Postoperative hypothermia and mortality in critically ill adults: review and meta-analysis

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KEY WORDS

hypothermia, core temperature, hospital mortality, intensive care unit, postoperative, critically ill.

ABSTRACT

Objective
To identify, appraise and synthesise published literature about hospital mortality associated with inadvertent postoperative hypothermia of adult patients directly transferred to the Intensive Care Unit (ICU) after surgery.

Design
Systematic literature review and meta-analysis.

Methods
Using key terms, a search was conducted in English-language, peer-reviewed journals indexed by CINAHL, PubMed and Cochrane Database focusing on articles published between 1980 and 2010. Data extraction and quality appraisal was performed. After evaluating heterogeneity among studies, quantitative synthesis was applied where possible.

Results
Seven observational studies met the inclusion criteria. In five of them, hospital mortality was significantly higher in hypothermic patients. Unadjusted odds ratio of core temperature<35^{0}C on hospital mortality was combined in a meta-analysis and the pooled estimate was 3.29 (95% confidence interval 1.58-6.85). In the multivariate level, independent associations between hypothermia and mortality were detected in four studies.

Conclusions
Existing evidence supports the positive association between postoperative hypothermia and hospital mortality in surgical ICU patients. Effective hypothermia prevention can be crucial for improving outcomes of this population, but further research is needed for confirming the independent contribution of hypothermia on mortality.

INTRODUCTION

Hypothermia is defined as body core temperature (T_c) decrease greater than one standard deviation below the mean value, under resting conditions in a thermoneutral environment (Buggy and Crossley 2000). T_c refers to core thermal compartment and normally ranges between 36.4-37.5^{0}C (Kempainen and Brunette 2004). Although there is no consensus concerning hypothermia threshold, hypothermia is generally considered to appear at a T_c<36^{0}C or <35^{0}C. During the perioperative period, incidence of inadvertent hypothermia may reach up to 70% (Burger and Fitzpatrick 2009), mainly coming as a result of body surface exposure to low ambient temperature and increased heat loss to the environment (Arndt 1999). In addition, vasodilation and lack of muscular tone, due to the action of general anaesthetic agents or regional anaesthesia, allows internal heat flow to periphery, resulting thus in T_c decrease (Sessler 2000).

Even mild hypothermia (32-35^{0}C) can be associated with adverse perioperative outcomes (Sessler 2001). Cold-induced post-anaesthetic shivering refers to involuntary contractions of small skeletal muscles (Buggy and Crossley 2000). In combination with increased catecholamine secretion due to thermal discomfort, and a left shift in oxyhemoglobin dissociation curve, shivering results in considerable increases in the heart, respiratory and metabolic rate (Sessler 2001). By raising oxygen consumption and cardiac activity, shivering may trigger myocardial ischaemia, especially in patients with pre-existing cardiovascular diseases (Frank et al 1997; Kurz et al 1995).

Besides increased cardiac morbidity, severe complications of mild perioperative hypothermia include increased blood loss (Winkler et al 2000) and high incidence of surgical infections (Kurz et al 1996). Increased allogeneic transfusion requirement can be a result of coagulation disorders, including the inhibition of normal platelet or clotting factor enzyme function, and fibrinolytic activity (Reynolds et al 2008; Sessler 2001). Local tissue vasoconstriction, decreased blood perfusion and oxygen availability, and suppression of immune system activity can be followed by impaired surgical wound healing and increased infection risk (Kumar et al 2005; Reynolds et al 2008).

Despite the documented hypothermia complications, association between inadvertent perioperative hypothermia and mortality has attracted little attention. In a recent large cohort study, perioperative hypothermia was not identified as an independent risk factor for mortality at 48 hours or 30 days after surgery (Fecho et al 2008). However, postoperative patients who need intensive care treatment can be particularly susceptible to hypothermia complications. Thus, the aim of this paper was to present a systematic literature review and meta-analysis of the association between inadvertent postoperative hypothermia and mortality of patients directly transferred to the Intensive Care Unit (ICU) after surgery.

