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석사학위 논문

척추유합수술 동안 저속 주입속도에서 중심체온유지에 대한 세가지 다른 수액 가온기의 효과

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Effect of three different fluid warming devices on maintaining core temperature at low flow rate during spinal fusion surgery

2019년 8월 23일

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지도교수 김 상 훈

이 논문을 의학 석사학위신청 논문으로 제출함

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조선대학교 대학원

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2019년 5월

조선대학교 대학원

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국 문 초 록

척추유합수술 동안 저속 주입속도에서 중심체온유지에 대한 세가지 다른 수액 가온기의 효과

수액가온기의 중심체온유지 효과

송 현

지도교수 : 김 상 훈

조선대학교 대학원 의학과

배경: 수술 중 저체온증은 많은 양의 수액 주입 또는 급속 주입에 의해 흔히 발생할 수 있지만, 수술 중 체액량 유지에 필요한 주입속도에서도 발생할 수 있습니다. 이에 금식에 의한 탈수와 수술 중 예상되는 체액손실을 보충 및 유지하기 위한 수액 주입속도에서 3 가지 서로 다른 수액 가온기의 가온 성능 및 중심체온 유지 효과를 비교하고자 한다.

대상 및 방법: 99 명의 환자를 Mega Acer Kit® (그룹 M), Ranger™ (그룹 R) 또는 ThermoSens® (그룹 T)를 사용한 3 군 중 한 군에 무작위로 배정하였다. 금식에 의한 예상 탈수량(4-2-1 공식으로 계산)의1/3과, 수술 중 예상되는 체액 소실의 보충을 위한 수액공급량(2 ml/kg)의 합을 시간당 주입속도로 계산하였다. 각 가온기로부터 76 cm 지점의 수액 온도(T_{Pout}) 와 원위 식도 체온(T_{eso})을 기록하였습니다. 이 연구의 1차 결과 변수는 수술 중 최종 및 최저 원위 식도 온도이고, 2차 결과 변수는 가온기 가동 후 3시간 뒤의 T_{Pout}이며, 3차 결과 변수는 저체온증의 발생 빈도이다.

결과: 최종 T_{eso}와 최저 T_{eso}는 세 그룹 간에 유의미한 차이는 없었지만, 세 군 모두 평균 35도 이상의 T_{eso}를 유지하였다($P = 0.512$, $P = 0.393$). T_{Pout}는 M군에서 R군과 T군에 비해 유의하게 높았다($P < 0.001$, $P < 0.001$).

각 가온기들의 수액가온능력은 M군, R군, T군의 순서대로 13.6도, 7.3도, 8.0도 이었으며, 모든 가온기들은 가온된 수액의 온도 변화가 모두 30분 후에 ±1도 이내로 안정화되었다($P = 0.507$).

최저 T_{eso}로 계산된 35.0도 이하의 저체온증 발생 빈도는 M군(10%)에서 가장 낮았고, 그 다음이 R군(18.8%), T군 (25.0%)으로 나타났다($P = 0.507$).

결론: 임상적으로 수술 중 수액유지요법을 위한 저속 주입속도에서 Mega Acer Kit®는 Ranger™ 및 ThermoSens®보다 뛰어난 수액 가온 능력을 지니고 있으며, 수술 중 35도 이하의 저체온증의 발생빈도를 감소시키는데 도움이 된다.

Abbreviations

ASA: American Society of Anesthesiologists

Base: Baseline

CI: 95% confidential intervals

BMI: Body mass index

EBL: Estimated blood loss

IQR: Interquartile range

MAK: Mega Acer Kit®

m*: Mean values of [*] from 30 min to 3 h after operating each device

T_{eso}: Distal esophageal temperature

T_{eso}_Lowest: Lowest T_{eso}

T_{exp}: Expected core temperature

T_{exp}_Lowest: Lowest T_{exp}

T_r: Room temperature

T_{Pin}: Fluid temperature at the inlet point of each fluid warmer

T_{Pout}: Fluid temperature at the outlet point of each fluid warmer

T_{tym}: Tympanic membrane temperature

T_{tym}_Lowest: Lowest T_{tym}

ΔT_{eso}_Lowest: Difference of T_{eso}_Lowest from baseline value

ΔT_{exp}_Lowest: Difference of T_{exp}_Lowest from baseline value

ΔT_{tym}_Lowest: Difference of T_{tym}_Lowest from baseline value

ΔT_{eso}(_Base): Difference of T_{eso} at each measured time point from that at baseline

ΔT_{eso}(_Prev): Difference of T_{eso} at each measured time point from that at previous time point

ΔT_{tym}(_Base): Difference of T_{tym} at each measured time point from that at baseline

ΔT_{tym}(_Prev): Difference of T_{tym} at each measured time point from that at previous time point

ΔT_{exp}(_Prev): Difference of T_{exp} at each measured time point from that at previous time point

ΔT_{Pout}(_Prev): Difference of T_{Pout} at each measured time point from that at previous time point

$\Delta(T_{eso}-T_{exp})$: Difference between T_{eso} and T_{exp}

$\Delta(T_{tym}-T_{eso})$: Difference between T_{tym} and T_{eso}

$\Delta(\Delta T_{exp}-\Delta T_{eso})]$: Difference between ΔT_{exp} and ΔT_{eso}

*_Base: * at time point (baseline)

*_Before: * at time point (before)

_: * at * time point

Ⅰ. Introduction

Intraoperative hypothermia commonly develops within the first 40 minutes of anesthesia due to the inhibition of normal thermoregulation [1], possibly resulting in delayed recovery and postoperative complications such as: surgical wound infections, coagulopathy, and cardiac events [2]. It was previously reported that postoperative hypothermic patients have a four-fold increase in mortality as well as a two-fold complication rate compared to normothermic patients [3]. Therefore, it is important to monitor and maintain the intraoperative core temperature. It is recommended to warm intravenous fluids, with infusion volumes greater than 500 ml, to 37°C using fluid warming devices to prevent or treat inadvertent perioperative hypothermia in adults [1,4,5].

There are a number of fluid-warming devices, which have been used prevent or treat hypothermia. These devices have been investigated for their effectiveness for rapid infusions with large volumes in patients in whom perioperative severe or moderate hypothermia was expected or developed. Previous studies show that these devices are helpful in maintaining the body temperature, while reducing hypothermia-related morbidity and complications [3,6-8].

Unfortunately, patients can also develop perioperative hypothermia at low to moderate flow rates, which can be prevented by warming the intravenous fluid during infusion. However, there are only a small number of studies regarding such situations [9,10]. Mega Acer Kit®, 3M™ Ranger™ Blood/Fluid Warming System, and ThermoSens® are commonly used in all patients for prevention and treatment of hypothermia.

Here, I investigated whether the three fluid warmers used in my hospital were suitable to maintain the core temperature at low to moderate flow rates for replacement of clinical maintenance fluid, and whether their fluid warming performances were adequate.

Ⅱ. Materials and methods

This prospective, randomized, controlled and non-blinded study was approved by the Institutional Review Board of Chosun University Hospital, and registered with the Clinical Research Information Service (CRIS: https://cris.nih.go.kr/, ref: KCT0001957) on July 1, 2016. Written informed consent was obtained from each participant, a legal surrogate, or the parents or legal guardians of participants who were minors. This study was conducted in accordance with the Declaration of Helsinki.

I included patients who were scheduled to undergo elective spinal fusion surgery with over 3 hours of general anesthesia with the American Society of Anesthesiologists (ASA) Physical Status classification I or II. Patients with preoperative body temperature abnormality (below 36°C or above 38°C), thyroid disease, diabetes, hypertension, brain tumor, coagulopathy, and emergent situation were excluded.

Ninety nine patients were randomly distributed into three groups receiving intravenous warming fluid either through Mega Acer Kit® (MAK: Ace Medical, Seoul, Korea) (Group M), 3M™ Ranger™ Blood/Fluid Warming System (Ranger™ 245: Arizant Healthcare Inc., MN, USA) with standard flow disposable set (Group R), or ThermoSens® Warming Unit (ThermoSens® fluid warmer: Sewoon Medical Company, Seoul, Korea) with sterile single use blood & fluid warmer set (Group T), by using a random numbers table obtained via a computer program. Patients were blinded to the study devices, but investigators were not.

