Effect of Intraoperative Hypothermia on Surgical Outcomes after Colorectal Surgery within an Enhanced Recovery after Surgery Pathway

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ABSTRACT

Objective: The adverse effects of intraoperative hypothermia from the published literature were mainly based on non-enhanced recovery after surgery (ERAS) settings. This study aimed to determine association between intraoperative hypothermia and outcomes following colorectal surgery under ERAS pathway.

Methods: A prospectively collected database of patients undergoing elective colorectal surgery under ERAS pathway from 2011 to 2015 was reviewed. Patients were divided into 2 groups: hypothermic group (core temperature <36°C continuously exceeding 30 minutes during an operation) and normothermic group. Short-term outcomes were compared.

Results: This study included 195 patients: 150 (77%) in hypothermic group and 45 (23%) in normothermic group. Rectal surgery (OR=5.15), operative time exceeding 3 hours (OR=3.80), multi-organ resection (OR=3.12) and male gender (OR=2.62) were significant predictors for intraoperative hypothermia. Rates of postoperative complication and wound infection were comparable between hypothermic patients and normothermic patients (23% vs 13%; *p*=0.17 and 6.0 vs 6.7%; *p*=0.87, respectively). Hypothermic patients had a longer time to tolerate normal diet (2.0 days vs 1.3 days; *p*=0.023) but a comparable time to first bowel movement (2.6 days vs 2.6 days; *p*=0.84). Hypothermic patients had a significant longer hospitalization (5.7 days vs 4.4 days; *p*=0.048). A multivariate analysis showed that intraoperative hypothermia was an independent predictor for delayed food intake (OR=2.9, 95%CI=1.2-6.9; *p*=0.014) but not for prolonged hospitalization (OR=1.7, 95%CI=0.7-3.9; *p*=0.207).

Conclusion: Intraoperative hypothermia prolonged time to tolerate food intake after colorectal surgery within an ERAS setting but it did not adversely affect the return of bowel function, wound infection, complication and length of hospitalization.

Keywords: Hypothermia; enhanced recovery after surgery; colon; rectum; surgery; outcomes (Siriraj Med J 2019;71: 52-58)

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INTRODUCTION

During an intraabdominal operation, patient's body temperature decreases as a result of impaired thermoregulatory mechanisms secondary to anesthesia and heat loss through a surgical wound or to the environment.[1] According to the World Health Organization (WHO)[2] and the U.S. Agency for Healthcare Research and Quality,[3] intraoperative hypothermia is defined as a

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core temperature less than 36°C (96.8°F). Intraoperative hypothermia was associated with poor surgical outcomes after major abdominal operations including colorectal surgery.[4-6] It led to increased surgical bleeding and requirement of blood transfusion,[7] higher incidence of cardiac arrhythmia and ischemia,[4] higher rates of surgical site infection and prolonged hospitalization.[5] Maintaining perioperative normothermia in surgical patients is therefore an essential part of several surgical guidelines such as the latest WHO recommendations for surgical site infection prevention[2] and the Enhanced Recovery After Surgery (ERAS) society recommendations for perioperative care in elective colorectal surgery.[8,9]

Since the adverse effects of intraoperative hypothermia in colorectal surgery from the published literature were mainly based on non-ERAS settings,[5,10] strong evidence supporting this association in patients undergoing colorectal operations within an ERAS pathway is lacking. The current study aimed to determine the association between intraoperative hypothermia and surgical outcomes following colorectal surgery within an ERAS pathway.

MATERIALS AND METHODS

Patients

A prospective, observational study of adult patients undergoing elective segmental resection (colectomy and/or proctectomy) within an ERAS pathway from March 2011 to October 2015 in the Faculty of Medicine Siriraj Hospital, Thailand was conducted. Patients with clinical peritonitis or acute colonic obstruction were excluded. The study was approved by the Institutional Ethics Committee and written informed consent was obtained from each patient (Si 014/2013).

Perioperative and operative care

All of the studied patients were operated on and treated by a board-certified colorectal surgeon (the first author) who has applied an ERAS pathway into colorectal surgery since 2010. ERAS strategies in our institute were adopted from the ERAS society recommendations for perioperative care in elective colorectal surgery.[8,9] Some details of our ERAS program have been described previously.[11-13] Briefly, a practice of mechanical bowel preparation, prophylactic antibiotic regimen, prophylaxis of postoperative nausea and vomiting, anastomosis creation with or without stoma formation, analgesic regimen, early enteral feeding and immediate mobilization was standardized. However, there was no standardized protocol of active warming in an operating theater *except* blood warmer was used for intraoperative blood transfusion (if any). Notably, active warming was not standardized in our ERAS protocol due to the cost and availability of related equipment. Patients would be discharged from the hospital if they had no fever, good appetite, satisfactory gastrointestinal recovery and a good level of ambulation. All of the patients were scheduled for follow-up at 7-10 days and 30 days after an operation.

