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Efficacy and safety of remimazolam tosylate combined with sufentanil for sedo-analgesia in elderly patients undergoing percutaneous vertebroplasty: A randomized controlled trial

yang qu
West China Hospital Sichuan University Jintang Hospital. Jintang First People's Hospital
you hu
West China Hospital Sichuan University Jintang Hospital. Jintang First People's Hospital
yi he
West China Hospital Sichuan University Jintang Hospital. Jintang First People's Hospital
dan qiu
West China Hospital Sichuan University Jintang Hospital. Jintang First People's Hospital
deyuan li
1839077375@qq.com

West China Hospital Sichuan University Jintang Hospital. Jintang First People's Hospital

Research Article

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Abstract

Background

Osteoporotic vertebral compression fractures (OVCFs) are common among elderly individuals. Percutaneous vertebroplasty (PVP) performed under local anesthesia may cause considerable stress and anxiety. Remimazolam tosylate is a novel ultra-short-acting GABAA receptor agonist. This study evaluated the efficacy and safety of remimazolam tosylate for sedation during PVP.

Methods

In this single-center, randomized, double-blind, controlled trial, 78 elderly patients aged 60–90 years were randomly assigned in a 1:1 ratio to the Remimazolam group (Group R) or the Control group (Group C). Group R received a loading dose of 5 mg remimazolam followed by a continuous infusion at 0.2 mg/kg/h. Mean arterial pressure (MAP), heart rate (HR), RASS scores, CAM scores at 6 and 24 hours postoperatively, and adverse events were recorded.

Results

MAP remained more stable in Group R than in Group C ($P = 0.035$). Group R also achieved significantly higher RASS scores during the procedure ($P < 0.05$), indicating effective light sedation. No significant difference in CAM scores was observed between the two groups ($P > 0.05$). Respiratory depression occurred in 5.13% of patients in Group R; however, all cases were transient and manageable.

Conclusion

Remimazolam provides effective light sedation and maintains hemodynamic stability without increasing the risk of postoperative delirium in elderly patients undergoing PVP.

Clinical Trial Registration

ChiCTR2500099227 (registered on March 20, 2025).

1. Introduction

Osteoporotic vertebral compression fractures (OVCFs) represent a major public health challenge in the aging population, leading to chronic pain, spinal deformity, and a substantial reduction in quality of life. Percutaneous vertebroplasty (PVP) has emerged as a cornerstone minimally invasive treatment for OVCFs, providing rapid pain relief and facilitating early mobilization[1–3]. However, PVP is typically

performed under local anesthesia, which often fails to relieve procedure-related anxiety and surgical stress in elderly patients adequately. This psychological and physical stress may provoke significant hemodynamic fluctuations, including acute hypertension and tachycardia, thereby increasing the risk of adverse cardiovascular events in individuals with limited physiological reserve [4]. Consequently, there is an urgent need for “comfortable medical care” strategies that can provide effective sedation without compromising safety in this vulnerable demographic[5, 6].

Commonly used sedative agents, such as propofol and midazolam, have inherent limitations when administered to geriatric patients. Propofol is associated with dose-dependent cardiorespiratory depression, whereas midazolam may result in prolonged recovery and an increased risk of postoperative cognitive dysfunction due to its organ-dependent metabolism[7, 8]. Remimazolam tosylate, a novel ultra-short-acting γ-aminobutyric acid type A (GABAA) receptor agonist, has emerged as a promising alternative[9–11]. Unlike conventional benzodiazepines, remimazolam is metabolized by non-specific tissue esterases into inactive metabolites, resulting in a rapid onset, predictable recovery, and minimal drug accumulation regardless of hepatic or renal function[12, 13]. Although its efficacy has been demonstrated in gastrointestinal endoscopy and general anesthesia[7, 14, 15], high-quality clinical evidence supporting its use for sedoanalgesia in elderly patients undergoing PVP remains limited.

