Thermal care in the perioperative period

Andrea Kurz* MD
Vice Chair
Department of Outcomes Research, The Cleveland Clinic, 9500 Euclid Avenue — P77,
Cleveland, OH 44195, USA

Perioperative hypothermia is a common and serious complication of anesthesia and surgery. Core body temperature, which is normally regulated to within a few tenths of a degree centi-grade, can fall by as much as 6 °C during anesthesia. The combination of anesthetic-induced impairment of thermoregulatory control and exposure to a cool operating room environment causes most surgical patients to become hypothermic. Mild intraoperative hypothermia triples the incidence of postoperative wound infections, triples the incidence of postoperative myocardial events and increases perioperative blood loss. Furthermore, it prolongs postoperative recovery and prolongs the duration of action of almost all anesthetic drugs. Effective methods are available for preventing inadvertent perioperative hypothermia. Consequently, it is now routine to maintain intraoperative normothermia.

There is no widely accepted definition for the term 'mild hypothermia'. Furthermore, the term is not used consistently within the literature. For the purpose of this review, mild hypothermia refers to core temperatures between 34 and 36 °C.

Key words: anesthesia, general; anesthesia regional; complications; heat; surgery; temperature; thermoregulation; sweating; vasoconstriction; shivering.

GENERAL ANESTHESIA

General anesthesia obliterates behavioral thermoregulatory compensations, leaving only autonomic defenses to environmental perturbations.

Thermoregulation

Anesthetic-induced thermoregulatory inhibition is dose-dependent, and impairs vasoconstriction and shivering about three times as much as sweating. General anesthetics
linearly increase the warm-response thresholds. Opioids\(^1\) and the intravenous anesthetic propofol\(^2\) linearly decrease the vasoconstriction and shivering thresholds. In contrast, volatile anesthetics, such as isoflurane\(^3\) and desflurane\(^4\) decrease cold responses non-linearly.

Typical anesthetic doses can thus increase the inter-threshold range (core temperatures not triggering thermoregulatory defenses) by approximately 20-fold from the normal value of around 0.2 °C. As a result, anesthetized patients are poikilothermic over an approximately 4 °C range of core temperatures (Figure 1).

**Figure 1.** Anesthetic-induced inhibition of thermoregulatory control is usually the major factor determining perioperative core temperature. Graphs show concentration-dependent thermoregulatory inhibition by desflurane and isoflurane (halogenated volatile anesthetics), propofol (an intravenous anesthetic), and alfentanil (a \(\mu\)-agonist opioid). The sweating (triangles), vasoconstriction (circles), and shivering (squares) thresholds are expressed in terms of core temperature at a designated mean skin temperature of 34 °C. Anesthesia linearly, but slightly, increases the sweating threshold. In contrast, anesthesia produces substantial and comparable linear or non-linear decreases in the vasoconstriction and shivering thresholds. Typical anesthetic concentrations thus increase the inter-threshold range (difference between the sweating and vasoconstriction thresholds) approximately 20-fold from its normal value near 0.2 °C. Patients do not activate autonomic thermoregulatory defenses unless body temperature exceeds the inter-threshold range; surgical patients are thus poikilothermic over a 3–5 °C range of core temperatures. Isoflurane 1% and desflurane 6% have comparable anesthetic potencies.
The gain and maximum response intensity of sweating and active vasodilation are well preserved in patients given volatile anesthetics. Desflurane, however, reduces the gain of arterio-venous shunt vasoconstriction threefold, without altering the maximum intensity.¹ It seems likely that the thermoregulatory effects of general anesthetics are primarily central, since anesthetics of widely different types produce similar thermoregulatory inhibition. However, the possibility of peripheral inhibition has not been eliminated.

**Heat balance**

Inadvertent hypothermia during anesthesia is by far the most common perioperative thermal disturbance, and results from a combination of anesthetic-impaired thermoregulation and exposure to a cold operating room environment.

Body heat is usually unevenly distributed, with tonic thermoregulatory vasoconstriction maintaining a 2–4 °C core-to-peripheral temperature gradient. Induction of general anesthesia reduces the vasoconstriction threshold to below body temperature, thus opening arterio-venous shunts. The resulting core-to-peripheral redistribution of body heat decreases core temperature 1–1.5 °C during the first hour of general anesthesia.² Net loss of heat to the environment contributes little to this initial decrease.

In the subsequent few hours, core temperature usually decreases at a slower rate. This decrease is nearly linear and results simply from heat loss exceeding metabolic heat production.³ Approximately 90% of all heat is lost via the skin surface, with radiation and convection usually contributing far more than evaporative or conductive losses.

After 3–5 hours of anesthesia, core temperature often stops decreasing. This core-temperature plateau may be a simple thermal steady-state, with heat loss equaling heat production. This sort of steady-state plateau is especially likely in patients who are well insulated or effectively warmed. In patients becoming sufficiently hypothermic, however, the plateau results from re-activation of thermoregulatory vasoconstriction⁶, which decreases cutaneous heat loss and constrains metabolic heat to the core thermal compartment. Intraoperative vasoconstriction thus re-establishes the normal core-to-peripheral temperature gradient by preventing loss of centrally-generated metabolic heat to peripheral tissues. (Figure 2).

**REGIONAL ANESTHESIA**

Regional anesthesia impairs both central and peripheral thermoregulatory control. As a result, hypothermia is common in patients given spinal or epidural anesthesia. In patients becoming sufficiently hypothermic, shivering may again appear – and is often disturbing to patients as it increases pain sensation.