Patients were transported to the operating room, after premedication with intramuscular midazolam (0.05 mg/kg). Prior to anesthesia induction, standard patient monitoring devices to obtain electrocardiograms, non-invasive blood pressure, end-tidal partial pressure of carbon dioxide, and peripheral pulse oximetry were applied. Tympanic membrane temperature (T_{tym}) was then measured using ThermoScan® (IRT4020: Braun GmbH, Kronberg, Germany).

All devices were set at a warming temperature of 41°C according to the manufacturers'

instructions, and they were preheated for 10 m for Group M and 5 m for Group R, contrary to Group T, which was not preheated, to calibrate each device. The infusion set was primed with normal saline hung at a height of 1 m from the warming device and attached to a roller pump (TE-171, Terumo Corp., Tokyo, Japan) [11]. Equal distances from each device to the outlet point (76 cm) were achieved using a 55 cm long fluid extension line, three-way connectors [11], followed by a 55 cm long fluid extension line connected to the outlet of the fluid warmers in series [12] (Figure 1). These extended lines were exposed to ambient room temperature.

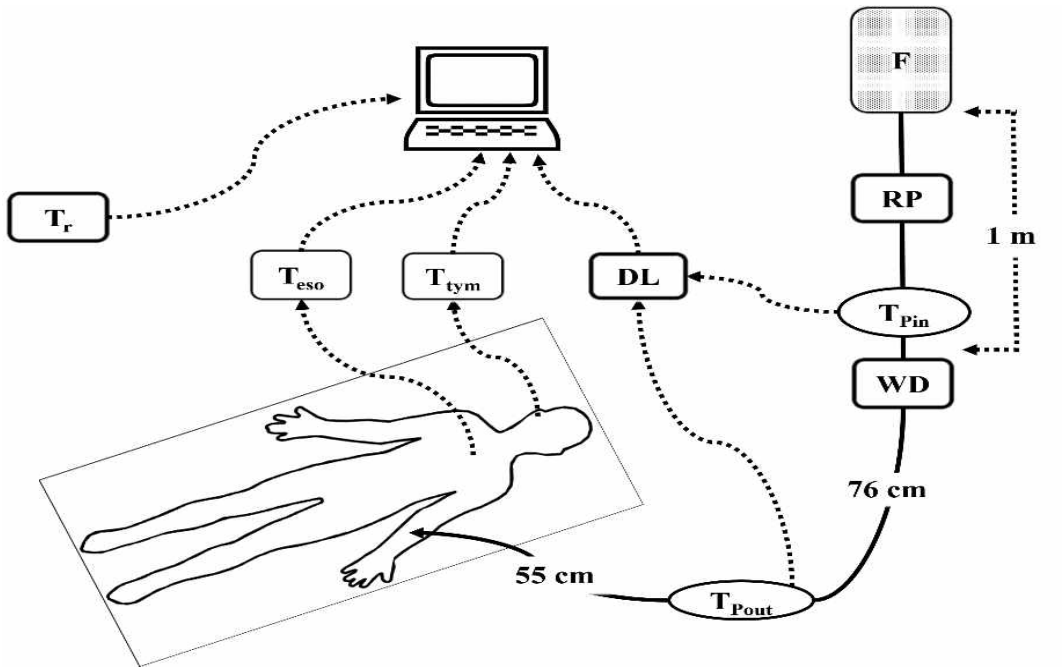

Figure1. Diagrammatic representation of method used for measurement.

F: Intravenous fluid, RP: Roller pump, WD: Warming device, DL: Kistock Datalogger, T_{eso}: Distal esophageal temperature, T_{Pin}: Fluid temperature at the inlet point of each fluid warmer, T_{Pout}: Fluid temperature at the outlet point of each fluid warmer, T_{tym}: Tympanic membrane temperature, T_r: Room temperature.

Two PT 100 temperature probes, as per IEC 751 standard [response time: $t_{0.63}$ = 32 s (V_{air} = 2 m/s), accuracy: ± 0.4% of reading ± 0.3°C; KRGA-50, Kimo Instruments, Edenbridge, UK], were connected to a Kistock Datalogger (KTH350: Kimo Instruments, Edenbridge, UK). The probes were inserted at the inlet and outlet points of each fluid warming device. The distal esophageal temperature (T_{eso}) was measured with an esophageal stethoscope with a temperature sensor (DeRoyal Industries, Inc., Powell, USA) after a total intravenous anesthesia induction with propofol, remifentanil, and rocuronium. The patient's fluid line was then switched with the prepared fluid line attached to each study device. The infusing volume of each device was the sum of one third of the volume (calculated with "4-2-1" formula based on weight and NPO time) and 2 ml/kg (replacement of deficit fluid due to losses of third space and evaporation during surgery with anticipated minimal to moderate tissue trauma) [11].

The fluid temperatures at the inlet and outlet points of each fluid warmer (T_{Pin}, T_{Pout}), distal esophageal and tympanic membrane temperatures (T_{eso} and T_{tym}), and room temperature (T_r) were recorded using the Kistock Datalogger before and immediately after anesthesia induction (baseline), and then at 30 min intervals for 3 h or until end of surgery.

The expected core temperatures (T_{exp}) of attended patients at each time points after 0.5 h of fluid infusion was estimated with the previous temperature by simple calculation [13]: $\frac{c_{fl} * m_{fl}}{c_{pt} * m_{pt}} = \frac{T_{end} - T_{start}}{T_{fl} - T_{end}}$, where c_{fl} is the specific heat of the infused fluid (≈ 1 cal/gm°C), m_{fl} is the mass of fluid infused (L), c_{pt} is the specific heat of the patient (≈ 0.83 cal/gm°C), m_{pt} is the mass of the patient (kg), T_{start} is the patient's temperature before the infusion (°C), T_{end} is the patient's temperature after the infusion (°C), and T_{fl} is the temperature of the fluid infused (°C).

Age, sex, ASA physical status, height, weight, body mass index (BMI), urine output, estimated blood loss (EBL), and infusion rate of intravenous fluid were noted. If patients' blood

loss exceeded maximal allowable blood loss and they demonstrated hemodynamic instability, they were managed by additional fluid and blood transfusion. These patients were excluded from data analysis.

I recorded the lowest T_{tym}, T_{eso}, and T_{exp} (T_{tym}_Lowest, T_{eso}_Lowest, and T_{exp}_Lowest) as well as their differences from baseline value (ΔT_{tym}_Lowest, ΔT_{eso}_Lowest, and ΔT_{exp}_Lowest). The difference between T_{tym} and T_{eso} at each measured time point from that at baseline [ΔT_{eso}(_Base) and ΔT_{tym}(_Base)] as well as a previous time point [ΔT_{eso}(_Prev), ΔT_{tym}(_Prev), and ΔT_{exp}(_Prev)] was recorded. I also recorded the differences between the T_{Pout} values at each measured time point from that at previous time point [ΔT_{Pout}(_Prev)].

I then calculated postoperative mean values of T_{Pin}, T_{Pout}, T_{tym}, T_{eso}, and T_r (mT_{Pin}, mT_{Pout}, mT_{tym}, mT_{eso}, and mTr) from 30 m to 3 h for each device. The mean values of ΔT_{eso}(_Base), ΔT_{tym}(_Base), ΔT_{eso}(_Prev), and ΔT_{tym}(_Prev) [$m\Delta T_{eso}$(_Base), $m\Delta T_{tym}$(_Base), $m\Delta T_{eso}$(_Prev), and $m\Delta T_{tym}$(_Prev) were also calculated.

I calculated the difference between T_{tym} and T_{eso} [$\Delta(T_{tym}-T_{eso})$] at each time point, and the mean values of $\Delta(T_{tym}-T_{eso})$ [$m\Delta(T_{tym}-T_{eso})$] from 30 m to 3 h after the procedure for each device, followed by the calculation of the difference between T_{eso} and T_{exp} [$\Delta(T_{eso}-T_{exp})$] at each time point, and difference between ΔT_{exp} and ΔT_{eso} [$\Delta(\Delta T_{exp}-\Delta T_{eso})$].

I classified the different body temperatures using grades, grade 1 (above 36.0°C), grade 2 (between 36.0°C and 35.0°C), and grade 3 (below 35.0°C). The incidence of grade 3 was recorded with the final and lowest T_{eso}.

