvertent hypothermia. Reflective blankets, prewarmed blankets, or several blankets cannot maintain intraoperative normothermia (Radford & Thurlow, 1979; Sessler & Schroeder, 1993; Ng et al., 2003).

6.2 The self-warming blanket

Preoperative warming with the SW blanket has been shown to decrease (but not totally prevent) the development of intraoperative hypothermia (Torossian et al., 2016; Rosenkilde et al., 2017; Koc et al., 2017). The findings of this thesis were similar. The SW blanket was capable of raising peripheral temperatures and of warming up three initially hypothermic patients during prewarming. Nevertheless, prewarming could not prevent the core temperature drop, and intraoperative hypothermia developed frequently (Study III).

The efficacy of the perioperative use of the SW blanket when compared with the FAW blanket remains unclear since the studies published so far each have some limitations. First, the SW blanket was compared with cotton clothes (Torossian et al., 2016). Second, intraoperative warming was conducted with a FAW blanket although an SW blanket was used during prewarming (Rosenkilde et al., 2017). Last, the FAW heater was initially set at 38 °C and the maximal heat available was not utilized (Study III).

The incidence of hypothermia has been shown to be statistically significantly greater in patients warmed intraoperatively with the SW blanket when compared with patients warmed with the FAW method (Verra et al., 2018; Tyvold, 2019). The results of this thesis were comparable to those reported previously, though the difference in the incidence of hypothermia did not reach statistical significance (Study III).

Although the SW blanket has some benefits over the FAW method, such as its silence and lack of need for electricity, its lower warming capacity makes it unfavorable compared with the FAW method. Further, the disadvantages of the SW blanket, such as the risk of burns and the nonadjustable temperature of the pads, do not promote its use. Moreover, the cost of the SW blanket is higher than that of the most-used FAW blankets.

6.3 Prewarming

In the Study III the body heat content was increased by prewarming more than it has been shown to decrease after epidural anesthesia induction (Matsukawa et al., 1995). Therefore, maybe core temperature did not decrease after spinal anesthesia

induction. It has been shown that spinal anesthesia impairs thermoregulation more than epidural anesthesia (Saito et al., 1998) Reasons for persistent normothermia may be either effective prewarming or, rather, anesthetic agents and the technique used that allowed only the leg undergoing surgery to be anesthetized, which also reduced redistribution.

Though core temperature remained unchanged at first, it decreased within forty minutes after admission to the OR (Study III). The core temperature decrease might result from: (1) redistribution that was only observed in the OR, (2) cold ambient temperature increasing cutaneous heat loss, or (3) a long interruption between pre- and intraoperative warming, which has been shown to diminish or even lose the effect of prewarming when it exceeds twenty minutes (Grote et al., 2019).

Prewarming is important, especially before short-lasting anesthesia, because the initial thermal redistribution exceeds the power of cutaneous warming devices. Patients who were prewarmed either with FAW blankets or an SW blanket have been shown to maintain core temperature better than patients who were only warmed intraoperatively (Horn et al., 2012; Perl et al., 2014; Koc et al., 2017). In Study III, many hypothermic patients were still hypothermic when admitted to the RR although they were actively warmed during surgery lasting sixty minutes.

6.4 Inadvertent perioperative hypothermia

Despite active warming, intraoperative hypothermia occurred relatively often and its incidence varied from 5% to 61%, which equals the incidence reported in previous studies (John et al., 2016; Scholten et al., 2018; Alfonsi et al., 2019). The incidence of hypothermia was lowest in Study II where contributory factors for reducing the risk of hypothermia—such as warm ambient temperature, a high core temperature value at the induction of anesthesia, and a relatively small exposed area for surgery—were fulfilled (Yi et al., 2017). The highest incidence of hypothermia in Study III was most obviously derived from a low ambient temperature (Morris & Wilkey, 1970; Yi et al., 2017), a quite large exposed area, and moreover, the propofol sedation used in 86% of the patients.

Propofol sedation was found to be the only statistically significant variable in multivariate logistic regression analysis determining the risk factors for intraoperative hypothermia. In contrast, age (Frank et al., 1992) and BMI (Kurz et al., 1995;

Fernandes et al., 2012) were not found to be predisposing factors for hypothermia. However, patients having a BMI of 25 or less were excluded from the study in order to diminish the variation of the study population.

Though perioperative hypothermia was common, most patients were only slightly hypothermic. Still, the recommendations for perioperative thermal management were followed, and active warming was enhanced when core temperature dropped below 36.0 °C (Scott et al., 2015; National Institute for Health and Clinical Excellence & (NICE), 2016). As a result, especially in Study III, most patients had both the SW blanket and the FAW blanket. Using several warming methods for a single patient increases the workload of healthcare professionals and is unecological and uneconomic.

Hypothermia-related adverse effects have been discovered in original randomized clinical trials (Leslie et al., 1995; Kurz et al., 1996; Schmied et al., 1996; Frank et al., 1997; Lenhardt et al., 1997) as well as in a large, retrospective study of 45,304 non-cardiac patients (Scott et al., 2015). The randomized trials were mostly targeted to at-risk patients (Kurz, Schmied, Frank), and thus, they lack generalizability. Moreover, hypothermic patients had a core temperature of approximately 35.0 °C, which is far lower than is typical at the present time when active warming is standard in care.

Recent studies indicate that mild hypothermia, 35.5 °C to 35.9 °C, is associated with increased transfusion requirements, but it is not related to other adverse effects found in colder patients (Sun et al., 2015; Brown et al., 2017; Schacham et al., 2018; Walters et al., 2020). In the studies of this thesis, the blood loss and the incidence of SSI that were observed were similar between the hypothermic and normothermic patients. However, the studies were underpowered when it came to detecting hypothermia-related adverse effects. Altogether, the proportion of urinary tract infection equals that reported (Riikonen et al., 2020), but the incidence of SSI after TKA was higher, 2.0%, than the earlier reported 0.5% (Bozzo et al., 2022).

The threshold temperature of IPH in surgical patients has been defined as a core temperature of 36.0 °C (Vaughan et al., 1981; Sessler, 1997). This threshold differs from generally accepted threshold of mild hypothermia, which is 35 °C in adults (Brown et al., 2012). It can be argued that the threshold for IPH is not valid for every patient. Each patient has personal risks for getting hypothermia-related adverse effects. Existing chronic diseases and the surgery performed influence the severity of adverse effects. For instance, a young adult of ASA Class I may become

hypothermic (35.5 °C) during appendectomy, but he or she has no hypothermia-related adverse effects. In contrast, a fragile geriatric patient undergoing total hip arthroplasty is vulnerable to hypothermia, and even slight hypothermia may predispose the patient to serious adverse effects. Thus, instead of focusing on the core temperature value, attention should be paid to the entirety of a patient and surgery.

6.5 Non-invasive deep-body temperature monitoring

Continuous non-invasive deep-body temperature monitoring is a pivotal method for the core temperature measurement of surgical patients. The method is well tolerated, even in conscious patients, and can be used pre-, intra-, and postoperatively. Further, the equilibrium time is short: three minutes with the ZHF method and ten minutes with the DS method, as stated by the manufacturer. However, the time required to reach equilibrium in this study was a bit longer at four minutes. Still, the time required is shorter than the time required by a nasopharyngeal probe.

The basal temperature of a patient who is awake can be obtained with the ZHF method and the DS method, unlike with conventional esophageal and nasopharyngeal probes that are set after induction. With conventional methods, the first recorded temperatures are probably lower than the temperatures measured before induction because of the thermal redistribution that has occurred. This was seen in Study I where core temperature was measured with an esophageal probe and hypothermia incidence was high after anesthetic induction.

The agreement of the ZHF method with nasopharyngeal temperature has been evaluated in four clinical studies (see Table 9). The results of Study II show that the mean difference between methods (0.15 °C) was slightly greater and the 95% LoAs (± 0.36 °C) was smaller than that reported in previous studies (Iden et al., 2015; Mäkinen et al., 2016; Pesonen et al., 2019; West et al., 2020). The smaller LoAs may be derived from the strictly controlled study protocol with no rapid thermal changes. Further, the LoAs were within the accepted limits of 0.5 °C, which has not been observed in any of four previous studies. It can be concluded that the ZHF method correlates well with the nasopharyngeal temperatures.

Table 9. Clinical studies evaluating the agreement of the ZHF method with conventional measurement methods in studies including adult patients.

Study	Year	Cohort, number of patients		Data samples	Comparison temperature	BA results	
						mean difference	±95% LoA
Eshraghi	2014	Cardiac surgery	105	13,900	PA	-0.08	0.88
Iden	2015	Gynecological and trauma surgery	83	249	Nasopharyngeal	0.05	0.44*
Kato	2015	ICU, cardiac surgery postop	20	16,407	PA	-0.28	0.88
Mäkinen	2016	Cardiac surgery	15	-	Nasopharyngeal	-0.05	0.51
		Vascular surgery	15	-	Esophageal	0.08	0.32*
DahyotFizelier	2017	ICU	52	61,298	Esophageal	0.19	0.53
				1,850	Iliac artery	0.00	0.36*
Boisson	2018	Abdominal surgery	49	2,446	Esophageal	0.07	0.55
			22	101	Axillary artery	-0.06	0.35*
Schell-Chaple	2018	ICU	38	748	Rectal	-0.24	0.57
					Bladder	-0.07	0.47*
Gomez-Romero	2019	Cardiac surgery	41	289	PA	0.21	2.50
Jack	2019	Surgery	29	2,511	Esophageal	0.02	0.50
Kollmann Camaiora	2019	Gynecological surgery	66	401	Esophageal	-0.27	0.58
Pesonen	2019	Craniotomy	29	-	Nasopharyngeal	0.11	0.65
Tachibana	2019	Laparoscopic surgery	30	303	Esophageal	0.01	0.48
Bräuer	2020	ICU	50	7,018	PA/iliac artery	-0.12	0.63
Morettini	2020	Abdominal or urologic surgery	99	1,347	Esophageal	0.005	0.49*
West	2020	Non-cardiac surgery	194	132,721	Nasopharyngeal	-0.06	0.65
					Oropharyngeal	0.00	0.56
Munday	2021	Orthopedic surgery	23	448	Esophageal	0.14	0.90
Verheyden	2021	Cardiac surgery	40	17,850	PA	-0.06	0.89
Lauronen	2022	Orthopedic surgery	30	1,261	ZHF	0.05	0.42*

BA = Bland-Altman; LoA = limits of agreement; PA = pulmonary artery; ICU = intensive care unit; ZHF = zero heat flux; * LoA within 0.5 °C

The nasopharyngeal temperatures only stabilized after thirty minutes. This might result from ambient, cooler air remaining in the nasopharynx. Another reason might be technical since the probes were reusable and possibly worn, which could have prolonged the equilibrium time.

In general, the accuracy of the ZHF method has been concluded to be acceptable for clinical use as the mean difference has been shown to be mostly below 0.1 °C (see Table 9). However, the LoAs are only within the usually adopted 0.5 °C in seven studies, of which, one is a study comparing two bilaterally placed ZHF sensors. There might be several reasons for the large LoAs observed in most of the studies. First, it has been shown that during rapid core temperature changes (that is, over 1 °C within 30 minutes), the inaccuracy of the ZHF method increases compared to esophageal or axillary artery temperatures (Boisson et al., 2018). Further, large LoAs have also been reported by studies conducted in cardiac surgical patients (Eshraghi et al., 2014; Kato et al., 2015; Gómez-Romero et al., 2019; Verheyden et al., 2021). Moreover, although the forehead side does not affect the temperature readings of the ZHF method per se (see Study IV), the lateral tilt of the head may change cerebral blood flow, causing the temperature value to vary. Lastly, the agreement of the ZHF method with esophageal temperature has been shown to depend on actual temperature and the agreement was better during low mean core temperatures (Munday et al., 2021).

The DS method has been evaluated in various clinical studies that have shown an acceptable mean difference between the DS method and a reference method (see Table 10). However, LoAs have been shown to be outside of 0.5 °C in all but one study (Soehle et al., 2019). The agreement of the DS method with the ZHF method can be said to be of the same magnitude as with the other reference method reported previously.

It has been observed in clinical and volunteer studies that the DS method underestimates the reference method (Gunga et al., 2008, 2009; Mazgaoker et al., 2017; Gómez-Romero et al., 2019; Sastre et al., 2019). A similar observation was found in Study IV as the temperatures obtained with the DS method decreased more than the temperatures obtained with the ZHF method when core temperature decreases.

The temperature readings of the DS method may be affected by ambient temperature. The borders of the DS sensor may unfasten because of the relatively

large size of the sensor. This can lead to the partial contact of the sensor with the skin, which may disturb the calculation of temperature.

The supposed imprecision of the DS method, especially during low core temperatures, may cause the false great prevalence of hypothermia. This may lead to excessive and prolonged warming of a patient which, in turn, may be harmful for the patient.

