

Perioperative hypothermia: Causes, consequences and treatment

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Abstract

Perioperative hypothermia, core temperature below 36.0 °C, transpires due to disruption of thermoregulation

by anesthesia coupled with cold exposure to procedural surroundings and cleansing agents. Although most publications have focused on thermoregulation disruption with general anesthesia, neuraxial anesthesia may also cause significant hypothermia. The clinical consequences of perioperative hypothermia are multiple and include patient discomfort, shivering, platelet dysfunction, coagulopathy, and increased vasoconstriction associated with a higher risk of wound infection. Furthermore, postoperative cardiac events occur at a higher rate; although it is unclear whether this is due to increased oxygen consumption or norepinephrine levels. Hypothermia may also affect pharmacokinetics and prolong postoperative recovery times and hospital length of stay. In order to combat perioperative hypothermia, many prevention strategies have been examined. Active and passive cutaneous warming are likely the most common and aim to both warm and prevent heat loss; many consider active warming a standard of care for surgeries over one hour. Intravenous nutrients have also been examined to boost metabolic heat production. Additionally, pharmacologic agents that induce vasoconstriction have been studied with the goal of minimizing heat loss. Despite these multiple strategies for prevention and treatment, hypothermia continues to be a problem and a common consequence of the perioperative period. This literature review presents the most recent evidence on the disruption of temperature regulation by anesthesia and perioperative environment, the consequences of hypothermia, and the methods for hypothermia prevention and treatment.

Key words: Body temperature regulation; Hypothermia prevention; Hypothermia; Hypothermia treatment; Intraoperative care

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Core tip: Thermoregulation tightly controls core temperature to ensure optimal organ and enzymatic

function. Anesthesia disrupts normal thermoregulation and, when combined with patient exposure to a cold procedural environment, leads to hypothermia. However, hypothermia is not a benign issue. It is associated with postoperative complications including infection, bleeding, cardiac events, changes in drug metabolism, patient discomfort, and increased length of stay. Although multiple preventive strategies have been explored, their utility varies. This review explores the impact of anesthesia on perioperative hypothermia and the evidence for associated complications and outcomes. Preventative strategies are also examined and future directions for research are discussed.

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INTRODUCTION

Normal core body temperature is approximately 37 °C. As strict temperature control is important for normal organ, enzymatic, and cellular function^[1], temperature control is tightly regulated by the body to within 0.2 °C. This is referred to as the interthreshold range. Within this range, active methods of heating or cooling are not triggered. In addition, a set point temperature exists in which the body maintains steady changes in core body temperature (0.5-1.0 °C) based on circadian rhythms. Temperature tends to be decreased during sleep and increased with physical activity^[1,2].

Precise temperature regulation involves both the peripheral and central nervous systems through behavioral and autonomic triggers. Afferent signals for cold and hot sensations are transmitted *via* A-delta and C nerve fibers, respectively^[2,3]. Sensory nerve fibers are thought to sense environmental temperature changes through skin projections^[3]. These cutaneous "sensors" are recently characterized as transient receptor potential receptors located in both skin and spinal cord^[4]. Temperature signals from the skin, spinal cord, deep abdominal/thoracic tissue, and other parts of the brain coalesce mainly within the anterior spinal cord and travel to the primary area of temperature regulation, the hypothalamus^[2-4]. The hypothalamus then activates both behavioral and autonomic responses to temperature changes^[3].

The human body tightly controls core temperature through a variety of mechanisms including behavioral modification, autonomic nervous system stimulation, surface skin sweating, and increased heat production *via* shivering and non-shivering thermogenesis^[2]. Behavioral changes, such as a change in dress or moving out of the wind, are more influenced by skin temperature. Conversely, autonomic regulation actions including peripheral

vasoconstriction or vasodilation are mostly dependent on core temperature^[1].