Diagnosis of intraoperative hypothermia

Intraoperative core temperature of the patients was continuously measured after induction of anesthesia using a single esophageal probe which was inserted by a staff anesthesiologist to the distal half of the esophagus. In this study patients were classified into a hypothermic group if their intraoperative core temperature was continuously below 36°C more than 30 minutes. A cut-off period of half an hour in a hypothermic state (< 36°C) was decided based on a previous study of >50,000 surgical patients which showed a trend of hypothermia-associated adverse outcomes from this time point.[14]

Data collection

Data including patient characteristics, operative details, and postoperative outcomes were prospectively collected. Patient characteristics included age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) grade, and ColoRectal Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity (CR-POSSUM) score.[15] Operative details included type of operation, operative time, and estimated blood loss. Overall ERAS protocol compliance of each case was determined based on the ERAS society recommendations for perioperative care in elective colorectal surgery.[8,9] Postoperative outcomes included postoperative complications (graded I-V according to the Clavien-Dindo classification system),[16] surgical site infection (based on the criteria of the U.S. Centers for Disease Control and Prevention),[17] time to first bowel movement, time to tolerate normal diet, length of postoperative stay, death and readmission within 30 days after the operation.

Statistical analysis

All of the data were prepared and compiled using the Statistical Package for the Social Sciences program version 18.0 for Windows (SPSS Inc, Chicago, IL). Continuous variables were expressed as mean ± standard deviation or median (interquartile; IQR), and were compared using the Student t-test or Mann-Whitney U test. Categorical data were expressed as number (percentage) and were compared using the Pearson Chi-square test or Fisher exact probability test. Factors influencing poor surgical outcomes were analyzed using a univariate analysis. Only significant variables from the univariate analysis were included in a multivariate model of logistic regression, and the odds ratio with 95% confidence intervals (95%CI) for each variable was determined. A *p*-value of <0.05 was considered statistically significant.

RESULTS

This study included 195 patients: 150 (77%) in hypothermic group and 45 (23%) in normothermic group. Maximum, minimum and average intraoperative core temperature was significantly lower in the hypothermic group (Table 1). Patients in the hypothermic group tended to had a greater volume of intraoperative IV fluid (2.4 L vs 1.7 L; *p*=0.141) and more median blood loss (200 mL vs 100 mL; *p*=0.074). Patient's characteristics of each group are shown in table 1. Factors strongly associated with intraoperative hypothermia were rectal surgery (OR=5.15, 95%CI=2.25-11.79; *p*<0.001), operative time exceeding 3 hours (OR=3.80, 95%CI=1.82-7.93; *p*<0.001), multi-organ resection (OR=3.12, 95%CI=1.04-9.32; *p*=0.034) and male gender (OR=2.62, 95%CI=1.30-5.26; *p*=0.006).

TABLE 1. Patient's characteristics and intraoperative parameters.

	Hypothermic group (n=150)	Normothermic group (n=45)	P-value
Age, year	64.3 ± 13.0	61.6 ± 13.8	0.227
Male	85 (56.7)	15 (33.3)	0.006*
BMI, kg/m^2	23.3 ± 4.5	23.3 ± 4.7	0.968
ASA class ≥ 3	29 (19.3)	8 (17.8)	0.815
CR-POSSUM predictive mortality, %	1.85 (0.98-3.38)	1.37 (0.95-2.58)	0.382
Hematocrit, %	36.7 ± 5.2	35.9 ± 5.7	0.355
Serum albumin, g/dL	3.8 ± 0.6	3.8 ± 0.6	0.368
Cancer surgery	138 (92.0)	39 (86.7)	0.278
Tumor staging ≥ 3	91 (60.7)	26 (57.8)	0.729
Rectal surgery	79 (52.7)	8 (17.8)	<0.001*
Multi-organ resection	35 (23.3)	4 (8.9)	0.034*
Laparoscopic surgery	23 (15.3)	11 (24.4)	0.158
Epidural analgesia	48 (32.0)	10 (22.2)	0.208
Total IV morphine consumption, mg/kg	0.11 (0-0.57)	0.10 (0-0.50)	0.976
Core temperature, °C			
Maximum	36.0 (35.7-36.3)	36.6 (36.4-36.9)	<0.001*
Minimum	35.4 (35.0-35.7)	36.1 (36.0-36.4)	<0.001*
Average	35.8 (35.4-36.0)	36.5 (36.2-36.6)	<0.001*
Duration of surgery, hour	3.7 ± 1.5	3.1 ± 1.4	0.010*
Intravenous fluid, L	2.4 ± 1.1	1.7 ± 1.0	0.141
Blood loss, mL	200 (100-400)	100 (50-300)	0.074
Intraoperative blood transfusion, yes	20 (13.3)	4 (8.9)	0.426
Overall ERAS protocol compliance[#], %	84.4 ± 6.2	85.8 ± 6.5	0.195

* P-value < 0.05

Values are expressed as mean ± standard deviation, median (interquartile range) or number (percentage).