Table 10. Clinical studies evaluating the agreement of the DS method with conventional measurement methods.

Study	Year	Cohort, number of patients		Data samples	Comparison temperature	BA results	
						mean difference	±95% LoA
Kimberger	2009	Surgery ICU	36 32	1,287	Esophageal	-0.08	0.58
Kimberger	2013	Trauma surgery (GA)	36	1,047	Esophageal	-0.01	0.60
		Orthopedic surgery (SA)	20	258	Bladder	-0.13	0.52
Gómez-Romero	2019	Cardiac surgery	41	289	PA	0.48	2.50
Sastre	2019	Cardiac surgery	40	960	PA Nasopharyngeal	-0.2 -0.2	1.16 1.09
Soehle	2019	Ovarian cancer	22	57,302	Iliac artery	-0.02	0.46
Janke	2021	Post cardiac arrest	25	1,319	Esophageal	0.02	1.046
Lauronen	2022	TKA (SA)	30	1,129	ZHF	0.33	0.88

BA = Bland-Altman; LoA = limits of agreement; ICU = intensive care unit; GA = general anesthesia; SA = spinal anesthesia; PA = pulmonary artery; TKA = total knee arthroplasty; ZHF = zero heat flux

6.6 Strengths and limitations

This study has several strengths. The most important are the study's coherence and the research design including three randomized controlled trials (RCTs) and one prospective observational study. For each RCT, a targeted study population was recruited and allocated to two study groups according to randomization. There were no changes between the groups. Further, the number of patients with missing data

or dropouts was small. The other essential strength is the research objects. There had been few published studies of both the thermal suit and the self-warming blanket when planning this study. The study results expanded and deepened the knowledge of the effectiveness and function of these warming methods. The results can be utilized in clinical decision-making. A further strength is the similar anesthesia and surgery procedures for all patients in each study, allowing for standardized circumstances and the predictable duration of the procedures. Another strength is the continuous core temperature monitoring and short intervals for data picking—especially in Studies II, III, and IV—that offered the chance to observe core temperature changes in real time. As the last, but not least, strength, we calculated changes in mean body temperature by measuring skin temperatures according to Ramanathan's formula.

Studies I–III were non-blinded due to the nature of the studies. Actually, the open label nature of the studies was not a limitation but an inevitable fact. However, it might increase the risk of detection and performance bias. The researcher, the nurses, and/or the patients might initially suppose either one of the warming methods to be better than the other. This supposition might especially affect patient-reported and nurse-reported outcomes. Nevertheless, the main outcome in each of Studies I–III was objectively measured core temperature. Further, the studies were conducted according to the strict study protocol. Thus, it can be assumed that the non-blinded manner did not influence the primary outcome, though it might have influenced the secondary outcomes.

There are limitations to the study. Firstly, the NICE recommendation for preventing inadvertent hypothermia was strictly adhered to and active warming was enhanced when core temperature dropped below 36°C. If the core temperature had been allowed to drop to 35.5°C, there might have been a bigger difference in the primary outcome between the groups in Studies II and III. Another limitation is the choice of the primary outcome in Studies II and III. Although core temperature on admission to the RR has been applied as a primary outcome in several previous studies comparing various warming methods, intraoperative core temperature change and especially the duration of hypothermia have been applied to assess the thermal condition or hypothermia burden of surgical patients (Sun et al., 2015). Lastly, one criticism that might be raised is that we did not have an acknowledged standard core temperature measurement site as a reference method in Study IV. However, the ZHF method has been shown to be accurate enough for clinical use

(Eshraghi et al., 2014). Moreover, the patients were under SA, and invasive core temperature monitoring methods could not have been used.

6.7 Suggestions for further research

The thermal suit and its perioperative use have been studied in four randomized clinical trials so far. The results of these studies mostly do not confirm the benefit of the suit in regard to preventing hypothermia. However, body heat content can be increased by preventing the cutaneous loss of metabolic heat. Increasing MBT by 1 °C requires 77 kcal (≈ 90 W), which is approximately the basal metabolic rate of an adult human per hour (Mcmurray et al., 2014). This is more than the amount usually redistributed in the first hour of GA (Matsukawa et al., 1995). Hence, there is need for studies concerning the ability of the thermal suit to increase body heat content preoperatively. Further, the effectiveness of the suit in preventing intraoperative cutaneous heat loss and hypothermia in a cool ambient temperature, such as the temperature in arthroplasty surgery, should be studied as well.

The number of publications concerning the effectiveness of the SW blanket in preventing IPH is limited, and the results of these studies are conflicting. In the future, the perioperative use of the SW blanket and especially the comparison of it with the FAW method should be studied in well-planned randomized clinical trials.

The ZHF method and its agreement with conventional core temperature monitoring methods have been evaluated in several studies. In contrast, the DS method has been studied in few clinical studies and should be compared with conventional core temperature monitoring methods in patients under GA and NA in the future. Further, it is not proven how ambient temperature, actual core temperature, and changes in head position affect the temperature readings of both methods. Moreover, the DS method and the ZHF method should be simultaneously compared with the conventional method.

The influence of large peripheral nerve blocks—such as femoral, popliteal, or interscalene nerve blocks—on thermoregulation and heat balance should be studied since there is no published data on how these blocks affect thermoregulation.

7 SUMMARY AND CONCLUSIONS

The aim of this study was to investigate the effectiveness and suitability of two new warming methods in regard to maintaining the normothermia of surgical patients. Further, two non-invasive temperature measuring methods were evaluated perioperatively.

The major findings in these studies follow:

1. A thermal suit does not provide additional benefit over cotton hospital clothes in maintaining normothermia during laparoscopic surgery in a setting where FAW and the warming of IV fluids are used.

2. The incidence of intraoperative hypothermia was statistically significantly lower in patients wearing the thermal suit connected to a FAW unit when compared with patients wearing hospital clothes. However, the difference was marginal, and the thermal suit was noticed to have poor breathability.

3. The SW blanket and the FAW blanket set to 38 °C raised the MST during prewarming. Despite this, both weakly prevented intraoperative hypothermia. The FAW blanket set to 43 °C was capable of raising core temperature intraoperatively.

4. The temperature readings of ZHF sensors were not dependent on the side of the forehead. The temperatures obtained by the DS sensors were mostly lower than those obtained by the ZHF sensors. The mean difference between the ZHF and DS sensors increased as the core temperature decreased.

To summarize, the thermal suit and the SW blanket are less effective than the FAW method in preventing intraoperative hypothermia. Moreover, their benefits do not

exceed their limited warming capacity. The ZHF method seems to have good internal validity. However, there is need for studies evaluating the accuracy of the ZHF method and the DS method, especially in hypothermic patients.

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PUBLICATIONS

PUBLICATION I

Thermal suit in preventing unintentional intraoperative hypothermia during general anaesthesia: A randomized controlled trial

Lauronen SL, Kalliomäki ML, Aho A, Kalliovalkama J, Riikonen J, Mäkinen MT, Leppikangas H, Yli-Hankala A

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Thermal suit in preventing unintentional intraoperative hypothermia during general anaesthesia: a randomized controlled trial

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Background: Unintentional perioperative hypothermia causes serious adverse effects to surgical patients. Thermal suit (T-Balance®) is an option for passive warming perioperatively. We hypothesized that the thermal suit will not maintain normothermia more efficiently than conventional cotton clothes when also other preventive procedures against unintentional hypothermia are used.
Methods: One hundred patients were recruited to this prospective, randomized trial. They were allocated to the Thermal Suit group or a Control group wearing conventional hospital cotton clothes. All patients received our institution's standard treatment against unintentional hypothermia including a warming mattress, a forced-air upper body warming blanket and a warming device for intravenous fluids. Eardrum temperature was measured preoperatively. In the operating room and post-anaesthesia care unit temperatures were measured from four locations: oesophagus, left axilla, dorsal surface of the left middle finger and dorsum of the left foot. The primary outcome measure was temperature change during robotic-assisted laparoscopic radical prostatectomy.
Results: The temperatures of 96 patients were analysed. There was no difference in mean core temperatures, axillary temperatures or skin temperatures on the finger between the groups. Only foot dorsum temperatures were significantly lower in the Thermal Suit group. Intraoperative temperature changes were similar in both groups. In the post-anaesthesia care unit temperature changes were minimal and they did not differ between the groups.
Conclusion: Provided that standard preventive procedures in maintaining normothermia are effective the thermal suit does not provide any additional benefit over conventional cotton clothes during robotic-assisted laparoscopic radical prostatectomy.

Editorial comment
In this clinical trial, a thermal insulation suit was tested to see if there would be any perioperative temperature retention advantage compared to routine operative patient clothing and routines during a laparscopic surgical procedure of moderate duration. No advantage was detected.

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Unintentional perioperative hypothermia causes well-known adverse effects: increased incidence of wound infections,[1] increased blood loss,[2] increased risk for myocardial ischaemia[3] and prolonged recovery post-operatively.[4] In addition to these shivering and the feeling of cold in the post-anaesthesia care unit are uncomfortable and distressing for the patient.

Laparoscopic surgery exposes the patients to heat loss by rather a large area of exposed skin in a comparable manner to open abdominal surgery.[5,6] Pre-heating the insufflating gas has little effect on body thermoregulation during laparoscopy.[7] Similarly, pre-warming the ambient temperature does not prevent intraoperative hypothermia[8] but the temperature of the operation room has a direct effect on the heat balance of the patients.

There are several methods to reduce heat loss in the perioperative setting. Active heating methods consist of warming of intravenous and irrigation fluids,[9] using forced-air warming devices and thermoadjustable mattresses. Passive warming methods such as space blankets, cotton and microfiber blankets, as well as low-flow anaesthesia are used during surgery.

Thermal suit (T-Balance®, TelesPro Finland Ltd., Kuopio, Finland) is an option for passive warming perioperatively. In a previous study, body temperature was maintained 0.5°C higher in patients wearing the T-Balance® thermal suit compared to patients wearing conventional hospital clothes during transurethral resection of the prostate under spinal anaesthesia.[10]

The aim of this prospective, randomized, controlled study was to investigate if using the T-Balance® thermal suit in addition to our institution's standard preventive procedure against unintentional perioperative hypothermia is beneficial during robotic-assisted laparoscopic radical prostatectomy (RALP) under general anaesthesia. Our null hypothesis was that the T-Balance® thermal suit will not maintain normothermia more efficiently than conventional cotton clothes during RALP. Primary aim was difference in core temperature during anaesthesia. Secondary aims were differences in peripheral temperatures and relevant surgical outcomes.

Methods

After approval from the Ethical Committee of Tampere University Hospital, Tampere, Finland (R12038) (Chairperson Prof. Amos Pasternack) on 21 February 2012 the study was registered with ClinicalTrials.gov (Code NCT01571544). The study was carried out at Tampere University Hospital, Tampere, Finland, during the period of November 2012 to April 2013. Written informed consent was obtained from all patients. The study was conducted according to rules and regulations of the Declaration of Helsinki.

Inclusion criteria were: age 18–90 years, American Society of Anesthesiologists ASA physical status I-III and scheduled for RALP. Exclusion criteria were: decreased mental status, neuromuscular disorders, Raynaud's phenomenon and unstable coronary artery disease.

Study design and trial protocol

One hundred patients were recruited to the study: 50 patients wearing conventional hospital cotton clothes (Control group) and 50 patients wearing the T-Balance® thermal suit (Thermal Suit group). Randomization was accomplished using a computerized random number generator. Blocked randomization was used including 10 patients in each block. During the pre-operative visit the patients were randomized to treatment groups. The randomization was kept blinded for the patient and the staff until the day of the surgery. The first patient of the day arrived from home to the hospital at seven o'clock and the second patient was scheduled to arrive at 11 o'clock. The attending nurse at the pre-operative holding area opened the sealed randomization envelope and instructed the patients to switch to study clothes accordingly.

All patients received standard methods against unintentional intraoperative hypothermia. At our institution the following are in use for RALP patients: warming mattress (Astopad®, Armstrong Medical, Coleraine, Northern Ireland) set to 38.5°C, warming of intravenous fluids to approximately 41°C (Hotline®, Smiths Medical, Ashford, UK) and upper body forced-air warming blanket set to 38°C (Bair Hugger®,

Arizant Heathcare, Eden Prairie, MN, USA). According to the routine care the patients in the Control group were administered single-use nonwoven leg stockings (Barrier®, Mölnlycke Health Care, French Forest, NSW, Australia) before induction of anaesthesia whereas the patients in the Thermal Suit group were barefoot.

Thermal suit

T-Balance® thermal suit has been developed to prevent inadvertent hypothermia perioperatively. It is dressed on the ward or in the preoperative holding area before surgery. The T-Balance® thermal suit can be worn throughout all kinds of surgeries and perioperative care. The thermal suit has multiple zippers that can be opened and closed as required for anaesthesia, surgery and post-operative care. The fabric of the thermal suit is three-layer laminate: the outermost layer is woven from smooth microfibers, the middle layer is made of waterproof, breathable fabric, and the innermost layer is made of microfleece. The reusable thermal suit can be washed in normal hospital laundry at 70–72°C. The thermal suit should be washed maximum of 80 times or maximal using time is 180 weeks if washing times cannot be calculated. New thermal suits were taken into use in the beginning of this study.