CAUSES OF PERIOPERATIVE HYPOTHERMIA

The human body loses heat to the atmosphere in four ways: radiation, conduction, convection, and evaporation^[1,5]. Radiation is the infrared transfer of heat. Conduction involves heat transfer through physical contact with an object (*i.e.*, operating room table). Convection is the movement of heat based on air flow (*i.e.*, cold air blowing over body). Finally, evaporation refers to the loss of heat through sweat from skin or fluid loss from exposure of organs to the open atmosphere. The most significant heat loss, approximately 60%, occurs by radiation^[2].

Multiple factors contribute to perioperative hypothermia development. Operating room temperature contributes to intraoperative hypothermia primarily through radiant heat loss. Although most operating rooms have in-room thermostats that are able to control the ambient temperature, disagreements about the optimal temperature settings may occur based on different levels of personal comfort, dress (surgical gowns), and other heat exposure (standing under hot lights)^[5]. Additional heat loss occurs through conduction as the patient is positioned on the cold operating room table and through convection by laminar airflow. Further, operative cleansing solutions aid in heat loss through evaporation.

Under normal conditions, the human body would initiate mechanisms to preserve or create heat. However, anesthesia disrupts these homeostatic mechanisms. Concurrently, exposure to the cold procedural environment and vasodilation induced by general or regional anesthesia contribute to intraoperative hypothermia development^[2,4].

General anesthesia

Regardless of maintenance with volatile agents, dexmedetomidine, or propofol, general anesthesia impairs autonomic temperature control^[2-4]. In fact, it may increase the interthreshold temperature range 5-20 fold, allowing temperatures to vary by 2-6 °C.

After induction of general anesthesia, body heat redistributes from the central compartment to the periphery *via* vasodilation, causing heat loss to the environment^[6]. Approximately 90% of this heat loss is through the skin *via* radiation and convection, with evaporation and conduction playing smaller roles^[3]. This redistribution of heat mainly occurs during the first hour of general anesthesia and is responsible for about 80% of the core temperature drop; however, after induction redistribution continues for at least 3 h, making it the major contributor to intraoperative heat loss during general anesthesia^[7]. Ventilation with dry gas, cutaneous heat loss, and cold surgical prep

solutions further contribute to overall intraoperative temperature decline^[6,7]. After several hours, core temperature decline stops and autonomic-induced peripheral vasoconstriction occurs in an effort to bring heat back to the body's core. This is often referred to as the plateau phase which may occur 3-5 h into a general anesthetic^[3].

Neuraxial anesthesia

The mechanisms of heat loss with neuraxial anesthesia are similar to those of general anesthesia, but they also differ in important ways. Similar to general anesthesia, neuraxial anesthesia impairs autonomic temperature control^[7]. Although redistribution during regional anesthesia decreases core temperature approximately half as much as during general anesthesia, it still remains the most important cause of core heat loss during the first hour. Unlike general anesthesia, there is not a temperature plateau phase with neuraxial anesthesia^[8]. The blocked portion of the patient's body is unable to shiver or vasoconstrict regardless of the decrease in core temperature. For these reasons, a long case under neuraxial anesthesia may cause more heat loss than general anesthesia^[9]. Neuraxial anesthesia also alters behavioral responses to hypothermia^[10]. Patients do not feel cold despite being hypothermic, secondary to the peripheral vasodilation in the blocked extremities. Finally, core temperature is often not monitored with neuraxial anesthetics and accordingly hypothermia is not detected. Overall, hypothermia with neuraxial anesthesia may be as significant as with general anesthesia^[11].

CONSEQUENCES OF PERIOPERATIVE HYPOTHERMIA

Hypothermia affects over 60% of patients intraoperatively, and its effects are noteworthy^[12]. It adversely impacts blood loss, infection risk, and cardiac events, potentially increasing length of hospital stay. It also slows anesthetic drug metabolism and may alter pharmacodynamics, thus contributing to increased post anesthesia care unit (PACU) recovery time.