**Thermoregulation**

All thermoregulatory responses are neutrally mediated. Consequently, nerve blocks prevent regional manifestation of the major thermoregulatory defenses including sweating, vasoconstriction, and shivering. Spinal and epidural anesthesia disrupt nerve conduction to more than half the body. This peripheral inhibition of thermoregulatory defenses is a major cause of hypothermia during regional anesthesia.
Regional anesthesia, however, also impairs central thermoregulatory control. Inhibition is similar with spinal and epidural anesthesia. It appears that the regulatory system misinterprets skin temperature in blocked areas as being abnormally elevated.\(^7\) This apparent (as opposed to actual) elevation in leg skin temperature fools the regulatory system into tolerating lower-than-normal core temperatures before triggering cold defenses. Typically, the vasoconstriction and shivering thresholds are reduced by approximately \(0.5^\circ C\) whereas the sweating threshold is elevated by approximately \(-0.3^\circ C\).\(^8\) The result is a threefold increase in the normal inter-threshold range.

Although regional anesthesia typically causes core hypothermia, patients often feel warmer after induction of anesthesia.\(^9\) Increased thermal comfort, like inhibition of autonomic defenses, presumably results from the thermoregulatory system misinterpreting skin temperature as being elevated in the blocked area. Because core-temperature monitoring remains rare during spinal and epidural anesthesia, and because patients often fail to recognize that they are cold, undetected hypothermia is common during regional anesthesia.

**Heat balance**

Core hypothermia is comparable during regional and general anesthesia. As during general anesthesia, the initial hypothermia results from a core-to-peripheral redistribution of body heat.\(^10\) In this case, however, redistribution results primarily from peripheral rather than central inhibition of tonic thermoregulatory vasoconstriction. Although arterio-venous shunt vasodilation is restricted to the lower body, the mass of the legs is sufficient to produce substantial core hypothermia. Subsequent hypothermia results simply from heat loss exceeding heat production. Patients given
spinal or epidural anesthesia cannot, however, develop a regulated core-temperature plateau because vasoconstriction remains peripherally impaired. Consequently hypothermia tends to progress throughout surgery.

Patients becoming sufficiently hypothermic during spinal or epidural anesthesia shiver. Shivering is disturbing to patients and caregivers, but produces relatively little heat because it is restricted to the small muscle mass cephalad to the block.

**CONSEQUENCES OF HYPOTHERMIA**

Mild hypothermia is likely to be protective in some patients, yet surely harms others (see Table 1, below). Thermal perturbations, therefore, deserve the same risk/benefit analysis as other medical interventions. Fortunately, effective methods of cooling and warming surgical patients are now available.

**Potential benefits**

*Therapeutic hypothermia*

Temperatures only 1–3 °C below normal provide substantial protection against cerebral ischemia and hypoxemia in numerous animal species. Consistent with these data, core temperatures near 32 °C improve outcome after traumatic brain injury in patients with Glasgow Coma scores of 5–7. Consequently, most anesthesiologists believe mild hypothermia is indicated during operations likely to cause cerebral ischemia such as carotid endarterectomy and neurosurgery.

*Neurosurgery.* Surgery for intracranial aneurysm often results in postoperative neurologic deficits. A prospective, randomized trial at 30 centers determined whether intraoperative cooling during open craniotomy would improve the outcome among patients with acute aneurysmal subarachnoid hemorrhage. A total of 1001 patients with a preoperative World Federation of Neurological Surgeons score of I, II, or III (‘good-grade patients’), who had had a subarachnoid hemorrhage no more than 14 days before planned surgical aneurysm clipping, were randomly assigned to intraoperative hypothermia (target temperature = 33 °C, with the use of surface cooling techniques) or normothermia (target temperature = 36.5 °C). Patients were followed closely postoperatively and examined approximately 90 days after surgery, at which time a Glasgow Outcome Score was assigned. There were no significant differences between the group assigned to intraoperative hypothermia and the group assigned to normothermia in the duration of stay in the intensive care unit, the total length of hospitalization, the rates of death at follow-up (6% in both groups), or the destination at discharge among surviving patients (home or another hospital). At the final follow-up, 329 out of 499 patients in the hypothermia group had a Glasgow Outcome Score of 1 (good outcome), compared with 314 out of 501 patients in the normothermia group (66% vs. 63%; odds ratio = 1.14; 95% confidence interval = 0.88–1.48; \( P = 0.32 \)). Postoperative bacteremia was more common in the hypothermia group than in the normothermia group (5% vs. 3%; \( P = 0.05 \)). Thus, intraoperative hypothermia did not improve the neurologic outcome after craniotomy among good-grade patients with aneurysmal subarachnoid hemorrhage.