Temperature measurement

Baseline body temperature was measured with an eardrum thermometer (Covidien Genius 2, Tympanic Thermometer and Base, Covidien llc, Mansfield, MA, USA) before patient changed to study clothes. The temperature measurement points in the operating room were oesophagus (core temperature, T1), left axilla (T2), dorsal surface of the middle phalanx of the left middle finger (T3) and the dorsum of the left foot (T4). As soon as the patient had moved onto the operating table the measurement of the skin temperatures (T2, T3 and T4) were started using disposable probes (Skin Temperature Probe®, GE Healthcare Finland, Helsinki, Finland). The disposable oesophageal thermometer (General Purpose Temperature Probe®, GE Healthcare Finland, Helsinki, Finland) was placed immediately after endotracheal intubation. All temperature data were collected at 10-s intervals on a laptop computer with S5 Collect software (GE Healthcare Finland, Helsinki, Finland) for offline analysis. Ambient temperature at one-metre distance from the patient (Prologue® Digital Thermometer, Model No RS3010, Clas Ohlson, Insjön, Sweden) and humidity (from the digital display on the operating room wall) of the operating room were also measured and recorded every 15 min. In the post-anaesthesia care unit the measuring and recording of all temperatures continued until the patient was transferred to the ward or up to 3 h.

If core temperature (T1) rose over 38°C the anaesthesiologist was instructed to: turn off the forced-air warming blanket, turn off the warming device for intravenous fluids, and turn off the warming mattress. If core temperature (T1) fell below 35°C the following steps were instructed: temperature of the warming mattress would be set to 40°C, and temperature of the forced-air warming blanket would be set to 43°C. It was also instructed to warm up the patient until the core temperature was over 35°C at tracheal extubation.

Anaesthesia

Patients received per os paracetamol 1000 mg and if needed also midazolam 7.5 mg per os 0.5–1 h before surgery. All patients were anaesthetized with target controlled infusions (TCI, Asena™ PK, Alaris Medical Systems, Basingstoke, UK) of propofol and remifentanil. Pharmacokinetic models of Schnider and Minto were used for administration of propofol and remifentanil, respectively.[11,12] Total amounts of anaesthetics were recorded at the end of anaesthesia. The administration of anaesthetics was targeted to keep State Entropy (GE Healthcare, Helsinki, Finland) values between 30 and 60. Rocuronium 0.6 mg/kg was used to facilitate endotracheal intubation and additional doses were given according to clinical needs. Neuromuscular transmission was monitored with the M-NMT Mechanosensor™ (Datex-Ohmeda, Helsinki, Finland) and assessed using the train of four stimulation mode.

Positive end-expiratory pressure was set to 5 cm H_2O and maintained throughout the anaesthesia. The end-tidal oxygen concentration of

45% and fresh gas flow of 1.2 l/min were used during surgery. To avoid anaesthetic-induced relative hypovolemia the study protocol permitted infusing 1000 ml of Ringer's acetate (Ringer-Acetat Baxter Viaflo®, Baxter Healthcare Ltd, Thetford, Norfolk, Great Britain) and 500 ml of hydroxyethyl starch (Tetraspan® 60 mg/ml, B. Braun Melsungen AG, Melsungen, Germany) intraoperatively via Hotline® fluid warmer. The noninvasive mean arterial pressure was maintained over 65 mmHg; additional intravenous fluids and/or infusion of noradrenaline were used if needed.

Surgery

Robotic-assisted laparoscopic radical prostatectomy was carried out with the aid of a four-arm da Vinci S robot (Intuitive Surgical, Sunnyvale, CA, USA). Pneumoperitoneum was established by the Hasson technique 2 cm above the umbilicus and maintained by unheated CO_2 insufflation. A transperitoneal six-port approach was used. During the operation the patient was in the 30° Trendelenburg position, hips were abducted and knees flexed. Intra-abdominal pressure was 12 mmHg, excluding division of the deep venous complex when pressure was raised up to 18–20 mmHg. The prostate specimen was removed via periumbilical incision.

At our institution two RALP surgeries are performed daily (in the text referred to as order of the patient, 1 or 2). The planned discharge from hospital is the first day after surgery. The removal of the urinary catheter is planned from 6 to 9 days post-operatively. The post-operative complications from surgery to catheter removal are collected using Clavien-Dindo classification.[13]

Statistical analysis

We aimed to detect a difference of 0.5°C in core temperature between the study groups as this is considered clinically significant. Based on the previous study[10] standard deviation of 0.7°C in the core temperature was assumed. The study was designed to have a power of 0.80, assuming alpha error of 0.05. To meet the criteria of power calculation 42 patients per group were needed. To allow for dropouts we enrolled 50 patients per study group.

Statistical analyses were performed using SPSS 21.0 (IBM, Chicago, Ill, USA). T-test was used for parametrical continuous independent data and Mann–Whitney for non-parametrical data. ANOVA was performed for the comparison of several groups. Paired *t*-test was used for analysing statistical difference in paired samples. *P* value <0.05 was considered statistically significant.

Results

One hundred patients were enrolled. Four patients, all from the Control group, were left out of the final analyses (Fig. 1). The patient characteristics and the relevant intraoperative data are presented in Table 1. All patients except one in the Control group received paracetamol 1000 mg for pre-medication. Seven patients in the Control group and eleven patients in the Thermal Suit group received also midazolam 7.5 mg per os. Before surgery the mean time spent at the pre-operative holding area was 55 min (median 45 min) in the Control group and 70 min (median 80 min) in the Thermal Suit group ($P = 0.015$). Altogether mean pre-operative waiting time was 63 min and median 47 min. To maintain mean arterial pressure >65 mmHg the infusion of noradrenaline was used in 20 and 13 patients in Control and Thermal Suit groups, respectively. Additionally 13 controls and 10 patients wearing the thermal suit needed noradrenaline boluses (total dose 8–24 μg, no statistical difference). Ambient temperature (Control 21.3°C ± 0.38, Thermal Suit 21.4°C ± 0.39) and humidity (Control 47.4% ± 1.0, Thermal Suit 47.4% ± 1.0) were similar in both groups. Mean volume of gas delivered was 267 l ± 130 (median 245) in the Control group and 253 l ± 121 (median 216) in the Thermal Suit group. The warming devices were not regulated during the anaesthesia. Four patients in the Control group and five patients wearing the thermal suit needed additional warming in the post-anaesthesia care unit.

Core temperature

No over 0.5°C differences were found in the mean core temperatures between the two groups. Neither did the minimal core

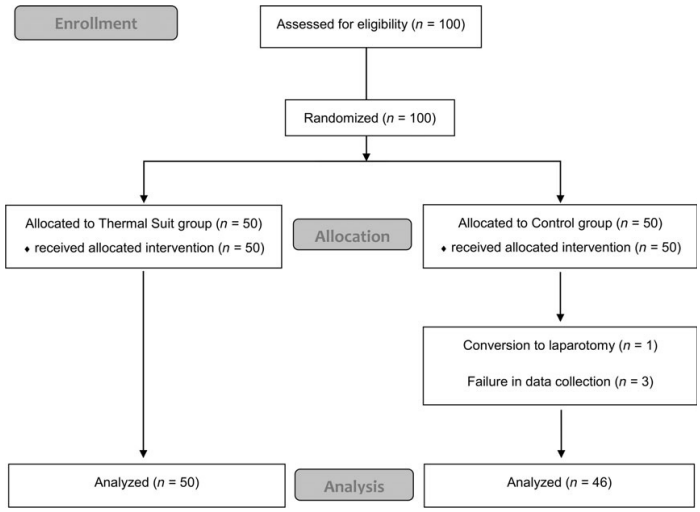

Fig. 1. CONSORT flow diagram. [Colour figure can be viewed at wileyonlinelibrary.com]

temperatures differ significantly. There was, however, a 0.6°C difference in the maximal core temperature for the benefit of the Control group at time point 120 min (Fig. 2, Table 2). Sixteen patients in the Control group and nineteen patients in the Thermal Suit group had a temperature below 36.0°C during surgery. Time spent at the temperature below 36.0°C was not different between the groups (Table 2). The core temperature at the time of tracheal extubation was below 36°C in two and five patients in Control and Thermal Suit groups, respectively. The differences in the core temperatures between Control and Thermal Suit –groups were not dependent on the order of the patient (data not shown). In addition the core temperature of both groups rose significantly during anaesthesia, more prominently in the Control group (Fig. 2).

The difference between the groups in the post-anaesthesia care unit was not significant, and in both groups the temperature rose to a similar extent (Fig. 3).

Skin temperatures

The axillary temperatures followed the oesophageal temperatures (Fig. 4). The skin temperatures in the finger and foot dorsum rose significantly in the both groups during the first hour of anaesthesia. The finger temperatures (T3) did not differ significantly between the study groups. The minimal and maximal foot dorsum temperatures (T4) were statistically significantly lower in the patients wearing the thermal suit (Table 3).

The skin temperatures in the post-anaesthesia care unit were similar in both groups. The axillary temperatures rose in both groups. The finger temperatures decreased first and then rose. The foot temperatures did not change. There were no differences in thermal distribution between the Control and the Thermal suit groups.

Relevant surgical outcomes

Eighty-four percent (81/96) of the patients were discharged from the hospital on the first post-operative day. Clavien-Dindo classification was available for 73 patients, 23 patients went for post-operative control in their local hospitals. In 53 (73%) patients no complications were observed. One patient from each group required cystoscopy. One patient in the Thermal Suit group needed antibiotics for urinary tract infection and another one analgesics for pain in the perineum. No differences in discharge time or

Table 1 Demographic data.

	Thermal suit (N = 50)	Control (N = 46)	P value
Age (years)	60.38 (6.76)	62.04 (5.54)	0.193
Body mass index (kg/m^2)	27.76 (3.51)	27.85 (4.15)	0.903
Pre-operative eardrum temperature (°C)	36.55 (0.39)	36.61 (0.36)	0.404
Blood loss (ml)	172.45 (163.54)	161.52 (122.13)	0.714
Hydroxyethyl starch (ml)	340.00 (194.83)	370.65 (162.47)	0.407
Remifentanil (μg)	2149.43 (669.00)	2292.13 (670.85)	0.305
Propofol (mg)	2287.61 (591.05)	2288.64 (509.20)	0.986
Preoperative waiting time (h)	1:10:02 (0:32:35)	0:55:04 (0:25:18)	0.015
Order of the patient (N1)/(N2)	23/27	29/17	0.105
Duration of surgery (h)	2:41:46 (0:36:20)	2:41:56 (0:32:32)	0.983
Duration of anaesthesia (h)	3:18:09 (0:37:13)	3:19:43 (0:34:28)	0.832
ASA class I/II/III (number of patients)	10/28/12	6/24/16	

Otherwise values mean (SD). Order of the patient: (N1) is amount of the patients being the first patient in the operating room, (N2) is amount of the patients being the second patient in the operating room. ASA American Society for Anesthesiologists.

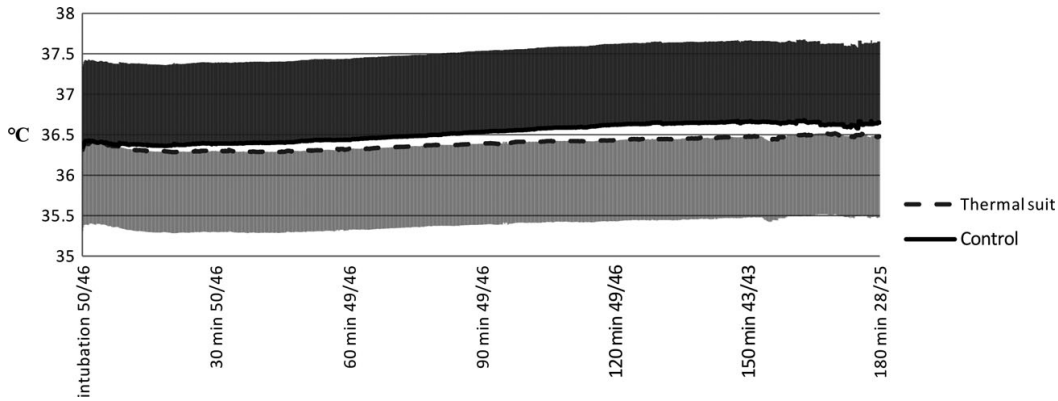

Fig. 2. Diagram showing the core temperature change within groups Control and Thermal Suit in the operating room. There is no significant difference between the groups during the anaesthesia. The *X*-axis shows time in minutes and number of patients in each group (Thermal Suit/Control).

complication rates were found between the Control and Thermal Suit groups.