Abbreviations: ASA = American society of Anesthesiologists, BMI = body mass index, CR-POSSUM = ColoRectal Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity, ERAS = enhanced recovery after surgery, IV = intravenous

#Overall compliance of each patient was determined based on the ERAS® society recommendations for perioperative care in elective colorectal surgery.

The incidences of postoperative complication and wound infection were comparable between hypothermic patients and normothermic patients (23% vs 13%; *p*=0.17 and 6.0 vs 6.7%; *p*=0.87, respectively). One patient in the normothermic group had a 30-day mortality while the other did not (*p*=0.12). Hypothermic patients had a longer time to tolerate normal diet (2.0 days vs 1.3 days; *p*=0.023) but a comparable time to first bowel movement (2.6 days vs 2.6 days; *p*=0.84). Hypothermic patients had a significant longer hospitalization (5.7 days vs 4.4 days; *p*=0.048) (Table 2).

A multivariate analysis adjusted for risk factors associated with delayed time to tolerate normal food (> 2 days) showed that intraoperative hypothermia was an independent predictor (OR=2.9, 95%CI=1.2-6.9; *p*=0.014) (Table 3). For predicting prolonged hospitalization (>5 days), a multivariate analysis showed that postoperative complication (OR=5.2, 95%CI=2.3-11.9; *p*<0.001) and operative time exceeding 3 hours (OR=3.4, 95%CI=1.8-6.4; *p*<0.001) were two significant risk factors. Intraoperative hypothermia was not associated with prolonged hospitalization (OR=1.7, 95%CI=0.7-3.9; *p*=0.207).

TABLE 2. Postoperative outcomes.

	Hypothermic group (n=150)	Normothermic group (n=45)	P-value
Overall complication	34 (22.7)	6 (13.3)	0.174
Complication excluding grade I[#]	19 (12.7)	3 (6.7)	0.265
Wound infection	9 (6.0)	3 (6.7)	0.870
30-day death	0	1 (2.2)	0.231
30-day readmission	5 (3.3)	3 (6.7)	0.389
Time to tolerate normal diet, days	2.0 ± 2.0	1.3 ± 1.3	0.023*
Time to first bowel movement, days	2.6 ± 1.1	2.6 ± 1.1	0.838
Length of hospitalization, days	5.7 ± 4.2	4.4 ± 2.6	0.048*

*P-value < 0.05
Values are expressed as mean ± standard deviation or number (percentage).
#According to the Clavien-Dindo classification of surgical complications

TABLE 3. Multivariate analysis of factors potentially associated with delayed time to tolerate normal diet (>2 days).

	Odds ratio	95% confidential interval	P-value
Intraoperative hypothermia	2.88	1.20-6.90	0.014*
Postoperative complication	1.99	0.97-4.09	0.059
Operative time exceeding 3 hours	1.81	0.97-3.38	0.059
Rectal surgery	1.58	0.86-2.92	0.142
Open surgery	1.32	0.61-2.89	0.482
Hypoalbuminemia	1.04	0.50-2.19	0.912
No epidural analgesia	0.84	0.44-1.64	0.621
Multi-organ resection	0.75	0.34-1.66	0.483

*P-value < 0.05

DISCUSSION

This study of 195 patients showed that intraoperative hypothermia was an independent risk factor for prolonged time to tolerate normal food in patients undergoing elective colorectal surgery. However, there was no association between intraoperative and time to first bowel movement, overall complication, surgical site infection or length of hospitalization. Rectal surgery, operative time exceeding 3 hours, multi-organ resection and male patients perceived greater risks of intraoperative hypothermia.

This study showed that intraoperative hypothermia was associated with delayed time to tolerate normal diet. Hypothermia-associated prolonged GI recovery could be explained by several possible mechanisms. First, the sympathetic nervous system is stimulated during the period of hypothermia to generate heat production and prevent further heat loss[18]. Neurotransmitters of the sympathetic nervous system such as adrenaline and noradrenaline are known to decrease GI motility and reduce luminal secretion.[19,20] Sympathetic stimulation also led to an inhibition of the vagus nerve-mediated gastric contractions[21] and decreased food appetite.[22] Second, the abnormal activities of the sympathetic nervous system in the GI tract may cause gut inflammation and motility disorders.[23] Third, in animal studies cold temperature diminished spontaneous movements of small bowel and depressed acetylcholine-induced contraction thus indicating that the tonic and phasic component of small bowel contraction are sensitive to cold temperature.[24] Although intraoperative hypothermia was an independent predictor for delayed time to tolerate solid food, it did not affect time to first bowel movement or time to discharge patients.