*Hypothermia and aortic aneurysm repair.* Traumatic great vessel injuries are frequently lethal events. Rarely, due to the location of the injury and delayed presentation,
<table>
<thead>
<tr>
<th>Consequence</th>
<th>Reference</th>
<th>$N$</th>
<th>$\Delta T_{\text{core}}$ (°C)</th>
<th>Normothermic</th>
<th>Hypothemic</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical wound infection</td>
<td>Kurz et al. (1996)\textsuperscript{27}</td>
<td>200</td>
<td>1.9</td>
<td>6%</td>
<td>19%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Duration of hospitalization</td>
<td>Kurz et al. (1996)\textsuperscript{27}</td>
<td>200</td>
<td>1.9</td>
<td>12.1 ± 4.4 days</td>
<td>14.7 ± 6.5 days</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Intraoperative blood loss</td>
<td>Schmied et al. (1996)\textsuperscript{64}</td>
<td>60</td>
<td>1.6</td>
<td>1.7 ± 0.3 L</td>
<td>2.2 ± 0.5 L</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Allogeneic transfusion requirement</td>
<td>Schmied et al. (1996)\textsuperscript{64}</td>
<td>60</td>
<td>1.6</td>
<td>1 unit</td>
<td>8 units</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Morbid cardiac events</td>
<td>Frank et al. (1997)\textsuperscript{8}</td>
<td>300</td>
<td>1.3</td>
<td>1%</td>
<td>6%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Postoperative ventricular tachycardia</td>
<td>Frank et al. (1997)\textsuperscript{8}</td>
<td>300</td>
<td>1.3</td>
<td>2%</td>
<td>8%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Urinary excretion of nitrogen</td>
<td>Carli et al. (1989)\textsuperscript{79}</td>
<td>12</td>
<td>1.5</td>
<td>982 mmol/day</td>
<td>1798 mmol/day</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Duration of vecuronium</td>
<td>Heier et al (1991)\textsuperscript{21}</td>
<td>20</td>
<td>2.0</td>
<td>28 ± 4 min</td>
<td>62 ± 8 min</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of atracurium</td>
<td>Leslie et al. (1995)\textsuperscript{24}</td>
<td>6</td>
<td>3.0</td>
<td>44 ± 4 min</td>
<td>68 ± 7 min</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Postoperative shivering</td>
<td>Just et al. (1992)\textsuperscript{50}</td>
<td>14</td>
<td>2.3</td>
<td>141 ± 9 ml min$^{-1}$ m$^{-2}$</td>
<td>269 ± 60 ml min$^{-1}$ m$^{-2}$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of postanesthetic recovery</td>
<td>Lenhardt et al. (1997)\textsuperscript{27}</td>
<td>150</td>
<td>1.9</td>
<td>53 ± 36 min</td>
<td>94 ± 65 min</td>
<td>&lt;0.001</td>
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<td>Adrenergic activation</td>
<td>Frank et al. (1995)\textsuperscript{30}</td>
<td>74</td>
<td>1.5</td>
<td>330 ± 30 pg/ml</td>
<td>480 ± 70 pg/ml</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Thermal discomfort</td>
<td>Kurz et al. (1993)\textsuperscript{53}</td>
<td>74</td>
<td>2.6</td>
<td>50 ± 10 mm VAS</td>
<td>18 ± 9 mm VAS</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Only prospective, randomized human trials are included; subjective responses were evaluated by observers blinded to treatment group and core temperature. $N$, total number of subjects; $\Delta T_{\text{core}}$, difference in core temperature between the treatment groups. Different outcomes of the first three studies are shown on separate lines. VAS is a 100-mm-long visual analog scale (0 mm = intense cold, 100 mm = intense heat).
standard techniques can be used and hypothermic cardiac circulatory arrest is required.\textsuperscript{13} Studies have shown improved outcome after repair of descending and thoracoabdominal aortic aneurysms.

**Adult respiratory distress syndrome.** Therapeutic hypothermia seems to be used mainly in the field of intensive care medicine. Core temperatures near \(34 \, ^\circ\text{C}\) facilitate recovery and reduce mortality from septic adult respiratory distress syndrome.\textsuperscript{14} Furthermore, mild hypothermia improves neurologic outcome and mortality in patients after cardiac resuscitation, as well as in brain trauma patients.

**Hypothermia and traumatic brain injury.** Based on the potential beneficial effects of therapeutic hypothermia, several clinical trials have been performed to evaluate the effect of different levels of hypothermia on neurologic outcome in patients after brain injury. Several trials have shown that mild hypothermia reduces intracranial pressure (ICP). Furthermore, there is evidence that therapeutic hypothermia (\(33 \, ^\circ\text{C}\)) for 24–72 h improves neurologic outcome in patients after brain trauma.\textsuperscript{15,16}

**Stroke.** Animal data suggests that therapeutic hypothermia might improve outcome after stroke. Moderate hypothermia reduces ICP in stroke patients\textsuperscript{17}, However, this indication has yet to be evaluated in prospective, randomized studies in patients.

**Myocardial infarction.** During the past three decades, there have been tremendous advances in our understanding of ischemia. Ischemia occurs when blood flow, oxygen, and substrate delivery are inadequate to meet the metabolic demand of the tissue. This is fundamentally the same for myocardial cells and for neuronal cells. Hypothermia has a protective effect against ischemia. Therapeutic hypothermia, although initially applied to the heart in the setting of cardiac bypass surgery, has recently received considerable attention because of its profound neuroprotective effects. Ironically, limitations in reperfusion therapy for acute myocardial infarction have recently rekindled interest in hypothermic myocardial protection. The precise mechanisms by which hypothermia provides protection during myocardial ischemia–reperfusion are not well defined. However, the beneficial effect of myocardial cooling appears to be independent of hypothermia-induced bradycardia, as the effect persists when heart rate is maintained with pacing.\textsuperscript{18} Recently, a pilot study examining the feasibility of endovascular cooling during primary percutaneous cardiac intervention (PCI) demonstrated trends in reduced infarct volume with no increase in hemodynamic instability or cardiac dysrhythmias.\textsuperscript{19}

The extent to which hypothermia becomes a valued therapeutic option will depend on the clinician's ability to rapidly reduce core body temperature and safely maintain hypothermia. So far, general anesthesia is the best way to block autonomic defences during induction of mild-to-moderate hypothermia; unfortunately general anesthesia is not an option in most patients likely to benefit from therapeutic hypothermia. Induction of hypothermia in awake humans (after myocardial infarction or stroke) is complicated by both the technical difficulties related to thermal manipulation and the remarkable efficacy of thermoregulatory defenses, especially, vasoconstriction and shivering. The most effective thermal manipulation devices are generally invasive and, therefore, more prone to complications than surface methods. In an effort to inhibit thermoregulation in awake humans several agents have been tested either alone or in combination. Many drugs and drug combinations have proven helpful for the induction of therapeutic hypothermia: dexmedetomidine, meperidine, buspirone.
The combination of meperidine and buspirone has already been applied to facilitate induction of hypothermia in human trials (Figure 3). Nefopam, a benzoxazocine compound, lowers the shivering threshold without affecting the vasoconstriction threshold and does not cause sedation, respiratory depression or nausea. Furthermore, it decreases the gain of shivering. The combination of skin warming and meperidine additively lowers the vasoconstriction and thresholds. However, pharmacologic induction of thermoregulatory tolerance to cold without excessive sedation, respiratory depression, or other serious toxicity remains a major focus of current therapeutic hypothermia research.

