

Comparison of Remimazolam and Sevoflurane on Perioperative Body Temperature Changes in Older Patients Undergoing Transurethral Resection of Prostate or Bladder Tumors Under General Anesthesia: A Randomized Prospective Clinical Trial

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Purpose: Perioperative hypothermia is a common complication of general anesthesia, especially in older patients undergoing transurethral resection of the prostate (TURP) or bladder tumors (TURB). Age-related thermoregulatory impairment increases vulnerability to hypothermia, and large-volume irrigation during these procedures further elevates the risk. Preclinical and clinical studies suggest that remimazolam may reduce perioperative hypothermia and shivering compared with volatile anesthetics. This study compared remimazolam and sevoflurane on perioperative body temperature (BT) changes in older patients undergoing TURP or TURB.

Patients and Methods: This prospective, randomized clinical trial enrolled 84 patients aged 65–85 years undergoing TURP or TURB under general anesthesia. Patients were randomized to receive either remimazolam ($n = 42$) or sevoflurane ($n = 42$). Preoperative tympanic temperature was measured immediately before induction, and intraoperative core BT was monitored with an esophageal temperature probe. Postoperative BT was recorded using tympanic thermometry. The primary outcome was the incidence of perioperative hypothermia ($BT < 36.0^{\circ}\text{C}$). Secondary outcomes included intraoperative decrease in BT, incidence of profound hypothermia ($BT < 35.0^{\circ}\text{C}$), need for active warming in the PACU, postoperative nausea, vomiting and shivering, pain scores, and perioperative hemodynamic variables.

Results: The change over time in BT in operating room was significantly different between 2 groups ($P = 0.010$). The remimazolam group exhibited significantly smaller intraoperative reductions in core BT compared to the sevoflurane group ($0.83 \pm 0.38^{\circ}\text{C}$ vs $1.08 \pm 0.48^{\circ}\text{C}$, $P = 0.011$). The incidence of profound hypothermia occurred in the sevoflurane group (17%) and was not observed in the remimazolam group (0%) ($P = 0.029$). Significantly fewer patients in the remimazolam group required active warming in the PACU (19% vs 40%, $P = 0.032$). Hemodynamic variables and postoperative shivering rates were comparable between the groups.

Conclusion: These findings suggest that remimazolam may offer thermoregulatory advantages in older surgical patients at high risk for hypothermia.

Keywords: remimazolam, sevoflurane, hypothermia, older patients, thermoregulation, general anesthesia

Introduction

Perioperative hypothermia is a common general anesthesia complication and is associated with numerous adverse outcomes, including increased risks of surgical site infection, coagulopathy, delayed drug metabolism, prolonged

hospitalization, and cardiovascular complications.^{1–3} Older patients are particularly vulnerable to hypothermia because of their diminished thermoregulatory capacity, reduced metabolic rate, and decreased subcutaneous fat insulation.^{4,5}

Transurethral resection of bladder tumor (TURB) and transurethral resection of the prostate (TURP) are among the most commonly performed urological procedures in older patients because of the high prevalence of bladder tumors and benign prostatic hyperplasia in this age group.^{6,7} Although minimally invasive, these procedures are often performed under general anesthesia and involve continuous irrigation with large volumes of fluid. This can lead to significant intraoperative heat loss, further compounding the risk of hypothermia in susceptible older patients.^{8,9} Although spinal anesthesia is widely used for transurethral resection surgeries, it may be technically difficult in older patients due to vertebral deformities and degenerative changes.¹⁰ Previous work has also suggested potential advantages of general anesthesia in older patients undergoing short transurethral procedures, reporting shorter induction and recovery times compared to spinal anesthesia.¹¹ In addition, transurethral resection requires large-volume irrigation fluid, and previous study demonstrated that systemic absorption of irrigation fluid was significantly greater during spinal anesthesia than during general anesthesia.¹² In addition, other previous reports have demonstrated that bladder perforation is a recognized complication of TURB performed under spinal anesthesia, largely due to obturator reflex.¹³ Although obturator nerve block can reduce this risk, its efficacy is not absolute, and in cases of block failure, obturator jerks may still occur, potentially leading to perforation. Therefore, general anesthesia was selected in the present study to minimize technical difficulties, enhance patient safety, and allow direct comparison between remimazolam and sevoflurane.

