The Impact of Intraoperative Hypothermia on Early Postoperative Adverse Events After Radical Esophagectomy for Cancer: A Retrospective Cohort Study

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Objective: **To investigate the correlation between intraoperative body temperature and postoperative adverse effects in patients who underwent esophagectomy procedures.**

Design: **Retrospective cohort study.**

Setting: **University Hospital.**

Participants: **One hundred twenty-one patients undergoing esophagectomy were enrolled.**

Interventions: **None.**

Measurements and Main Results: **Various perioperative and intraoperative variables were recorded. Hypothermia was defined as a urinary bladder temperature <35°C. Multiple logistic regression analysis was conducted to identify independent significant predictors of postoperative complications. In addition, the authors also determined a cutoff point for intraoperative minimum urinary bladder temperature by analyzing receiver operating characteristic (ROC) curves for occurrence of adverse events at 1 month after surgery. No patients died within 1 month after the surgery. There were 53 patients with early postoperative complications, and 51 had experienced intraoperative hypothermia. Factors that were correlated significantly with complications included age ($p = 0.02$); hypothermia ($p < 0.01$); and doses of ephedrine ($p < 0.01$), phenylephrine ($p < 0.01$), and fentanyl ($p < 0.01$). Multiple logistic regression analysis identified intraoperative hypothermia as a significant independent predictor for the development of early perioperative complications (odds ratio 2.57; 95% confidence interval 1.09-6.08). The area under the ROC curve for body temperature was 0.71, and the cutoff point was 35°C (sensitivity = 0.65, specificity = 0.72).**

Conclusions: **Intraoperative hypothermia was identified as an independent risk factor for early postoperative adverse events following esophagectomy.**

KEY WORDS: body temperature, intraoperative hypothermia, esophageal cancer, esophagectomy

MINIMALLY INVASIVE SURGERY, early enteral nutrition, and perioperative steroids recently have contributed to improvements[1–3] in postoperative complications following esophageal cancer surgeries. However, the mortality and morbidity rates for esophageal cancer surgery remain relatively higher compared with those for other major abdominal surgeries. Therefore, it is important to investigate perioperative factors that may influence esophageal cancer surgery outcomes. In fact, it has been reported that the amount of perioperative fluid infusion and epidural anesthesia are related to postoperative complications following esophageal cancer surgery.[4,5] However, there has been no definitive evidence that intraoperative anesthetic management ensures a favorable outcome following esophageal cancer surgery.

Intraoperative hypothermia is known to contribute to postoperative clinical problems such as wound infections, hemorrhage, morbid cardiac events, and longer intensive care unit (ICU) stays.[6,7] Therefore, perioperative warming is recognized as a significant anesthetic management tool. Esophagectomy is known to be associated with long surgery, lateral position, and large surgical fields, which appear to impair body temperature management.[8] In addition, a large area of the patient's body is exposed to the air in the room during several changes in position, possibly resulting in more severe hypothermia during esophagectomy procedures. However, to the best of the authors' knowledge, there has been no report on the harmful effects exerted by intraoperative hypothermia on patients who underwent esophagectomy procedures. In this study, the authors retrospectively evaluated the correlation between intraoperative body temperature and postoperative adverse effects in esophagectomy cases.

SUBJECTS AND METHODS

This study was approved by the authors' institutional ethics committee and the requirement for written informed consent was waived by their institutional review board. A total of 121 consecutive patients who underwent esophagectomy for cancer performed by a single surgical team between April 2010 and February 2012 were identified using hospital records.

Patients were not premedicated prior to surgery. An epidural thoracic catheter was inserted at the T6-7 level for patients with normal coagulation immediately before administration of general anesthesia with propofol (1.5-2 mg/kg), remifentanil (0.2-0.5 μg/kg/min), and rocuronium (0.6-1.0 mg/kg). The trachea was intubated with double-lumen endotracheal tubes: 37-Fr for men and 35-Fr for women. Anesthesia was maintained with propofol (5-8 mg/kg/h) or sevoflurane (1%-1.5%). In addition, remifentanil (0.1-0.5 μg/kg/min) and fentanyl (50-150 μg/h) were administered intravenously for analgesia. Rocuronium was administered as a muscle relaxant. In addition, in patients with an epidural catheter, 0.25% levobupivacaine (3-5 mL/h) was administered. To prevent postoperative respiratory complications, 500 mg of methylprednisolone was administered intravenously immediately before skin incision. During surgery, all patients were treated with upper body forced air warming systems (Bair Hugger model 750®, Arizant Healthcare, St. Paul, MN) and fluid warming units (Ranger®, Arizant Healthcare) to prevent hypothermia. The cover for the forced air warming system was applied to the lower limbs of patients, and the system was set initially at the middle level (38°C). When the patient's urinary bladder temperature decreased below 36°C, the system was set at a higher level (43°C). Operating room air temperature was maintained at 24.5°C. Patient body temperature was measured in the urinary

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Table 1. Number of Postoperative Adverse Events

Adverse Event	Total Adverse Events (n = 72)
Severe arrhythmia*	8
Mini-tracheostomy	6
Anastomotic leakage	19
Thoracic empyema	4
Wound infection	7
Pneumothorax	5
Pneumonia	14
Catheter-related infection	2
Necrosis of a gastric graft	1
Respiratory dysfunction requiring reintubation	4
Hemorrhage requiring surgical reintervention	2

