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ORIGINAL ARTICLE

Perfusion index as a possible predictor for postanesthetic shivering

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Abstract
Background Postanesthetic shivering can be triggered by surgical stress and several aspects of anesthetic management and is frequently preceded by a decrease in peripheral blood flow due to thermoregulatory vasoconstriction. As perfusion index correlates with peripheral blood flow, we examined whether perioperative perfusion index, measured using pulse oximetry, might be correlated with postanesthetic shivering.
Methods Twenty-eight patients presenting for elective abdominal surgery were enrolled. Core (esophagus) and peripheral (finger) temperatures and perfusion index were recorded in the perioperative periods. Correlations between perfusion index and peripheral temperature and core-to-peripheral temperature gradient were then explored. Plasma levels of epinephrine and norepinephrine were also measured. The extent of shivering was graded after emergence from anesthesia.
Results Perfusion index declined before emergence from anesthesia in patients who then developed postanesthetic shivering. This coincided with the time at which the difference between core and peripheral temperature became dissociated and peripheral temperature declined. Perioperative perfusion index was correlated with peripheral temperature and peripheral-core temperature gradient. Perfusion index at closure of the peritoneum predicted postanesthetic shivering and was significantly correlated with the extent of shivering. Plasma levels of both epinephrine and norepinephrine were significantly elevated after shivering events.
Conclusions Perfusion index was significantly lower in patients with postanesthetic shivering before emergence from anesthesia, indicating that measurement of perfusion index during and before the end of anesthesia might be a useful means of predicting postanesthetic shivering.

Keywords Postanesthetic shivering · Perfusion index · Core-to-peripheral temperature gradient

Introduction

Postanesthetic shivering occurs in approximately 40 % of unwarmed patients recovering from general anesthesia and is associated with substantial adrenergic activation and discomfort [1]. Shivering can increase tissue oxygen consumption and cardiac output and is occasionally associated with deleterious sequelae such as cardiopulmonary compromise [2, 3]. Postanesthetic shivering is often preceded by core hypothermia and peripheral vasoconstriction, which are the first signs of autonomic thermoregulatory responses [4].

The perfusion index is a noninvasive measure of peripheral perfusion that can be calculated using pulse oximetry: the proportion of pulsatile signal (arterial blood) is expressed as a percentage of the nonpulsatile signal (skin, other tissues, and nonpulsatile blood) derived from

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the amount of infrared light absorbed [5]. Perfusion index has been used to evaluate the efficacy of epidural anesthesia, the circulatory status of neonates and critically ill patients, and to confirm adequate blood flow after revascularization procedures [6–9]. Peripheral perfusion is influenced by local blood flow and sympathetic nervous tone [1, 10]. It has been reported that forearm-skin temperature gradient or skin temperature alone influences skin blood flow measured using laser Doppler flowmetry [11, 12]. Skin temperature has been found to contribute nearly 20 % to the control of vasoconstriction and postanesthetic shivering threshold under isoflurane anesthesia [13, 14]: increasing mean skin temperature linearly reduces core temperature thresholds for vasoconstriction and shivering [14], suggesting that skin temperature itself might correlate with the incidence of postanesthetic shivering. However, the correlation between perfusion index and postanesthetic shivering has not been investigated. Therefore, we examined whether perianesthetic changes in perfusion index correlated with the incidence of postanesthetic shivering and therefore whether perfusion index could predict postanesthetic shivering before emergence. In addition, we investigated the correlation between changes in perfusion index and body temperature measured at a finger (peripheral) and the esophagus (core) to evaluate whether perfusion index reflects thermoregulatory vasoconstriction in the perianesthetic period.

Table 1 Patient characteristics and intraoperative data

	Shivering group	Nonshivering group	*P* value
Age (years)	58.5 ± 16.0	60.1 ± 17.3	0.82
Male/female (*n*)	3/7	6/11	1.00
Body mass index	21.4 ± 3.9	23.6 ± 3.5	0.14
ASA 1/2 (*n*)	2/8	5/12	0.62
Surgery type (general/gynecological) (*n*)	4/6	11/6	0.26
Duration of anesthesia (min)	430 ± 133	397 ± 166	0.61
Duration of operation (min)	277 ± 97	296 ± 153	0.74
Volume of infused fluid (ml)	3522 ± 1151	3225 ± 1547	0.61
Volume of transfused blood (ml)	312 ± 349	128 ± 241	0.12
Blood loss (ml)	658 ± 640	275 ± 337	0.06
Shivering grade (0/1/2/3/4) (*n*)	0/0/6/3/1	13/1/0/0/0	
VAS score (mm)	7.6 ± 12.5	12.7 ± 18.4	0.45