METHODS

Search strategy and selection criteria

Articles published between January 1980 and June 2010 in English-language peer-reviewed journals indexed by the Cumulative Index for Nursing and Allied Health Literature (CINAHL), PubMed (National Library of Medicine) and Cochrane Database, were systematically searched for clinical studies on inadvertent hypothermia and mortality of patients transferred to the ICU after surgery. Online searches took place at the first week of June 2010. Additional articles were retrieved through hand-searches, from reference lists of online found articles. A combination of the following search terms was used: hypothermia, temperature, postoperative, surgery/surgical, mortality, intensive/critical care unit, ICU/CCU, critically ill. Specific criteria for considering studies for this review were:

- study subjects: adult, postoperative patients directly transferred to surgical or general ICUs after surgery;
- study design: observational, prospective or retrospective, single-or multi-centre;
- exposure: early postoperative hypothermia, evident on ICU admission or at the first

temperature measurement after ICU admission. Hypothermia was generally defined as T_c<36⁰C measured at any appropriate site; T_c threshold for hypothermia could differ among studies; and

- outcome measure: hospital mortality.

Retrieved studies were screened for inclusion by two independent reviewers (P.K., N.S.) by using titles and abstracts. Discrepancies between reviewers were resolved by discussion. The full text of selected articles was obtained and thoroughly read by both reviewers for a final determination regarding eligibility of each study for inclusion.

Data analysis and synthesis

Main study characteristics and findings were summarised in tables. Quantitative synthesis method was applied to a limited extent, according to the number of studies that reported comparable exposures. Due to the small number of included studies, both Q statistic and I^2 index were used for evaluating heterogeneity among studies, with a p value of Q statistic <0.10 and a value of I^2>50% indicating significant heterogeneity (Huedo-Medina et al 2006). Study findings were reported as odds ratios (ORs). A Forest plot was constructed to describe the range and distribution of effects across studies, and unadjusted ORs were pooled. Since heterogeneity was relatively high among studies, ORs were combined with DerSimonian and Laird random effects model. Appraisal criteria for the quality of studies were discussed. Data analysis was conducted using Comprehensive Meta-Analysis 2.0 (Biostat; Englewood, NJ).

RESULTS

Study characteristics and quality

Online searches revealed 18 potentially relevant citations. Six articles were selected based on abstract evaluation (12 were excluded, mainly as duplicate entries) and the searches of their reference lists revealed five citations. Full text of these 11 articles was evaluated and four articles were excluded. Of these, one was a preliminary report of an already included study, in two there was no separate report on surgical patients admitted to the ICU, while in the rest one, there was no separate report on patients admitted to the ICU after surgery. Thus, seven articles finally met the inclusion criteria for this review.

Table 1: Main characteristics of reviewed studies

Author (year)	Study design / country	Study subjects	Hypothermia definition / incidence	Tc measurement site
Slotman et al (1985)	Retrospective, single-center / USA	100 pts after general, non-cardiac surgery)	T_c<36⁰C at 2 hours after the end of surgery / 39.2%	Esophagus / rectum
Bush et al (1995)	Prospective, single-center / USA	262 pts after elective abdominal aortic aneurysm repair	T_c<34.5⁰C on ICU admission / 25.2%	Pulmonary artery
Insler et al (2000)	Retrospective, single-center / USA	5,701 pts after coronary artery bypass grafting with cardiopulmonary bypass	T_c<36⁰C on ICU admission / 28.0%	Bladder
Kongsayreepong et al (2003)	Prospective, single-center / Thailand	194 pts after elective or emergency non-cardiac surgery	T_c<36⁰C on ICU admission / 57.1% of pts had T_c<36⁰C, 41.3% had T_c<35.5⁰C, 28.3% had T_c<35⁰C	Tympanic membrane (thermometer)
Abelha et al (2005)	Prospective, single-center / Portugal	185 pts after elective or emergency non-cardiac surgery (non-neurosurgical)	T_c<35⁰C on ICU admission / 57.8%	Tympanic membrane (thermometer)
Inaba et al (2009)	Prospective, single-center / USA	1,252 pts after laparotomy / thoracotomy due to trauma	T_c<35⁰C on ICU admission / 15.1% of pts had T_c<35⁰C, 4.9% had T_c<33⁰C	Not defined
Karalapillai et al (2009)	Retrospective, single-center / Australia	5,050 pts after cardiac (23.8%) and general surgery (76.2%)	T_c<36⁰C within 24 hours of ICU admission / 35% of pts had T_c<36⁰C, 5.8% had T_c<35⁰C	Tympanic membrane (thermometer)