To that end, we conducted a single-center, randomized, double-blind, controlled clinical trial to evaluate the efficacy and safety of remimazolam tosylate combined with sufentanil in elderly patients undergoing PVP[1]. We surmised that remimazolam-based sedation would provide superior hemodynamic stability and effective light sedation compared with conventional local anesthesia plus analgesia, without increasing the incidence of postoperative delirium or respiratory complications. Importantly, the findings of this study (registered at ChiCTR2500099227) may help establish a standardized sedation protocol to improve perioperative comfort and safety in the geriatric population.

2. Materials and Methods

2.1 Study Design and Ethics

This single-center, randomized, double-blind, parallel-controlled clinical trial was approved by the Institutional Review Board of Jintang County First People’s Hospital (No. 20240912001) and conducted in accordance with the Declaration of Helsinki. The trial was prospectively registered at the Chinese Clinical Trial Registry (ChiCTR2500099227; registered on March 20, 2025). Written informed consent was obtained from all participants or their legal representatives before enrollment.

2.2 Participants

Patients aged 60–90 years with American Society of Anesthesiologists (ASA) physical status I–III and New York Heart Association (NYHA) functional class I–III who were scheduled for elective PVP were eligible for inclusion. Additional inclusion criteria included a body mass index (BMI) of 18.5–30 kg/m².

Meanwhile, exclusion criteria were as follows: (1) severe dysfunction of vital organs (heart, lung, or kidney failure); (2) acute or chronic systemic infection; (3) history of long-term use of antipsychotic medications, severe depression, or myasthenia gravis; (4) known allergy to any of the study medications; and (5) current participation in other clinical trials.

2.3 Randomization and Blinding

A total of 80 patients were randomly assigned in a 1:1 ratio to either the Remimazolam group (Group R, n = 40) or the Control group (Group C, n = 40) using a computer-generated random number table. Allocation concealment was ensured using sealed, opaque envelopes. To ensure the integrity of blinding, study medications were prepared and administered by an independent anesthesiologist who was not involved in subsequent data collection or data analysis. Patients and the investigators responsible for postoperative outcome assessments remained blinded to group allocation until study completion.

2.4 Anesthesia and Sedation Protocol

Upon arrival in the operating room, patients were monitored for mean arterial pressure (MAP), heart rate (HR), and peripheral oxygen saturation (SpO_2). All patients received local infiltration anesthesia at the surgical site. In group R, patients received an intravenous loading dose of sufentanil (0.1 μg/kg) combined with remimazolam tosylate (5 mg), followed by a continuous infusion of remimazolam at 0.2 mg/kg/h until the end of the procedure. Meanwhile, patients in Group C received the same loading dose of sufentanil (0.1 μg/kg), followed by a continuous infusion of 0.9% normal saline at a volume-matched rate.

2.5 Outcome Measures

The primary outcome was hemodynamic stability, assessed by MAP at eight time points: T1 (1 min after drug loading), T2 (skin incision), T3 (trocar insertion), T4–T7 (various intraoperative stages), and T8 (end of surgery). Secondary outcomes were as follows:

1. Sedation depth, assessed using the Richmond Agitation-Sedation Scale (RASS). In accordance with international standards, RASS scores were recorded as negative values (0 = alert/calm; −1 to −3 = light-to-moderate sedation) to quantify sedation depth.

2. Postoperative cognition, evaluated using the Confusion Assessment Method (CAM) at 6 and 24 hours postoperatively to screen for delirium.

3. Safety, assessed by the incidence of adverse events, including respiratory depression, hypotension, and bradycardia.

2.6 Sample Size Calculation

The sample size was calculated based on the primary outcome (MAP stability). According to our preliminary study, 36 participants per group were required to detect a statistically significant difference

in MAP with 80% power (1 − β = 0.80) and a two-sided significance level of 5% (α = 0.05). Given an anticipated dropout rate of approximately 10%, a total of 80 patients (40 per group) were planned for enrollment to ensure robustness of the findings.