Date are expressed as mean ± standard deviation

ASA American Society of Anesthesiologists, *VAS* visual analog scale

Methods

Patient backgrounds

This study was approved by the ethics committee of Kagoshima University Hospital, Japan. Written informed consent was obtained from all participants. A total of 28 consecutive American Society of Anesthesiologists (ASA) physical status I and II patients undergoing elective gastrointestinal or gynecologic laparotomy under general anesthesia between September and December 2011 were enrolled (Table 1). Patients requiring a continuous intravenous catecholamine infusion or those <20 years of age were excluded from the study.

Anesthetic management

In all patients, an electrocardiogram, radial arterial blood pressure, and arterial oxygen saturation were monitored routinely after their arrival in the operating room. After the insertion of an epidural catheter at the thoracic level (Th10–12), patients received total intravenous anesthesia, with a target-controlled infusion of propofol aiming for a serum concentration of 2.5–3.0 μg/ml to maintain bispectral index (BIS) between 40 and 60 during anesthesia. As high-dose remifentanil increases postoperative shivering due to acute opioid tolerance [15] rather than hypothermia, a continuous infusion of remifentanil was maintained in the serum concentration range of 0.2–0.4 μg kg^{-1} min^{-1} during anesthesia. Rocuronium 0.6 mg/kg was administered before tracheal intubation, and further boluses of 10 mg were administered as required, indicated by monitoring of the train of four ratio. Controlled ventilation was established with a fraction of inspired oxygen (FiO_2) of 0.35–0.5 and tidal volume between 8 and 10 ml/kg. End-tidal carbon dioxide (CO_2) was maintained between 35 and 40 mmHg. At the time of peritoneal closure, 0.3 % bupivacaine 5–10 ml was administered via the epidural catheter, and fentanyl 2 μg/kg given intravenously for postoperative analgesia. Sugammadex 2 mg/kg was administered before extubation. Postanesthetic shivering was evaluated according to the shivering grade (0, no shivering; 1, piloerection or peripheral vasoconstriction but no visible shivering; 2, muscular activity in only one muscle group; 3, muscular activity in more than one muscle group but not generalized shivering: 4, shivering involving the whole body) for 30 min after tracheal extubation until room exit [16, 17]. Shivering grades 0 and 1 were classified as nonshivering; shivering grades 2–4 were considered as shivering. Postoperative pain was assessed with a visual analog scale (VAS) at room exit. If patients developed postanesthetic shivering, they were treated with oxygen by mask and an additional intravenous bolus of fentanyl 2 μg/kg.

Management of body temperature

Core temperature was measured in the esophagus. Peripheral temperature was measured at the tip of the middle finger on the same side as the measurement of perfusion index and pleth variability index. Pleth variability index is used as a parameter for volume responsiveness defined as change in arterial pulse pressure with respiratory variation [18, 19]. Perfusion index and pleth variability index were measured at a forefinger (BMS-9101, Nihon Kohden, Japan) contralateral to the side in which intravenous catheters had been placed to avoid the possible influence of infusions or transfusions on local temperature. The ambient temperature was maintained at 28 °C before and after the operation and at 25 °C during the operation. Patients were covered with a cotton blanket before induction of anesthesia. After induction of anesthesia and during surgery, the upper body was covered with a 38 °C forced-air warming blanket (Warm-Touch, Mallinckrodt, St. Louis, MO, USA), which was reoriented to cover the whole body from the end of surgery until operating room exit. All fluid was kept at room temperature before infusion. Body temperature and perfusion index were compared between shivering (grade 2–4) and nonshivering (grade 0–1) patients at T_1, the time of arrival in the operating room; T_2, before the start of the operation; T_3, at the closure of the peritoneum; T_4, at emergence from anesthesia; T_5, within 10 min of tracheal extubation, and T_6, on exit from the operating room.