Discussion

In this randomized controlled trial no difference was found in the core temperature between groups wearing conventional hospital cotton clothes or the T-Balance® thermal suit. To our knowledge this is the first study comparing the conventional hospital cotton clothes and the T-Balance® thermal suit during laparoscopy under general anaesthesia. A statistically but not clinically significant difference (0.6°C) of the maximal core temperature for the benefit of the Control group was seen at 120 min after intubation. The patients in the Control group were more prone to be warmed up during anaesthesia. The thermal suit most probably acts as an insulator, i.e. external warming devices do not reach the patient through the thermal suit, but on the other hand these patients do not loose thermal energy through convection, evaporation and conduction in comparison with control

Table 2 Core temperature parameters.

	Group	*N*	Mean	SD	Lowest-highest	*P*
Min	Control	46	36.15	0.52	34.90–37.40	0.57
	Thermal suit	50	36.07	0.51	34.90–37.00	
Max	Control	46	36.82	0.44	35.80–37.90	0.19
	Thermal suit	50	36.71	0.37	35.90–37.40	
Mean	Control	46	36.54	0.41	35.61–37.53	0.09
	Thermal suit	50	36.40	0.41	35.54–37.16	
Mean 120	Control	46	36.62	0.47	35.60–37.90	0.04
	Thermal suit	49	36.43	0.45	35.60–37.30	
Extubation	Control	46	36.69	0.49	35.70–37.90	0.06
	Thermal suit	50	36.51	0.45	35.60–37.60	
Time spent at <36°C (min)	Control	16	17.02	41.81	0.3–198	0.32
	Thermal suit	19	27.55	58.75	0.5–200	

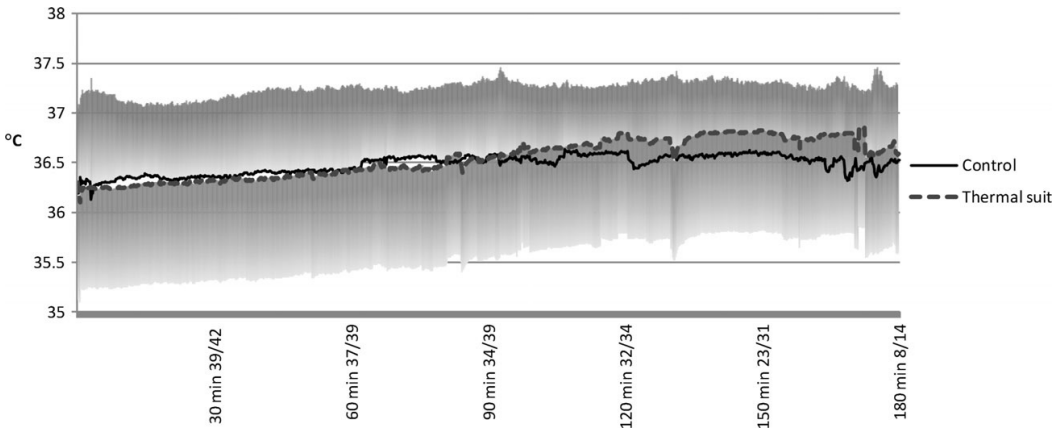

Fig. 3. Diagram showing the core temperature change within groups Control and Thermal Suit in the post-anaesthesia care unit. The difference in between the groups is not significant ($P = 0.08$). The temperature rises significantly in both groups, $P = 0.000$ (Lower Bound), and the difference is more pronounced in the Control group, $P = 0.036$ (Lower Bound). Black line=Control group, Grey line=Thermal Suit group. The *X*-axis shows time in minutes and number of patients in each group (Thermal Suit/Control). [Colour figure can be viewed at wileyonlinelibrary.com]

patients. The lack of benefit of the suit cannot be explained by excessive washing of the reusable suits since all thermal suits were brand new in this study.

It can be argued that there was a statistically significant difference in the temperature of the foot between the study groups but, in our opinion, it is justifiable to claim that this difference is not clinically relevant. Patients wearing the thermal suit had lower foot temperatures already at the induction of anaesthesia. This may be a sum effect of longer waiting time and lack of leg stockings in the Thermal Suit group compared to the Control group. This discrepancy may be considered as a limitation of the study. A method for equalizing the waiting times could have been randomizing the days first and second patients separately into hospital clothes and thermal suits. We recommend this to be considered in further studies.

The manufacturer claims that the longer the thermal suit is on the patient the better the benefit from it. In our study population the waiting time at the pre-operative holding area was significantly longer in the Thermal Suit group. Even so we did not find any significant

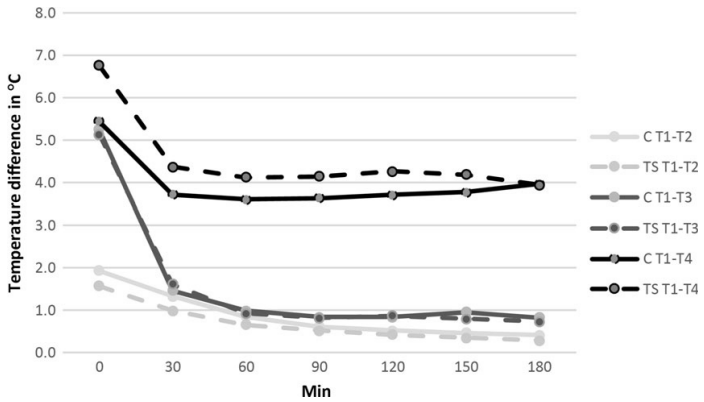

Fig. 4. Thermal distribution during anaesthesia. There was no difference in the oesophagial (T1) and axillary temperatures (T2). The temperature difference between oesophagial (T1) and peripheral (T3, finger and T4, foot dorsum) is largest at the beginning and diminishes during the first 30 min after the induction of anaesthesia whereafter it stays stabile. C, Control; TS, Thermal Suit. [Colour figure can be viewed at wileyonlinelibrary.com]

Table 3 Peripheral temperatures.

	Group	Mean TC	SD	Range	*P*
Mean	T2 Control	35.82	0.46	34.7–37.1	0.47
	Thermal suit	35.75	0.49	34.6–36.6	
	T3 Control	35.10	0.69	33.4–36.5	0.28
	Thermal suit	34.93	0.75	32.8–36.2	
	T4 Control	32.73	1.68	28.1–35.2	0.01
	Thermal suit	31.90	1.53	26.8–33.9	
TC at 120 min	T2 Control	36.12	0.48	34.7–37.5	0.24
	Thermal suit	36.00	0.50	34.7–36.8	
	T3 Control	35.78	0.64	34.0–36.8	0.13
	Thermal suit	35.56	0.77	32.4–36.5	
	T4 Control	32.92	1.78	28.0–35.3	0.05
	Thermal suit	32.16	1.87	26.4–34.6	

T2 axilla, T3 finger and T4 foot dorsum. Means of temperatures in degrees Celsius (TC) and mean of temperatures at 120 min from the induction of anaesthesia, when the temperature differences were largest. SD, stardard deviation.

changes of body temperatures in favour of the thermal suit. The manufacturer recommends the thermal suit to be worn for several hours before entering the operating room. This, however, is not possible in the era of day- and short-term surgery when the patients come to the hospital in the morning of their surgery. In order to find out the benefit of wearing the thermal suit for a longer time patients should be able to wear the thermal suit from the previous evening of surgery.

Thermal redistribution after the induction of anaesthesia happens due to the disturbance of central thermoregulation and the peripheral vasodilatation.[14] In our study the thermal distribution during anaesthesia was similarly affected in both clothing groups – the difference between core and skin temperatures diminished with time from the beginning of anaesthesia. We hypothesize that because the thermal suit acts as an insulator it does not prevent or change the pattern of thermal redistribution. It would be of interest to investigate the efficacy of thermal suit in preserving body's thermal energy. This should be done in a separate, well planned setting with a long enough pre-operative period.

Hypothermia during surgery is a sum effect of radiation, convection, evaporation and conduction of the body surfaces and the respiratory tract. Factors affecting these are: type of surgery, exposed area of skin, volume and temperature of irrigation and intravenous fluids, ventilation with cold gases and the length of anaesthesia. Two earlier studies have compared the open surgical technique with a laparoscopic technique for cholecystectomy[5] and gastric bypass surgery.[6]Neither of the studies detected difference in the core temperature[5,6] nor the thermal balance[5] between the open and laparoscopic surgical groups. It is thus unlikely that the thermal suit could provide any benefit in other types of surgery under general anaesthesia.

One of the limitations in our study is that we aimed for a 0.5°C difference but according to our analysis the 0.2°C difference in the mean core temperature between Thermal Suit and Control groups was statistically significant. However, at this time point there was a larger (0.6°C) temperature difference in the maximal temperatures, which explains the statistical difference. This discrepancy occurred because the variation in temperatures was smaller in our study sample than in the reference[10] study sample. It may be considered yet as another limitation that neither the patients nor the nurses were asked for the convenience of the thermal suit. Patient-related features of importance for thermoregulation during laparoscopy are the radius of abdomen, the thickness of the distended abdominal wall, initial blood mass flow rate and body metabolic heat ratio[15] which were not calculated in our study.

In conclusion, in a setting where routine procedures against unintentional perioperative hypothermia are effective, as in our hospital, the thermal suit does not bring additional value to maintaining normothermia during general anaesthesia in major laparoscopic surgery.

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PUBLICATION II

Thermal suit connected to a forced-air warming unit for preventing intraoperative hypothermia: A randomised controlled trial

Lauronen SL, Mäkinen MT, Annila P, Huhtala H, Yli-Hankala A, Kalliomäki ML

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ORIGINAL ARTICLE

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Thermal suit connected to a forced-air warming unit for preventing intraoperative hypothermia: A randomised controlled trial

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Abstract

Background: Inadvertent intraoperative hypothermia is a common occurrence in surgical patients. A thermal suit is an option for passive insulation. However, active warming is known to be more effective. Therefore, we hypothesised that a forced-air warming (FAW) unit connected to the thermal suit is superior to a commercial FAW blanket and a warming mattress in breast cancer surgery.

Methods: Forty patients were randomised to this prospective, clinical trial to wear either the thermal suit or conventional hospital clothes under general anaesthesia. The Thermal suit group had a FAW unit set to 38°C and connected to the legs of the suit. The Hospital clothes group had a lower body blanket set to 38°C and a warming mattress set to 37°C. Core temperature was measured with zero-heat-flux sensor. The primary outcome was core temperature on admission to the recovery room.

Results: There was no difference in mean core temperatures at anaesthetic induction ($P = .4$) or on admission to the recovery room ($P = .07$). One patient in the Thermal suit group (5%) vs six patients in the Hospital clothes group (32%) suffered from intraoperative hypothermia ($P = .04$, 95% CI 1.9%-49%). Mean skin temperatures (MSTs) were higher in the Thermal suit group during anaesthesia. No burns or skin irritations were reported. Two patients in the Thermal suit group sweated.

Conclusions: A thermal suit connected to a FAW unit was not superior to a commercial FAW blanket, although the incidence of intraoperative hypothermia was lower in patients treated with a thermal suit.

1 | INTRODUCTION

Inadvertent perioperative hypothermia (IPH), defined as a core temperature below 36°C,[1] is common in patients undergoing surgery. Hypothermia can lead to several adverse effects, such as decreased drug metabolism,[2] impaired coagulation,[3] increased blood loss[4] and wound infections,[5] increased risk of myocardial ischaemia[6] and delayed recovery.[7] In addition, feeling cold and experiencing shivering post-operatively are uncomfortable and distressing for the patient.

Many active and passive warming techniques are used to prevent IPH. However, active warming has been reported to be more effective than passive insulation.[8] Despite the effective warming techniques currently in use, as many as half of all surgical patients still experience hypothermia.[9] The most efficient method for preventing IPH is pre-operative warming,[10] but it is not always available. Hence,

M-TM was a member of the 3M Patient Temperature Management Advisory Board until 31 December 2016.

multiple warming methods are often applied during surgery. Using several warming methods for one particular patient, however, increases costs and waste and the workload of healthcare professionals.

One option for passive perioperative warming of patients is a thermal insulating suit that is worn instead of hospital cotton clothes. The jumpsuit is made of a three-layer laminate fabric composed of an outer layer of woven smooth microfiber, a waterproof, breathable fabric middle layer and a microfleece inner layer. The thermal suit can be used for various surgical procedures due to multiple zippers. The suit is reusable and can be washed up to 80 times or until 180 weeks, if the number of washes cannot be calculated.

The benefit of a thermal suit in preventing IPH is unclear since recently published studies show conflicting results.[11,12] To optimise the feasibility of the suit, the manufacturer has developed an adapter that leads forced warm air to the inside of the suit.