Anesthetic agents also play a crucial role in thermoregulation. Most general anesthetics impair the central thermoregulatory response by reducing vasoconstriction and shivering threshold, making patients more prone to core temperature reduction.¹⁴ In contrast, midazolam exerts a relatively mild thermoregulatory suppression.¹⁵ Remimazolam, a novel ultrashort-acting benzodiazepine, combines the cardiovascular stability of midazolam with a rapid onset and offset, similar to propofol.¹⁶ Remimazolam undergoes organ-independent metabolism by tissue esterases, resulting in a predictable onset and recovery profile even in older patients, with minimal accumulation.¹⁷ In contrast, volatile anesthetics such as sevoflurane demonstrate an age-dependent reduction in the minimum alveolar concentration (MAC), indicating increased pharmacodynamic sensitivity in older patients.¹⁸ In older patients, these pharmacodynamic differences between two anesthetics may result in different perioperative thermoregulation during surgery compared to younger adult patients. Although efficacy and safety of remimazolam have been demonstrated under procedural and general anesthesia, its effects on intraoperative thermoregulation remain under explored. In animal experiments, remimazolam suppressed shivering even after anesthesia, suggesting potential benefits in preventing postoperative shivering.¹⁹ In addition, a randomized controlled trial in gynecologic laparoscopic surgery reported that remimazolam use was associated with a significantly lower incidence of intraoperative hypothermia and postoperative shivering compared with sevoflurane.²⁰ Given its pharmacological profile, remimazolam may offer advantages in maintaining core temperature in older patients during the surgery with a high hypothermia risk. We hypothesized that remimazolam might be associated with a lower incidence of perioperative hypothermia and a reduced need for postoperative warming interventions than sevoflurane in older patients. Therefore, this study aimed to compare the effects of remimazolam and sevoflurane on intraoperative and postoperative thermoregulation in older patients undergoing TURB or TURP.

Materials and Methods

This prospective, randomized, controlled study was conducted at Gachon University Gil Medical Center from May 2023 to February 2025, following approval by the institutional review board of Gachon University Gil Medical Center (GFIRB2023-073). This study was registered with the Clinical Research Information Service (CRIS) prior to patient enrollment (registration no. KCT0008417). This study complies with the Declaration of Helsinki. Prior to the operation, written informed consent was obtained from all patients. Patients aged 65 to 85 years classified as American Society of Anesthesiologists (ASA) physical status 1 or 2 and scheduled for TURP or TURB under general anesthesia were eligible for inclusion. Only individuals capable of reading and understanding the informed consent documents were enrolled. The exclusion criteria were as follows: preoperative body temperature (BT) greater than 37.5°C or less than 36°C; hemodynamic instability or respiratory failure; known hypersensitivity to study-related medications; anticipated difficulty

with endotracheal intubation (eg, limited mouth opening, restricted cervical extension, or Mallampati class IV); morbid obesity (body mass index >35 kg/m²); and total anesthesia duration (from induction to emergence) of less than 45 min.

The patients were randomized into 2 groups using a computer-generated randomization protocol: the remimazolam and sevoflurane groups. No premedications were administered. Upon arrival at the preanesthetic room, the patients were covered with a forced-air warming blanket, and after 5 min, the tympanic temperature and hemodynamic parameters were measured.

Study Population, Randomization and Data Collection

A total of 84 older patients scheduled for TURB or TURP were randomized to receive either sevoflurane (sevoflurane group, $n = 42$) or remimazolam (remimazolam group, $n = 42$). No patients were lost to follow-up or excluded from the final analysis (Figure 1). Baseline characteristics included age, sex, body weight, height, type and duration of surgery, volumes of intravenous and irrigating fluid, operating room temperature, and emergence time.

Anesthesia Induction

All patients underwent preoxygenation with 100% oxygen for 1 min. Standard monitoring, including electrocardiography, noninvasive blood pressure measurement, and pulse oximetry, was performed. In the remimazolam group, patients received intravenous administration of remimazolam at 6 mg/kg/h and fentanyl at 1 μ g/kg. After loss of consciousness, rocuronium was administered, a supraglottic airway (I-gel) was inserted. Endotracheal intubation was performed only when i-gel placement failed or in patients with conditions known to make supraglottic airway insertion difficult, such as edentulous or unstable dentition, cervical spine instability, high BMI, or upper airway abnormalities. An esophageal stethoscope with

