

Perioperative hypothermia and myocardial injury after non-cardiac surgery: abridged secondary publication

MTV Chan *, CKM Lam, BCP Cheng, T Gin, CW Cheung

KEY MESSAGES

1. In patients who were randomly assigned to either aggressive warming with targeted intraoperative temperatures of 37.0°C or routine thermal care with temperatures around 35.5°C, there were similar incidences of myocardial injury (9.9% vs 9.6%), surgical site infection (7.2% vs 6.3%), and need for transfusion (10% vs 9.5%).
2. Over a range of 1.5°C—from very mild hypothermia to full normothermia—there was no evidence of any substantial effect on patient outcomes. The maintenance of core temperature of $\geq 35.5^\circ\text{C}$ in surgical patients appears to be sufficient to avoid major hypothermia-related complications.

Hong Kong Med J 2023;29(Suppl 4):S36-8

HMRP project number: 06170306

¹ MTV Chan, ² CKM Lam, ² BCP Cheng, ¹ T Gin, ³ CW Cheung

¹ Department of Anaesthesia and Intensive Care, The Chinese University of Hong Kong, Hong Kong SAR, China

² Department of Anaesthesia and Operating Theatre Services, Tuen Mun Hospital, Hong Kong SAR, China

³ Department of Anaesthesiology, School of Clinical Medicine, The University of Hong Kong, Hong Kong SAR, China

* Principal applicant and corresponding author: mtvchan@cuhk.edu.hk

Background

Myocardial injury is among the most common causes of death within 1 month of non-cardiac surgery. Hypothermia increases sympathetic activation, promotes tachycardia, and causes hypertension; all of these can lead to myocardial injury. Mild hypothermia (35.5°C) increases morbid myocardial outcomes. Moderate perioperative hypothermia (34.5°C) increases the risk of surgical site infections and increases transfusion requirements. Consequently, international guidelines recommend maintaining normothermia in surgical patients, and active intraoperative warming has become routine. We tested the primary hypothesis that aggressive intraoperative warming reduces the incidence of major cardiovascular complications in patients undergoing major non-cardiac surgery.

Methods

In a multicentre, parallel group, superiority trial (perioperative hypothermia and myocardial injury after non-cardiac surgery trial [PROTECT]), adult patients at risk for postoperative cardiovascular complications who underwent major non-cardiac surgery at 12 sites in China and at the Cleveland Clinic in the United States were randomly assigned

to receive either ‘aggressive warming’ to achieve a target intraoperative core temperature of 37°C or ‘routine thermal management’ with rescue intraoperative forced-air warming to prevent core temperature from decreasing below 35.5°C. Patient characteristics and perioperative details were recorded. In addition, venous blood samples for plasma cardiac troponin assays were collected before surgery and on each of the first 3 days after surgery.

The primary outcome was a composite of myocardial injury (elevated troponin because of ischaemia), non-fatal cardiac arrest, and all-cause mortality within 30 days of surgery. Secondary 30-day outcomes were deep or organ-space surgical site infection (ie, serious wound infection), intraoperative transfusion requirement, duration of hospitalisation, and readmission.

Results

In total, 5013 patients (mean age, 67 years, 33% women) were randomly assigned to receive ‘aggressive warming’ (n=2507) or ‘routine thermal management’ (n=2506) during surgery (52% of surgeries were laparoscopic intra-abdominal procedures). The final intraoperative temperatures in the respective groups were 37.1±0.3°C and 35.6±0.3°C. The two groups

were similar in terms of the incidences of major cardiovascular complications (9.9% vs 9.6%, relative risk [RR]=1.04, 95% confidence interval [CI]=0.87-1.24, P=0.69), serious wound infection (7.2% vs 6.3%, RR=1.13, 95% CI=0.87-1.47, P=0.25), transfusion requirement (10.2% vs 9.5%, RR=1.07, 95% CI=0.87-1.33, P=0.41), duration of hospitalisation (hazard ratio=0.98, 95% CI=0.91-1.05, P=0.46), and readmission (6.5% vs 5.5%, RR=1.19, 95% CI=0.89-1.57, P=0.13).