Measurement of plasma catecholamines

Samples were collected from the arterial catheter at T_1, T_2, T_3, and T_6 (as described earlier) and centrifuged at 1,000*g* for 5 min. Plasma fraction was separated and kept at −80 °C until measurement. Plasma levels of epinephrine and norepinephrine were assayed using an automated catecholamine analyzer HLC-725CAII (Tosho Corporation, Japan).

Statistical analysis

Data are presented as mean ± SD. A power analysis based on a pilot study indicated that the sample size required for the study was 25. Data were compared by two-way analysis of variance (ANOVA) followed by Bonferroni's post hoc test. The unpaired two-tailed *t* test, the Mann–Whitney test, or Fisher's exact test was used when appropriate to evaluate the influence of patient demographic characteristics. Correlations between perfusion index and finger temperature, peripheral-core temperature gradient, and shivering grade were assessed using the Spearman rank correlation coefficient. Receiver operating characteristic (ROC) curve analysis was used to evaluate whether perfusion index could predict the incidence of postanesthetic shivering; results are reported with 95 % confidence interval (CI). $P < 0.05$ was considered statistically significant. Statistical analyses were performed using Graph Pad Prism 5 (Graph Pad Software Inc., San Diego, CA, USA).

Results

Table 1 shows patients' characteristics and a summary of intraoperative data. Of 28 patients, one was excluded, as a catecholamine infusion was required. Ten patients exhibited postanesthetic shivering (grade 2–4). There was no difference in body mass index (BMI) between patients with and without shivering ($P = 0.14$). Neither the amount of infused fluid nor the volume of transfused red cell concentrate was significantly different between groups. There was a trend suggesting that blood loss might be higher in patients with shivering, although this did not reach statistical significance ($P = 0.06$).

During anesthesia, esophageal temperature was maintained at a constant level of around 36.0 °C in both groups while the upper body was covered by the forced-air warming blanket (Fig. 1a). In contrast, finger temperature was significantly lower in patients with shivering between T_3 and T_5 compared with patients without shivering (T_3; shivering 34.4 ± 1.11 °C, nonshivering 35.5 ± 1.08 °C; $P = 0.019$) (Fig. 1b). As a consequence, the difference in esophageal–skin temperature was dissociated from T_3 in patients with shivering (T_3; shivering 1.99 ± 1.11 °C, nonshivering 1.02 ± 0.99 °C; $P = 0.008$) (Fig. 1c). It has been reported that perfusion index reflects peripheral perfusion and the change in difference of central-to-peripheral temperature [6]. Consistent with the decrease in skin temperature and increased esophageal–skin temperature gradient, perfusion index declined between T_3 and T_6 in patients with postanesthetic shivering (T_3; shivering 1.19 ± 0.63 %, nonshivering 2.52 ± 1.03 %; $P = 0.001$) (Fig. 2a). In addition, perfusion index significantly correlated with forefinger temperature ($R = 0.49$, $P < 0.0001$, $n = 135$) (Fig. 2b) and peripheral–core temperature gradient ($R = 0.58$, $P < 0.0001$, $n = 135$) (Fig. 2c). Furthermore, perfusion index at T_3 predicted postanesthetic shivering [receiver operator characteristic (ROC) area 0.91, 95 % confidence interval (CI) 0.78–1.0, $P < 0.001$) (Fig. 3a). Peripheral–core temperature gradient (ROC area 0.75, 95 % CI 0.57–0.94, $P = 0.03$) and peripheral temperature alone (ROC area 0.81, 95 % CI 0.63–0.98, $P = 0.008$) also predicted postanesthetic shivering, as previously reported [14, 20]: however, the optimal area