ICU: Intensive Care Unit, pts: patients, T_c: core temperature

Four studies were conducted in USA, with the remaining being conducted in Australia, Thailand and Portugal (table 1). All studies were single-centre, with four of them employing prospective data collection. Hypothermia was defined as T_c<36⁰C in four studies; among them, Karalapillai et al (2009) and Kongsayreepong et al (2003) also provided data for T_c<35⁰C. Hypothermia was defined as T_c<35⁰C in two studies and T_c<34.5⁰C in one study. In five studies, T_c measurements for defining hypothermia were conducted on ICU admission. Hypothermia incidence ranged between 28-57.1% when hypothermia was defined as T_c<36⁰C, and between 15-57.8% when it was defined as T_c<35⁰C.

Besides data collection method, the quality of reviewed studies also differed according to the number and subgroups of patients included, and temperature measurement site used (table 1). Four studies employed small convenience samples ranging between 100-262 patients, while in the other three the samples were considerably larger (1,252-5,701 patients). Only one study enrolled both cardiac and general surgery patients and three studies enrolled non-cardiac, general surgery patients. In three studies, T_c was measured at tympanic membrane. Although a widely accepted method, infrared tympanic thermometry has been considered to be less accurate and reliable than the other T_c measurement methods (thermistors at pulmonary artery, bladder, oesophagus and rectum) (O'Grady et al 2008).

Study findings

Overall hospital mortality ranged between 1.8-15.7% (table 2). Irrespective from the hypothermia definition threshold, unadjusted hospital mortality of hypothermic patients was significantly higher in five studies, while it was remarkably higher in the other two studies, without reaching statistical significance (Abelha et al 2005; Kongsayreepong et al 2003). Of importance, in the studies of Karalapillai et al (2009) and Kongsayreepong et al (2003), ORs for hospital mortality were higher for T_c<35⁰C compared with ORs for T_c<36⁰C. Likewise, in the study of Inaba et al (2009), OR for hospital mortality was higher for T_c<33⁰C compared with OR for T_c<35⁰C.