2.7 Statistical Analysis

Statistical analysis was performed using SPSS version 25.0. Continuous data are expressed as mean ± standard deviation ($\bar{x} \pm s$). Repeated-measures ANOVA was used for hemodynamic and sedation data across multiple time points. Independent-samples t-tests were used for between-group comparisons at specific time points. Categorical data were analyzed using the chi-square test or Fisher's exact test, as appropriate. A two-sided *P*-value < 0.05 was considered statistically significant.

3. Results

3.1 Participant Flow and Baseline Characteristics

A total of 80 patients were initially enrolled and randomized. During the study, two patients were excluded (one in Group R due to conversion to general anesthesia and one in Group C due to incomplete data recording). Ultimately, 78 patients (39 in each group) completed the study and were included in the final analysis (Fig. 1). There were no significant differences between the two groups in age, sex, or weight (*P* > 0.05) (Table 1)

Table 1
Baseline demographic and clinical characteristics of the patients

Variables	**Group R (n = 39)**	**Group C (n = 39)**	**T or chi-square values**	***P*-value**
Age (years)	74.05 ± 5.68	76.95 ± 6.01	2.188	0.052
Male [n (%)]	22 (56.4%)	19 (48.7%)	0.463	0.496
Female [n (%)]	17 (43.6%)	20 (51.3%)		
Weight (kg)	54.08 ± 9.13	53.23 ± 10.12	0.388	0.699

Note: Data are expressed as mean ± SD or number (percentage). Group R: remimazolam group; Group C: control group. *P* > 0.05 indicates no significant difference between the two groups.

The diagram illustrates the recruitment, randomization, and follow-up process. Initially, 80 patients were enrolled, and 78 completed the study after two cases were excluded (one due to conversion to general anesthesia and one due to incomplete data).

3.2 Hemodynamic Parameters (MAP and HR)

The dynamic changes in MAP and HR are summarized in Table 2, Table 3, Fig. 2, and Fig. 3. Notably, statistical analysis revealed a significant difference in MAP trends between the two groups ($P = 0.035$). In Group R, MAP remained stable at approximately 100 ± 10 mmHg throughout the procedure. Although MAP values in this group were significantly lower than baseline (T1) at multiple time points (T2, T4–T8; $P < 0.05$), they remained within a clinically acceptable range. In contrast, Group C exhibited greater fluctuations in MAP in response to surgical stimuli. There was no statistically significant difference in HR between the two groups ($P = 0.709$). However, intra-group analysis showed that Group C exhibited significant HR fluctuations relative to T1 ($P < 0.05$), suggesting a heightened surgical stress response in the absence of sedation.

Table 2
Comparison of Mean Arterial Pressure at different time points between the two groups.

Time Points	**Group R (n = 39)**	**Group C (n = 39)**	***P* -value**
T1 (Baseline)	110.23 ± 12.03	108.97 ± 16.84	0.706
T2	105.56 ± 13.97*#	111.28 ± 13.14	0.066
T3	116.67 ± 11.42	111.08 ± 11.44	0.740
T4	99.41 ± 14.16*#	112.23 ± 12.73	0.000
T5	101.08 ± 11.91*#	112.31 ± 13.53	0.000
T6	104.74 ± 14.91*#	111.08 ± 13.09	0.050
T7	99.54 ± 13.34*#	111.46 ± 14.27	0.000
T8	104.41 ± 11.00*#	112.56 ± 13.52	0.005

Note: Data are expressed as mean ± standard deviation (**± s**). MAP: Mean Arterial Pressure (mmHg). Group R: remimazolam group; Group C: control group. T1: 1 min after drug loading; T2: skin incision; T3: trocar insertion; T4: bone cement perfusion preparation; T5–T7: specific surgical stages; T8: end of surgery.