The primary outcome of this study was the intraoperative final and lowest T_{eso}. Secondary outcome was T_{Pout} and T_{exp} at 3 h after operating devices. Third outcome was the incidence of hypothermia with grade 3.

Ⅲ. Statistical analysis

The necessary sample size for one-way ANOVA using G*Power software (ver. 3.1.9.1, Heinrich-Heine-Universität Düsseldorf, Germany) was calculated by taking the level of statistical significance as $\alpha = 0.05$ and $\beta = 0.1$, and using an expected effect size of 0.4, due to lack of data to calculate the effect size. The study needed a total of 84 patients, thus we enrolled 99 patients, allowing for a dropout rate of approximately 15%.

SPSS (Windows ver. 24.0, IBM Corp., Armonk, NY, USA) was used for statistical analysis. All measured values were presented as mean (95% confidential intervals [CI]), median [interquartile range (IQR)], or number (percentage) of patients [n (%)].

The normality of probability distribution was analyzed with Kolmogorov-Smirnova test and Shapiro-Wilk test. The continuous normally distributed variables were analyzed with the one-way ANOVA followed by Scheffe's post-hoc test in the presence of a homogeneity of variance according to Levene's test. In the absence of the same, we performed the Games-Howell post-hoc test. The continuous variables with non-normal probability distribution were analyzed with the Kruskal-Wallis test followed by pairwise-comparisons. Nominal variables were analyzed with χ^2 or Fisher's exact. P values < 0.05 were considered statistically significant.

Ⅳ. Results

Total 94 patients were enrolled in the study. As the surgery was finished early in 3 patients and was canceled in 2 patients, these patients were excluded from the final data analysis (Figure 2).

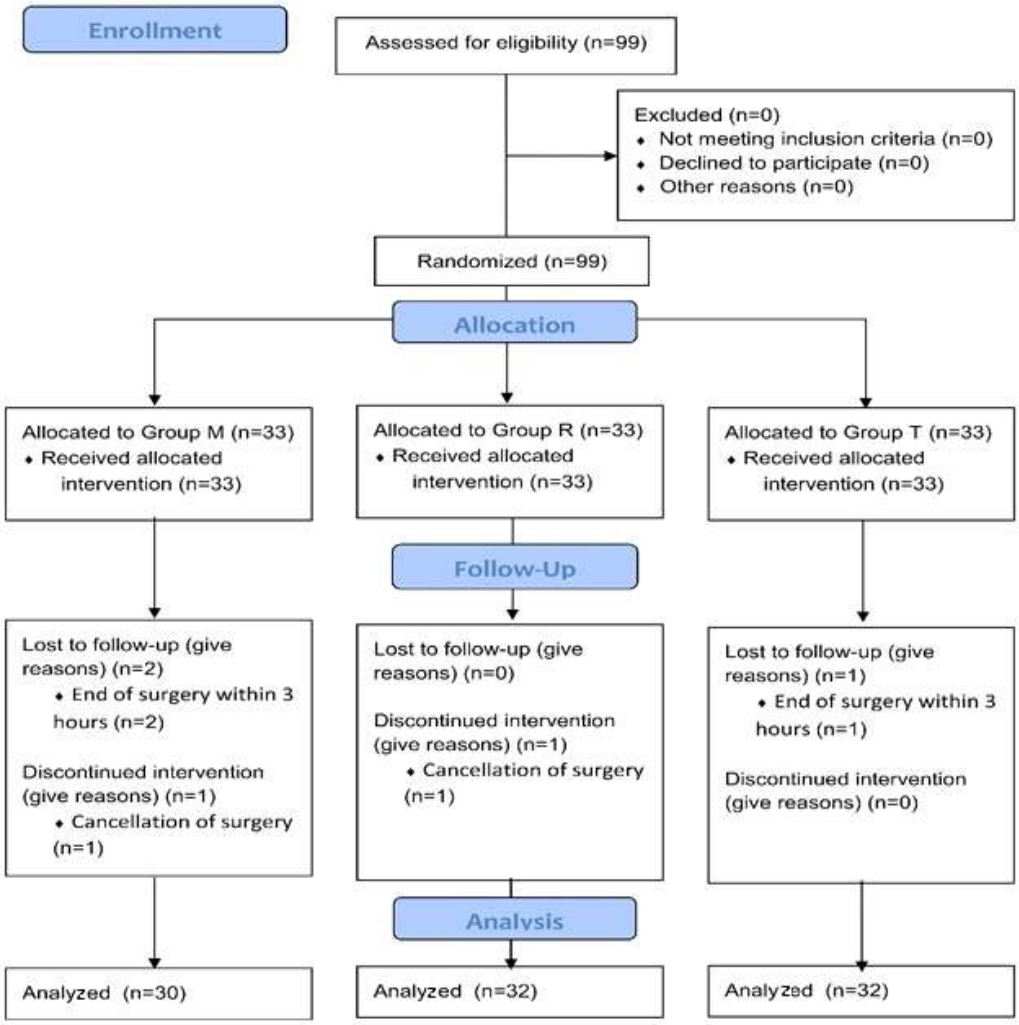

Figure 2. CONSORT (Consolidated Standards of Reporting Trials) diagram. Group M: Group using Mega Acer Kit®, Group R: Group using Ranger™, Group T: Group using ThermoSens®.

A. Demographic and intraoperative data

No statistically significant differences were observed in demographic data, intraoperative EBL, urine output, and infusion rate (Table 1).

Table 1. Demographic and intraoperative data

	Group M (n=30)	Group R (n=32)	Group T (n=32)	P value
Age (years)	60.3 (54.8-65.8)	64.3 (60.2-68.4)	64.6 (61.6-67.6)	0.281
Sex(male/female)	10/20	9/23	11/21	0.849
Height (cm) [a]	157.0 (153.0-162.3)	155.0 (153.0-164.5)	158.0 (152.0-167.3)	0.711
Weight (kg)	58.6 (54.8-62.5)	61.3 (56.8-65.7)	63.8 (59.6-68.0)	0.220
BMI (kg/m^2)	23.2 (22.2-24.1)	24.4 (23.1-25.7)	24.9 (23.6-26.2)	0.108
ASA status (I/II)	15/15	11/21	11/21	0.352
EBL (ml) [a]	300.0 (100.0-300.0)	300.0 (225.0-500.0)	300.0 (200.0-300.0)	0.094
Surgical time (min) [a]	215.0 (200.0-255.0)	240.0 (207.5-322.3)	230.0 (211.3-277.5)	0.117
Urine output (ml) [a]	450.0 (200.0-825.0)	450.0 (300.0-700.0)	400.0 (212.5-600.0)	0.608
Infusion rate (ml/h)	380.3 (362.2-398.4)	392.5 (371.7-413.3)	404.3 (384.6-424.0)	0.220

The values are expressed as mean (95% confidential intervals), median (interquartile range), or number of patients. There are no significant differences among groups. ASA: American Society of Anesthesiologists, BMI: body mass index, EBL: Estimated blood loss. $P < 0.05$ was considered to indicate statistical significance. [a]: median (interquartile range).

B. Performances of three fluid warming devices

No significant difference in the room temperature (T_r) was observed among the three groups throughout the study period (Table 2, Figure 3A). The mean T_r, T_r_Before, and T_r_Base were not significantly different among the groups (Table 2).