Blood loss

Studies that attempted to determine whether mild hypothermia leads to increased blood loss and transfusions have given inconsistent results^[13]. A recent meta-analysis found that a median patient temperature of 35.6°C resulted in increased blood loss (4%-26%) and an increased relative risk of transfusion (3%-37%)^[13]. Notably, some studies included in the meta-analysis were from the 1990s when blood conservation techniques and transfusion thresholds may have been more liberal. However, in a recent large retrospective study of noncardiac surgeries published in 2015, transfusion requirements increased in proportion to the decrease in temperature and the increased duration of

hypothermia^[12].

Potential causes for increased blood loss include hypothermia-induced platelet dysfunction and coagulation cascade enzyme dysfunction. To evaluate coagulopathy, prothrombin time (PT) and partial thromboplastin time (PTT) were measured at different temperatures. For a given blood sample, PT and PTT increased from 11.8 ± 0.3 s and 36.0 ± 0.7 s to 12.9 ± 0.5 s and 39.4 ± 1.0 s, respectively, as the temperature of the sample decreased from 37 to 34 °C^[14]. Both PT and PTT continued to increase as temperature further decreased. It is important to note that blood samples are warmed to 37 °C prior to performing the lab tests^[14]. Therefore, laboratory values may not reflect what is occurring physiologically in the patient.

Surgical wound infection

Mild hypothermia has been associated with increased risk of surgical wound infection due to vasoconstriction and change in oxygen tension. At 34.5°C, thermoregulation leads to peripheral vasoconstriction^[12]. When this occurs, oxygen delivery to subcutaneous tissues decreases impairing the strength of the collagen lattice that supports the healing scar^[15,16]. Decreased oxygen delivery also impairs chemotaxis, phagocytosis, and antibody production by white blood cells and the immune system^[17]. In patients undergoing colorectal surgery, the last intraoperative core temperature was strongly correlated with the incidence of postoperative wound infection. The hypothermic group (34.7 ± 0.6 °C) had a 19% incidence of wound infections compared with 6% in the normothermic group (36.6 ± 0.5°C)^[16].

Length of hospital stay and PACU recovery time

Although most studies show that hypothermia contributes to increasing length of hospital stay and PACU recovery time, results are not consistent. A large study published in 1996 in colorectal surgery patients found that hypothermia (34.7 ± 0.6°C) at the end of surgery delayed patients' ability to tolerate solid food and suture removal by one day compared to patients with normothermia. Hospital length of stay also increased 20% (2.6 d) and length of stay was prolonged even after correcting for the increased risk of infection in the hypothermic group^[16].

PACU discharge times are also impacted by hypothermia. Discharge from the PACU was observed to significantly increase by 40 min in hypothermic patients based on a modified Aldrete and Kroulik scoring system^[18]. If discharge criteria included normothermia, then recovery was prolonged over 2 h^[18].

Drug metabolism

Mild hypothermia impairs temperature-sensitive enzymes that metabolize and clear anesthetic drugs, thus increasing their duration of action; the effect on potency differs depending on the drug. In animal models, moderate-severe hypothermia increases volatile anest-

hetic potency, thus decreasing minimum alveolar concentration (MAC)^[19].

The duration of actions of midazolam, morphine, propofol, and several nondepolarizing neuromuscular blocking agents (*e.g.*, vecuronium, rocuronium, atracurium) are prolonged due to the pharmacokinetic effect of hypothermia. In nonsurgical healthy patients, midazolam clearance decreases 11.1% per 1°C below 36.5°C^[20]. The same decrease in clearance has been noted for vecuronium^[21-24]. Additionally, mild hypothermia can cause a decrease in the twitch response even when neuromuscular blocking drugs are not given^[25]. The twitch tension starts to decrease 16% per 1°C once the temperature of the adductor pollicis muscle is below 35.2°C^[26]. With moderate hypothermia to 30°C, morphine also has decreased potency, clearance, and volume of distribution; although, its concentration is elevated in the plasma and cerebral spinal fluid^[27,28]. Notably, the efficacy of neostigmine and naloxone seems to be preserved during hypothermia^[29].