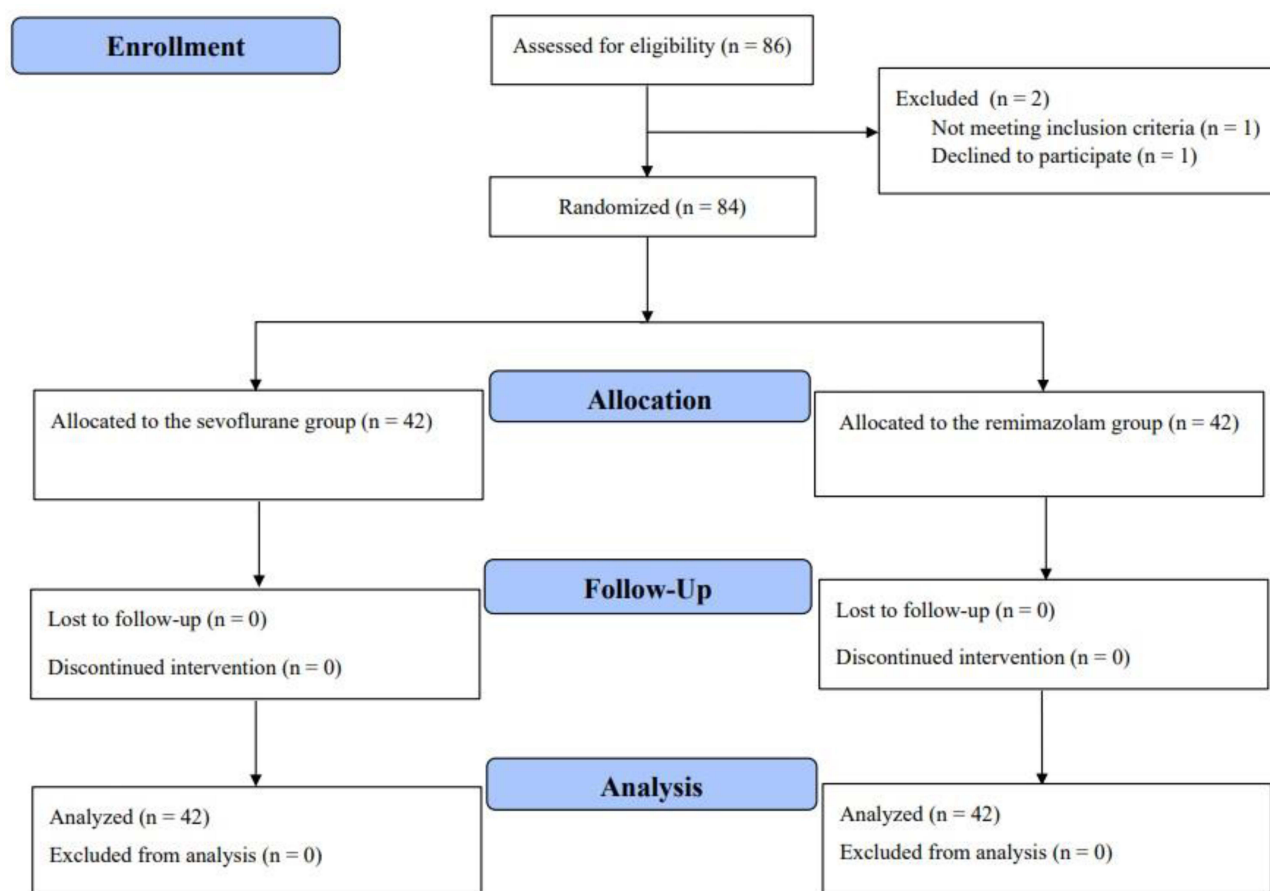


Figure 1 Flowchart of patient allocation.

temperature sensor was then placed. Anesthesia was maintained with remimazolam (1–3 mg/kg/h) and a continuous infusion of remifentanyl. In sevoflurane group, patients received propofol (1.5–2 mg/kg) and fentanyl (1 µg/kg) intravenously. After loss of consciousness, rocuronium was administered, followed by I-gel insertion or endotracheal intubation, if necessary. An esophageal stethoscope was then placed. Anesthesia was maintained using an infusion of sevoflurane and remifentanyl. Bispectral index (BIS) was continuously monitored using a BIS monitor (Covidien LLC, Mansfield, MA, USA) placed on the forehead. The BIS score was maintained between 40 and 60 for all patients.

Temperature and Hemodynamic Monitoring

In the operating room, the tympanic temperature was recorded immediately before anesthesia induction. Core BT was measured using an esophageal stethoscope at 5, 15, and 30 min after induction, and at the end of the operation. In the postanesthetic care unit (PACU), the tympanic temperature was measured upon arrival and at 15, 30, and 45 min after arrival and at discharge.