Table 2. Temperatures of inlet and outlet points of warming device, and operating room (°C)

	Group M (n=30)	Group R (n=32)	Group T (n=32)	P value
mT_r	21.8 (21.4-22.2)	22.2 (21.9-22.5)	22.0 (21.7-22.3)	0.313
T_r_Before	21.7 (21.3-22.1)	21.8 (21.4-22.3)	21.6 (21.3-21.9)	0.698
T_r_Base	21.7 (21.2-22.1)	21.9 (21.5-22.3)	21.6 (21.3-21.8)	0.380
mT_{Pin} [a]	21.9 (21.8-22.0)	21.8 (21.4-22.3)	21.9 (21.5-22.2)	0.194
T_{Pin}_Before [a]	21.5 (21.4-22.0) [†]	21.5 (21.5-21.8)	21.7 (21.6-22.0)	0.023
T_{Pin}_Base [a]	21.5 (21.4-21.9)	21.6 (21.5-21.8)	21.7 (21.6-21.9)	0.135
mT_{Pout} [a]	34.1 (33.1-34.8) [*†]	27.2 (26.9-27.6) [†]	28.4 (27.4-28.8)	< 0.001
T_{Pout}_Before [a]	21.5 (21.4-22.0) [*†]	21.2 (20.9-21.2) [†]	21.3 (21.1-22.2)	< 0.001
T_{Pout}_Base [a]	29.7 (29.0-30.4) [*†]	21.2 (21.1-21.3)	21.3 (21.2-21.9)	< 0.001

The values are expressed as mean (95% confidential intervals) or median (interquartile range). mT_r: mean room temperature (T_r), T_r_Before: room temperature before anesthesia induction, T_r_Base: room temperature immediately after anesthesia induction, T_{Pin}: temperature at inlet point ($_{Pin}$), T_{Pout}: temperature at outlet point ($_{Pout}$), mT_{Pin}: mean T_{Pin}, mT_{Pout}: mean T_{Pout}, T_{Pin}_Base: T_{Pin} just after anesthesia induction, T_{Pout}_Base: T_{Pout} just after anesthesia induction, T_{Pin}_Before: T_{Pin} before anesthesia induction, T_{Pout}_Before: T_{Pout} before anesthesia induction. $P < 0.05$ was considered to indicate statistical significance. [*]: $P < 0.05$ compared with group R, [†]: $P < 0.05$ compared with group T. [a]: median (interquartile range).

No significant difference in T_{Pin} throughout the study period was observed among the three groups, except for T_{Pin} before (T_{Pin}_Before) and 3 h after operating warming device (T_{Pin}_3.0h) (P =0.023, P =0.013, respectively) (Table 2, Figure 3B). T_{Pin}_Before and T_{Pin}_3.0h of group M were significantly different when compared with that of group T (P =0.020, P =0.017, respectively). Mean T_{Pin} (mT_{Pin}) from baseline to 2.5 h after the procedure for each device was not significantly different among the three groups (P =0.207, Table 2).

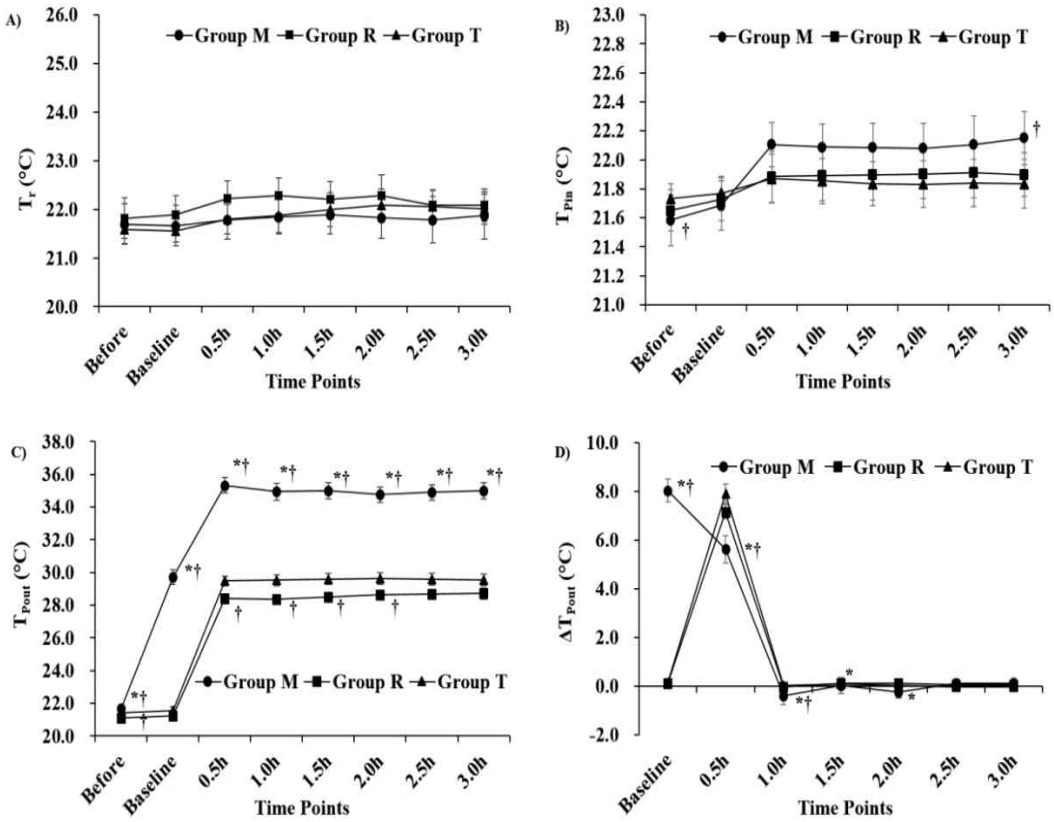

Figure 3. Temperatures of inlet (T_{Pin}) and outlet points (T_{Pout}) of warming device, and operating room (T_r) (°C). A) T_r, B) T_{Pin}, C) T_{Pout} at each measuring time point. D) Difference of T_{Pout} at each measured time point from that at previous time point [ΔT_{Pout}(_Prev)]. *: P < 0.05 compared with group R, †: P < 0.05 compared with group T.

I observed significant differences in the T_{Pout} values among three groups throughout the study period (P <0.001), and it was highest in group M, followed by group T, and lowest in group R (Table 2, Figure 3C). T_{Pout} of group M was significantly higher when compared with that of groups R and T. T_{Pout} of group T was significantly higher than that of group R, except for the T_{Pout}_Base, T_{Pout}_2.5h, and T_{Pout}_3.0h values. T_{Pout} before anesthesia induction (T_{Pout}_Before) was significantly higher in group M compared to that in groups R and T (P <0.001, P =0.004, respectively), and it was higher in group T than group R (P =0.003) (Table 2). T_{Pout} immediately after anesthesia induction (T_{Pout}_Base) was significantly different among three groups (P <0.001) (Table 2). The T_{Pout}_Base was significantly higher in group M compared to that of groups R and T (P <0.001, P <0.001, respectively), with no significant difference between the values of groups R and T (P =0.140). Mean T_{Pout} (mT_{Pout}) from baseline to 2.5 h post-surgery each device was significantly different among three groups (P <0.001, Table 2). The mT_{Pout} was significantly higher in group M compared to that in groups R and T (P <0.001, P <0.001, respectively), and its values were also significantly higher in group T than group R (P =0.004).

ΔT_{Pout}(_Prev), which is difference between T_{Pout} values at each measured time point from that at previous time point, was significantly different at several time points (Figure 3D). The ΔT_{Pout}(_Prev) of group M showed significant differences at baseline, 0.5 h, and 1.0 h post-surgery for each device, compared with that of groups R and T (P <0.001, P <0.001, respectively). The ΔT_{Pout}(_Prev) of group M was higher at 1.5 h and 2 h after operating each device than that of group R (P =0.029, P =0.001, respectively). However, the ΔT_{Pout}(_Prev) of each device was within ± 1°C and was stable after 30 m of activation.

C. Effect on temperatures of Tympanic membrane and distal esophagus (T_{tym}, T_{eso})

No statistically significant differences in the T_{tym} and ΔT_{tym}(_Prev) values were observed among the groups throughout the study period (Figures 4A and 4B). Mean values of T_{tym} (mT_{tym}) and ΔT_{tym}(_Prev) [$m\Delta T_{tym}$(_Prev)] were not significantly different among the groups (Table 3). ΔT_{tym}(_Base), tympanic temperature changes at each measured time point compared with baseline value, and its $m\Delta T_{tym}$(_Base) were lowest in group M; however the differences between the three groups were not significant (Table 3, Figure 4C).