Table 2: Findings of reviewed studies

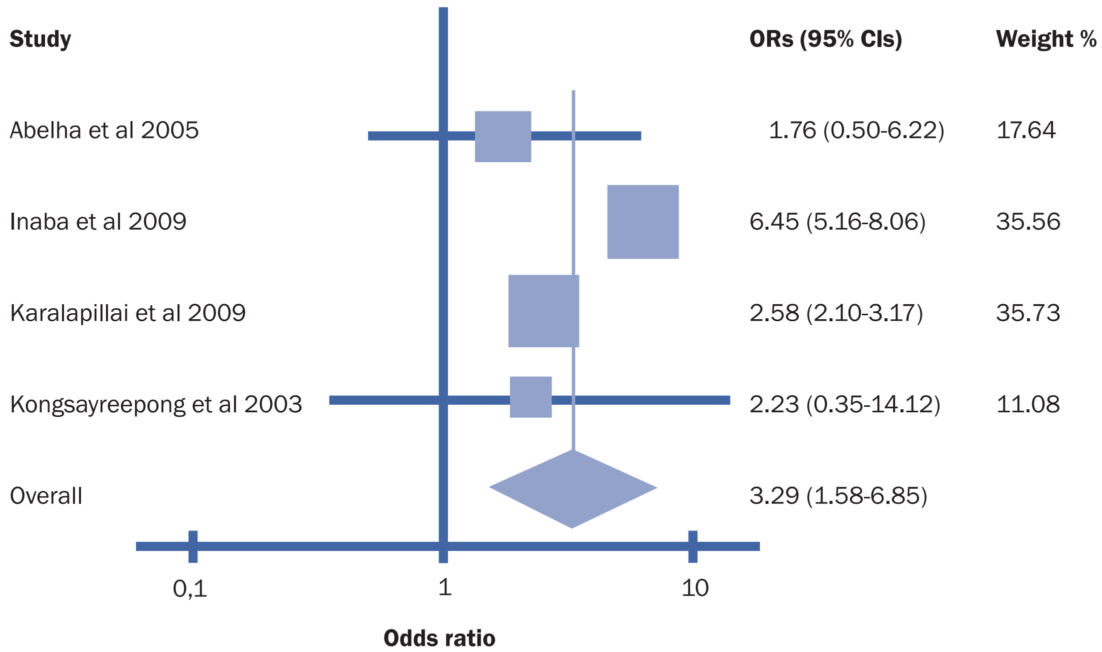
Author (year)	Overall hospital mortality	Unadjusted hospital mortality of hypothermic vs normothermic pts / OR (95% CI)	Adjusted hospital mortality
Slotman et al (1985)	12.2%	31.8% vs 4.6% / 6.84 (1.31-35.74), *p*=0.011	-
Bush et al (1995)	4.2%	12.1% vs 1.5% / 8.87 (2.28-34.54), *p*<0.01	T_c<34.5⁰C was associated with multiple organ dysfunction (*p*=0.030), which was a significant predictor of death (*p*=0.003)
Insler et al (2000)	1.8%	Pts with T_c<36⁰C had a higher mortality, *p*=0.02 (univariate ORs not presented)	After excluding pts <35⁰C and >37⁰C: pts <36⁰C had a higher mortality (*p*=0.02)
Kongsayreepong et al (2003)	6.2%	For pts with T_c<36⁰C: 2.09 (0.54-8.14), *p*=0.279 For pts with T_c<35.5⁰C: 1.77 (0.52-6.01), *p*=0.358 For pts with T_c<35⁰C: 2.23 (0.65-7.67), *p*=0.191	-
Abelha et al (2005)	15.7%	18.7% vs 11.5% / 1.76 (0.76-4.11), p=0.190	-
Inaba et al (2009)	11.8%	For pts with T_c<35⁰C: 35.1% vs 7.7% / 6.45 (4.44-9.39), *p*<0.001 For pts with T_c<33⁰C: 55.0% vs 10.4% / 10.53 (5.50-20.17), *p*<0.001	OR (95% CI) for <35⁰C: 3.15 (1.88-5.27), *p*<0.001
Karalapillai et al (2009)	6.8%	For pts with T_c<36⁰C: 8.9% vs 5.6% / 1.64 (1.32-2.05), *p*<0.001 For pts with T_c<35⁰C: 14.7% vs 6.3% / 2.58 (1.83-3.65), *p*<0.001	OR (95% CI) per 1⁰C decrease: 1.83 (1.28-2.60), *p*<0.001

ICU: Intensive Care Unit, pts: patients, OR: odds ratio, CI: confidence interval, T_c: core temperature

For the hypothermia definition threshold of <36⁰C, unadjusted ORs for hospital mortality in hypothermic patients extracted from three studies (Karalapillai et al 2009; Kongsayreepong et al 2003; Slotman et al 1985) demonstrated significant heterogeneity (Q=4.874, p=0,087, I^2=58.969%), thus these could not be combined in a meta-analysis. Two of these studies showed significantly higher ORs for hospital mortality in hypothermic patients. In the study of Insler et al (2000), unadjusted hospital mortality was also significantly higher in patients with T_c<36⁰C, but ORs were not presented. For the hypothermia definition threshold <35⁰C, unadjusted ORs for hospital mortality in hypothermic patients extracted from four studies (Inaba et al 2009; Karalapillai et al 2009; Abelha et al 2005; Kongsayreepong et al 2003) did not demonstrate significant heterogeneity (Q=5.008, *p*=0,171, I^2=40.099%) and were combined in a Forest plot (figure 1). Two of these studies showed significantly higher ORs for hospital mortality in hypothermic patients, with an overall OR of 3.29 (95% confidence interval, 1.58-6.85).