We are unaware of any previous studies that have examined the thermal suit connected to a forced-air warming (FAW) unit in clinical practice. We hypothesised that this new method is superior to the conventional intraoperative warming method, comprising a commercial lower body FAW blanket and a warming mattress. We chose breast cancer patients as a study group because in unilateral breast surgery, all circumstances are easily standardised, allowing a strictly controlled study of warming methods. The primary aim of this clinical trial was to investigate the effectiveness of the thermal suit connected to a FAW unit in preventing IPH in patients under general anaesthesia. Secondary aims were to evaluate the usability, compliance and related costs of this new method.

2 | METHODS

This prospective, randomised study was approved by the Ethics Committee of Tampere University Hospital, Tampere, Finland (R17137) on 12 December 2017, and registered at ClinicalTrials.gov on 2 February 2018 (Code NCT03420924). Written informed consent was obtained from all patients. Valvira (the National Supervisory Authority for Welfare and Health in Finland) was notified at the beginning of the study.

The study population consisted of females who were scheduled for primary, unilateral mastectomy or resection of the breast with or without lymphadenectomy of the axilla due to breast cancer. The inclusion criteria were age 20-90 years, American Society of Anesthesiologists (ASA) physical status I-III classification and body mass index (BMI) 25 to 40.[13] The exclusion criteria were insufficient knowledge of the Finnish language or any other impediment that prevented the participants from giving informed consent. During the pre-operative visit, participants were assessed for eligibility and recruited to the study by an anaesthesiologist (S-LL). The patients were then randomised to this parallel, 1:1 allocated study. In the morning of the surgery, the attending nurse opened the sealed randomisation envelope and the patients were dressed in either a thermal suit (T-Balance®, Telespro Finland Ltd.; Thermal suit group) or conventional hospital cotton clothes (Hospital clothes group).

Editorial comments

The advantages of perioperative forced-air warming include both a reduction in post-operative complications and improved patient comfort. However, the present randomised study demonstrates that forced-air warming by means of a thermal suit probably is not superior to using a conventional forced-air warming blanket.

Patients did not receive any premedication or active pre-warming. Non-invasive blood pressure, electrocardiography and pulse oximetry monitoring were initiated before anaesthetic induction. General anaesthesia was induced and maintained with target-controlled infusions (TCI, Asena™ PK, Alaris Medical Systems). Propofol was administered with the Schnider model and remifentanil with the Minto model. State Entropy (GE Healthcare) values were kept between 40 and 60. A laryngeal mask (i-gel®, Intersurgical Ltd) was used to secure the airway. Inspiratory oxygen fraction was 0.5 at a fresh gas flow of 2 L/min. The end-tidal partial pressure of carbon dioxide was kept between 4.5 and 5.0 kPa.

All patients received FAW (3M™ Bair Hugger™, Arizant Healthcare) intraoperatively. The nozzle of the FAW (Warming Unit model 750) was connected to the legs of the T-Balance thermal suit using a Y-piece adapter newly developed for the thermal suit system (Figure 1). The Hospital clothes group had a lower body FAW blanket (model 52500). In both groups, the FAW was turned on at 38°C immediately after surgical draping. The Hospital clothes group also had a warming mattress (Astopad®, Armstrong Medical) set at 37°C from the beginning. Intravenous fluids were taken from the warming cabinet (Heraeus Function Line B12, Thermo Fischer Scientific Inc) set at 36.5°C, but the fluids were not actively warmed perioperatively.

Hypothermia was defined as a core temperature ≤35.9°C.[1] If hypothermia occurred, the warming mattress was set to 39°C and intravenous fluids were actively warmed at 38°C (BW 585M, Biegler GmbH) in both groups. For the Hospital clothes group, the FAW was set at 43°C. If the core temperature exceeded 38°C, active warming was discontinued.

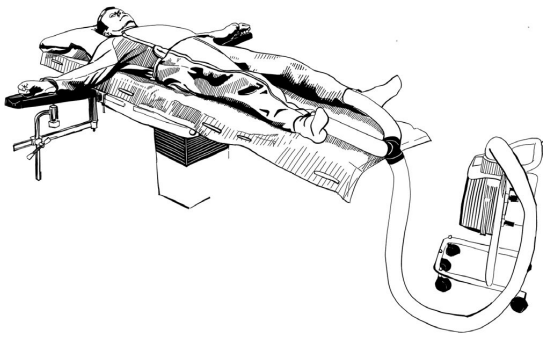

FIGURE 1 T-Balance® thermal suit connected to the forced-air warming unit

If the patient felt cold post-operatively, a warm blanket or FAW was initiated, depending on the decision of the nurse. Otherwise, post-operative active warming was not used.

Intra- and post-operatively, the core temperature ($Temp_{ZHF}$) was measured using a non-invasive Zero-heat-flux sensor (3M™ Bair Hugger™ Temperature Monitoring System, Arizant Healthcare) that was placed on the patients' lateral forehead before anaesthetic induction. During anaesthesia, the nasopharyngeal temperature ($Temp_{Naso}$; General purpose probe®, GE Healthcare) was used as the reference method. The probe was inserted to the depth of the distance between the nostril and the auditory canal. Pre-operative core temperature was measured once from the eardrum (Genius™, 2 Tympanic Thermometer and Base, Covidien llc). Skin temperatures (Skin Temperature Probe®, GE Healthcare) were measured from the chest (t_{chest}), upper arm (t_{arm}), thigh (t_{thigh}) and leg (t_{leg}).[14] The core and skin temperatures were continuously recorded intraoperatively and for up to 1 hour post-operatively, and the data were saved every 10 minutes. Patients' characteristics and relevant perioperative data as well as temperatures were documented in a data collection file.

The primary outcome was the core temperature value on admission to the recovery room. Secondary outcomes were changes in the core and peripheral temperatures intraoperatively and post-operatively, the level of satisfaction with the warming method of both patients and nurses and the costs of the warming methods used.

We aimed to detect a difference of 0.5°C in mean core temperature between groups. Based on a previous study,[15] a SD of 0.5°C was chosen. With an alpha error of 0.05 and a power of 80%, the sample size of 16 patients per group was calculated. To allow for dropouts, 20 patients were enrolled for each study group.

Statistical analysis was performed using SPSS Version 25.0. (IBM Corp). Normally distributed data are presented as mean (SD). The Shapiro-Wilk test of normality was used to confirm normal distribution of data. *T*-test was used for continuous data, Fisher's exact test for binominal data and Spearman's correlation for calculating statistical relationship. In order to evaluate the thermal redistribution, we applied Ramanathan's formula,[14] where four peripheral temperatures are used to calculate mean skin temperature (MST): $MST_R = 0.3 \times (t_{chest} + t_{arm}) + 0.2 \times (t_{thigh} + t_{leg})$.

A $P < .05$ was considered statistically significant.

3 | RESULTS

The data were collected between February and July 2018. After screening 126 patients, 40 patients were randomised either to the Thermal suit group (n = 20) or the Hospital clothes group (n = 20). One patient allocated to the Hospital clothes group was excluded from the final analysis due to missing data (Figure 2). Patients' characteristics and relevant perioperative data were similar between groups (Table 1). No patient was hypothermic on admission to the hospital or at anaesthetic induction. Time spent in the holding area varied and was longer in patients operated in the afternoon. General anaesthesia was induced 13 (4) minutes after admission to the operating room (OR) in both groups and FAW was turned on 19 (4) and 20 (4) minutes after induction in the Thermal suit group and Hospital clothes group respectively. During the first 40 minutes of surgery, $Temp_{Naso}$ was statistically lower than $Temp_{ZHF}$. Thereafter, both temperatures paralleled closely with each other until the end of anaesthesia, although $Temp_{Naso}$ remained 0.14° lower.

After anaesthetic induction, the drop in mean core temperature was 0.8 (0.2)°C and 0.9 (0.3)°C in the Thermal suit and Hospital clothes groups respectively (Figure 3). Intraoperatively, one patient in the Thermal suit group (5%) and six patients in the Hospital clothes group (32%) became hypothermic ($P = .04$, 95% CI 1.9%-49%). The

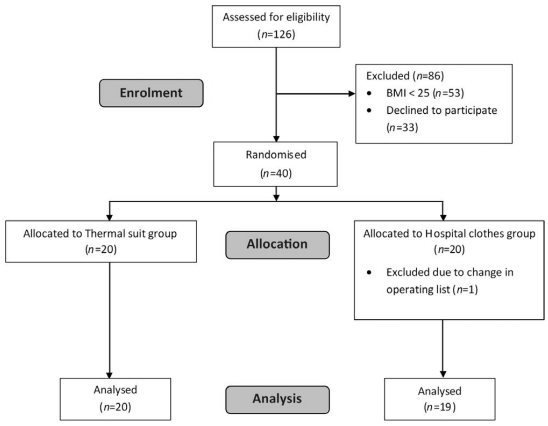

FIGURE 2 Consort flow diagram [Colour figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Patients' characteristics and perioperative data

	Thermal suit (n = 20)	Hospital clothes (n = 19)
Age (y)	66.7 (10.9)	62.3 (15.0)
Height (cm)	162 (7)	163 (7)
Weight (kg)	79 (10)	76 (11)
Body mass index (kg/m^2)	29.9 (3.2)	28.6 (3.4)
ASA class 1/2/3 (n)	1/16/3	3/11/5
Order in OR I/II/III (n)	4/7/9	7/6/6
Pre-operative waiting time depending on the order (h:min)	0:58/2:04/4:19	0:29/2:30/3:57
Duration of anaesthesia (h:min)	1:44 (0:17)	1:55 (0:22)
Duration of surgery (h:min)	1:17 (0:19)	1:24 (0:23)
Propofol (mg)	1066 (271)	1111 (333)
Remifentanil (μg)	701 (290)	744 (278)
Crystalloid (mL)	655 (202)	722 (207)
Estimated blood loss (mL)	25 (21)	24 (15)

Note: Values mean (SD) or number. Order in OR (operating room): quantity of the patients being the first, second or third patient of the day in the operating room.

Abbreviation: ASA, American Society for Anesthesiologists.

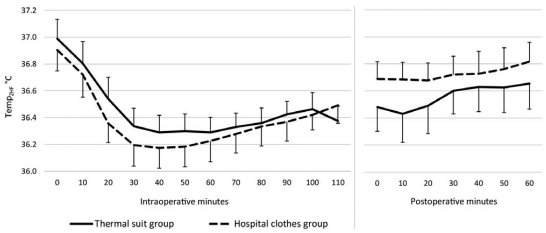

FIGURE 3 Core temperature ($Temp_{ZHF}$) change during anaesthesia and in the recovery room. Mean with 95% confidence interval

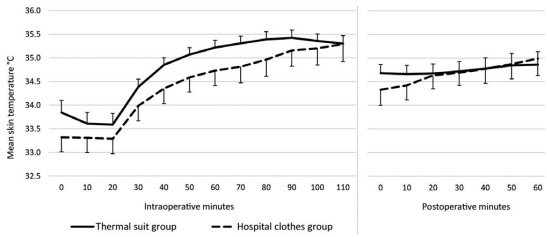

FIGURE 4 Mean skin temperature change during anaesthesia and in the recovery room. Mean with 95% confidence interval

lowest $Temp_{ZHF}$ was 35.5°C in the Thermal suit group, and 35.4°C in the Hospital clothes group. All seven patients were already hypothermic at the 30 minutes time point after induction. The mean duration of hypothermia in the six patients randomised to wear hospital clothes was 35 minutes (10-60 minutes), whereas the only Thermal suit group patient was hypothermic for 60 minutes, and her hypothermia lasted for the post-operative period of the treatment. All hypothermic patients in the Hospital clothes group regained normothermia during general anaesthesia. There was no inter-group difference in mean core temperatures on admission to the recovery room (primary outcome) (Table 2). All patients were normothermic except for one patient in the Thermal suit group.

TABLE 2 Perioperative temperatures and incidence of inadvertent perioperative hypothermia

	Thermal suit (n = 20)	Hospital clothes (n = 19)	*P*-value
Pre-operative eardrum temperature	36.5 (0.3)	36.3 (0.4)	.08
Holding area temperature	23.0 (0.4)	23.1 (0.4)	.67
Operating room temperature	21.9 (1.0)	21.8 (0.9)	.93
$Temp_{ZHF}$			
Anaesthetic induction	37.0 (0.3)	36.9 (0.4)	.44
End of anaesthesia	36.4 (0.3)	36.6 (0.3)	.07
Admission to the recovery room	36.5 (0.4)	36.7 (0.3)	.07
After 1 h in the recovery room	36.7 (0.4)	36.8 (0.3)	.20
Intraoperative skin temperatures			
Chest (min-max)	35.1 (31.0-36.7)	34.5 (31.1-36.5)	.03
Arm (min-max)	33.9 (32.2-35.5)	33.0 (29.3-35.3)	<.00
Thigh (min-max)	35.1 (29.8-36.7)	35.6 (30.3-38.0)	.35
Leg (min-max)	35.4 (31.1-36.7)	35.5 (31.2-38.0)	.70
IPH intraoperatively	1 (5%)	6 (32%)	.04
IPH on admission to the recovery room	1 (5%)	0 (0%)	.33

Note: Temperature (°C), values mean (SD) or number (proportion).
Abbreviations: IPH, inadvertent perioperative hypothermia (core temperature ≤35.9°C); $Temp_{ZHF}$, core temperature measured with zero-heat-flux sensor.