Table 3. Tympanic membrane temperature (°C)

	Group M (n=30)	Group R (n=32)	Group T (n=32)	P value
mT_{tym}	36.1 (36.0-36.3)	36.1 (36.0-36.2)	36.1 (36.0-36.2)	0.938
$m\Delta T_{tym}$(_Prev)	-0.10 [-0.14-(-0.07)]	-0.13 [-0.15-(-0.10)]	-0.13 [-0.15-(-0.10)]	0.383
$m\Delta T_{tym}$(_Base)	-0.51 [-0.67-(-0.35)]	-0.62 [-0.71-(-0.52)]	-0.61 [-0.74-(-0.49)]	0.393

The values are expressed as mean (95% confidential intervals). There are no significant differences among groups. mT_{tym}: mean tympanic membrane temperature (T_{tym}), $m\Delta T_{tym}$(_Prev): mean value of T_{tym} changes at each measured point compared with previous time points, $m\Delta T_{tym}$(_Base): mean value of T_{tym} changes at each measured point compared with baseline value. $P < 0.05$ was considered to indicate statistical significance.

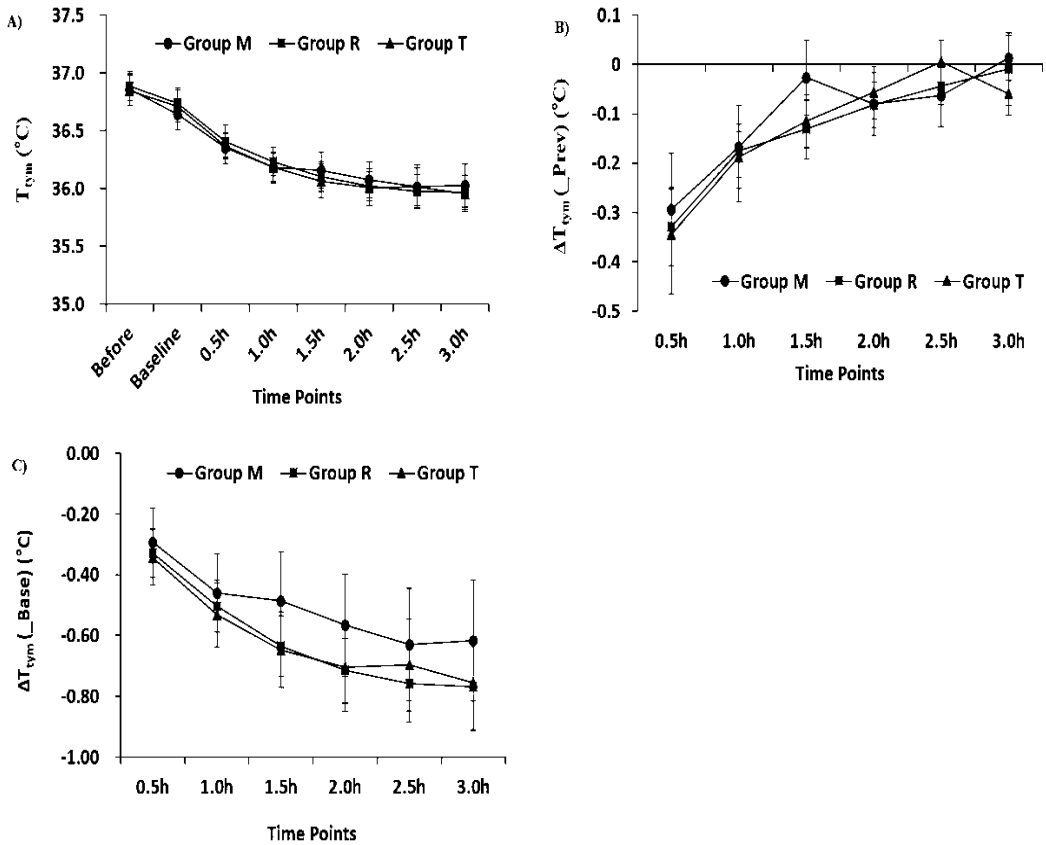

Figure 4. Tympanic membrane temperature (T_{tym}). A) T_{tym} at each measuring time point, B) Difference of T_{tym} at each measured time point from that at previous time point [ΔT_{tym}(_Prev)], C) Difference of T_{tym} at each measured time point from that at baseline [ΔT_{tym}(_Base)].

No statistically significant differences in values of T_{eso} and ΔT_{eso}(_Prev) were observed among the groups throughout the study period, except with regards to ΔT_{eso}(_Prev) which at 1.0 h after operating of each device was higher in group M than in group R (P =0.028) (Figures 5A and 5B). Mean of T_{eso} (mT_{eso}) values were not significantly different among the groups (P =0.881) (Table 4). However, mean of ΔT_{eso}(_Prev) [$m\Delta T_{eso}$(_Prev)] was significantly different among the groups (P =0.044), with that of group M being significantly higher than that of

Group T (P =0.048) (Table 4). ΔT_{eso}(_Base), difference of distal esophageal temperatures at each measured point compared with baseline value, and its $m\Delta T_{eso}$(_Base) were lowest in group M (Table 4, Figure 5C). Although there were no significant differences among the three groups, ΔT_{eso}(_Base) of group M was significantly lower than that of group T (P =0.033) (Figure 5C).

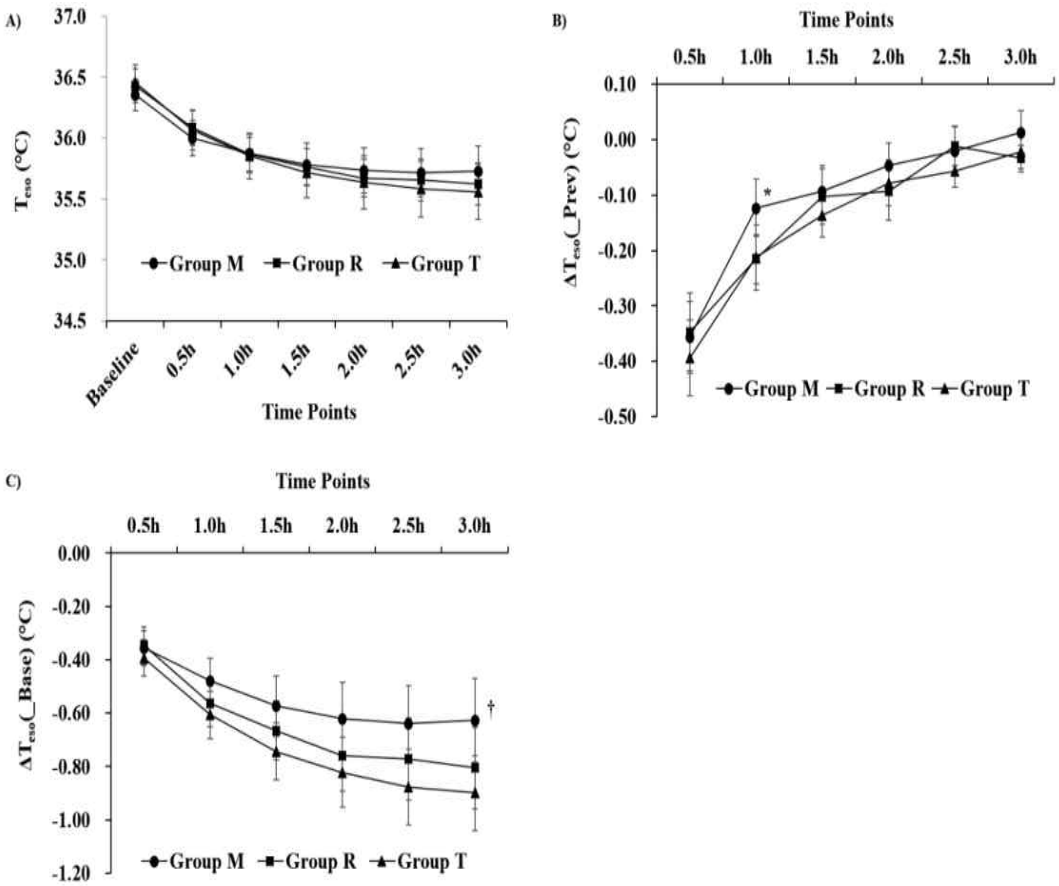

Figure 5. Tympanic membrane temperature (T_{eso}). A) T_{eso} at each measuring time point. B) Difference of T_{eso} at each measured time point from that at previous time point [ΔT_{tym}(_Prev)]. C) Difference of T_{eso} at each measured time point from that at baseline [ΔT_{eso}(_Base)]. *: $P < 0.05$ compared with group R, †: $P < 0.05$ compared with group T.