Multivariate analyses were conducted in four studies. T_c<35⁰C in the study of Inaba et al (2009) and T_c<36⁰C in the study of Insler et al (2000) was independently associated with higher hospital mortality (*p*<0.001). In the study of Karalapillai et al (2009), T_c as a continuous variable was independently associated with higher hospital mortality (*p*<0.001). In the study of Bush et al (1995), T_c<34.5⁰C was independently associated with longer hospital length of stay (*p*=0.047) and risk for multiple organ dysfunction (*p*=0.030). Multiple organ dysfunction after hypothermia was a significant predictor of death (*p*=0.003).

Figure 1: Forest plot with odds ratios (ORs) and 95% confidence intervals (CIs) of hospital mortality for patients with core temperature <35⁰C



DISCUSSION

This systematic review investigated the associations between postoperative inadvertent hypothermia and hospital mortality of patients directly transferred to the ICU after surgery. Findings from four studies indicated a significantly higher pooled unadjusted OR for mortality for T_c<35⁰C, while significantly higher mortality for T_c<36⁰C was reported in three studies. In addition, three studies indicated an increase in unadjusted mortality with decreasing thresholds of T_c. Existing evidence also provided considerable suspicion that T_c below normal can be an independent predictor of mortality. In the multivariate level, significant positive associations between hypothermia and mortality were reported in three studies, with a fourth study reporting independent associations between hypothermia, multiple organ dysfunction and subsequent mortality.

Diverse patient subgroups enrolled among studies, in combination with differences in T_c measurement methods and hypothermia prevention methods used, are possibly responsible for the considerable variation in hypothermia incidence among studies. The use of a higher T_c threshold for defining hypothermia can be justified in cardiac surgery patients, who are actively warmed during cardiopulmonary bypass, and are expected to be warmer on ICU admission than non-cardiac surgery ones. This hypothesis was corroborated by a prospective audit (Karalapillai and Story 2008), in which a significantly lower proportion of cardiac surgery patients had T_c<36^{0}C on ICU admission (31% vs 55% in non-cardiac surgery patients, p=0.004).

In all included studies, patient outcome used was mortality during hospitalisation. This is considered to be more reliable than ICU mortality, which can be influenced by decisions to discharge patients from ICU. Mortality has the most robust operational definition as an outcome measure, has been commonly used for safety assessment of patient care and is expected to be more sensitive in case its rate is high, as in critically ill population (Numata et al 2006). However, due to differences in clinical severity among patients, individual mortality risk is a major confounding factor that has to be adjusted when mortality is studied. Otherwise, considering that severely ill patients are more susceptible to hypothermia, high clinical severity may account for high incidence of both death and hypothermia. In the reviewed studies that presented multivariate analyses, adjustment included factors associated with patient baseline characteristics or abnormal physiologic variables. However, none of them included standardised scores for stratifying overall patient mortality risk, and this may have led to incomplete risk adjustment.

Can early hypothermia of critically ill surgical patients not only be a marker but also a mediator of mortality? Severe complications of mild hypothermia could account for direct negative effects on patient survival. During hospitalisation, attributable mortality of surgical infections has been reported to be particularly high (Kirkland et al 1999). Similarly, in non-cardiac surgery patients, perioperative cardiac events have been followed by a considerably high mortality rate (Deveraux et al 2005). As regards allogeneic blood transfusion, this can be followed by severe complications, mainly transfusion-related acute lung injury and hemolytic transfusion reactions, which are also associated with high mortality (Vamvakas and Blajchman 2009).

Associations between hypothermia and adverse outcomes have also been reported for other patient groups. In a mixed medical-surgical ICU population (Peres Bota et al 2004), ICU mortality was significantly higher in patients with T_c<36^{0}C at some time during ICU stay (33.3% vs 10.3%, p<0.01). Although independent associations were not investigated, organ failure was significantly more common in hypothermic patients, raising the possibility that higher mortality was rather attributed to their worse physical status. In trauma patients, hypothermia on Emergency Department admission was independently associated with higher hospital mortality in two studies that analysed data from the National Trauma Data Banks (Martin et al 2005; Shafi et al 2005). However, trauma patients often have multiple physiological derangements, being in critical condition on hospital admission, and may not be comparable to postoperative ICU patients, who are expected to be healthy enough to sustain an operation. In addition, highest mortality rates were reported for T_c<32^{0}C in trauma patients, while postoperative patients generally manifest mild hypothermia with T_c barely reaching such low values.