Intraoperative skin temperatures are presented in Table 2. In the Hospital clothes group, the maximum values were measured from the leg and thigh. The MSTs were higher in the Thermal suit group (Figure 4). The differences in MST between groups were significant with the exception of the 10-, 20- and after 70-minute time points. A longer time spent in the holding area did not correlate with higher MST on admission to the OR ($r_S = -.208$).

Post-operatively, the mean $Temp_{ZHF}$ was 36.6°C in the Thermal suit group and 36.7°C in the Hospital clothes group ($P = .20$) (Figure 3). In the Hospital clothes group, no patients were hypothermic. In the Thermal suit group, however, three patients had $Temp_{ZHF}$ below 36°C for periods of between 10 and 60 minutes, but they did not report feeling cold. In the recovery room, MSTs were similar between groups (Figure 4).

No tissue irritation or burns were reported by the patients or the medical staff. However, two patients in the Thermal suit group experienced sweating. In one case, sweating was noticed intraoperatively by the surgeon, and in another case post-operatively by a nurse. With the exception of one patient from each group and two nurses from the Hospital clothes group, patients and nursing staff were satisfied with the warming method. In total, the acquisition and operating costs per patient were 14.55 EUR (13.34 GBP) for the Thermal suit group and 11.53 EUR (10.57 GBP) for the Hospital clothes group.

4 | DISCUSSION

Our study evaluated a new method of forced warm air delivery and compared it with conventional intraoperative warming methods. The results showed a lower prevalence of intraoperative hypothermia and higher MSTs in the Thermal suit group compared with those of the Hospital clothes group. Still, the superiority of the thermal suit connected to a FAW unit over the standard warming method lacked evidence, since there was no difference in the mean core temperature of patients on admission to the recovery room.

The National Institute for Health and Care Excellence (NICE) clinical guideline recommends the core temperature to be over 36°C perioperatively.[1] Because the disadvantages of hypothermia are well known, we strictly followed the NICE recommendation, and active warming

was enhanced when the core temperature dropped below 36°C. As a result, all six hypothermic patients in the Hospital clothes group were normothermic by the end of anaesthesia. The commercial lower body FAW blanket with maximum set temperature was effective in warming up hypothermic patients, a finding also reported in a previous study by Röder and collegues.[16] By contrast, the medium set FAW together with maximal set warming mattress and on-line warmed intravenous fluids were insufficient to warm up the hypothermic patient in the Thermal suit group. The most obvious reason for the persistent hypothermia is the avoidance of the maximum set temperature of FAW. Another reason might be the insulation effect of the suit that prevented the external warming device, the warming mattress in our study, from reaching the patient through the multi-layered fabric of the Thermal suit. This 'thermos phenomenon' was seen in our previous study[12] and also by Brodshaug and co-workers.[17] In their study, the re-establishment of normothermia took a significantly longer time in the Thermal suit group.

To the best of our knowledge, this clinical trial was only the second in which FAW was used in patients without a commercial blanket. Kabbara and colleagues[18] utilised standard hospital blankets and blew warm air between them. Similarly to Kabbara and colleagues, we also used the medium set temperature of 38°C and no thermal injuries were reported. The design and size of commercial blankets are known to be associated with heat distribution,[19] whereas it is not known how the heat is distributed inside the thermal suit. In small FAW blankets, heat is distributed more evenly, and therefore they are more efficient than larger blankets.[20] Conversely, the larger the area covered under the blanket, the more effective is the warming. Inside the thermal suit, warm air can diffuse up to the upper body. This results in higher skin temperatures on the arm and chest, as seen in our study. Overall, the maximum skin temperatures remained below 37°C in the Thermal suit group, which can be regarded as safe. The main disadvantage of the suit is the poor breathability that resulted in sweating of two patients.

Pre-warming is the most efficient method for preventing the decrease in core temperature caused by body heat redistribution after anaesthetic induction.[21] However, active pre-warming was not implemented in our study due to a lack of resources and time, especially with the first patients of the day. Instead, we assumed that the longer the thermal suit is worn pre-operatively, the higher the core and peripheral temperatures on admission to the OR because a thermal suit is designed to prevent thermal loss.[22] Indeed, the Thermal suit group had higher peripheral temperatures on admission to the OR but there was no correlation with pre-operative suit time. Still, the warmer periphery might account for the minor thermal redistribution in the Thermal suit group seen in the difference in the number of cases of intraoperative hypothermia (one vs six patients). Ramanathan's method for calculating MSTs was chosen to measure thermal redistribution, since the method is non-invasive, simple and approved.[23]

The incidence of hypothermia (core temperature <36°C) was only 5% in the Thermal suit group but 32% in the Hospital clothes group. Older age is a known risk factor for intraoperative hypothermia,[24] as is a low pre-operative normothermic baseline core temperature.[25] In our study, patients were on average younger than 70 years, and at induction, $Temp_{ZHF}$ was 37 (0.3)°C in the Thermal suit group and 36.9 (0.3)°C in the Hospital clothes group. Moreover, a cool ambient temperature and exposing the patient to surgery predispose to hypothermia.[26] The NICE guideline recommends that the ambient temperature be at least 21°C while patients are exposed and that they should be adequately covered throughout the intraoperative phase.[1] Both these recommendations were accomplished in our study as the OR temperature was over 21°C and a patient was covered except for the lateral side of chest, shoulder and upper arm.

The strengths of our study are the standard anaesthesia and type of surgery, allowing a similar area disposal for surgery and predictable duration of the procedure. Furthermore, the continuous core temperature monitoring with ZHF method is superior to bladder or oesophagus catheter methods, as it is non-invasive and indifferent to exact positioning or urine outflow. The standardisation of a patient BMI of between 25 and 40 was applied to permit more reliable results regarding the effect of the warming methods. However, this restriction made the enrolment of patients more difficult, since 53 women were slender and failed to meet the inclusion criteria.

One limitation of our study is the choice of primary outcome and consequently, the resultant small sample size. The mean core temperature on admission to the recovery room has been applied as a primary outcome in several previous studies comparing various warming methods. Recently, however, intraoperative core temperature change and especially duration of hypothermia have been applied to assess the thermal condition or hypothermia burden of surgical patients.[7]

Further, for the sample size calculation, we assumed a 0.5°C difference in the mean core temperature between groups on admission to the recovery room, as was the case in the study by Janicki et al[15] However, the actual difference was smaller (0.2°C) and favoured the Hospital clothes group. In our study, we adhered to the NICE recommendations. However, had we allowed the core temperature to drop to 35.5°C before enhancing warming, as was done in the study by Janicki et al, there might have been a bigger difference between groups favouring the Thermal suit group because the incidence of hypothermia was higher and the minimum $Temp_{ZHF}$ was lower in the Hospital clothes group.

Another limitation of the study is that we did not follow-up on the use of the thermal suit for up to 24 hours. Although nearly all patients were satisfied with the suit, we know that some of them changed back to hospital clothes once in the ward since, despite our efforts, the suits were not always of an optimal size for the patients. The full benefits of the thermal suit may only be gained if the suit is worn from admission to discharge in this type of 24-hour in-hospital care. Further, the suit has an inner layer of fleece that is harmful to the environment, especially during washing.[27] Commercial FAW blankets, on the other hand, are single use, and waste is thus produced every time they are used. Moreover, the higher operating costs of thermal suits are not an advantage in hospital bids in which every cent is summed.

In the future, this new warming method should be studied in pre-warming and during different types of surgeries in which exposed areas vary and the OR temperature has different demands.

The breathability of the suit and the safety of the maximum set temperature should also be investigated. Moreover, the impact of body weight on the effect of these warming methods and perioperative heat balance should be studied in further clinical trials.

In conclusion, the thermal suit connected to the FAW unit was not found to be superior to the lower body FAW blanket and a warming mattress. Although the incidence of hypothermia was lower in the Thermal suit group, the mean core temperature did not differ between groups on admission to the recovery room. There was no difference in satisfaction of using thermal suit or hospital clothes, but the thermal suit costs are higher.

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CONFLICT OF INTEREST

The other authors declare that they have no conflict of interest.

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PUBLICATION III

Self-warming blanket versus forced-air warming blanket during total knee arthroplasty under spinal anaesthesia: A randomised noninferiority trial

Lauronen SL, Kalliovalkama J, Aho A, Mäkinen MT, Huhtala H, Yli-Hankala A, Kalliomäki ML

Submitted

PUBLICATION IV

Comparison of zero heat flux and double sensor thermometers during spinal anaesthesia: a prospective observational study

Lauronen SL, Kalliomäki ML, Kalliovalkama J, Aho A, Huhtala H, Yli-Hankala A, Mäkinen MT

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ORIGINAL RESEARCH

Comparison of zero heat flux and double sensor thermometers during spinal anaesthesia: a prospective observational study

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Abstract
Because of the difficulties involved in the invasive monitoring of conscious patients, core temperature monitoring is frequently neglected during neuraxial anaesthesia. Zero heat flux (ZHF) and double sensor (DS) are non-invasive methods that measure core temperature from the forehead skin. Here, we compare these methods in patients under spinal anaesthesia. Sixty patients scheduled for elective unilateral knee arthroplasty were recruited and divided into two groups. Of these, thirty patients were fitted with bilateral ZHF sensors (ZHF group), and thirty patients were fitted with both a ZHF sensor and a DS sensor (DS group). Temperatures were saved at 5-min intervals from the beginning of prewarming up to one hour postoperatively. Bland–Altman analysis for repeated measurements was performed and a proportion of differences within 0.5 °C was calculated as well as Lin`s concordance correlation coefficient (LCCC). A total of 1261 and 1129 measurement pairs were obtained. The mean difference between ZHF sensors was 0.05 °C with 95% limits of agreement − 0.36 to 0.47 °C, 99% of the readings were within 0.5 °C and LCCC was 0.88. The mean difference between ZHF and DS sensors was 0.33 °C with 95% limits of agreement − 0.55 to 1.21 °C, 66% of readings were within 0.5 °C and LCCC was 0.59. Bilaterally measured ZHF temperatures were almost identical. DS temperatures were mostly lower than ZHF temperatures. The mean difference between ZHF and DS temperatures increased when the core temperature decreased.
Trial registration: The study was registered in ClinicalTrials.gov on 13th May 2019, Code NCT03408197.

Keyword Non-invasive core temperature measurement · Zero heat flux · Double sensor · Spinal anaesthesia

1 Introduction

Body core temperature monitoring is often neglected during neuraxial (i.e., spinal or epidural) anaesthesia (NA) [1, 2] even though NA is known to predispose a patient to hypothermia [3] and resultant adverse effects [4–9]. Conscious patients under NA do not perceive temperature changes, and thus, although hypothermic, will not report feeling cold [10]. Vigilance by the anaesthesia team and adequate temperature measurement are therefore mandatory to ensure the detection and prevention of perioperative temperature disturbances.

Core temperature can be reliably measured from a pulmonary artery (PA) or other well perfused sites, such as the oesophagus, nasopharynx and tympanic membrane. The bladder and rectum are less reliable sites because they are poorly perfused. Because all these measurement sites are invasive, they are unsuitable for conscious patients. Moreover, the conventional sites used for the core temperature measurement of conscious patients (e.g., oral, axillar or infrared measurements from the tympanic membrane or temporal region of the head) typically lack the desired clinical accuracy and reliability [11].

In recent years, other core temperature measurement devices have been developed. In 1971 Fox and Solman

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demonstrated a non-invasive zero heat flux (ZHF) method for measuring core temperature from the intact skin surface [12, 13]. This technique was subsequently further developed in Japan [14, 15]. The ZHF system (3M™ BairHugger™ Temperature Monitoring System, previously 3M™SpotOn™, Arizant Healthcare, Eden Prairie, MN, USA) has been proven to be accurate and precise enough when compared with standard invasive core temperature measurements [16–19]. Another non-invasive core temperature measurement system, which incorporates the double-sensor (DS) technique, was released in 2006 (Tcore™ Temperature Monitoring System, Drägerwerk AG & Co, Lübeck, Germany). In noncardiac clinical studies, the DS method was estimated to be sufficient for routine clinical use [20, 21], whereas the agreement between DS and PA temperature measurements in cardiac surgical patients was less satisfactory [22, 23].