Table 4. Distal esophageal temperature (°C)

	Group M (n=30)	Group R (n=32)	Group T (n=32)	P value
mT_{eso} [a]	35.4 (35.8-36.2)	35.4 (35.8-36.0)	35.3 (35.6-36.3)	0.881
$m\Delta T_{eso}$(_Prev)	-0.10 [-0.13-(-0.08)]†	-0.13 [-0.16-(-0.11)]	-0.15 [-0.17-(-0.13)]	0.044
$m\Delta T_{eso}$(_Base)	-0.55 [-0.66-(-0.44)]	-0.65 [-0.77-(-0.54)]	-0.72 [-0.83-(-0.61)]	0.090

The values are expressed as mean (95% confidential intervals) or median (interquartile range). mT_{eso} : mean distal esophageal temperature (T_{eso}), $m\Delta T_{eso}$(_Prev): mean value of T_{eso} changes at each measured point compared with previous time points, $m\Delta T_{eso}$(_Base): mean value of T_{eso} changes at each measured point compared with baseline value. $P < 0.05$ was considered to indicate statistical significance. †: $P < 0.05$ compared with group T. [a]: median (interquartile range).

The difference between T_{tym} and T_{eso} [$\Delta(T_{tym}-T_{eso})$], showed no statistically significant differences between the groups throughout the study period (Figure 6), and mean $\Delta(T_{tym}-T_{eso})$ [$m\Delta(T_{tym}-T_{eso})$] was not significantly different among the groups (Table 5).

Table 5. Mean value of difference between T_{tym} and T_{eso} at each time point (°C)

	Group M (n=30)	Group R (n=32)	Group T (n=32)	P value
$m\Delta(T_{tym}-T_{eso})$	0.33 (0.24-0.41)	0.34 (0.26-0.42)	0.36 (0.24-0.49)	0.887

The values are expressed as mean (95% confidential intervals). There are no significant differences among groups. $m\Delta(T_{tym}-T_{eso})$: mean value of difference between T_{tym} and T_{eso} at each time point. T_{eso}: distal esophageal temperature, T_{tym}: tympanic membrane temperature.

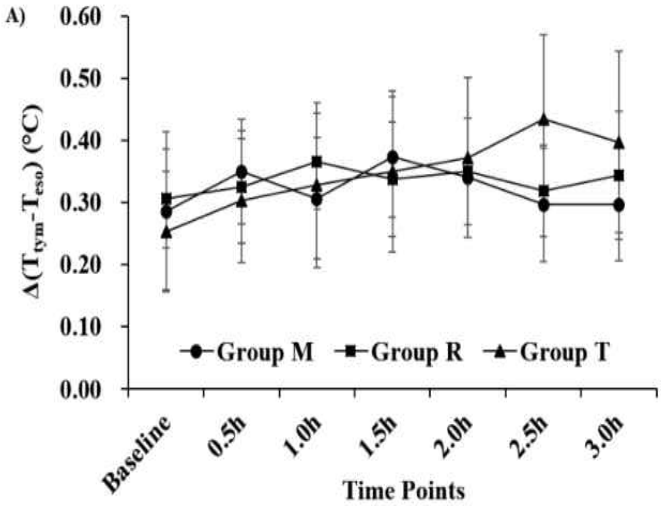

Figure 6. Difference between T_{tym} and T_{eso} [$\Delta(T_{tym}-T_{eso})$]. A) $\Delta(T_{tym}-T_{eso})$ at each measuring time point.

The values for final T_{tym} and T_{eso} (T_{tym}_Final, T_{eso}_Final), lowest T_{tym} and T_{eso} (T_{tym}_Lowest, T_{eso}_Lowest), and change of T_{tym} and T_{eso} from baseline value to T_{tym}_Lowest and T_{eso}_Lowest (ΔT_{tym}_Lowest, ΔT_{eso}_Lowest) were not significantly different among groups (Table 6).

Table 6. Final and lowest temperatures of tympanic membrane and distal esophagus (°C)

	Group M (n=30)	Group R (n=32)	Group T (n=32)	P value
T_{tym}_Final	36.0 (35.8-36.2)	36.0 (35.8-36.1)	36.0 (35.8-36.1)	0.820
T_{tym}_Lowest	35.9 (35.7-36.1)	35.9 (35.7-36.0)	35.9 (35.7-36.0)	0.965
ΔT_{tym}_Lowest	-0.75 [-0.92-(-0.56)]	-0.87 [-0.99-(-0.74)]	-0.83 [-0.98-(-0.68)]	0.496
T_{eso}_Final	35.7 (35.5-35.9)	35.6 (35.4-35.8)	35.6 (35.3-35.8)	0.512
T_{eso}_Lowest	35.7 (35.3-35.8)	35.6 (35.4-35.7)	35.5 (35.3-35.7)	0.393
ΔT_{eso}_Lowest	-0.72 [-0.86-(-0.58)]	-0.87 [-1.00-(-0.73)]	-0.94 [-1.08-(-0.80)]	0.076

The values are expressed as mean (95% confidential intervals). There are no significant differences between the groups. T_{tym}: tympanic membrane temperature, T_{eso}: distal esophageal temperature. T_{tym}_Final: final T_{tym}, T_{eso}_Final: final T_{eso}. T_{tym}_Lowest, T_{eso}_Lowest: Lowest T_{tym}, Lowest T_{eso}. ΔT_{tym}_Lowest, ΔT_{eso}_Lowest: differences of T_{tym}_Lowest, T_{eso}_Lowest from each baseline value.

D. Incidence of intraoperative hypothermia based on final and lowest distal esophageal temperature (%)

There were no significant differences among groups (Table 7). Incidence of intraoperative hypothermia below 35.0°C was lowest in group M, followed groups R and T with no significant differences.

Table 7. Incidence of intraoperative hypothermia based on final and lowest distal esophageal temperature

Parameter	Grade	Group M (n=30)	Group R (n=32)	Group T (n=32)	P value
T_{eso}_Final					0.750
	grade 1	10 (33.3%)	8 (25.0%)	8 (25.0%)	
	grade 2	17 (56.7%)	18 (56.2%)	17 (53.1%)	
	grade 3:	3 (10.0%)	6 (18.8%)	7 (21.9%)	
T_{eso}_Lowest					0.507
	grade 1	6 (20.0%)	6 (18.8%)	8 (25.0%)	
	grade 2	21 (70.0%)	20 (62.5%)	16 (50.0%)	
	grade 3	3 (10.0%)	6 (18.8%)	8 (25.0%)	

The values are expressed as numbers of patients (%). There are no significant differences among groups. T_{eso}: distal esophageal temperature, T_{eso}_Final: final T_{eso}, T_{eso}_Lowest. Grade 1: Above 36.0°C, grade 2: Between 36.0°C and 35.0°C, grade 3: Below 35.0°C

E. Estimated core temperatures by simple equation (T_{exp})

No statistically significant differences for both T_{exp} (Figure 7A) and mean T_{exp} (mT_{exp}) values (P =0.968) (Table 8) were observed between the groups throughout the study period. Final T_{exp} (T_{exp}_Final), lowest T_{exp} (T_{exp}_Lowest), and change in the T_{exp} values from baseline value to T_{exp}_Lowest (ΔT_{exp}_Lowest) also did not show statistically significant differences among the groups (Table 8).

Table 8. Expected core temperatures calculated by simple equation (T_{exp}) (°C)

	Group M (n=30)	Group R (n=32)	Group T (n=32)	P value
mT_{exp} [a]	35.9 (35.7-36.4)	36.0 (35.7-36.2)	35.9 (35.5-36.5)	0.958
T_{exp}_Final	35.7 (35.5-35.9)	35.6 (35.5-35.8)	35.6 (35.3-35.8)	0.557
T_{exp}_Lowest	35.6 (35.5-35.8)	35.6 (35.4-35.7)	35.5 (35.3-35.8)	0.700
ΔT_{exp}_Lowest	-0.71 [-0.84-(0.58)]	-0.86 [-1.00-(-0.73)]	-0.92 [-1.06-(-0.78)]	0.073

The values are expressed as mean (95% confidential intervals) and median (interquartile range). There are no significant differences among groups. T_{exp}: Estimated core temperatures, mT_{exp}: mean T_{exp}. T_{exp}_Final: final T_{exp}, T_{exp}_Lowest: Lowest T_{exp}, ΔT_{exp}_Lowest: differences of T_{exp}_Lowest. $P < 0.05$ was considered to indicate statistical significance. a: median (interquartile range).