The following parameters were recorded in the PACU: vital signs, the presence of shivering, episodes of hypertension or hypotension, postoperative nausea and vomiting (PONV), and numerical rating scale (NRS) pain scores. Active warming was initiated if body temperature dropped below 35°C.

Hemodynamic parameters were recorded at the following time points: 5 min after arrival in the preanesthesia room; immediately before induction; at 5, 30, 45, and 60 min after induction; at the end of the procedure; at 0, 15, 30, and 45 min after PACU arrival; and at PACU discharge.

Primary and Secondary Outcomes

The primary outcome measure was the incidence of perioperative hypothermia. Hypothermia was defined as core BT (an esophageal or tympanic temperature) below 36.0°C at any point during the perioperative period. Secondary outcomes included the difference in intraoperative core body temperature between the remimazolam and sevoflurane groups, incidence of postoperative nausea and vomiting (PONV), incidence of postoperative shivering, postoperative pain intensity measured using the NRS in the PACU, and perioperative hemodynamic variables such as mean arterial pressure and heart rate. These parameters were recorded at predefined time points before, during, and after the procedure.

Statistical Analysis

A previous study reported that the incidence of perioperative hypothermia in patients undergoing TURP or TURB was approximately 54%.²¹ Assuming that a reduction of more than 50% in the incidence of hypothermia would be clinically significant, we calculated the required sample size with a 2-sided α -level of 0.05 and a power of 80% ($1-\beta = 0.80$). Based on these assumptions, a minimum of 40 patients were required per group. To account for potential dropouts or protocol violations, the total sample size was increased to 84 (42 per group).

All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS Inc., Chicago, Illinois, USA) version 17.0. Continuous variables are expressed as mean \pm standard deviation (SD) and compared using the independent *t*-test or Mann–Whitney *U*-test, as appropriate, based on the normality of distribution. Categorical variables are presented as counts and percentages and compared using the chi-square test or Fisher's exact test when the expected frequencies were small. Changes in core BT over time were analyzed using repeated measures ANOVA. Interaction effects between group and time were evaluated to assess the differences in temperature trends between the remimazolam and sevoflurane groups. A *P* value < 0.05 was considered statistically significant.

Results

Baseline demographic and perioperative characteristics were not significantly different between the 2 groups (all *P* > 0.05) (Table 1).

In the operating room, the change in BT over time differed significantly between the 2 groups (*P* = 0.010), and the sevoflurane group showed a significantly lower BT at the end of the procedure than the remimazolam group. The BT decreased significantly in both groups from before anesthesia induction (preoperative value) to 15 min after induction (*P* < 0.001) (Figure 2). The mean difference from preoperative to the end of the procedure in BT (Δ BT) was significantly smaller in the

Table 1 Patient Characteristics and Perioperative Clinical Data

Variables	Sevoflurane (N = 42)	Remimazolam (N = 42)	P value
Age (yr)	73.7 ± 7.7	72.1 ± 5.4	0.183
Sex (M/F)	36/6	39/3	0.290
In preanesthetic room			
Room temperature (°C)	20.8 ± 1.05	21.1 ± 1.52	0.359
Body temperature (°C)	36.6 ± 0.21	36.6 ± 0.24	0.739
Type of procedure (n)			0.811
TURB/TURP	30/12	29/13	
Weight (kg)	66.6 ± 9.8	64.8 ± 9.7	0.401
Height (cm)	163.5 ± 6.9	164.9 ± 7.9	0.388
Emergence time (min)	7.9 ± 5.1	8.3 ± 3.2	0.074
Duration of anesthesia (min)	74.1 ± 35.1	71.8 ± 23.1	0.725
Operative time (min)	44.3 ± 34.4	43.1 ± 22.2	0.836
Intravenous fluid (mL)	297 ± 175	281 ± 124	0.635
Irrigating fluid (L)	13.4 ± 15.4	13.2 ± 10.1	0.922

Note: Values are mean ± SD.

Abbreviations: TURB, transurethral resection of bladder tumor; TURP, transurethral resection of the prostate.

remimazolam group than in the sevoflurane group ($0.83 \pm 0.38^{\circ}\text{C}$ vs $1.08 \pm 0.48^{\circ}\text{C}$, $P = 0.011$). Furthermore, the incidence of profound hypothermia (body temperature $34.5\text{--}34.9^{\circ}\text{C}$) occurred only in the sevoflurane group (17%) and was not observed in the remimazolam group (0%) ($P = 0.029$). A higher proportion of patients maintained intraoperative normothermia ($\geq 36.0^{\circ}\text{C}$) in the remimazolam group (38% vs 21%) (Table 2). In addition, the changes in mean arterial pressure and heart rate over time were not significantly different between the 2 groups (both $P > 0.05$) (Figure 3).