Shivering and thermal discomfort

If a patient is hypothermic, there is an increased incidence of thermal discomfort, oxygen consumption, vasoconstriction, and shivering^[30]. Shivering is four times more dependent on core temperature than skin temperature^[30]. However, core normothermia does not guarantee that shivering will not occur. During shivering, all patients are vasoconstricted^[30]. In a study by Kurz *et al.*^[16], intraoperative vasoconstriction, measured by comparing forearm temperature with fingertip temperature, was noted in 74% of hypothermic patients vs 6% of normothermic patients. Postoperatively, hypothermic patients experienced persistent vasoconstriction for up to 6 h, decreased thermal comfort, and increased rates of shivering^[16]. Although postoperative cutaneous warming decreases thermal discomfort, shivering intensity, and maximum oxygen consumption during shivering, it does not stop or affect the duration of shivering^[30]. Fortunately, vasoconstriction and hypothermia usually resolve by postoperative day one^[31].

Cardiac events

The mechanism behind the increased postoperative cardiac risk with mild hypothermia is still unclear. Studies are inconsistent in determining whether the increased risk of myocardial infarction is due to shivering or stress hormones^[32]. Although plasma catecholamine concentrations increase to three times normal in PACU, this finding has not been proven to be the cause^[32]. To further this conundrum, hypothermia is thought to be cardioprotective during cardiopulmonary bypass and after cardiac arrest.

Although normothermia does not change the incidence of intra-operative cardiac events, it does reduce the postoperative risk by 55%^[33]. In a study evaluating patients with high risk of coronary artery disease who had abdominal, thoracic or vascular surgery, those who were

hypothermic had an increased incidence of postoperative cardiac events, including angina, ischemia, infarction, and cardiac arrest^[33]. In the hypothermic group, cardiac events (6.3%) and ventricular tachycardia (7.9%) were significantly greater compared to the normothermic group (1.4% and 2.4%) respectively^[33]. Similarly in the first 24 h following lower extremity revascularization surgery, hypothermic patients were significantly more likely to experience myocardial ischemia compared to normothermic patients (36% vs 13%, respectively)^[34]. However, the incidence of intraoperative cardiac events was similar in the two groups^[33]. In contrast, a significant difference in cardiovascular events or mortality was not noted between moderate hypothermic (33.3 ± 0.8°C) and normothermic patients undergoing intracranial aneurysm surgery^[35].

The mechanism for the increased risk of myocardial ischemia in patients with mild hypothermia remains unclear. Shivering leads to increased metabolic demands but oxygen consumption alone has not proven to be the culprit^[34]. Physiologic responses to hypothermia in nonsurgical patients include vasoconstriction^[36] and sympathetic nervous system stimulation leading to increased epinephrine, norepinephrine, blood pressure, and heart rate^[37,38]; however, stress hormones in surgical patients seem to respond differently. In a study by Frank *et al.*^[31] examining patients over 60 years old with two or more coronary artery disease risk factors and undergoing thoracic, abdominal, or lower extremity vascular surgery, hypothermic patients had significantly higher norepinephrine concentrations and arterial blood pressures but lower heart rates in the early postoperative period. While postoperative norepinephrine, epinephrine and cortisol concentrations increased in all patients, norepinephrine was significantly higher in the hypothermic group compared to the normothermic group^[31]. Alternatively, during cerebral aneurysm surgery, intraoperative norepinephrine and cortisol levels decreased similarly in both the mild hypothermic and normothermic groups, while epinephrine had a significant decrease in the hypothermic group^[39]. Intraoperative mild hypothermia also did not affect blood pressure when compared to normothermic patients. The difference between intraoperative and postoperative stress hormone levels may suggest that a time lag exists between stressful stimuli and hormone response; alternatively, anesthetics may attenuate the stress response and protect the myocardium. This would be consistent with the risk of myocardial infarction increasing and occurring postoperatively instead of intraoperatively.

HYPOTHERMIA PREVENTION AND TREATMENT

Hypothermia treatment involves minimizing cold exposure while providing heat sources, such as heat transfer systems or pharmacologic agents, to equalize heat loss. Heat transfer systems may be passive or active.