**Practice points**

- Hypothermia provides marked protection against ischemia
- It improves neurologic outcome after cardiac resuscitation
- It does not improve outcome in patients undergoing aneurysm clipping
- Therapeutic hypothermia has to be initiated as soon as possible after the event
  - Currently core temperatures of approximately 34 °C are used for a duration of up to 72 h
  - Careful monitoring of side effects is necessary (i.e. coagulopathy)
Perioperative complications

The major in vivo complications of mild perioperative hypothermia in humans are listed in Table 1, and will be discussed further below.

Pharmacokinetics and pharmacodynamics

The enzymes that moderate organ function and metabolize most drugs are highly temperature sensitive. Hypothermia alters the pharmacodynamics of volatile anesthetics, as well as many drugs routinely administered during anesthesia.

For example, the duration of action of vecuronium is more than doubled in patients assigned to 2 °C core hypothermia.21 This duration thus exceeds that of pancuronium in a normothermic patient. Caldwell et al. demonstrated temperature-related differences in the pharmacodynamics of vecuronium. The keo (rate constant for equilibration between plasma concentration and effect) decreased (0.023 min⁻¹ per °C) with lower temperature, suggesting a slightly delayed drug equilibration between the circulation and the neuromuscular junction during hypothermia.22 Thus, the onset of vecuronium is significantly delayed, and recovery may be minimally prolonged. However, the efficacy of neostigmine as an antagonist of vecuronium-induced neuromuscular block is not altered by mild hypothermia.23 Atracurium duration is less dependent on core temperature than vecuronium: a 3 °C reduction in core temperature increases the duration of muscle relaxation by ~60%.24 With both atracurium and vecuronium the recovery index (time for 25–75% twitch recovery) remains normal during hypothermia.

Tissue solubility of volatile anesthetics increases in hypothermic patients. At a given steady-state plasma partial pressure, body anesthetic content thus increases at subnormal temperatures. The minimum alveolar concentration (MAC) of halothane and isoflurane in rats both decrease roughly 5% per °C reduction in core body temperature. Furthermore, Liu et al. demonstrated a decrease in isoflurane MAC of 5.1% for each 1 °C reduction in the body temperature in children.25

During a constant infusion of propofol, plasma concentration is ≈30% greater than normal when individuals are 3 °C hypothermic. The increase apparently results from reduced inter-compartmental clearances between the central and shallow compartments. Interestingly, mild hypothermia does not appear to significantly alter hepatic blood flow. Hypothermia also increases steady-state plasma concentrations of fentanyl by about 5% per °C.26

Research agenda

- Further research is warranted to study the effect of therapeutic hypothermia after:
  - Stroke
  - Myocardial infarction
  - Brain trauma
- Duration and depth of hypothermia need further evaluation

Perioperative hypothermia
Post-operative recovery and thermal comfort

A prospective randomized trial demonstrated that mild hypothermia significantly delayed discharge of adult patients from the post-anesthesia care unit. Recovery duration was prolonged even when core normothermia was not a discharge criterion. Interestingly, similar prolongation of recovery duration was not observed in infants and children.

Body core and skin temperatures contribute about equally to thermal comfort, whereas core predominates in the regulation of the autonomic and metabolic responses. Even mild hypothermia produces marked post-operative thermal discomfort. Patients often identify feeling cold in the immediate post-operative period as the worst part of their hospitalization, sometimes rating it as worse than surgical pain. It is also likely that thermal discomfort is physiologically stressful, and contributes to observed increases in post-operative blood pressure, heart rate, and plasma catecholamine concentrations.

Shivering and shivering-like tremor

The incidence of post-operative shivering-like tremor is reportedly about 40%, but nowadays appears to be less as more patients are kept normothermic and opioids are administered more frequently and in larger doses. It is a potentially serious complication, increasing oxygen consumption by roughly 100%. Interestingly, though, myocardial ischemia is poorly correlated with shivering, suggesting that increased metabolic rate is not the primary etiology of this complication. In addition to increasing intraocular and intracranial pressures, post-operative shivering likely aggravates wound pain by stretching incisions.

Most postoperative shivering is thermoregulatory, i.e. preceded by core hypothermia and arterio-venous shunt vasoconstriction. However, there appears to be a distinct incidence of non-thermoregulatory tremor in normothermic post-operative patients; similar non-thermoregulatory tremor has been observed in women during labor. The etiology of this tremor, and why volunteers and patients should respond differently, remains unknown; however, preliminary data suggest that pain is a contributor.

Post-anesthetic shivering can be treated by skin-surface warming because the regulatory system tolerates more core hypothermia when cutaneous warm input is augmented. Post-anesthetic shivering can also be treated using a variety of drugs, including clonidine (75 μg intravenously (iv)), ketanserin (10 mg, iv), physostigmine (0.04 mg/kg), tramadol (1 mg/kg), and magnesium sulfate (30 mg/kg). The specific mechanisms by which clonidine, ketanserin, physostigmine, and magnesium sulfate stop shivering are unknown.

Alfentanil, a pure μ-receptor agonist, significantly impairs thermoregulatory control. However, meperidine is reportedly far more effective in treating shivering than equi-analgesic doses of other μ agonists. Clinically, this efficacy is manifested as a shivering threshold that is reduced twice as much as the vasoconstriction threshold without a decrease in the gain or maximum intensity of shivering.