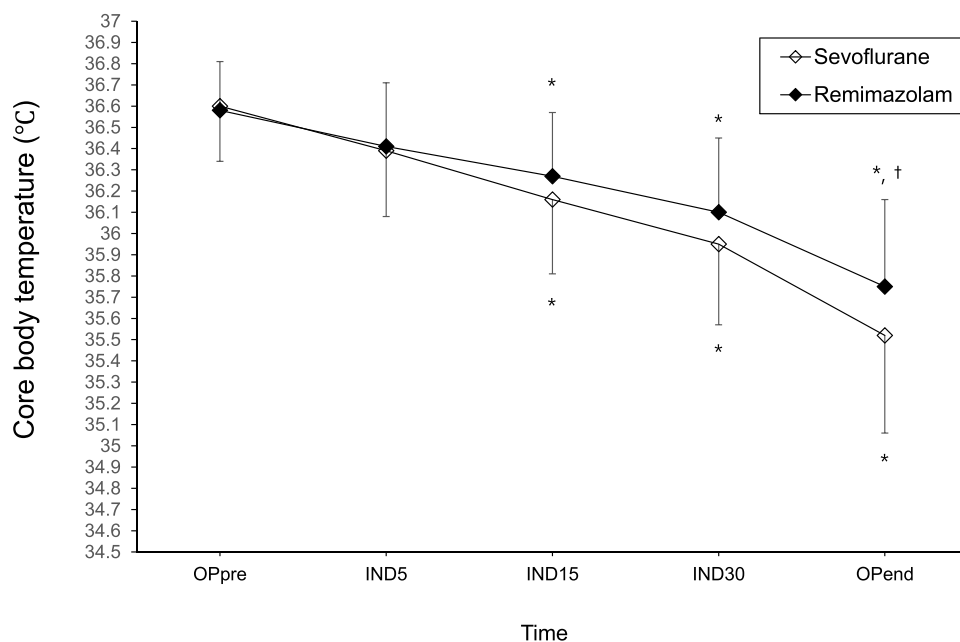


Figure 2 Changes in core body temperature in the operating room during transurethral resection of the bladder or prostate in older patients. Error bars represent the standard deviation. The change over time in body temperature was significantly different between 2 groups ($P = 0.010$). In both the sevoflurane and remimazolam groups, body temperature decreased significantly 15 min after anesthesia induction ($P < 0.001$). * $P < 0.05$, vs OPpre within the group; † $P < 0.05$, vs sevoflurane group. **Abbreviations:** OPpre, preoperative; IND5, IND15, and IND30, 5, 15, and 30 min after anesthetic induction, respectively; OPend, end of the procedure.

Table 2 Incidences of Hypothermia and Shivering During the Perioperative Period

Variables	Sevoflurane (N = 42)	Remimazolam (N = 42)	P value
Intra-operative period (in OR)			0.029
Normothermia ($\geq 36.0^{\circ}\text{C}$)	9 (21%)	16 (38%)	
Mild hypothermia ($35.5\text{--}35.9^{\circ}\text{C}$)	13 (31%)	14 (33%)	
Moderate hypothermia ($35.0\text{--}35.4^{\circ}\text{C}$)	13 (31%)	12 (29%)	
Profound hypothermia ($34.5\text{--}34.9^{\circ}\text{C}$)	7 (17%)	0 (0%)	
ΔBT ($^{\circ}\text{C}$)	1.08 ± 0.48	0.83 ± 0.38	0.011
Postoperative period (in PACU)			
Hypothermia ($< 36.0^{\circ}\text{C}$) on arrival	33 (79%)	26 (62%)	0.152
Shivering (n)	1 (2%)	1 (2%)	1.00
Needing rescue warming (n)	17 (40%)	8 (19%)	0.032
Needing rescue medication (n)	1 (2%)	0 (0%)	1.00

Note: Data are expressed as mean \pm SD or numbers of patients (%).

Abbreviations: OR, operating room; PACU, postanesthetic care unit; ΔBT , difference between preoperative and intraoperative minimum body temperature.