Clinical guidelines for preventing perioperative hypothermia have been developed by the American Society of PeriAnesthesia Nurses (2001) and the American College of Surgeons (Forbes et al 2009). Despite these guidelines, hypothermia incidence in patients transferred to the ICU after surgery has been remarkably high in recent studies. Continuous perioperative T_c monitoring by the use of accurate and reliable methods along with maintaining warm operating room temperature are the first steps for preventing hypothermia in the high-risk population of surgical ICU patients. In addition, since these patients generally sustain extensive surgical procedures or have high pre-existing comorbidity, a combination of active warming methods is needed. Forced air warming is a non-invasive, low-cost, easy to apply, effective method, and its use is recommended both intraoperatively and preoperatively, to prevent heat redistribution. Heating crystalloid solutions or blood / blood products is necessary, especially when large amounts of fluids are administered, while airway rewarming with humidified oxygen decreases evaporative heat loss (McCullough and Arora 2004). Implementing a perioperative normothermia care plan is strongly recommended, since it has been shown to decrease hypothermia incidence of patients undergoing elective abdominal operations in post-anaesthesia care unit from 39% to 2% (Forbes et al 2008).

Study limitations

A major limitation of this literature review was the small number of original studies included and methodological weaknesses identified in some of them, such as retrospective design. All studies were single-centre, most of them focused on specific surgical patient subgroups, while four studies were underpowered. Another four studies were coming from the same country which, in combination with the inclusion of articles published only in English language, may limit generalisability of findings to other countries. A second limitation was that the meta-analysis performed should be seen with caution. Although high proportions of positive results are expected to be published, analytical methods for studying publication bias were not used. Moreover, the number of studies combined was very small, while study heterogeneity was considerable, although not significant. Finally, it cannot be excluded that hypothermia-mortality associations reported in some studies were due to non-adjusted confounders.

CONCLUSIONS AND RECOMMENDATIONS

This review has confirmed that, in patients transferred to the ICU after surgery, hospital mortality is higher among those with early inadvertent hypothermia. Considerable possibility was also raised that hypothermia can be a mediator of mortality due to its well-described severe complications. The importance of effective perioperative hypothermia prevention has been previously highlighted in terms of decreasing morbidity, but it seems further to be a priority in surgical critically ill patients, since it may have a beneficial effect on their survival. Being at the front line in the management of perioperative hypothermia, nursing personnel are called to be aware of hypothermia complications and vigilant for signs/symptoms of hypothermia, actively participate to the application of preventive measures for hypothermia and evaluate the effectiveness of available warming methods.

Adequately powered, prospective studies are necessary for confirming the association between inadvertent hypothermia and mortality in postoperative ICU patients. To elucidate whether hypothermia independently contributes to mortality, future studies should control for patient clinical severity, as well as for other potential confounders, such as age, infections or sepsis, complications not associated with hypothermia, injury severity, magnitude of surgery and baseline characteristics. In case an independent association between hypothermia and mortality is confirmed, the impact of hypothermia degree on mortality should be investigated. Moreover, since ICU admission T_c may poorly correlate with T_c intraoperative values, hypothermia during surgery should separately be studied for associations with adverse outcomes. Evaluating hypothermia-mortality associations among subgroups of postoperative ICU patients is also recommended, especially for patients after cardiac, emergency or trauma surgery, since hypothermia threshold for increased mortality risk may differ among these subgroups. Determining the effectiveness of intraoperative preventive measures for hypothermia with regard to adverse patient outcomes can finally be suggested.

REFERENCES

Abelha, F.J., Castro, M.A., Neves, A.M., Landeiro, N.M. and Santos, C.C. 2005. Hypothermia in a surgical intensive care unit. *BMC Anesthesiology*, 5:7.