Within an ERAS setting this study failed to demonstrate a correlation between intraoperative hypothermia and postoperative complications including wound infection. These findings are similar to those reported in several large and recent studies examining an association between perioperative hypothermia and surgical site infection following colorectal surgery.[10,25,26] For example, Baucom and her colleagues showed that, regardless of how hypothermia was defined, intraoperative temperature did not predict infectious complications after laparoscopic and open colorectal operations.[10] Linking to the American College of Surgeons National Surgical Quality Improvement Program, Melton et al also did not find any correlation between intraoperative hypothermia and 30-day surgical site infection in 1008 colorectal procedures.[26]

Our findings were in contrast to the 1996 landmark study by Kurz et al which was a randomized prospective trial of routine care versus additional intraoperative warming in 200 patients undergoing open colorectal resection in non-ERAS setting.[5] Kurz et al reported that patients with hypothermia had three times higher rates of wound infection (19% vs 6%) and 2.6-days longer hospitalization compared with normothermic patients. Although hypothermic patients in our study had 1.3-days longer hospitalization than the other group, in a multivariate analysis the prolonged hospitalization was a result of postoperative complications – not intraoperative hypothermia. Notably, in our study the rates of wound infection in both studied groups were comparable (6% in hypothermic patients and 6.7% in normothermic patients) and almost identical to those with active warming in the study of Kurz et al. It is conceivable that the detrimental effects of 'mild' intraoperative hypothermia on surgical site infection may be negligible in an ERAS setting. Within an ERAS pathway, the implementation of bundled interventions including appropriate administration of prophylactic antibiotics and better glycemic control significantly decreased the rates of surgical site infection after colorectal operation to 4-7%.[27]

The incidence of intraoperative hypothermia in our study was high (77%). This may be explained by the fact that active warming protocol and standardized maneuvers for preventing hypothermia are lacking in our institute even an ERAS pathway has been applied for several years.[11-13] In some institutes, where the routine use of body-warming devices and other efforts to prevent and manage perioperative hypothermia, the incidence of intraoperative hypothermia may be as low as 7%.[28] Forced air warming system appeared to be the most efficient in maintaining perioperative normothermia compared with reflective blanket and warmed cotton blanket.[29] Warming of large amounts of intravenous fluid, blood and inspired air is also commonly used in the theater to preventing hypothermia in developed countries.[26,30] However, the rate of active warming of patients during an operation is low in resource-poor countries including Thailand and other Asian countries.[31-33]

Our data indicated that rectal surgery, operative time exceeding 3 hours, multi-organ resection and male gender were significant predictors for intraoperative hypothermia. Several risk factors for intraoperative hypothermia have been identified in the literature including high ASA physical status, major surgery, operative time exceeding 2-3 hours, use of combined epidural and general anesthesia and intravenous administration of un-warmed fluid or blood components.[33] Meanwhile, active warming, overweight, high baseline core temperature before anesthesia and high ambient temperature were significant protective factors for intraoperative hypothermia.[32]

Our study benefits from the use of a single-center database of ERAS pathway in colorectal operations. Notably, the patients in this registry were taken care of by single surgeon's team with good adherence to the ERAS protocol. However, there are several limitations of this observational study. First, the sample size was relatively small. Potential negative impact of hypothermia on surgical outcomes reported in non-ERAS setting, such as prolonged hospitalization,[5] may be not clearly evident in this study due to the low sample size. Second, the effect of intraoperative hypothermia was evaluated only in patients undergoing colorectal surgery – mainly open surgery for colorectal cancer, making it difficult to extrapolate our results to patients undergoing other operations. Third, it could be argued that active warming is currently the accepted standard of care and laparoscopic surgery has become a common approach with a less incidence or less degree of intraoperative hypothermia. We acknowledge that it is true in developed countries but maybe not in developing and underdeveloped regions[31,33] – thus making this study a great opportunity to re-evaluate the effect of intraoperative hypothermia in the current surgical practice. Furthermore, it would be interesting to examine in the future whether cost savings from the omission of active warming is off-set by additional costs to provide care in the postoperative period. Finally, our findings were analyzed based on a definition of 'mild' intraoperative hypothermia. Whether moderate or severe hypothermia will adversely affect surgical outcomes under an ERAS pathway needs to be examined.

In conclusion, despite these limitations, our data indicated that intraoperative hypothermia prolonged time to resume normal food after colorectal surgery within an ERAS setting but it did not adversely affect the return of bowel function, surgical site infection, postoperative complications and length of hospitalization. These findings suggest that the detrimental effects of 'mild' intraoperative hypothermia on surgical outcomes may be minimal in an ERAS setting.

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