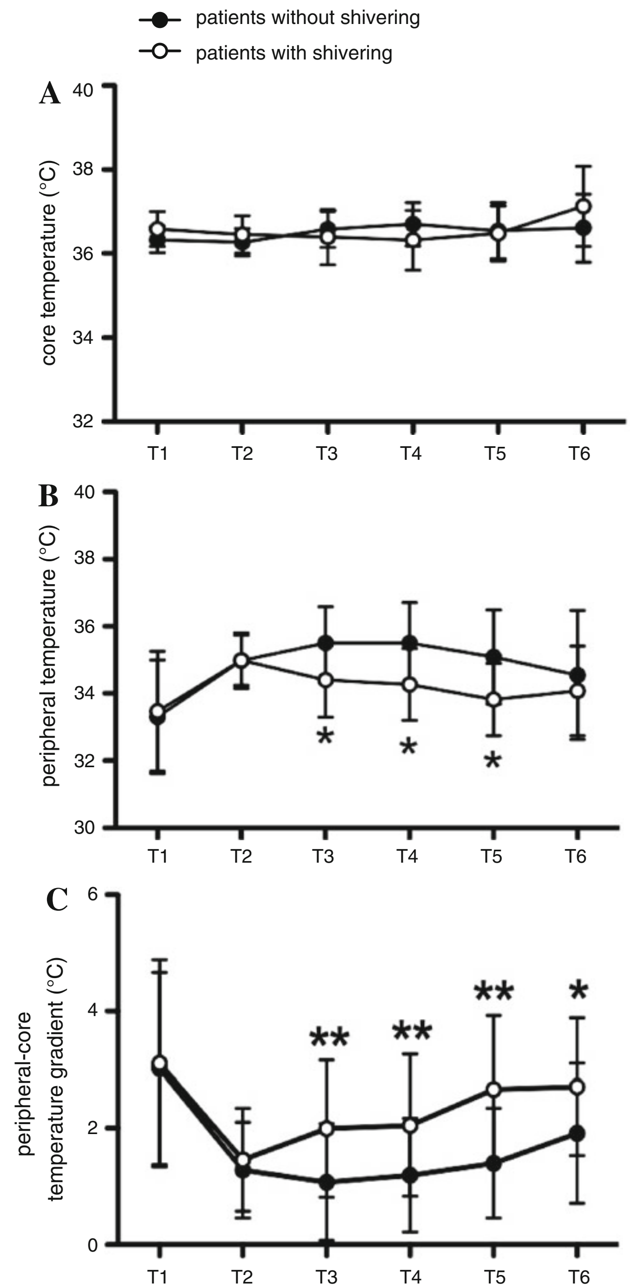

Fig. 1 Dissociation of peripheral–core temperature gradient was observed with decrease in peripheral temperature before anesthetic emergence. Core (esophagus) temperature (**a**), peripheral (skin) temperature (**b**), and the difference between core and peripheral temperature (**c**) were evaluated at T_1, room entrance; T_2, within 30 min of induction of anesthesia; T_3, closure of peritoneum; T_4, end of surgery; T_5, within 10 min of tracheal extubation, and T_6, operating room exit. *Data* are presented as mean ± standard deciation. Statistically significant differences between patients with and without postanesthetic shivering at each point are indicated as $*P < 0.05$ or $**P < 0.01$