Nefopam, a benzoxazocine compound is a centrally acting analgesic with both supra-spinal and spinal sites of action. Nefopam does not induce respiratory depression, even in postoperative patients. It differs from other tested drugs in reducing the shivering threshold without altering the vasoconstriction or sweating thresholds.

Adverse myocardial events

Myocardial infarction is one of the leading causes of unanticipated perioperative morbidity and mortality. In a landmark study using prospective randomized data, Frank
et al. demonstrated that patients assigned to only 1.4 °C core hypothermia were three times as likely to experience adverse myocardial outcomes.

The mechanism by which mild hypothermia triggers myocardial events remains unclear, although shivering is clearly not the primary mechanism. Hypothermia causes hypotension and tachycardia in elderly patients and those at high risk for cardiac complications. In this regard, they differ from young, healthy subjects who demonstrate virtually no hemodynamic response to mild hypothermia. Cold-induced hypertension in the elderly is associated with a threefold increase in plasma norepinephrine concentrations, which is at least likely to augment cardiac irritability and facilitate development of ventricular arrhythmias.

It has long been suggested that patients with cardiopulmonary disease may not tolerate the increased metabolic demands associated with post-operative shivering and may have adverse outcomes. However, post-operatively, oxygen consumption (i.e. metabolic rate) rarely increases even by a factor of 3, and then only during extreme circumstances. Because advanced age and opioid administration are associated with reduced shivering, it is likely that the average elderly patient who is undergoing surgery and receives adequate analgesia experiences a relatively small increase in metabolism due to post-operative shivering.

A temperature threshold of approximately 1 °C below normothermia activates sympathoneural (noradrenaline), as well as adrenomedullary (adrenaline) responses in awake healthy volunteers during cold exposure. The cardiovascular physiology associated with these reactions involves an increase in the various indices of cardiac work. In addition, studies demonstrate that this β-adrenoceptor-mediated increase in the myocardial work in normal, mildly hypothermic volunteers is linked to an increase in myocardial perfusion. Thus, mild core hypothermia does not evoke coronary vasoconstriction in healthy human subjects, and actually increases myocardial tissue perfusion, in a manner that matches the increase in the heart rate–systolic pressure product, an index of myocardial oxygen consumption. However, even in the absence of vasoconstriction, increased myocardial metabolic requirements in the presence of flow-limiting coronary lesions may predispose patients to myocardial ischemia.

Strict thermoregulation attenuates myocardial injury during coronary artery graft surgery as reflected by reduced levels of cardiac specific troponin.

**Coagulation**

Three general mechanisms contribute to temperature-related coagulation disorders: platelet function, clotting factor enzyme function, and fibrinolytic activity.

Platelet counts remain normal during mild hypothermia. Nevertheless, hypothermia has been shown to induce morphologic changes in the platelet structure suggestive of activation. Faraday & Rosenfeld found that moderate and profound degrees of in vitro hypothermia enhanced the binding of platelets to fibrinogen through activation of GPllb-IIIa receptors. These findings suggest that inhibition of intrinsic platelet function is not the cause of this coagulopathy. Further observations supporting the hypothesis that hypothermia results in coagulopathy by reducing the availability of platelet activators include: (1) The generation of thrombin, a potent platelet agonist, decreases under hypothermic conditions, and (2) hypothermia results in the release of a circulating anticoagulant with heparin-like effects.

An insidious feature of hypothermic coagulopathy is that standard coagulation timing tests remain normal. The reason is that the tests are normally performed at 37 °C – no matter what the patient’s temperature might be. These same tests, though,
are prolonged by hypothermia when they are performed at the patient’s actual core temperature. The isolated effect of hypothermia on hemostasis has been also investigated in healthy humans: reduction of core temperature to 32 °C was associated with a small decrease in the prothrombin time and platelet count, whereas coagulation variables at 34 °C did not differ from normothermia.

The fibrinolytic system normally regulates the balance between formation of hemostatic plugs and restoration of blood flow after clot formation. Fibrin is a major structural element in formed clots, but is subject to degradation by plasmin (the activated enzymatic form of plasminogen). Multivariate analysis of 232 adult trauma patients demonstrated a significant hypercoagulability associated with enzyme activity slowing and decreased platelet function at core temperatures <34 °C, whereas fibrinolysis was not significantly affected at any of the measured temperatures. Preliminary data suggests that fibrinolysis remains normal during mild hypothermia, but is significantly increased during hyperthermia.

Schmied et al. showed that mild hypothermia increases blood loss during surgery. In that study, patients were randomly assigned to normothermia or mild hypothermia during elective primary hip arthroplasty. A reduction of 1.6 °C in core temperature increased blood loss by 500 ml (30%) and significantly augmented allogeneic transfusion requirements. The same group subsequently confirmed the hemostatic benefits of maintaining intraoperative normothermia in a retrospective analysis. In contrast, another study during hip arthroplasty failed to identify a temperature-dependence of blood loss. Why the results should differ so much in similar, and apparently well conducted, studies remains unclear. Possibilities include differences in surgical technique or even in the populations evaluated. Additional randomized controlled trials have confirmed that only a ≈ 0.5 °C core hypothermia increases blood loss by 200–300 ml in patients undergoing hip arthroplasty under spinal anesthesia.

**Wound infection and healing**

Wound infections are common and are serious complications of anesthesia and surgery. For example, the wound infection risk in patients undergoing colon surgery is approximately 10%. Surgical wound infections prolong hospitalization by 5–20 days per infection, and substantially increase costs.

Hypothermia may facilitate perioperative wound infections in two ways. First, sufficient intraoperative hypothermia triggers thermoregulatory vasoconstriction. Thermoregulatory vasoconstriction significantly decreases subcutaneous oxygen tension in humans and the incidence of wound infections correlates with subcutaneous oxygen tension.