American Society of PeriAnesthesia Nurses 2001. ASPAN clinical guideline for the prevention of unplanned perioperative hypothermia. *Journal of PeriAnesthesia Nursing,* 16(5):305-314.

Arndt, K. 1999. Inadvertent hypothermia in the OR. *AORN Journal,* 70(2):204-214.

Buggy, D.J.and Crossley, A.W. 2000. Thermoregulation, mild perioperative hypothermia and postanaesthetic shivering. *British Journal of Anaesthesia,* 84(5):615-628.

Burger, L. and Fitzpatrick, J. 2009. Prevention of inadvertent perioperative hypothermia. *British Journal of Nursing,* 18(18):1114, 1116-1119.

Bush, H.L., Hydo, L.J., Fischer, E., Fantini, G.A., Silane, M.F. and Barie, P.S. 1995. Hypothermia during elective abdominal aortic aneurysm repair: the high price of avoidable morbidity. *Journal of Vascular Surgery,* 21(3):392-402.

Deveraux, P.J., Goldman, L., Cook, D.J., Gilbert, K., Leslie, K. and Guyatt, G.H. 2005. Perioperative cardiac events in patients undergoing noncardiac surgery: a review of the magnitude of the problem, the pathophysiology of the events and methods to estimate and communicate risk. *Canadian Medical Association Journal,* 173(6):627-634.

Fecho, K., Lunney, A.T., Boysen, P.G., Rock, P. and Norfleet, E.A. 2008. Postoperative mortality after inpatient surgery: incidence and risk factors. *Therapeutics and Clinical Risk Management,* 4(4):681-688.

Forbes, S.S., Stephen, W.J., Harper, W.L., Loeb, M., Smith, R., Christoffersen, E.P. and McLean, R.F. 2008. Implementation of evidence-based practices for surgical site infection prophylaxis: results of a pre- and post-intervention study. *Journal of the American College of Surgeons,* 207(3):336-341.

Forbes, S.S., Eskicioglu, C., Nathens, A.B., Fenech, D.S., Laflamme, C., McLean, R.F. and McLeod, R.S. Best Practice in General Surgery Committee, University of Toronto. 2009. Evidence-based guidelines for prevention of perioperative hypothermia. *Journal of the American College of Surgeons,* 209(4):492-503.

Frank, S.M., Fleisher, L.A., Breslow, M.J., Higgins, M.S., Olson, K.F., Kelly, S. and Beattie, C. 1997. Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. A randomized clinical trial. *Journal of the American Medical Association,* 277(14):1127-1134.

Huedo-Medina, T.B., Sanchez-Meca, J., Marin-Martinez, F. and Botella, J. 2006. Assessing heterogeneity in meta-analysis: Q statistic or I^2 index? *Psychological Methods,* 11(2):193-206.

Inaba, K., Teixeira, P.G., Rhee, P., Brown, C., Salim, A., DuBose, J., Chan, L.S. and Demetriades, D. 2009. Mortality impact of hypothermia after cavitary explorations in trauma. *World Journal of Surgery,* 33(4):864-869.

Insler, S.R., O'Connor, M.S., Leventhal, M.J., Nelson, D.R. and Starr, N.J. 2000. Association between postoperative hypothermia and adverse outcome after coronary artery bypass surgery. *Annals of Thoracic Surgery,* 70(1):175-181.

Karalapillai, D. and Story, D. 2008. Hypothermia on arrival in the intensive care unit after surgery. *Critical Care and Resuscitation*, 10(2):116-119.

Karalapillai, D., Story, D.A., Calzavacca, P., Licari, E., Liu, Y.L. and Hart, G.K. 2009. Inadvertent hypothermia and mortality in postoperative intensive care patients: retrospective audit of 5050 patients. *Anaesthesia,* 64(9):968-972.

Kempainen, R.R. and Brunette, D.D. 2004. The evaluation and management of accidental hypothermia. *Respiratory Care,* 49(2):192-205.

Kirkland, K.B., Briggs, J.P., Trivette, S.L., Wilkinson, W.E. and Sexton, D.J. 1999. The impact of surgical site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. *Infection Control and Hospital Epidemiology*, 20(11):725-730.