In the PACU, the change in BT over time differed significantly between the 2 groups ($P = 0.025$), and the sevoflurane group showed significantly lower BT upon arrival at the PACU and at 15 min after PACU arrival than the remimazolam group. The BT increased significantly in both groups from PACU arrival to 45 min after arrival ($P < 0.01$) (Figure 4). Upon arrival to the PACU, hypothermia ($< 36.0^{\circ}\text{C}$) was observed in 62% of patients in the remimazolam group and 79% in the sevoflurane group, though this difference was not statistically significant ($P = 0.152$). Additionally, significantly fewer patients in the remimazolam group required active warming in the PACU (19% vs 40%, $P = 0.032$). The incidence of postoperative shivering was low and similar in both groups (2%). However, the need for rescue warming was significantly lower in the remimazolam group (19%) than in the sevoflurane group (40%; $P = 0.032$). Only 1 patient in the sevoflurane group required rescue medication for thermoregulation ($P = 1.00$) (Table 2).

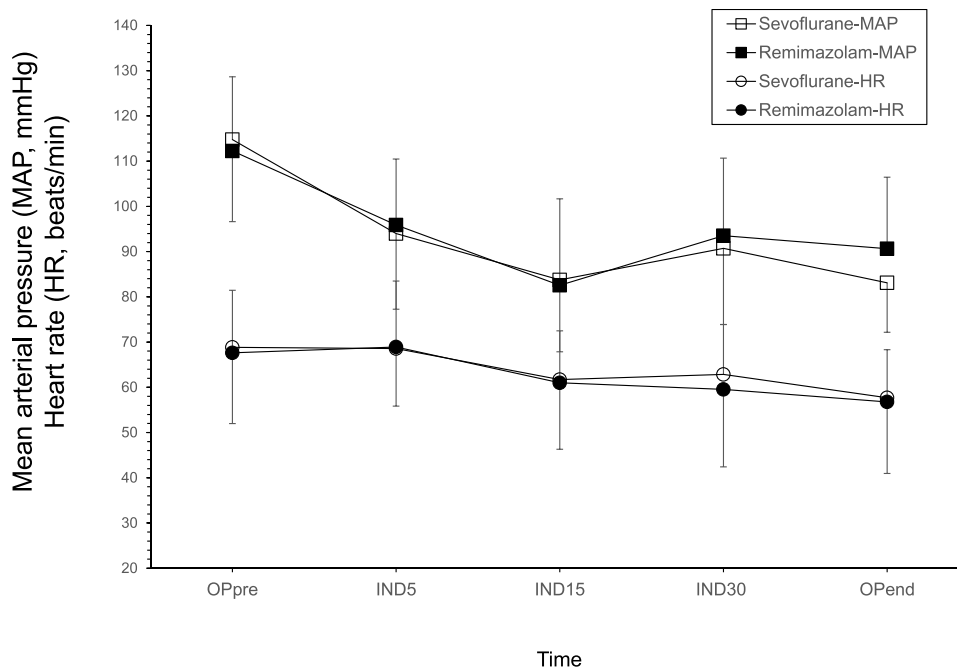


Figure 3 Changes in the mean arterial pressure and heart rate during transurethral resection of the bladder or prostate in older patients. Error bars represent the standard deviation. The changes in mean arterial pressure and heart rate over time were not significantly different between the 2 groups (both $P > 0.05$).

Abbreviations: OPpre, preoperative; IND5, IND15, and IND30, 5, 15, and 30 min after anesthetic induction, respectively; OPend, end of the procedure.