*$P < 0.05$ was considered statistically significant for comparisons between Group R and Group C at the same time point (independent-samples t-test);

# $P < 0.05$ was considered statistically significant for comparisons with baseline (T1) within the same group (paired t-test or repeated-measures ANOVA).

Table 3
Comparison of HR at different time points between the two groups.

Time Points	Group R (n = 39)	Group C (n = 39)	*P*-value
T1 (Baseline)	77.10 ± 14.55	77.10 ± 10.48	1.000
T2	79.13 ± 14.83	77.64 ± 12.51[#]	0.634
T3	77.92 ± 14.75	77.03 ± 11.00[#]	0.761
T4	75.62 ± 14.69	76.90 ± 10.64[#]	0.660
T5	74.59 ± 13.69	78.85 ± 12.32[#]	0.153
T6	78.03 ± 15.44	76.18 ± 11.86[#]	0.556
T7	75.36 ± 13.87	77.44 ± 12.46[#]	0.489
T8	75.95 ± 14.00	80.97 ± 13.71[#]	0.113
Note: Data are expressed as mean ± standard deviation (**± s**). HR: Heart Rate (beats/min). Group R: remimazolam group; Group C: control group.			
**P* < 0.05 compared with Group C at the same time point;			

[#] *P* < 0.05 compared with baseline (T1) within the same group.

3.3 Sedation Depth (RASS Score)

Sedation efficacy was assessed using RASS scores (Table 4 and Fig. 4). Of note, patients in Group R achieved and maintained light-to-moderate sedation (RASS scores ranging from − 1.74 to − 2.79) from T2 to T8, which differed significantly from the alert state observed in Group C (*P* < 0.05). Importantly, this level of sedation in Group R effectively reduced procedural anxiety and improved patient comfort without compromising airway safety.

Table 4
Comparison of RASS scores between the two groups at different time points.

Time Points	Group R (n = 39)	Group C (n = 39)	*P*-value
T1	-0.10 ± 0.31	-0.10 ± 0.31	>0.05
T2	-2.03 ± 1.39*	-0.10 ± 0.31	<0.05
T3	-2.79 ± 1.40*	-0.13 ± 0.34	<0.05
T4	-2.51 ± 1.41*	-0.38 ± 0.59	<0.05
T5	-1.82 ± 1.17*	-0.33 ± 0.48	<0.05
T6	-1.74 ± 1.33*	-0.13 ± 0.34	<0.05
T7	-2.59 ± 1.31*	-0.33 ± 0.58	<0.05
T8	-0.77 ± 0.84*	-0.03 ± 0.16	<0.05

Notes: Data are expressed as mean ± standard deviation. RASS: Richmond Agitation-Sedation Scale. Group R: remimazolam group; Group C: control group.

T1: 1 min after drug administration; T2: skin incision; T3: trocar insertion; T4: biopsy (if applicable) or bone cement perfusion preparation; T5-T7: specific stages of vertebral stabilization; T8: end of surgery.

* $P<0.05$ compared with Group C.

3.4 Postoperative Cognitive Function (CAM Score)

Postoperative cognitive status was evaluated using the CAM at 6 and 24 hours post-surgery (Table 5). There were no significant differences in CAM scores between Group R and Group C at 6 hours (11.56 ± 1.12 vs. 11.28 ± 0.61, $P = 0.19$) or at 24 hours (11.26 ± 0.90 vs. 11.33 ± 0.55, $P = 0.511$) postoperatively. No cases of postoperative delirium were observed in either group, suggesting that remimazolam did not adversely affect early cognitive recovery in this particular cohort.

Table 5
Comparison of Confusion Assessment Method (CAM) scores between the two groups.