Discussion

PROTECT is more than tenfold larger than prior thermoregulatory trials, most of which were conducted >20 years ago. Despite a difference of 1.5°C (ranging from very mild hypothermia to full normothermia), there was no significant or clinically meaningful difference in the primary composite outcome of myocardial injury, non-fatal cardiac arrest, and all-cause mortality within 30 days after surgery. The incidence of myocardial infarction was also similar. Furthermore, the 95% CIs around the primary outcome were relatively small, indicating that a type II error was relatively unlikely.

Our findings differ from the those of prior trials in which mild hypothermia did not influence postoperative cardiovascular events.¹ However, the previous trials had few events and did not use the sensitive cardiac troponin marker to detect myocardial injury; therefore, they were prone to bias.² We also found no difference in the incidences of serious wound infection between groups. This finding also distinctly differed from that of previous observational analyses^{3,4} and a randomised trial.⁵ Importantly, the extent of hypothermia was more severe in previous studies. Furthermore, the previous studies had a small sample size and wide confidence intervals; its finding of a threefold reduction in the incidence of infection seems biologically implausible. The results of the present study indicate that mild hypothermia of $\geq 35.5^{\circ}\text{C}$ did not result in serious wound infections, although more severe hypothermia might have different effects.

There were some limitations in this study. First, the preoperative and intraoperative teams could not be blinded to thermal management. Similarly, patients knew that they were pre-warmed, although they were not informed about possible consequences. However, the primary outcome (a composite of myocardial injury, non-fatal cardiac arrest, and all-cause mortality) was objective and unlikely to be influenced by patient perception of warming.

Secondary outcomes were also objective, and they were unlikely to be influenced by the lack of blinding. Second, we did not evaluate some thermoregulatory responses such as postoperative thermal comfort or shivering. However, both complications are minor and transient. Similar to other trials, our conclusions are directly applicable to the enrolled patients and can reasonably extrapolated to similar patients. Results may differ in obese patients, patients undergoing emergency surgery, and patients with greater risk of cardiovascular complications.

Conclusions

In patients randomly assigned to receive either 'aggressive warming' or 'routine thermal management' during surgery, there were similar incidences of composite major cardiovascular outcomes within 30 days after surgery. The incidences of serious wound infection and transfusion were also similar, as were the duration of hospitalisation and incidence of hospital readmission. The maintenance of core temperature of $\geq 35.5^{\circ}\text{C}$ in surgical patients appears to be sufficient to avoid major perioperative adverse outcomes.

Funding

This study was supported by the Health and Medical Research Fund, Health Bureau, Hong Kong SAR Government (#06170306). The full report is available from the Health and Medical Research Fund website (<https://rfs2.healthbureau.gov.hk>).

Disclosure

The results of this research have been previously published in:

1. Sessler DI, Pei L, Li K, et al. Aggressive intraoperative warming versus routine thermal management during non-cardiac surgery (PROTECT): a multicentre, parallel group, superiority trial. *Lancet* 2022;399:1799-808.

References

1. Frank SM, Fleisher LA, Breslow MJ, et al. Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. A randomized clinical trial. *JAMA* 1997;277:1127-34.
2. Devereaux PJ, Chan MT, Eisenach J, Schricker T, Sessler DI. The need for large clinical studies in perioperative medicine. *Anesthesiology* 2012;116:1169-75.
3. Scott AV, Stonemetz JL, Wasey JO, et al. Compliance with surgical care improvement project for body temperature management (SCIP Inf-10) is associated with improved

- clinical outcomes. *Anesthesiology* 2015;123:116-25.
4. Seamon MJ, Wobb J, Gaughan JP, Kulp H, Kamel I, Dempsey DT. The effects of intraoperative hypothermia on surgical site infection: an analysis of 524 trauma laparotomies. *Ann Surg* 2012;255:789-95.
 5. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. *N Engl J Med* 1996;334:1209-15.