Passive warming methods include passive insulation, environmental warming, and closed or semi-closed anesthesia systems. Active warming requires heat transfer to the patient through warmed fluids, circuit humidification, radiant heaters, forced or convective air warmers, infrared lights or circulating hot water systems. Alternatively, pharmacologic means may minimize heat loss through medications that decrease heat redistribution or through intravenous nutrients that stimulate metabolism and heat production. A combination of these methods is likely most effective in practice; however, prevention of hypothermia is likely a superior approach to treatment^[40-42].

Passive warming

Passive warming methods, including environmental heating and passive insulation, minimize but do not eliminate heat loss. The operating room temperature is the most critical factor influencing heat loss^[43,44]. Heat loss increases as the difference between the skin and environment grows. Consequently, the simplest method to reduce heat loss is raising ambient temperature. Unfortunately, most operating room personnel find elevated temperatures intolerable making this approach impractical as a singular solution. Thermal insulation may be accomplished through mass or reflective covering. Reflective coverings prevent radiant heat loss by reflecting radiant heat back to the body. Mass coverings halt airflow between the covering materials. Surgical drapes and blankets are common examples, and covering patients with blankets is a standard practice. Heat loss may be reduced by as much as 33% with a single layer covering; however, prevention of heat loss is limited and multiple blankets are only slightly more effective than one blanket^[45-47]. Unfortunately, effective covering of the body surface is often not feasible in the intraoperative setting making passive methods ineffective to prevent hypothermia.

Active warming

Active warming is required in most situations to maintain normothermia. Methods include warming of intravenous fluids, cutaneous warming, pharmacologic vasoconstriction, and intravenous nutrients. Of these choices, cutaneous warming (*e.g.*, forced air warming, electrical resistance, circulating hot water device) is the most widely used^[48].

Cutaneous warming: Likely the most common warming system, forced air warming is effective, safe, relatively inexpensive, easy to use^[45,49], and superior to many other warming systems^[50,51]. Forced air warmers were initially utilized to treat postoperative hypothermia before they were introduced for intraoperative warming. In this method, warmed air is forced into a receptacle, commonly a two-layer blanket, which lies in direct contact with a large surface area of the body. The forced air escapes through pores of the blanket material creating a warm microclimate over the area of contact.

Heat transfer is dependent on both the amount of surface area covered and the temperature difference between the skin and blanket. Consequently, the effectiveness is dependent upon utilization of a properly shaped warming blanket, appropriate placement on the body, and selection of a high warming temperature.

The utility and consequences of forced air warmers have also been scrutinized. A recent, large retrospective study of over 58000 patients undergoing noncardiac surgery and utilizing forced air warmers found that 64.4% of patients were hypothermic 45 min after induction and 20% of patients continued to be hypothermic after 6 h of anesthesia^[12]. Additionally, much discussion has occurred recently in regard to the potential for bacterial dispersion in the operating room by forced air warmers. However, studies examining contamination with and without forced air warmers did not find a difference^[52,53].

Electrical resistance may also be used for heat production by sending an electrical current through a resistant polymer blanket or mattress^[54]. These systems utilize conduction and are only effective when the warmed surface directly contacts the skin. This differs from forced air warmers, which create a carrier (air) for heat to travel from the warming blanket to the patient. Benefits of these devices include noiseless operation and slower temperature changes compared to the continuous supply of warmed air required with forced air warmers^[54]. While the efficacy of electrical resistance warming blankets are similar to forced air warmers, they are expensive albeit reusable^[54-56]. Additionally, an electrical mattress alone is insufficient to prevent hypothermia due to the negligible amount of body surface area contacting the operating table and the low amount of heat transfer^[56,57]. Consequently, warming blankets (forced air warming or electrical resistance) must be utilized concurrently to prevent intraoperative hypothermia.