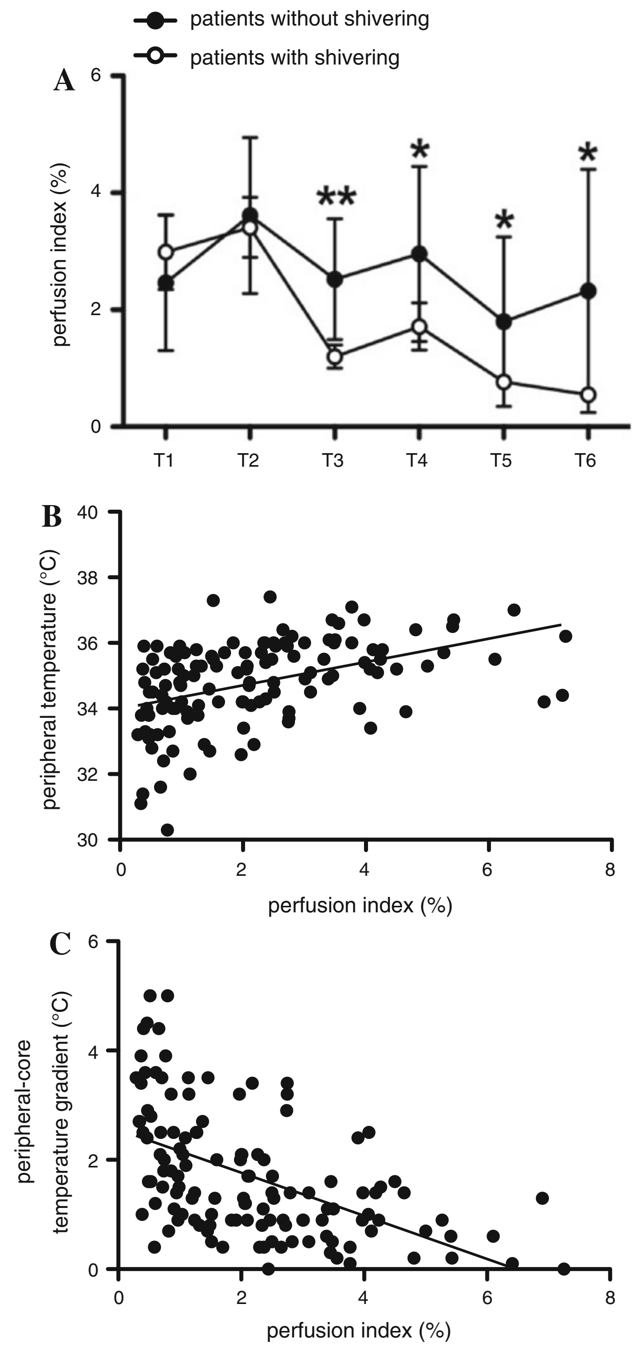

Fig. 2 Perfusion index declined before anesthetic emergence in patients with postanesthetic shivering. Perfusion indices of shivering and nonshivering patients were compared (**a**). Statistically significant differences between patients with and without postanesthetic shivering at each point are indicated as $*P < 0.05$. Correlations between perfusion index and peripheral temperature (**b**) ($R = 0.49$, $P < 0.0001$, $n = 135$) and peripheral–core temperature gradient (**c**) ($R = 0.58$, $P < 0.0001$, $n = 135$) were evaluated. *Data* are presented as mean ± standard deviation

under the ROC curve was obtained with perfusion index. A perfusion index <1.30 discriminated between patients with and without shivering, with a sensitivity of 78 % (95 % CI 40–97 %) and a specificity of 93 % (95 % CI 68–100 %) at T_3. In addition, perfusion index at T_3 was significantly correlated with shivering grade ($R = 0.38$, $P < 0.001$, Fig. 3b).

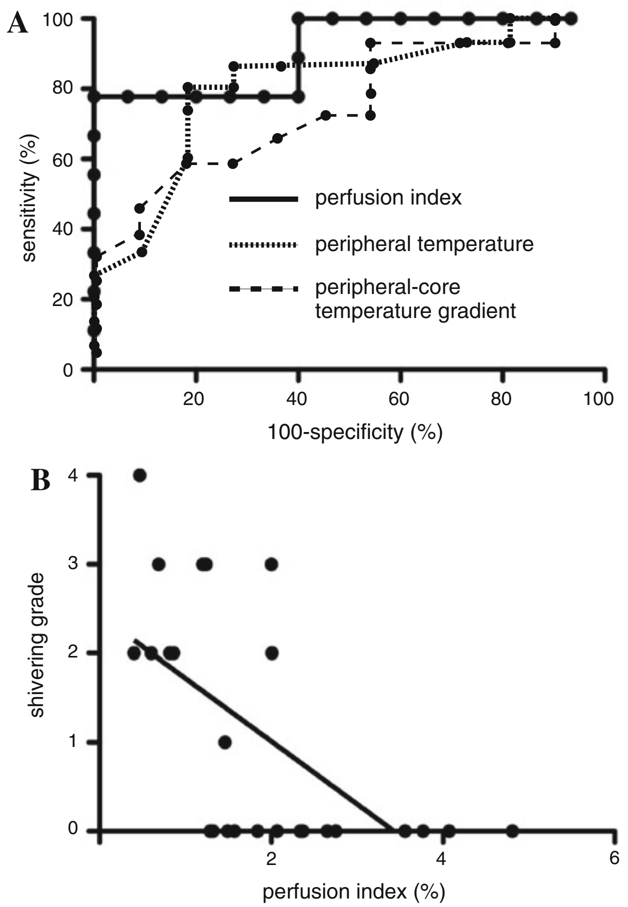

Fig. 3 Postanesthetic shivering can be predicted by intraoperative perfusion index. Receiver operating characteristic *curves* showing the ability of perfusion index, peripheral temperature, and peripheral–core temperature gradient at the closure of the peritoneum (T_3) to predict the incidence of postanesthetic shivering (**a**). Extent of correlation between perfusion index at T_3 and shivering grade (**b**)