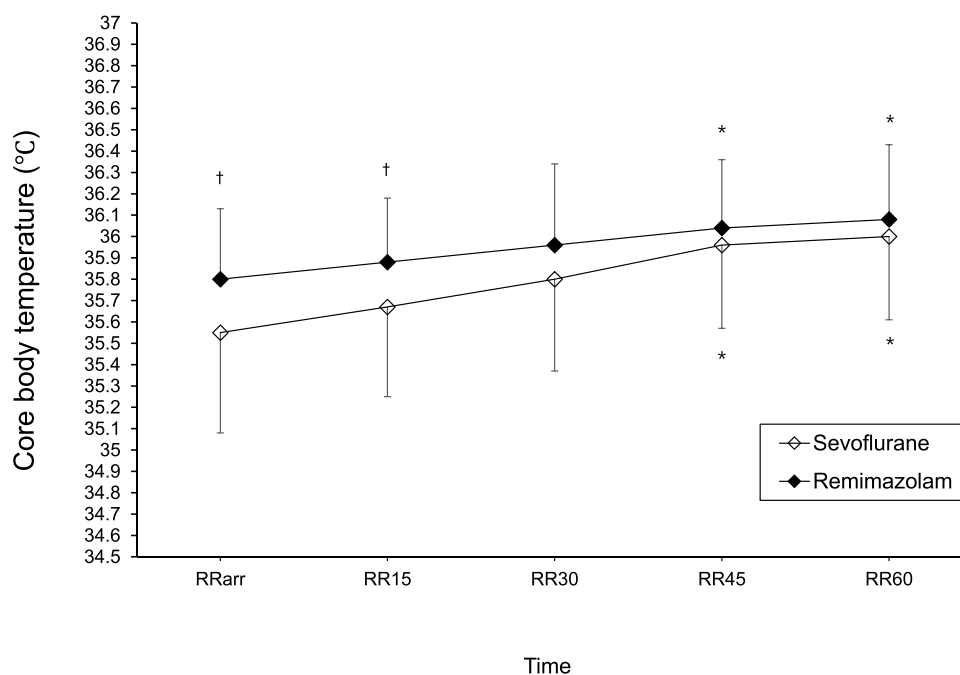


Figure 4 Changes in core body temperature in the postanesthetic care unit (PACU) after transurethral resection of the bladder or prostate in older patients. Error bars represent the standard deviation. The change over time in body temperature was significantly different between 2 groups ($P = 0.025$). In both the sevoflurane and remimazolam groups, body temperature increased significantly from PACU arrival to 45 min after arrival ($P < 0.01$). Upon arrival at the PACU; PACU15, PACU30, and PCAU45: 15, 30, and 45 min after PACU arrival, respectively; discharge: at discharge from the PACU. * $P < 0.05$, vs Arrival within the group; † $P < 0.05$, vs sevoflurane group.

Discussion

This study demonstrated the effects of remimazolam and sevoflurane on perioperative thermoregulation in older patients who underwent TURB or TURP. The key findings indicated that remimazolam anesthesia resulted in significantly better preservation of the core BT throughout the perioperative period. Patients in the remimazolam group experienced a smaller reduction in core BT intraoperatively, a lower incidence of profound hypothermia, and a decreased need for postoperative active warming measures compared with those who received sevoflurane. These outcomes suggest that remimazolam may offer meaningful thermoregulatory advantages in older surgical patients who are particularly vulnerable to perioperative hypothermia and its associated complications.

Most anesthetic agents reduce the threshold for vasoconstriction and shivering in a dose- and drug-dependent manner, thereby impairing the body's ability to respond to cold stress and increasing the risk of hypothermia during anesthesia.^{22–24} During general anesthesia, the core-to-peripheral thermal redistribution promotes redistribution hypothermia by causing vasodilation and increasing peripheral heat loss, particularly during the early stages of anesthesia induction.²⁵ Compared with volatile anesthetics, midazolam, an intravenous benzodiazepine, has been reported to exert a milder influence on central thermoregulatory control, preserving the vasomotor tone to a greater extent.¹⁵

Remimazolam is an ultra-short-acting benzodiazepine that is structurally related to midazolam and is designed to offer rapid onset and recovery profiles.¹⁶ Previous studies have reported that remimazolam is associated with a higher vasoconstriction threshold and shorter time to vasoconstriction onset, suggesting a potential advantage in preserving thermoregulatory responses compared to other anesthetic agents.²⁶ Although current evidence on the effects of remimazolam on thermoregulation remains limited and somewhat inconsistent, some clinical data indicate favorable outcomes. For instance, during robotic or laparoscopic prostatectomy, remimazolam was shown to better preserve thermoregulatory function than propofol, resulting in higher core BTs within 60 min after induction and a faster onset of vasoconstriction.²⁶ Similarly, in gynecologic laparoscopic surgery, remimazolam use was associated with a reduced incidence of intraoperative hypothermia and postoperative shivering compared with sevoflurane.²⁰ These findings support the hypothesis that remimazolam may offer thermoregulatory benefits, possibly owing to its pharmacokinetic properties or differential effects on central temperature regulation pathways. However, not all studies have consistently demonstrated these

benefits. A study involving nasal procedures reported a higher incidence of hypothermia in patients receiving remimazolam than in those managed with inhalational anesthetics.²⁷ This discrepancy may be attributed to differences in surgical type, duration, ambient operating room temperature, or patient population, indicating that the thermoregulatory effects of remimazolam may be context dependent.