In previous studies, the ZHF and DS methods have been compared to standard core temperature measurement methods. To the best of our knowledge, however, no previous studies have compared the ZHF and DS methods or two bilateral ZHF sensors placed simultaneously on both sides of a patient`s forehead. Our study evaluates these two non-invasive methods perioperatively in patients undergoing unilateral total knee arthroplasty under spinal anaesthesia. We hypothesised that the core temperature measured on either side of the forehead is similar, regardless of the method used.

2 Methods

Ethical approval for the study (ETL R17136) was provided by the Regional Ethics Committee of the Expert Responsibility Area of Tampere University Hospital, Tampere, Finland (Chairperson Prof Matti Korppi) on 3rd October 2017. This observational study was registered in ClinicalTrials.gov on 13th May 2019 (Code NCT03408197). All patients gave their written informed consent prior to their inclusion in the study.

Sixty adult patients scheduled for elective, primary unilateral total knee arthroplasty under spinal anaesthesia were enrolled in the study. Exclusion criteria were body mass index (BMI) < 25 or > 40, American Society of Anesthesiologist (ASA) class > 3, general anaesthesia (GA) or inability to give written consent.

2.1 Protocol

Patients arrived at the hospital and were recruited to the study on the day of the surgery. Paracetamol 1 g and cetirizine 10 mg were used as premedication. Before surgery, patients were prewarmed in supine position for thirty minutes in the preoperative holding area. Either a forced-air warming (FAW) blanket (3M™BairHugger™, model 62200,) or self-warming blanket (Barrier® EasyWarm®, Mölnlycke Health Care AB, Gothenburg, Sweden) was placed longitudinally on a patient`s body and legs during prewarming. After prewarming, standard monitoring (non-invasive blood pressure, electrocardiogram and SpO_2) was applied, intravenous access was opened, and spinal anaesthesia was induced with isobaric bupivacaine (Bicain Spinal 5 mg/ml, Orion Pharma, Espoo, Finland) in lateral position. After ensuring the complete motor and sensory block of the lower limb to be operated, patients were transferred to the operating room (OR). During surgery, patients received propofol sedation for their comfort, if desired, which was induced and maintained with target-controlled infusion (TCI, Asena™ PK, Alaris Medical Systems, Basingstoke, UK). Propofol was initially administered with Schnider model effect-site concentration set to 1.0 µg/ml and adjusted when needed. Patients were under light sedation (score -2), or moderate sedation (score -3) as measured with The Richmond Agitation–Sedation Scale. No other sedation or opiates were used intraoperatively. Active warming was continued intraoperatively. Both blankets were placed on the chest and arms during surgery. The head of the patient was left uncovered.

Patient characteristics and relevant perioperative data were saved on an information security data collection file. Personal data were processed in accordance with the European Union`s General Data Protection Regulation requirements.

2.2 Temperature monitoring

The ZHF and DS temperature monitoring systems consist of a disposable sensor, which is attached to the forehead skin above the eyebrow, and a reusable control unit or an adapter. The ZHF sensor is 41 mm high, 41 mm wide and 5 mm thick; the DS sensor is 49 mm high, 58 mm wide and 5 mm thick. The control unit of the ZHF system is compatible with existing monitors, but it requires current to work. However, the battery-powered adapter of the DS system is only compatible with Dräger monitors.

The ZHF and DS systems are both based on vertical heat flow from deep tissue to the skin surface. According to the manufacturer, the ZHF sensor consists of two thermistors and a covering flex circuit, which are separated by insulating foam. The flex circuit regulates its temperature to create a zone of perfect insulation. Thus, heat loss to the environment is eliminated and core temperature can be measured from the skin surface [24]. The DS sensor consists of two thermistors separated by insulating foam and a cover. The DS system determines core temperature by using the formula: $T_c = T_1 + K_{insul}/K_{tis} \times (T_1 - T_2)$. Core temperature ($T_c$) is estimated from the measured temperatures at each point

of the thermistors (T_1 and T_2), and the ratio of the thermal conduction coefficient of the insulating foam (K_{insul}) to that of human tissue (K_{tis}) [25].

All patients had a ZHF sensor (3M™ Bair Hugger™ Temperature Monitoring System) placed on the right side of the forehead as the reference core temperature ($T_{ZHF\text{-}R}$). The study sensor, either a ZHF sensor ($T_{ZHF\text{-}L}$; ZHF group) or a DS sensor (Tcore™ Temperature Monitoring System; T_{DS}; DS group), was placed on the left side of the forehead.

Temperatures were measured preoperatively, in the OR and up to one hour postoperatively. Temperature monitoring was temporarily interrupted while the patient was transferred to the OR or the recovery room. Temperatures of the ZHF group were collected at 10-s intervals using S5Collect software (GE Healthcare Oy, Helsinki, Finland) and retrieved for statistical analysis at 5-min intervals. Temperatures of the DS group were saved on the data collection file at 1-min intervals from the beginning up to ten minutes, and thereafter at 5-min intervals.

2.3 Statistical analysis

For each patient, temperature data consisted of multiple measurements taken pre-, intra- and postoperatively. Bland–Altman (BA) analysis was used to assess the agreement between the two temperatures obtained by either two ZHF sensors or by a ZHF and a DS sensor. Mean difference and 95% limits of agreement (LoA: ± 1.96 standard deviation (SD) around the mean difference) with 95% confidence intervals (CI) were calculated as described by Zou with multiple observations per patient [26]. BA analysis was computed separately for the pre-, intra- and postoperative data. A difference of ± 0.5 °C between two temperatures was determined to be clinically acceptable [27]. The percentage of measurement differences within 0.5 °C were counted. Lin`s concordance correlation coefficient (LCCC) for repeated measures with 95% CI was calculated.

Statistical analyses were performed using SPSS Version 25.0. (IBM Corp: Armonk, NY), and STATA (StataCorp. 2019. College Station, TX: StataCorp LLC). BA plot with 95% CIs were calculated using Microsoft Excel 2010 (Microsoft, Redmond, WA, USA). Continuous data are reported as median and quartiles (Q_1–Q_3). Categorical data are expressed as number (n) and percentage (%).

3 Results

Sixty patients were recruited to the study between May and November 2019. Of these, thirty patients were fitted with bilateral ZHF sensors (ZHF group), and thirty patients were fitted with both a ZHF sensor and a DS sensor (DS group). The postoperative data of two patients in the DS group were lost due to problems in data collection (Fig. 1). Patient characteristics and relevant perioperative data are presented in Table 1.

The ZHF and DS sensors were placed on the forehead before initiating preoperative warming. As the temperature value of the ZHF sensor stabilised within four minutes, the value of the DS sensor only stabilised after ten minutes. The unstable temperature data were excluded from the statistical analyses.

3.1 Comparison between two ZHF sensors

A total of 1261 measurement pairs were obtained at 5-min intervals perioperatively (preoperative n = 332, intraoperative n = 512, postoperative n = 417). Results and BA plot are presented in Table 2 and in Fig. 2, respectively. Chronological changes of $T_{ZHF\text{-}R}$ and $T_{ZHF\text{-}L}$ are illustrated in Fig. 3.

3.2 Comparison between ZHF and DS methods

A total of 1129 measurement pairs were obtained at 5-min intervals perioperatively (preoperative n = 301, intraoperative n = 484, postoperative n = 344). Results and BA plot are presented in Table 2 and in Fig. 4, respectively. Chronological changes of $T_{ZHF\text{-}R}$ and T_{DS} are presented in Fig. 5.

4 Discussion

The findings of this observational prospective study demonstrate that the side of the forehead does not influence the temperature reading of ZHF sensors. The mean difference between temperatures obtained by ZHF and DS sensors was bigger than that between two ZHF sensors. Further, the lower the core temperature was, the larger the mean difference between the ZHF and DS sensors.

The ZHF method has previously been evaluated in many clinical studies, whereas only a few clinical studies have compared the DS method to standard invasive temperature monitoring. The agreement of ZHF temperature with PA, oesophageal and nasopharyngeal temperatures has been shown to be sufficiently accurate [16–18, 28–30]. The DS method has been estimated to be comparable to oesophageal, bladder and femoro-iliac artery temperatures [20, 21, 31]. Although the mean difference between DS and PA temperatures in cardiac surgical patients was small, the 95% limits of agreement were over a degree [22, 23].

We are unaware of previous studies that have compared two simultaneous ZHF sensors in a single patient. Regardless of the identical method, the observed dispersion of temperature difference was small, but greater than we expected. There may be several patient- or sensor-related reasons for this greater than expected dispersion of temperature

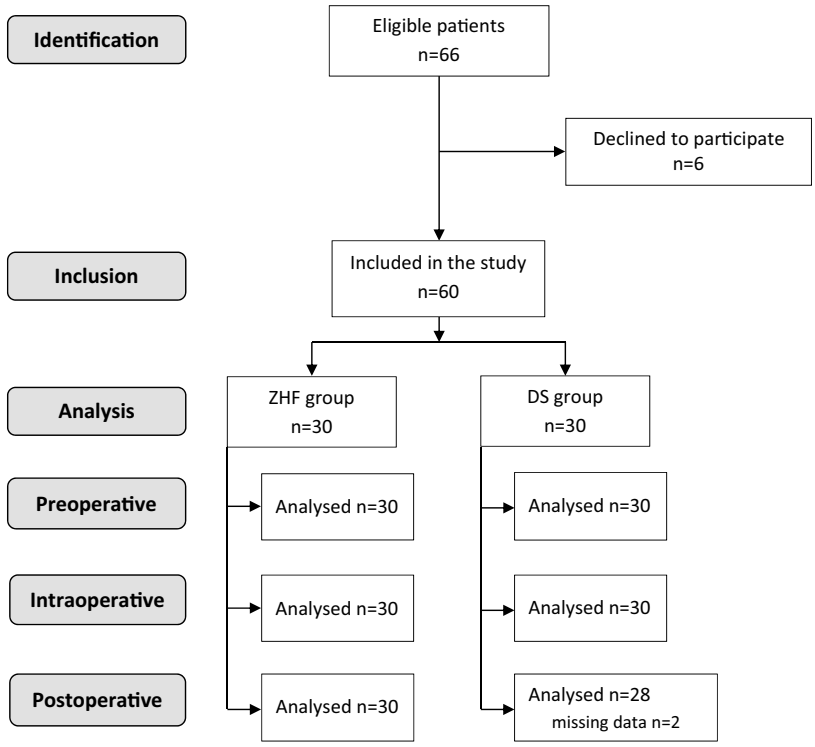

Fig. 1 Flow diagram

difference. First, changes in body and head position may have influenced cerebral blood flow [32], causing bilateral temperature values to diverge. Second, according to the manufacturer, the sensor reaches a depth of 1 to 2 cm below the skin [16]. Finally, the anatomical focus of the sensor cannot be determined, and therefore the temperature measurement point remains inexact [29], leading to measurement inaccuracy.

In general, the DS sensor yielded lower temperature values than the ZHF sensor throughout the study. Further, intraoperative temperature drop was greater with the DS sensor than with the ZHF sensor. The increased difference between the temperatures yielded by the DS sensor and the rectal temperature recordings at lower core temperatures has also been reported in volunteer studies by Gunga [33, 34]. In our study, the drop was seen in a cool ambient temperature, where many patients became hypothermic. In addition, we noticed that the size of the DS sensor sometimes hampers a perfect fit to the forehead skin and may therefore have contributed to a partial unfastening of the sensor, leading to unsatisfactory contact and even inaccurate readings. The possible partial insulation of the sensor may have allowed heat loss to influence the temperature recording and heat flux calculation, which results in a lower observed temperature. However, the anaesthesia management itself does not appear to have had an influence on the sensor feasibility, since the DS sensor has been shown to perform equally well in patients undergoing both regional and general anaesthesia [21].

The sufficient accuracy of a thermometer is considered an offset from the reference temperature of 0.5 °C, because normal circadian fluctuations are within this range [35]. Further, 0.5 °C is the smallest difference that has been shown to be associated with hypothermia-induced complications [36]. The mean difference with 95% LoAs remained within 0.5 °C between the ZHF sensors. The mean difference between the ZHF and DS sensors was 0.33 °C, which is acceptable, but the difference together with the observed 95% LoAs (i.e., 0.88 °C) exceeds the proposed limit of 0.5 °C and was therefore unsatisfactory.