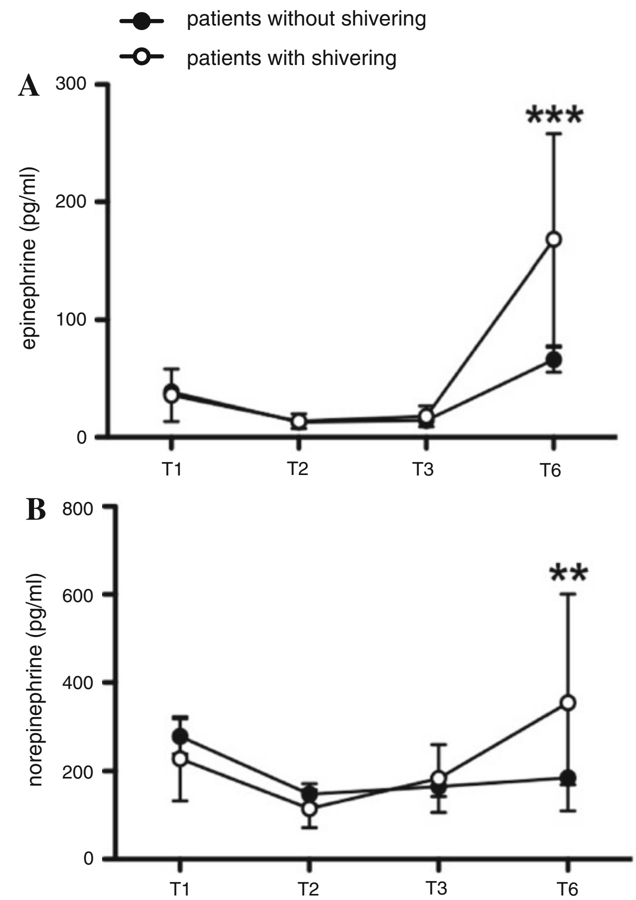

Fig. 4 Plasma levels of epinephrine and norepinephrine were elevated after emergence from anesthesia in patients with postanesthetic shivering. Plasma levels of epinephrine (**a**) and norepinephrine (**b**) were measured. *Data* are presented as mean ± standard deviation. The statistically significant differences between patients with and without postanesthetic shivering at each time point are indicated as $^{**}P < 0.01$ or $^{***}P < 0.001$

As blood loss was slightly (but not significantly) greater in patients with shivering, we examined the influence of perioperative pleth variability index, mean arterial pressure, and heart rate. As the evaluation of fluid responsiveness using pleth variability index requires mechanical ventilation (tidal volume >8 ml/kg) in the absence of spontaneous respiratory activity [21], the influence of pleth variability index was only evaluated between T_2 and T_4. Despite the gradual decline in perfusion index of patients with shivering, there was no difference in gradients of pleth variability index (T_3, shivering 8.40 ± 4.06 %, nonshivering 7.54 ± 5.36 %; $P = 0.68$), mean arterial pressure (T_3, shivering 74.90 ± 10.59 mmHg, nonshivering 72.47 ± 10.64 mmHg; $P = 0.57$), or heart rate (T_3, shivering 68.50 ± 12.48/min, nonshivering 68.18 ± 10.38/min; $P = 0.94$) between groups throughout the perioperative period, indicating that there were no differences in volume responsiveness or systemic circulatory status. Catecholamine levels were measured as an index of stress response due to sympathetic nervous system activation. Epinephrine (T_6, shivering 168.5 ± 90.2 pg/ml, nonshivering 66.1 ± 41.2 pg/ml; $P = 0.0008$) (Fig. 4a) and norepinephrine (T_6, shivering 355.2 ± 245.5 pg/ml, nonshivering 184.7 ± 61.7 pg/ml; $P = 0.016$) (Fig. 4b) were both significantly elevated in patients with shivering at T_6.

Discussion

Perianesthetic perfusion index was significantly lower before emergence from anesthesia in patients who developed postanesthetic shivering. Postanesthetic shivering was predicted by perfusion index before emergence from anesthesia. Perfusion index also correlated with skin temperature and peripheral–core temperature gradient. These data suggest that perfusion index might reflect the change in peripheral temperature due to thermoregulatory vasoconstriction in the perianesthetic period.