No statistically significant differences in ΔT_{exp}(_Prev) was observed among the groups throughout the study period; however, the values of ΔT_{exp}(_Prev) at 0.5 h after operating fluid warming device (P <0.001, Figure 7B) were significantly different. ΔT_{exp}(_Prev) at 0.5 h was higher in group M than groups R and T (P <0.001, P <0.001, respectively).

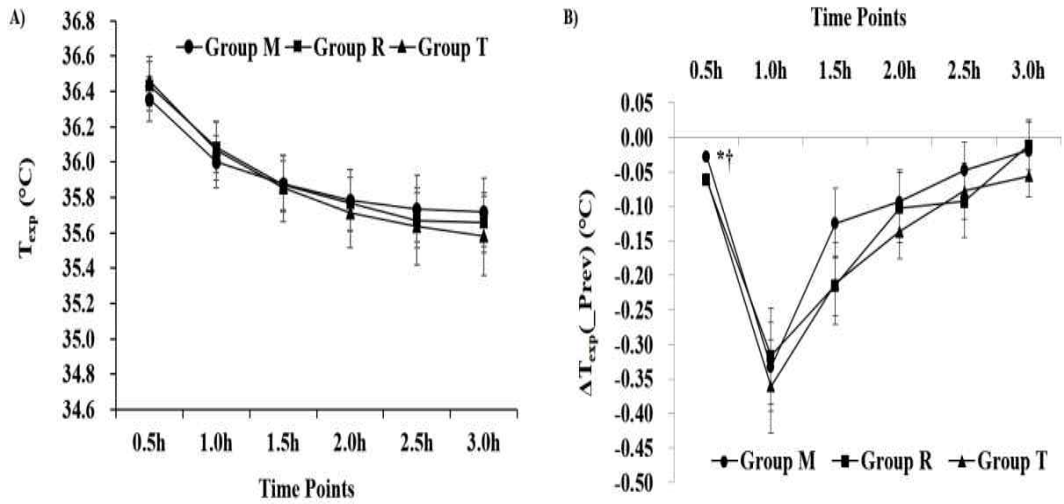

Figure 7. Expected core temperatures (T_{exp}) calculated by simple equation (°C). A) T_{exp} at each measuring time point, B) Difference of T_{exp} values at each measured time point from that at previous time point [ΔT_{exp}(_Prev)]. *: $P < 0.05$ compared with group R, †: $P < 0.05$ compared with group T.

Difference between T_{eso} and T_{exp} [$\Delta(T_{eso}-T_{exp})$], at each time point was not significant different (Figure 8).

Statistically significant differences in $\Delta(\Delta T_{exp}-\Delta T_{eso})$, difference between ΔT_{exp}(_Prev) and ΔT_{eso}(_Prev), were observed among the groups throughout the study period (Figure 8). The values for $\Delta(\Delta T_{exp}-\Delta T_{eso})$ were lower in group M than groups R and T. Furthermore, $\Delta(\Delta T_{exp}-\Delta T_{eso})$ values of group T were significantly lower than that of group R, except in the case of T_{Pout}_0.5h.

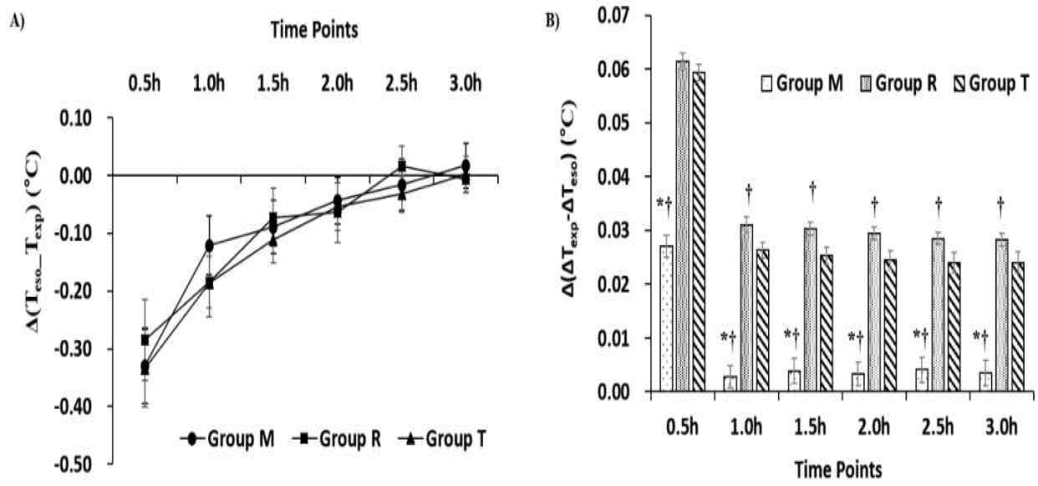

Figure 8. Difference between T_{eso} and T_{exp}. A) Difference between T_{eso} and T_{exp} [$\Delta(T_{eso}-T_{exp})$] at each measuring time point, B) Difference between ΔT_{exp} and ΔT_{eso} [$\Delta(\Delta Texp-\Delta Teso)$] at each measuring time point. *: $P < 0.05$ compared with group R, †: $P < 0.05$ compared with group T.

Ⅴ. Discussion

Here, we demonstrated that Mega Acer Kit® was more effective than Ranger™ and ThermoSens® in terms of heating capability for groups M, R and T, which was 13.6°C, 7.3°C, and 8.0°C, respectively. Although neither of them delivered the normothermic (37°C) fluid to patients consequently, they were effective in preventing intraoperative hypothermia (core temperature < 35°C).

Mega Acer Kit® is based on a heating mechanism that is different from ThermoSens® and Ranger™. Mega Acer Kit® is made up of a heated and humidified circuit, regulating the fluid warming function with a convective warming system, which can warm the fluid directly using heated convective air currents [14,15]; however, ThermoSens® and Ranger™ employ a dry heat technology. ThermoSens® uses plastic cassettes in contact with a heating plate [16,17], and Ranger™ uses using a flat plastic sheet in contact with a counter-current metal heating plate [18], thus showing differences in their effectiveness in preventing intraoperative hypothermia and successfully heating the fluid.

Most studies with Mega Acer Kit®, ThermoSens®, or Ranger™ were performed to investigate the performance in the laboratory [11,12,14-17,19], and only a few studies were performed to evaluate their effects on changes to the core temperature [14,15]. A few of them even studied their effectiveness at low and moderate flow rates similar to this study [11,12,14,15].

Clinical studies demonstrated that the Mega Acer Kit® was effective in maintaining the T_{eso} above 35°C [14,15], despite the decrease in the T_{tym} and T_{eso} values, caused because of an impairment of the central thermoregulation (which controls body heat redistribution) under the effects of the anesthesia [20]. Jung et al. [14] reported that the T_{eso} was significantly higher in group using the Mega Acer Kit® than groups using the Ranger™ throughout the study period, and it was 35.8 ± 0.3°C and 35.1 ± 0.1°C, respectively 3 h post-surgery. Kim et al. [15] reported that the T_{eso} decreased by 0.5 ± 0.5℃ from baseline values at the end of surgery in a

group with Mega Acer Kit®. In spinal surgery, this lowest T_{eso} was significantly decreased, which was -0.8℃ in group received with Mega Acer Kit®, -1.4℃ in group the Ranger™, and -1.7℃ in group without warmer [14]. This study also showed similarity in the values of the final T_{eso}, which was 35.7°C with Mega Acer Kit® and 35.6°C with the Ranger™, and the lowest T_{eso} was -0.72℃ with Mega Acer Kit®, -0.87℃ in group the Ranger™, and −0.94℃ in group with the ThermoSens® in patients who underwent spinal fusion surgery. These values were similar to that of the expected core temperatures (T_{exp}) using the equation described in Presson's study [13].

None of the fluid warmers used in this study was successful in offsetting the intraoperative redistribution hypothermia, even though their use could prevent the marked decrease of T_{eso}. While the incidence of lowest T_{eso} (< 35.0°C) was 100% in group without the use of fluid warmer, it was 0% and 57% in group with Mega Acer Kit® and the Ranger™, respectively [14]. However, this study showed a 10.0%, 18.8%, 21.9% incidence of hypothermia in groups with Mega Acer Kit®, Ranger™, and ThermoSens®, respectively. This discrepancy may be explained by the mean final delivered fluid temperature, which was comparatively higher in Jung's study [14].