Second, considerable evidence indicates that mild core hypothermia directly impairs immune function including T-cell-mediated antibody production and 'non-specific' oxidative bacterial killing by neutrophils. Thus, hypothermia may directly impair neutrophil function, or impair it indirectly by triggering subcutaneous vasoconstriction and thereby producing tissue hypoxia.

Vasoconstriction-induced tissue hypoxia may also impair wound healing. Scar formation requires hydroxylation of abundant proline and lysine residues, allowing cross-linking within and between collagen strands to provide tensile strength. The hydroxylases catalyzing this reaction depend on the substrate oxygen. Hypothermic vasoconstriction decreases oxygen supply to tissues and thus results in decreased collagen deposition.

The first few hours following bacterial contamination constitute a decisive period during which infection is established. The effects of antibiotic administration and
of hypoperfusion are especially important during this period.\textsuperscript{75,76} Similarly, wound hypoperfusion (achieved by epinephrine infiltration or ‘dehydration shock’) aggravates test infections when induced up to 2.5 h after the inoculation, but has no effect when induced later.\textsuperscript{75}

Only 1.9 $^\circ\text{C}$ core hypothermia triples the incidence of surgical wound infection following colon resection.\textsuperscript{67} This is clinically important, as indicated by the fact that patients with wound infections were hospitalized for 1 week longer, on average, than patients without infection. In addition, hypothermia increases the duration of hospitalization by 20\% even when infected patients were excluded from the analysis – apparently because healing \textit{per se} was significantly impaired.\textsuperscript{77,78}

This result is consistent with studies by Carli et al. showing that mild hypothermia aggravates post-operative protein wasting.\textsuperscript{79} In addition, disorders of hemostasis are characterized not only by prolonged bleeding, but also by slow wound healing. Hemostatic reactions, particularly platelet plug formation, play a primary role in initiating the first and perhaps the second stage of wound healing Activated platelets initiate wound healing and angiogenesis by the release of growth and chemotactic factors.\textsuperscript{80} It is, thus, likely that hypothermia-induced coagulopathy because of low availability of platelet activators also contributes to impaired wound healing.

\textbf{Cancer recurrence}

Removing the primary tumor is important for eliminating the major pool of metastasizing cells, but the surgical procedure itself might promote metastases. This is attributed to several mechanisms acting in synergy, including mechanical release of tumor cells, enhanced angiogenesis and immunosuppression. The immune system, in particular, is affected by perioperative hypothermia. Inadvertant hypothermia might thus increase cancer recurrence in patients undergoing cancer surgery.\textsuperscript{81}

<table>
<thead>
<tr>
<th>Practice points</th>
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<tbody>
<tr>
<td>● Hypothermia is common in the perioperative period</td>
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<tr>
<td>● It is associated with major complications, namely:</td>
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<td>○ Increased incidence of adverse cardiac arrests</td>
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<td>○ Increased blood loss</td>
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<td>○ Increased incidence of surgical wound infections</td>
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<td>○ Prolonged duration of recovery</td>
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<td>● It is also associated with minor complications, namely:</td>
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<td>○ Prolonged duration of action of inhalation agents, muscle relaxants and propofol</td>
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<td>○ Electrolyte imbalances</td>
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**TEMPERATURE MONITORING**

Temperature monitoring devices vary according to the type of transducer used and the monitoring site. The most commonly used transducers are thermistors and
thermocouples. A more recent development is monitors that use infrared emission to measure temperature; these are seen commonly in aural thermometers. Liquid crystal sensors also can be used to measure skin temperature.

Core temperature is the best indicator of body temperature. Therefore all non-core sites need to be judged by their ability to accurately assess core temperature. Core temperature monitoring is necessary in all patients undergoing general anesthesia.

Monitoring sites

**Pulmonary artery catheter:** This allows the measurement of central blood temperature and is considered the gold standard for measuring core body temperature. It is usually used as a reference for all other monitoring sites. The obvious disadvantage is the high cost and invasiveness of the catheter and the difficulty of insertion.

**Esophageal temperature:** This is usually monitored using a thermistor or thermocouple that is incorporated into an esophageal stethoscope. It accurately reflects core body temperature. The optimal position for the sensor is approximately 45 cm from the nose in adults, which is 12–16 cm distal from where heart and breath sounds are best heard.

**Nasopharyngeal temperature:** This is reasonably close to brain and core temperature.

**Tympanic membrane temperature:** This is a reliable measure of core temperature. This measurement requires the transducer to be placed in contact with the tympanic membrane. Infrared tympanic thermometers are difficult to handle and might not reflect tympanic temperature.

**Bladder Temperature:** This can be measured with a foley catheter, either by using an attached temperature thermistor or a thermocouple. Although bladder temperature is a close approximation of core temperature, the accuracy of this site decreases with low urine output and during abdominal surgery. Rectal temperature is another site that approximates to core temperature, but these readings may be affected by

![Figure 4](image-url)  
*Figure 4.* The difference between tympanic membrane (core) and forehead skin–surface temperature (open squares) decreases after induction of general anesthesia, but the decrease is not statistically significant. The difference between tympanic membrane (core) and neck skin–surface temperature (filled squares) decreased significantly after induction of general anesthesia. Elapsed time zero indicates induction of anesthesia. Asterisks (*) indicate values differing significantly from elapsed time zero; results are presented as mean ± SD.
the presence of stool or bacteria which generate heat. Thus rectal temperature is usually slightly higher than core temperature. Rectal and bladder temperatures lag behind other monitoring sites during rapid temperature changes, such as during cardiopulmonary bypass surgery. They are reliable choices during regional anesthesia.