Although the correlation between perfusion index and thermoregulatory responses has not been well investigated, studies using laser Doppler flowmetry reveal that there is a linear relationship between peripheral blood flow and forearm–fingertip temperature gradients [11]. As perfusion index changes with peripheral blood flow, perfusion index could reflect peripheral temperature gradient and hence the thermoregulatory responses, such as peripheral vasoconstriction that precedes shivering. Indeed, it has been reported that core-to-peripheral temperature difference correlates with peripheral perfusion index [6] and that increasing skin temperature linearly reduces the core temperature thresholds for arteriovenous shunt vasoconstriction and shivering [14]. These reports support our findings that both peripheral and core temperatures contribute to the threshold for shivering and that perfusion index reflects the vasoconstriction induced by thermoregulatory responses that precede shivering.

Furthermore, in our study, core-to-peripheral temperature difference, which correlated with the change in perfusion index (Fig. 2c), was significantly different between patients with and without shivering. Although the core temperature of patients with shivering was similar to that of patients with nonshivering throughout the perioperative period, shivering developed in those whose skin temperature fell during the operation (Fig. 1). This suggests that declining skin temperature, or dissociation of core-to-peripheral temperature, might trigger postanesthetic shivering without core hypothermia. However, in this study, esophageal temperature was maintained throughout the perianesthetic periods; therefore, it is unclear whether perfusion index reflects the thermoregulatory responses that precede shivering during core hypothermia.

Pleth variability index is an indicator of volume responsiveness [18, 19]. The amount of infused fluid and transfused blood did not differ between groups; although blood loss appeared to be greater in patients with shivering, the difference was not significant (Table 1). Although a decline in perfusion index was observed only in patients with shivering, there were no significant differences in pleth variability index, mean arterial pressure, or heart rate between patients with and without shivering (Fig. 3), indicating that there was little difference in intravascular volume responsiveness or circulatory status. As perfusion index correlated with peripheral–core temperature gradient (Fig. 2c), the decline in perfusion index may mainly reflect thermoregulatory vasoconstriction as a precursor of shivering.

Most shivering occurs as a thermoregulatory response to hypothermia. It has been proposed that postanesthetic shivering is associated with three independent risk factors: young age, endoprosthetic surgery, and core hypothermia [22]. In our study, neither age nor core temperature differed between groups, nor was endoprosthetic surgery performed. In addition, shivering-like tremor after general anesthesia is aggravated by inadequate pain control [23]. However, VAS scores suggested adequate control of postoperative pain in both groups, implying that nonthermoregulatory shivering due to inadequate pain control was unlikely (Table 1).

Activation of the sympathetic nervous system due to surgical stress and inadequate anesthetic management may result in increased release of catecholamines. It has been reported that plasma epinephrine and norepinephrine levels are increased in the postanesthetic period in the presence of perioperative hypothermia [24]. In our study, the levels of epinephrine and norepinephrine were not different between groups during anesthesia but were elevated after emergence from anesthesia only in patients with shivering, suggesting that the sympathetic nervous system was activated after emergence from anesthesia, probably after shivering was triggered. In addition, although neither plasma epinephrine nor norepinephrine was elevated at T_3, before emergence from anesthesia, a decline in perfusion index at this time was only observed in patients with postanesthetic shivering. This suggests that perfusion index might be controlled by a local vasoregulatory reflex independent of plasma catecholamines.

It is well recognized that perfusion index differs between individuals, reflected in the breadth of the normal range (0.1–20 %) [25]. However, neither the difference between perfusion index at T_1 and at later time points, nor the rate of decline compared with T_1, were significantly correlated with the incidence of postanesthetic shivering (data not shown). Therefore, absolute values of perfusion index might be useful for predicting postanesthetic shivering.

In conclusion, perfusion index, which reflects peripheral perfusion, declined before emergence from anesthesia in patients with postanesthetic shivering, correlating with the decline in peripheral temperature and increased peripheral–core temperature gradient. The decline in perfusion index in patients with shivering was not accompanied by changes in pleth variability index, suggesting that with optimal fluid volume management, the decrease in perfusion index might reflect preshivering factors, such as thermoregulatory vasoconstriction. Preventative treatment for postanesthetic shivering could be started based on intraoperative perfusion index before emergence from anesthesia.

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