Ideally, fluid of approximately 37° C should be delivered to the patient [21,22], but the final delivered fluid temperature can be influenced by the length of the extended tube from warmer in an extended length-dependent manner, apart from the effects of a wide range of flow rates in clinical conditions [18,23,24]. Mega Acer Kit® warmed the fluid (33.6 ± 1.4℃) at an 18 cm distance at flow rates of 400 ml/h, and 31.0 ± 1.0℃ at a 118 cm distance at a mean 442 ml/h [15]. The Mega Acer Kit® at a warming temperature of 38°C was fit to deliver warmed fluid with 37°C at 108 cm distance in patients with the flow rate of 400 ml/h, but the Ranger™ at a warming temperature of 41°C was not [14]. Furthermore, at a distance of 198 cm, both the devices did not achieve the delivery temperature of 37°C, and the final delivered

fluid temperatures were 35.4°C with the Mega Acer Kit® and 32.8°C with the Ranger™ [14]. This study also showed that the final delivered fluid temperature did not achieve 37°C despite the use of a shorter tube (76 cm) than that of Jung's study [14].

This discrepancy may be explained by differences in the flow rates and absence of covering the extended tube. First, the minimal (about 300 ml/h) and maximal (about 550 ml/h) flow rates were different according to the body weight of each patient in this study, even though the mean flow rate in this study was similar with that of Jung's study fixed at 400 ml/h [14]. If more number of patients receiving the fluid at a flow rate above 400 ml/h, the final delivered fluid temperature would have decreased further. This difference in the flow rate would have influenced the warming capacity of each device and the final fluid temperature. Therefore, we should consider a device-specific maximum flow rate in order to maintain the final temperature of 37°C [14]. The Bair Hugger, which is suitable for prolonged minor surgeries, has a maximal flow rate of up to 1 l/h (17 ml/min) [18]. The most effective performance could be achieved at low to moderate flow rate (< 860 ml/h) using the Mega Acer Kit®, and at high flow rate (> 1140 ml/h) using the Ranger™ and the ThermoSens® with a shorter tubing distance [12,25]. Mega Acer Kit® presented the highest fluid temperature (34.3°C) at 440 ml/h and 76 cm tubing distance. However, none of the fluid warmers achieved a constant normothermic temperature (> 36.5°C) regardless of flow rates and distances [12]. Therefore, the Mega Acer Kit® seems to be effective in preventing intraoperative hypothermia in cases with a shorter extended tube length and lower flow rates.

Second, the presence of covering on the extended tubing line can influence the final fluid temperature. The Mega Acer Kit® was more effective in demonstrating fluid warming (above 35.5℃) than Ranger™ and ThermoSens®, in an experimental study with similar study design to study the effectiveness of fluid warmer, performed at 440 ml/h for 60 m after preheating for 10 m with 41℃ [11]. The delivered fluid temperature was slightly higher at 76 cm from the device, compared to this study, by covering the extended tube with drape. However, none of

the fluid warmers delivered the fluid above 37℃ in this study as well as in Kim's study [11]. Here, if we had covered the extended tube, the delivered fluid temperature would have been higher.

The ThermoSens® and Ranger™ have typically been studied at higher flow rates [16,17,24], except for a few studies which do so at lower and moderate flow rates [11,12,14]. In high flow rates such as 1.8 l/h and 3 l/h, the warmer with the similar technology of ThermoSens® could delivered 39.4°C and 39.7°C fluid at an 18 cm tubing distance; however, the temperature subsequently decreased by 1.6°C ± 1.3°C and 1.2°C ± 1.0°C at 60 cm tubing distance [17]. However, at the low and moderate flow rates, they could not deliver the normothermic fluid (37°C) at a tubing distance greater than 75 cm [13,26,27]. Presson et al. [13] suggested that a flow rate of at least 300 ml/h was required to deliver fluids above 32℃ at 108 cm of tubing distance, and the fluid temperature did not increase above 35℃ despite increasing the flow rate to 1 L/h. Patel et al. [27] also reported that the delivered fluid temperatures were 29.5℃ at 390 ml/h and 30.8℃ at 780 ml/h, similar to my results as well as that of Kim's study using ThermoSens® [11]. Ranger™ also did not successfully achieve delivered fluid temperatures greater than 35℃ at 78-103 cm tubing distance [11,14]. I excluded the potential factors that could influence the results of this study. First, the Mega Acer Kit®, Ranger™, and ThermoSens® have the unequalled extended tubing line themselves, so, we utilized a fluid tube of equal length from each device to the outlet point (76 cm), and from the outlet point to the patient's intravenous cannula (55 cm). Second, the delivered fluid temperature demonstrates a negative correlation with humidity and a positive correlation with temperature of the inspired gas [11]. The Mega Acer Kit® showed the differences in the fluid warming performance at a flow rate within range of this study based on the presence of humidification [11,14,15]. The delivered warmed fluid temperature was above 36℃ using the Mega Acer Kit® without humidification [11,14]; however, it decreased below 33.6℃ under humidification despite a

shorter outlet distance (18 cm) [15]. Therefore, we did not include the effects of humidification on the warming fluid, and set the Mega Acer Kit® at a warming temperature of 41°C to increase the temperature of the inspired gas.

Based on the temperature of warmed fluid, we can anticipate the degrees of the decrease in intraoperative body temperature with ΔMBT, as calculated using Horowitz's equation [24]. If the ΔMBT is more than 0.5℃, a fluid warmer should be applied. However, a fluid warmer is generally not used, as the minimal expected ΔMBT in cases required low to moderate flow rates. Although the ΔMBT was below 0.5℃ after the infusion of unwarmed fluid, the intraoperative hypothermia below 35℃ could be observed after 3 h infusion at 400 ml/h [14]. This study showed that the use of fluid warmers regardless of ΔMBT was related to the decrease in the incidence of intraoperative hypothermia below 35°C. Hence, the fluid warmer should be used for preventing and treating intraoperative hypothermia even if the ΔMBT is below 0.5℃ and if the fluid infuses at low to moderate flow rate [11].

This study had several limitations. First, there are several factors that may be considered as confounding factors: the T_{Pin}_3.0h, T_{Pout}_before, and T_{Pout}_base. With regards to, T_{Pout}_before and T_{Pout}_base, it was impossible to eliminate the heating due to the heated circuit in the preheating period, as the fluid line of the Mega Acer Kit® was instilled thorough the circuit. I checked whether these differences influence the results of T_{eso} and found that there was no significant effect on the results. Second, we exposed the extended tubing line into the cold environment without the use of a covering, which might influence the fluid temperature. Third, we could not ignore the effect of extension tubing line (55 cm) from outlet points, thus, we re-estimated the final expected core temperatures (T_{exp}_Final) in the patients using the previous temperatures after calculating the expected fluid temperatures at the nearest point from patient, which was a distance of 55 cm from the outlet point by following equation [28]: [Delivery temperature (°C): Td = Ti − f(Ti-Ta), Equilibration fraction: f = L/(24Q +L)], where Ti is the

initial saline temperature (°C), Ta is ambient air temperature (°C), Q is flow rate (ml/min), L is intravenous tubing length (cm), f is equilibration fraction, and Td is delivery temperature (°C). Even though we did not show this result, these expected delivered fluid temperatures were lower than the outlet point (76 cm), and the re-estimated $T_{exp_}$Final was not significantly changed.

In conclusion, we demonstrate that the Mega Acer Kit® was more effective in heating the fluid than Ranger™ and ThermoSens® at flow rates ideal to replace clinical maintenance fluid; however, all the fluid warmers used could not produce a normothermic fluid temperature at such infusion rates. Nevertheless, Mega Acer Kit® was effective in preventing intraoperative hypothermia (core temperature <35°C) than Ranger™ and ThermoSens®. I suggest that the most effective performance could be achieved using the Mega Acer Kit® at low flow rates, with a shorter tubing distance, and with a covered extension line, even though they do not provide the normothermic delivered fluid temperature.

Ⅵ. References

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