Since water has much greater heat capacity than air, it may be hypothesized that water systems would supply a great amount of heat. However, similar to electrical resistance systems, direct contact must be made with the skin. In addition, these devices have been found to be ineffective with posterior body warming alone^[51]. As a result, water-warming blankets have been designed to wrap around the limbs^[58] and trunk^[59] depending on the surgical procedure. While anterior and posterior warming with water systems have demonstrated improved maintenance of normothermia in large upper abdominal surgeries compared to forced air warming alone, posterior water mattresses combined with anterior forced air warmers are comparable^[60]. Further, thermal injury remains a concern for circulating water devices; especially mattresses^[61]. Price and technological problems have also largely limited use of these systems.

The timing to initiate cutaneous warming is also important. Hypothermia prevention is less effective after anesthesia induction^[40-42]. Warming patients prior to anesthesia induction substantially prevents the decrease

in core temperature caused by redistribution^[62]. Pre-warming may also lessen intraoperative heat loss by increasing peripheral tissue temperature to resemble core temperature.

Warming intravenous fluids: Although heating intravenous fluids does not warm patients, it does assist in hypothermia prevention with administration of large volumes of IV fluids^[63]. Multiple different systems and technologies have been developed to warm intravenous fluids and blood products. These include water baths, conductive warming with metal, countercurrent heat exchange, microwave technology, and forced-air warming. All systems provide a range of flow velocities and temperatures with built-in prevention technologies for excessive warming and air detection. However, while 42 °C is considered safe for blood administration^[64], the safe upper limit is not well defined. Although reports have described heating intravenous fluids to 54 °C^[65], this practice is not studied and should not be utilized.

Pharmacologic vasoconstriction: Pharmacologic means to minimize heat loss caused by core-to-peripheral redistribution have been explored with a predominant focus on maintaining precapillary vasoconstriction. Induction with ketamine was associated with greater core temperatures throughout surgery compared to patients induced with propofol^[66]. Similarly, phenylephrine infusion (0.5 µg/kg per minute) initiated immediately prior to general anesthesia induction was associated with a smaller reduction in core temperature compared to controls.

Intravenous nutrients: Administration of intravenous nutrients, such as amino acids and fructose, has been examined to maintain normothermia through endogenous heat production. Protein/amino acid administration increases whole-body heat content by 20% with a significant increase in body temperature in awake subjects^[67]. Intravenous infusion of amino acids minimized core temperature decline and postoperative shivering following general anesthesia for open abdominal surgery^[68]. Notably, the timing of amino acid administration was variable. In hip arthroplasty patients receiving neuraxial anesthesia, preoperative intravenous amino acid administration one hour prior to surgery elevated subjects' temperatures prior to spinal placement resulting in improved intraoperative normothermia with decreased blood loss compared to control patients receiving saline^[69]. Oxygen uptake was also increased in subjects receiving amino acids. Intravenous fructose has also been examined. Patients receiving preoperative fructose infusions demonstrated greater core temperatures after anesthetic induction and throughout the study period^[70]. Interestingly, improvement in normothermia was attributed to both amplified metabolic heat production and an elevated threshold for vasoconstriction.

CONCLUSION

Despite the well-documented incidence of perioperative hypothermia, it continues to be a very common and avoidable anesthesia-related complication. Both general and neuraxial anesthesia impair normal physiologic temperature regulation. The consequences of perioperative hypothermia are significant and may include increased intraoperative blood loss, increased chance of surgical wound infection, increased length of PACU and overall hospital stay, decreased patient comfort, and increased rates of cardiac events. Although both passive and active cutaneous warming minimize heat loss and are commonly used strategies in most operating rooms today, these methods do not completely eliminate intraoperative hypothermia.

Few published studies characterize intraoperative temperature patterns. Rather, most publications have focused on postoperative temperatures and outcomes. Consequently, the impact of various normothermia strategies on intraoperative temperature patterns is not well elucidated. This is especially true in patients receiving neuraxial anesthesia, where temperature monitoring is often inconsistent or absent.

As intraoperative hypothermia may be difficult to prevent in many cases, future studies should further characterize intraoperative hypothermia development and the impact on outcomes. Intraoperative characterization should investigate the impact of both preventative strategies and anesthesia type. Postoperative outcome studies should examine the extent and duration of hypothermia and how it relates to negative perioperative outcomes.

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