**Skin temperature monitors:** These can be confounded by core-to-peripheral redistribution, thermoregulatory changes in vasomotor tone and changes in ambient temperature. Ikeda et al.\(^8\) showed that there were only slight differences induced by these factors, with the smallest difference of only 0.5–1.0°C being on the forehead when using liquid crystal thermometers (Figure 4). Infrared temporal artery thermometry is a non-invasive core temperature measurement method that has been introduced recently. However, trials have shown that it is not sensitive enough to correctly detect hypothermia as well as fever.

**Axillary and oral temperature:** These are close to core temperature and may be a reasonable choice in selected patients, such as, for example, post-anesthesia care unit (PACU) patients.

### Practice points

- Temperature monitoring should be performed in all patients undergoing general and regional anesthesia lasting longer than 1 h
- The most accurate monitoring sites during general anesthesia are: pulmonary artery, esophagus, tympanic membrane, bladder, rectum
- The most accurate monitoring sites during regional anesthesia are:
  - Temporal artery, bladder, rectum, tympanic membrane
  - Liquid crystal thermometers used on forehead and neck, with offset calculation
  - Axilla, mouth
- **Not recommended:**
  - Tympanic infrared thermometers
  - Infrared temporal artery measurements
  - Peripheral skin temperatures

### Research agenda

- Further research is warranted to develop non-invasive skin temperature monitoring devices (especially for core temperature measurements during regional anesthesia and in the postoperative period)

## TEMPERATURE MANAGEMENT

Thermal management can be performed by means of passive methods, which mainly decrease cutaneous heat loss, and active warming or cooling methods, which actively transfer heat into or out of the body.
Passive warming

Heat loss through radiation accounts for roughly 60% of the total perioperative heat loss. Operating-room temperatures determine the rate at which metabolic heat is lost through radiation and convection from the skin and by evaporation from within surgical incisions. However, room temperatures exceeding 23 °C are generally required to maintain normothermia in patients undergoing all but the smallest procedures. Increasing ambient temperature is, thus, rarely a practical way of keeping surgical patients warm.83

Thermal insulators that are readily available in most operating rooms include cotton blankets, surgical drapes, plastic sheeting and reflective composites ('space blankets'). A single layer of any of these reduces heat loss by approximately 30%, and there are no clinically important differences among the insulation types.74 Unfortunately, adding more layers doesn’t appreciably reduce heat loss further.

Active warming

Convective warming

The most common perioperative warming system is convective warming with forced air.84 The best forced-air systems eliminate loss of metabolic heat and even transfer some heat across the skin surface. Forced air usually maintains normothermia even during large operations.

Conductive warming

In certain patient populations (the old and the very ill) forced-air warming might be insufficient for maintaining normothermia during surgical procedures such as, for example, liver transplantation, off pump coronary artery bypass surgery (OPCAB), polytrauma and major abdominal surgery in the lithotomy position. Cardiac surgery, in particular, poses unique challenges to perioperative temperature management. On-pump procedures expose patients to the risk of temperature afterdrop following disconnection from the heat pump, whereas OPCAB grafting requires close temperature management both perioperatively and postoperatively. For this and other high-acuity procedures, technologies are needed that can warm limited skin surface areas with maximum efficiency. Specialized circulating-water garment systems85, some of them servo-regulated, that circulate temperature-controlled water, can be wrapped around patients’ trunks and extremities and transfer large amounts of heat because water has a higher capacity to transfer heat than does air (Figure 5).86

However, conductive warming with circulating-water mattresses placed underneath the patient is almost ineffective.87 Presumably patients are unable to maintain normothermia because little heat is lost from the back. Furthermore, the combination of heat and decreased local perfusion (which results when the patient’s weight reduces capillary blood flow) increases the propensity for pressure/heat necrosis ('burns').88 Circulating water is more effective — and safer — when placed over or around patients rather than under them and, in that position, can almost completely eliminate metabolic heat loss.56

Another conductive device, the Arctic Sun temperature-management system, uses a flexible adherent hydrogel matrix combined with a conductive water-delivery
system to provide uninterrupted skin contact. The biocompatible pads can be positioned to provide an intimate interface with the patient’s skin that allows optimal energy transfer from the heated water to the patient. The consequence of this close contact is that less patient coverage is required to achieve effective thermal management. A study in volunteers showed that the rate of increase of core temperature from 34°C to 36°C was 1.2 ± 0.2°C/h with the Kimberly Clark warming system, 0.9 ± 0.2°C/h with the Allon system, and 0.6 ± 0.1°C/h with the Bair Hugger (P = 0.002). Thus the warming rate with the Kimberly Clark system was 25% faster than with the Allon system, and twice as fast as with the Bair Hugger. Both circulating-water systems thus warmed hypothermic volunteers in significantly less time than the forced-air system.

Several other studies have shown the effectiveness of the above devices in preventing or treating perioperative hypothermia. Stanley et al.90 noted that patients warmed with the Arctic Sun device achieved a faster temperature increase compared to forced-air warming (0.3 versus 0.14°C/h). Measurements of SvO2 revealed fewer perturbations during recovery. Another study using the Artic Sun device examined the effect of the pads on outcomes in cardiac surgery, and found that using the device led to significantly higher blood temperatures (36.6 ± 0.5 versus 35.4 ± 0.9°C; P < 0.001) on arrival at the intensive care unit, less afterdrop among those whose temperature was <37°C (0.5 ± 0.5 versus 1.7 ± 0.7°C; P < 0.001) and a lower average rate of temperature increase (0.14 versus 0.3°C/h). Measurements of SvO2 revealed fewer perturbations during recovery. Recently, a retrospective study in 50 off-pump coronary artery bypass graft (OCABG) patients showed that active warming treatment resulted in significantly higher temperatures intraoperatively. Patients warmed using the hydrogel-pad device required fewer units of transfused blood. They were also extubated sooner and had shorter stays in the intensive care unit (1.3 ± 0.1 versus 2.0 ± 0.3 days; P < 0.01) and in the hospital (4.3 ± 0.1 versus 5.1 ± 0.3 days; P < 0.05).