In this study, the mean intraoperative decrease of BT (Δ BT) was significantly smaller in the remimazolam group than in the sevoflurane group ($0.83 \pm 0.38^\circ\text{C}$ vs $1.08 \pm 0.48^\circ\text{C}$, $P = 0.011$), and profound hypothermia ($<34.9^\circ\text{C}$) occurred exclusively in the sevoflurane group. Additionally, a higher proportion of patients maintained normothermia ($\geq 36.0^\circ\text{C}$) intraoperatively with remimazolam, and significantly fewer required active warming in the PACU. These findings not only demonstrate a statistically significant difference but also have important clinical implications. Maintaining normothermia reduces the risk of surgical site infections, coagulopathy, delayed wound healing, and perioperative cardiac events, particularly in older patients.¹⁻³

Time-course analysis of the temperature change (Figure 2) further reinforced the superiority of remimazolam in temperature preservation. Although both groups exhibited significant decreases in temperature following induction, the remimazolam group consistently maintained higher core temperatures throughout the surgical procedure ($P = 0.010$ for interaction), suggesting a more stable thermoregulatory control. This observation supports the hypothesis that remimazolam causes less impairment of autonomic thermal defense mechanisms than sevoflurane.

Interestingly, despite differences in temperature trends and recovery profiles, both groups had similarly low incidences of postoperative shivering (2%). This may be because of the relatively short operative time and anesthesia (approximately 70 min), which limited the extent of hypothermia and allowed for prompt warming interventions.

This study had several limitations. First, the relatively short procedure time may have attenuated the differences in thermoregulatory outcomes, especially in terms of complications, such as shivering or delayed recovery. Second, although the study focused on older patients, a population at higher risk of hypothermia, the findings may not be directly generalizable to younger or more diverse surgical populations. Third, prewarming was performed for only 5 minutes, which may not be sufficient to fully prevent redistribution hypothermia. Previous evidence indicates that 15–30 minutes of prewarming provides greater benefit in reducing perioperative hypothermia.²¹ Therefore, the relatively short prewarming duration in our protocol should be considered when interpreting the results. Fourth, this study did not include a systematic assessment of emergence delirium, which is an important concern in older patients. Although no patient required pharmacologic treatment for agitation or confusion in the PACU, the lack of formal delirium evaluation represents a limitation and should be addressed in future trials. This study was limited to a comparison of remimazolam- and sevoflurane-based general anesthesia. We did not include a spinal anesthesia group, not only because spinal anesthesia is technically challenging in older patients, but also because temperature measurement methods often differ between spinal and general anesthesia studies, making direct comparison difficult. Another limitation is that patient-specific factors such as basal metabolic rate or skin condition, which may also influence perioperative thermoregulation, were not included in our exclusion criteria. And future studies could investigate their potential impact on perioperative body temperature regulation.

Despite these limitations, our results support the use of remimazolam as a favorable anesthetic option for older patients undergoing procedures with a high risk of heat loss, such as those involving large-volume irrigation. Its ability to preserve core temperature and reduce the need for postoperative warming may contribute to improved perioperative outcomes and a reduced incidence of hypothermia-related complications. Future studies should explore the effects of remimazolam in longer and more invasive procedures, including comparisons with other intravenous agents such as propofol or dexmedetomidine, and investigate its potential benefits in broader clinical endpoints such as wound healing, recovery time, and patient satisfaction. And future research directly comparing volatile-based general anesthesia, TIVA-based anesthesia, and spinal anesthesia would be necessary to provide a more comprehensive understanding of perioperative thermoregulation in older patients.

Conclusion

In conclusion, remimazolam anesthesia resulted in significantly better preservation of the BT throughout the perioperative period in older patients undergoing TURB or TURP. These findings suggest that remimazolam may offer meaningful thermoregulatory advantages in older surgical patients who are particularly vulnerable to perioperative hypothermia and its associated complications.

Abbreviations

TURB, transurethral resection of bladder tumor; TURP, transurethral resection of the prostate; BT, Core body temperature; PACU, postanesthetic care unit; BIS, Bispectral index; PONV, postoperative nausea and vomiting; NRS, numerical rating scale; SD, standard deviation; OR, operating room; Δ BT, difference between preoperative and intraoperative minimum body temperature.

Ethics Approval

This study was conducted following approval by the institutional review board of Gachon University Gil Medical Center (GFIRB2023-073). This study was registered with the Clinical Research Information Service (CRIS) prior to patient enrollment (registration no. KCT0008417). This study complies with the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

No conflicts of interest are declared by the authors.

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