Core temperature should be maintained over 36.0 °C perioperatively, and a patient with hypothermia should be actively warmed [37]. Such warming, though mandatory, increases costs and the workload of personnel, produces waste and may cause sedation and intubation-related risks when performed in the postanaesthetic care unit. For proper patient care, the appropriate monitoring system should be used but possible limitations of the measuring methods must be recognised. The incidence of hypothermia has been shown to vary from 11 to 60% in previous prospective

Table 1 Patient characteristics and relevant perioperative data

	Zero heat flux group		Double sensor group	
	n = 30		n = 30	
	n/median	%/$Q_1 - Q_3$	n/median	%/$Q_1 - Q_3$
Age (years)	71	62–74	69	64–73
BMI (kg/m^2)	29	27–32	30	28–33
Female	19	63.3	16	53.3
ASA				
I	1	3.3	7	23.3
II	18	60.0	9	30.0
III	11	36.7	14	46.7
Warming				
EasyWarm	16	53.3	14	46.7
BairHugger	14	46.7	16	53.3
Side of surgery				
Right	17	56.7	17	56.7
Bicain spinal 5 mg/ml (ml)	1.6	1.5–2.0	1.5	1.4–1.6
Preoperative holding area temperature (°C)	20.7	20.5–20.9	21.5	20.9–21.8
Operating room temperature (°C)	18.6	17.9–18.9	19.2	18.9–19.9
Duration of prewarming (min)	30	30–32	32	30–42
Duration of surgery (min)	60	55–70	57	49–63
Propofol sedation intraoperatively	25	83.3	25	83.3
Propofol (mg/kg/h)	3.2	2.5–4.4	4.0	3.3–4.2
Hypothermia[a] intraoperatively	17	56.7	11	36.7

BMI body mass index, *ASA* American Society for Anesthesiologists

[a]Core temperature value below 36.0 °C measured with zero heat flux sensor placed on the right side of the forehead

Table 2 Results of the evaluation of the ZHF and DS methods

	Preoperative	Intraoperative	Postoperative	Overall
ZHF group				
Temperature ranges (°C)				
ZHF-R	35.5–37.7	35.0–37.3	35.5–37.2	35.0–37.7
ZHF-L	35.3–37.4	35.2–37.4	35.0–37.1	35.0–37.4
Mean difference ± 95% LoA with 95% CI (°C)	0.07 ± 0.37 with ± 0.08	0.04 ± 0.46 with ± 0.13	0.06 ± 0.39 with ± 0.10	0.05 ± 0.42 with ± 0.08
Proportion of temperature differences ≤ 0.5 °C (%)	99	98	99	99
LCCC (± 95% CI)	0.86 (± 0.03)	0.84 (± 0.03)	0.85 (± 0.03)	0.88 (± 0.01)
DS group				
Temperature ranges (°C)				
ZHF-R	36.1–37.4	35.4–37.3	35.3–37.1	35.3–37.4
DS	35.2–37.8	34.4–37.9	34.6–36.8	34.4–37.9
Mean difference ± 95% LoA with 95% CI (°C)	0.13 ± 0.80 with ± 0.20	0.36 ± 0.90 with ± 0.24	0.46 ± 0.76 with ± 0.22	0.33 ± 0.88 with ± 0.20
Proportion of temperature differences ≤ 0.5 °C (%)	82	61	61	66
LCCC (± 95% CI)	0.51 (± 0.06)	0.51 (± 0.06)	0.45 (± 0.05)	0.59 (± 0.03)

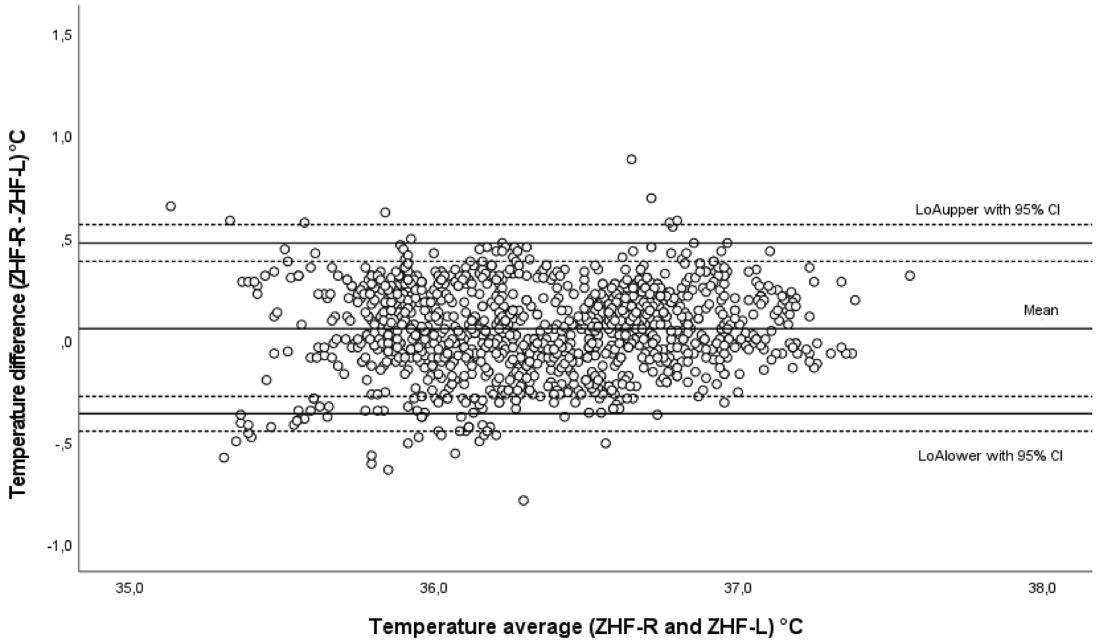

Fig. 2 Bland–Altman plot of the ZHF group. Comparison of bilateral ZHF sensors. *ZHF* zero heat flux, *R* right forehead, *L* left forehead, *LoA* 95% limits of agreement, *CI* confidence interval

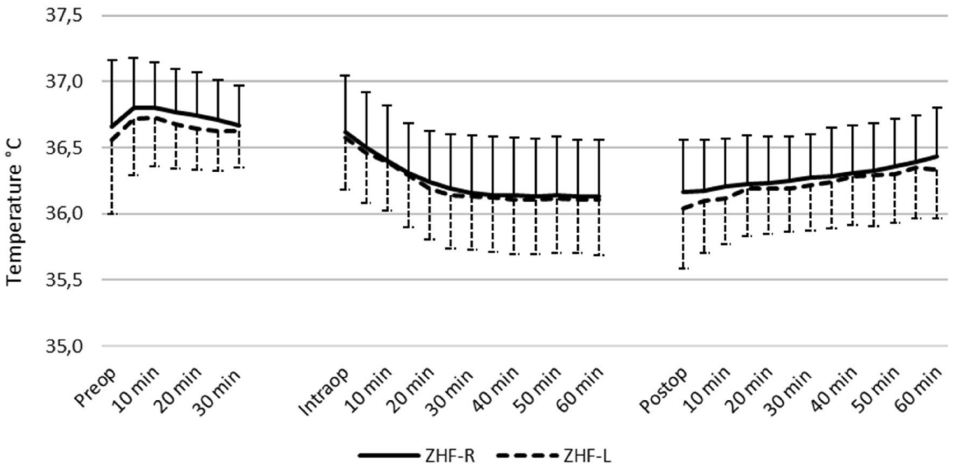

Fig. 3 Chronological temperature changes of the right and left ZHF sensors. Mean with standard deviation. *ZHF* zero heat flux, *R* sensor placed on the right side of the forehead, *L* sensor placed on the left side of the forehead

observational studies performed in patients receiving NA for joint arthroplasty [38, 39]. In our study, the overall incidence of intraoperative hypothermia measured with $T_{ZHF\text{-}R,}$ was 47%. Our results together with those of previous studies underline the need for the accurate and adequate non-invasive monitoring of core temperature.

The major limitation of our study was that we did not have a standard core temperature measurement site as a

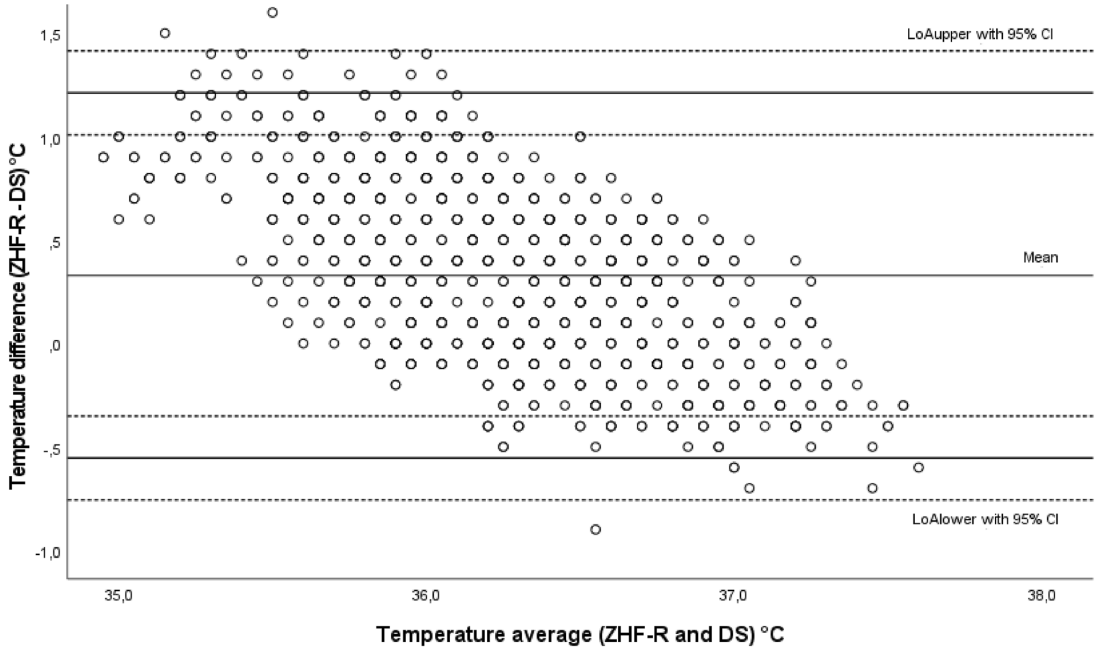

Fig. 4 Bland–Altman plot of the DS group. Comparison of ZHF and DS temperature measurement methods. *ZHF* zero heat flux, *R* right forehead, *DS* double sensor, *LoA* 95% limits of agreement, *CI* confidence interval

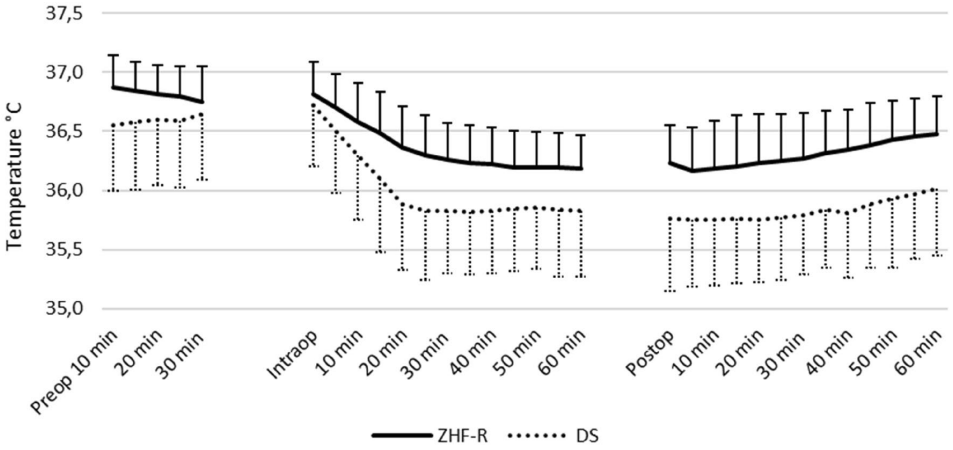

Fig. 5 Chronological temperature changes of the ZHF-R and DS sensors. Mean with standard deviation. *ZHF-R* zero heat flux sensor placed on the right forehead, *DS* double sensor placed on the left forehead

reference method. Hence, no conclusion on the superiority of either of these methods can be drawn based on these results. However, the agreement of the ZHF method with standard core temperature measurement methods has been shown to be precise and acceptable for clinical use [16, 17, 40]. The ZHF method was chosen as a reference because it is the primary core temperature measurement method used under NA in our hospital, and we could not

predispose the conscious patients to invasive core temperature measurements.

The strengths of this study were that our study included not only intraoperative, but also pre- and postoperative temperature measurements with multiple observations per patient. Further, surgery and anaesthesia were similar for all patients, and the same ZHF control and DS adapter units were used throughout the study. Finally, we measured the temperature from both sides of the forehead to ensure that two different measurement methods, placed either side of the forehead, may be compared.

In future, the ZHF method should be evaluated in different patient populations undergoing neuraxial anaesthesia. In addition, more studies that compare the DS method with other non-invasive and standard temperature measurement methods under various circumstances are needed, as the existing clinical studies are scarce and appear to report conflicting results.

In conclusion, based on the findings of our study, the ZHF method has good internal validity, and the temperature reading is not dependent on the side of the forehead. The DS method shows lower temperature values than the ZHF method, especially when the core temperature is low. However, based on our results we do not know which one of the two methods measures core temperature more accurately.

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Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethical approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Regional Ethics Committee of the Expert Responsibility area of Tampere University Hospital (ETL R17136/2017).

Informed consent Informed consent was obtained from all individual participants included in the study.

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