Kongsayreepong, S., Chaibundit, C., Chadpaibool, J., Komoltri, C., Suraseranivongse, S., Suwannanonda, P., Raksamanee, E.O., Noocharoen, P., Silapadech, A., Parakkamodom, S., Pum-In, C., Sojeoyya, L. 2003. Predictor of core hypothermia and the surgical intensive care unit. *Anesthesia & Analgesia,* 96(3):826-833.

Kumar, S., Wong, P.F., Melling, A.C. and Leaper, D.J. 2005. Effects of perioperative hypothermia and warming in surgical practice. *International Wound Journal,* 2(3):193-204.

Kurz, A., Sessler, D.I., Narzt, E., Bekar, A., Lenhardt, R., Huemer, G. and Lackner, F. 1995. Postoperative hemodynamic and thermoregulatory consequences of intraoperative core hypothermia. *Journal of Clinical Anesthesia,* 7(5):359-366.

Kurz, A., Sessler, D.I. and Lenhardt, R.A. 1996. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of wound infections and temperature group. *New England Journal of Medicine*, 334(19):1209-1215.

Martin, R.S., Kilgo, P.D., Miller, P.R., Hoth, J.J., Meredith, J.W. and Chang, M.C. 2005. Injury-associated hypothermia: an analysis of the 2004 National Trauma Data Bank. *Shock,* 24(2):114-118.

McCullough, L. and Arora, S. 2004. Diagnosis and treatment of hypothermia. *American Family Physician,* 70(12):2325-2332.

Numata, Y., Schulzer, M., van der Wal, R., Globerman, J., Semeniuk, P., Balka, E. and Fitzgerald, J.M. 2006. Nurse staffing levels and hospital mortality in critical care settings: literature review and meta-analysis. *Journal of Advanced Nursing,* 55(4):435-448.

O'Grady, N.P., Barie, P.S., Bartlett, J.G., Bleck, T., Carroll, K., Kalil, A.C., Linden, P., Maki, D.G., Nierman, D., Pasculle, W. and Masur, H. American College of Critical Care Medicine, Infectious Diseases Society of America. 2008. Guidelines for evaluation of new fever in critically ill adult patients. 2008 update from the American College of Critical Care Medicine and the Infectious Diseases Society of America. *Critical Care Medicine,* 36(4):1330-1349.

Peres Bota, D., Lopes Ferreira, F., Melot, C. and Vincent, J.L. 2004. Body temperature alterations in the critically ill. *Intensive Care Medicine,* 30(5):811-816.

Reynolds, L., Beckmann, J. and Kurz, A. 2008. Perioperative complications of hypothermia. Best practice and research. *Clinical Anaesthesiology,* 22(4):645-657.

Sessler, D.I. 2000. Perioperative heat balance. *Anesthesiology,* 92(2):578-596.

Sessler, D.I. 2001. Complications and treatment of mild hypothermia. *Anesthesiology,* 95(2):531-543.

Shafi, S., Elliott, A.C. and Gentilello, L. 2005. Is hypothermia simply a marker of shock and injury severity or an independent risk factor for mortality in trauma patients? Analysis of a large National Trauma Registry. *The Journal of Trauma,* 59(5):1081-1085.

Slotman, G.J., Jed, E.H. and Burchard, K.W. 1985. Adverse effects of hypothermia in postoperative patients. *American Journal of Surgery,* 149(4):495-501.

Vamvakas, E.C. and Blajchman, M.A. 2009. Transfusion-related mortality: the ongoing risks of allogeneic blood transfusion and the available strategies for their prevention. *Blood,* 113(15):3406-3417.

Winkler, M., Akça, O., Birkenberg, B., Hetz, H., Scheck, T., Arkiliç, C.F., Kabon, B., Marker, E., Grübl, A., Czepan, R., Greher, M., Goll, V., Gottsauner-Wolf, F., Kurz, A. and Sessler, D.I. 2000. Aggressive warming reduces blood loss during hip arthroplasty. *Anesthesia & Analgesia,* 91(4):978-984.