Figure 5. Core temperature (± 95% confidence intervals) as a function of rewarming time in 7 healthy volunteers on three separate study days, each with a different warming device. The three warming devices were (1) Kimberly Clark energy transfer pads (circles), (2) Allon circulating-water garment (squares), and (3) Bair Hugger forced-air warming (triangles). Even after volunteers reached 36°C on the KC day and the study was stopped, they are shown as continuing at that temperature in the figure.
Although noting the limitations of the retrospective study, the authors felt that the benefits were clear-cut enough that this active warming device has become standard in their practices not only for OPCAB but also for long non-cardiopulmonary bypass (CPB) procedures such as thoracoabdominal aortic repair, robotic procedures, operations involving profound hypothermic circulatory arrest and CPB cases that require prolonged pre- and post-CPB periods.

**Prewarming**

Thirty minutes of forced-air warming increases peripheral tissue heat content by more than the amount normally redistributed during the first hour of anesthesia. Therefore, prewarming substantially decreases redistribution hypothermia and decreases the incidence of postoperative wound infections.

![Figure 6](image)

**Figure 6.** Relative effects of warming methods on mean body temperature ($\Delta$MBT) as a function of time (upper portion) or administered fluid (lower portion). Mean body temperature is the average temperature of body tissues, and is usually somewhat less than core temperature. The calculations assume an undressed 70-kg patient with a metabolic rate of 80 kcal/h, in a thermal steady state with a typical 21 °C operating room environment. (a-d) Changes in MBT per liter of administered blood or crystalloid at various fluid temperatures. (e) Inspiring warmed, humidified gas. (f, g) Warmed or unwarmed blankets, with all skin below the neck covered. Savings are similar with a single layer of other passive insulators. (h) Full-length circulating-water mattress. (i) Full-length forced-air warmer.
Endovascular warming/cooling

One temperature-management approach that has gained more and more importance over the past few years is that of internal warming and cooling. These systems consist of a heat-exchanging catheter, usually inserted into the inferior vena cava via the femoral vein, and a servo-controller. They transfer heat into and out of the body in the range of 400–700 W and, thus, are very efficient. Internal warming increases core temperature faster than surface warming. Interestingly, core warming depends strongly on the vasomotor tone of the patients. Warming rates of 2 °C/h during peripheral arterio-venous shunt vasoconstriction were obliterated as soon as peripheral vasodilation occurred. The same catheter can be used for the induction of therapeutic hypothermia. These cooling catheters can decrease core temperature at rates approaching 4–6 °C/h.

Fluid warming

Warming intravenous fluids is an adjunct therapy that helps minimize the heat loss associated with the transfusion of large volumes of cool fluids. However, it must be kept in mind that in order to transfer heat into the body, large amounts of fluid are necessary (Figure 6).

Chemical warming

Perioperative amino acid infusion improves recovery and shortens duration of hospitalization after OCABG, it also shortens postoperative mechanical ventilation, duration of ICU stay, and improves fitness for discharge. Furthermore, amino acid infusion induces thermogenesis and reduces blood loss during hip arthroplasty under spinal anesthesia.

Despite all of the available warming and monitoring methods, thermal management has only slightly improved worldwide over the past decade. Ratnaraj et al. evaluated patients’ core temperature in the PACU and noted that hypothermia was still commonly observed in the operation room and PACU. Approximately 40% of the patients were discharged from the PACU with core temperatures below 36 °C. Furthermore, a survey performed in 800 European hospitals showed that temperature monitoring was performed in only 25% of the patients and only 30% of the patients were actively warmed.

Practice points

- Despite all of the available warming and monitoring devices, perioperative hypothermia is still common
- Active warming should be performed in all patients undergoing general and regional anesthesia lasting longer than 1 hour
- Core temperature should be maintained at > 36 °C
- Conductive and convective warming are the most commonly used warming methods
SUMMARY

Perioperative hypothermia is, even today, 15 years after the development of active warming devices, a common complication of anesthesia and surgery.

The combination of anesthetic-induced thermoregulatory impairment and exposure to cold operating room environments makes most surgical patients hypothermic. Hypothermia results initially from a core-to-peripheral redistribution of body heat, and subsequently from heat loss exceeding heat production. Patients becoming sufficiently hypothermic during general anesthesia develop a core-temperature plateau when arterio-venous shunt tone is re-established.

General anesthesia produces marked and dose-dependent inhibition of thermoregulatory control, typically increasing the sweating and vasodilation thresholds by approximately 1°C and reducing the vasoconstriction and shivering thresholds by approximately 3°C. As a result, the inter-threshold range increases roughly 20-fold, leaving patients poikilothermic over an approximately 4°C range of core temperatures. Regional anesthesia also impairs thermoregulatory control, producing both peripheral and central inhibition.

Even mild perioperative hypothermia, which can easily be prevented, is associated with adverse outcomes including morbid cardiac events, coagulopathy, surgical wound infections, and prolonged hospitalization. Consequently, body temperature should be measured in most surgical patients. Unless hypothermia is specifically indicated (e.g. for protection against ischemia), intraoperative core temperature should be maintained above 36°C.

REFERENCES


Research agenda

- Endovascular warming and cooling should be investigated
- The uses of therapeutic hypothermia (e.g. in stroke, myocardial infarction patients) should be investigated

Research agenda

Endovascular warming and cooling should be investigated

The uses of therapeutic hypothermia (e.g. in stroke, myocardial infarction patients) should be investigated


31. Panzer O, Ghazanfari N, Sessler DI et al. Shivering and shivering-like tremor during labor with and without epidural analgesia. Anesthesiology 1999; 90: 1609–1616. ref tremor has been observed in women during labor.