*Severe arrhythmia is defined as an event requiring medical intervention.

bladder using a temperature-sensing Foley catheter (Bard, Inc., Covington, GA). If the mean blood pressure was <60 mmHg, intermittent infusion of vasopressor drugs (5 mg of ephedrine or 100 μg of phenylephrine) and/or fluid administration was performed by referring to stroke volume variation as displayed on the Vigileo® monitor (Edwards Lifesciences, Tokyo, Japan). If intraoperative hypotension, mainly due to bleeding, was refractory to vasopressor drugs or fluid administration, blood transfusion was performed. Mediastinal lymph node dissection or gastric tube advancement posterior-mediastinally, which cause severe hypotension due to cardiac suppression, was performed by skilled surgeons with coordinating anesthesiologists. No circulatory deterioration occurred in any patients. All patients underwent thoracoscopic esophagectomy and mediastinal lymph node dissection with a right mini-thoracotomy.[9] In addition, a gastric tube that was perfused by the right gastroepiploic artery was created, and abdominal lymph node dissection was performed. Finally, cervical lymph node dissection and cervical esophagogastric anastomosis were completed.

At the end of the surgery, the double-lumen endotracheal tube was removed from the trachea, and a single-lumen endotracheal tube was inserted. All patients subsequently were transferred to the ICU. After transfer to the ICU, all patients were ventilated mechanically under propofol sedation until the following morning. When the patient's status was hemodynamically stable and the oxygenation was good, sedation was discontinued and extubation was performed.

Preoperative variables recorded were age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) classification, and prior chemoradiotherapy. Perioperative variables that were studied were early postoperative morbidity and mortality (≤1 month), operative time, amount of bleeding, use of blood products, occurrence of intraoperative hypothermia, use of epidural anesthesia, total intravenous anesthesia, amount of blood products and fluid infused, amount of urine produced, and dosage of anesthetic or vasoactive drugs administered. The authors defined intraoperative hypothermia as a minimum urinary bladder temperature of <35°C as described in a previous study.[10]

The authors' primary endpoint was adverse events within 1 month. Chylothorax, vocal cord paralysis, and pyloric or gastric tube stenosis, which possibly were affected by surgical techniques, were not included. In addition, the authors determined the cut-off point of intraoperative hypothermia resulting from the appropriate sensitivity–specificity balance in the receiver operating characteristic (ROC) curve for the occurrence of adverse events 1 month after surgery.

All of the data obtained were analyzed using StatFlex 6.0 statistical software (Artech Co., Ltd., Osaka, Japan). Kolmogorov–Smirnov tests and equal variance tests were applied to all data. When these tests confirmed a normal distribution pattern and equal variance of the data, the Student's t-test was conducted for comparison of preoperative and intraoperative characteristics between patients with and without adverse events 1 month after surgery. Results are expressed as mean ± standard deviation (SD). When the data were not distributed normally or the variance of the data was not equal, a Mann-Whitney U-test was performed, and the results were expressed as the median (interquartile range). Chi-square or Fisher's exact tests were used for the comparison of binary variables between groups. Multiple logistic regression analysis was used to identify independent significant predictors of perioperative complications. Hypothermia was treated as a binary variable; ie, it was either present or absent. A p value of < 0.05 was considered statistically significant.

RESULTS

Fifty-three of 121 patients (44%) had early postoperative complications (Table 1). No patients died within 1 month after surgery. Fifty-one of 121 patients (42%) experienced intraoperative hypothermia. Factors that did not correlate with complications included sex, BMI, ASA classification, prior chemoradiotherapy, operative time, and use of epidural anesthesia. Factors that correlated significantly with complications included age ($p = 0.02$), hypothermia ($p < 0.01$), ephedrine dosage ($p < 0.01$), phenylephrine dosage ($p < 0.01$), and fentanyl dosage ($p < 0.01$) (Tables 2 and 3). Multiple logistic regression analysis identified intraoperative hypothermia (odds ratio [OR], 2.57; 95% confidence interval [CI], 1.09-6.08; $p = 0.03$) and the intraoperative dosage of ephedrine (OR, 1.05; 95% CI, 1.00-1.10; $p < 0.04$) as significant independent predictors for the development of early perioperative complications (Table 4).

The usefulness of intraoperative minimum body temperature in predicting the incidence of morbidity 1 month after surgery was evaluated by ROC curves. The area under the ROC curve was 0.71 for body temperature, 0.61 for age, 0.68 for amount of

Table 2. Preoperative Patient Characteristics

Variable	No Adverse Events (n = 68)	Adverse Events (n = 53)	p Value
Age, mean ± SD (years)	63.5 ± 7.3	66.9 ± 8.3	0.02*
BMI, mean ± SD(%)	21.0 ± 2.0	21.0 ± 2.4	0.93
Female sex, No. (%)	15 (22)	8 (15)	0.33
ASA score 1/2/3, No. (%)	7(10)/59(87)/2(3)	6(11)/45(85)/2(4)	n.s.
Preoperative chemoradiation therapy, No. (%)	46 (67)	34 (64)	0.89

NOTE. For continuous variables, p values were calculated using a t-test for continuous variables. For binomial variables, P values were calculated using a chi-square test or Fisher's exact test.

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; n.s., not significant; SD, standard deviation.

*Indicates statistical significance.