Time Points	Group C (n = 39)	Group R (n = 39)	Statistic (*t*)	*P*-value
Postoperative 6 h	11.28 ± 0.61	11.56 ± 1.12	1.322	0.19
Postoperative 24 h	11.33 ± 0.55	11.26 ± 0.90	0.66	0.511

Note: Data are expressed as mean ± standard deviation (± s). CAM: Confusion Assessment Method. Group R: remimazolam group; Group C: control group. A higher CAM score indicates better cognitive orientation in this specific assessment tool; $P > 0.05$ indicates no statistically significant difference between the groups.

3.5 Safety and Adverse Events

The incidence of perioperative adverse events is presented in Table 6. In Group R, two cases (5.13%) of transient respiratory depression and two cases (5.13%) of oxygen desaturation (SpO_2 < 90%) occurred; all were promptly resolved with simple oxygen mask adjustments or verbal stimulation. One case of hypotension was recorded in each group. The overall incidence of adverse events was 12.8% in Group R and 2.6% in Group C, with no statistically significant difference between the groups (*P* = 0.198, Fisher's exact test). No severe cardiovascular events or delayed recovery were reported.

Table 6
Comparison of perioperative adverse events between the two groups [n (%)].

Group	Number of cases	Respiratory depression	Bradycardia	Body movement	Hypotension	Oxygen desaturation (SpO2 < 90%)
Group R	39	2 (5.13%)	0	0	0	2 (5.13%)
Group C	39	0	0	0	0	0
Total incidence	78	2 (2.56%)	0	0	0	2 (2.56%)
P(Fisher)	-	0.494	-	-	-	0.494

Note: Data are expressed as frequency (percentage). Group R: remimazolam group; Group C: control group. X: pulse oxygen saturation.

P-values were calculated using Fisher's exact test due to small expected frequencies.

P > 0.05 indicates that the safety profile of remimazolam is comparable to that of the control group in this study.

4. Discussion

The present study demonstrates that remimazolam tosylate provides effective and safe sedation in elderly patients undergoing percutaneous Vertebroplasty (PVP). Our primary findings indicate that remimazolam maintains superior hemodynamic stability and achieves a predictable level of light-to-moderate sedation without increasing the risk of early postoperative cognitive dysfunction (POCD)[5, 6, 16].

4.1 Hemodynamic Stability and Surgical Stress

Elderly patients often present with reduced cardiovascular reserve and multiple comorbidities, making them highly sensitive to hemodynamic fluctuations induced by surgical stress or anesthetic agents[6, 17]. Herein, Group R exhibited a more stable MAP trend compared with Group C. Although MAP in Group R decreased from baseline (T1) following drug induction, it remained within a clinically acceptable range

(± 20% of baseline), thereby avoiding the marked hypertensive peaks observed in Group C during noxious stimuli such as trocar insertion (T3) and bone cement injection (T4).

This stability can be attributed to the unique pharmacological profile of remimazolam. As a novel ultra-short-acting GABAA receptor agonist, remimazolam has high affinity for the receptor but exerts a more moderate effect on the cardiovascular system than propofol[17–21]. Previous studies have shown that remimazolam significantly reduces the incidence of injection pain and circulatory depression, which is particularly beneficial in the geriatric population[7, 22–24].

4.2 Sedation Depth and Patient Comfort

The concept of “Monitored Anesthesia Care (MAC)” or “comfortable medicine” is increasingly emphasized in minimally invasive surgery. Our results showed that patients in Group R maintained RASS scores between − 1 and − 3, representing a state of conscious sedation. This level of sedation was sufficient to alleviate procedural anxiety and reduce the psychological stress associated with being awake in the operating room environment. Unlike midazolam, which may cause unpredictable and prolonged sedation in elderly patients due to its active metabolites, remimazolam is metabolized by nonspecific tissue esterases into an inactive metabolite, ensuring rapid and predictable recovery [9, 25–27].

4.3 Postoperative Cognition and Safety

Postoperative delirium (POD) and POCD are major concerns in geriatric anesthesia[28, 29]. In the present study, CAM scores did not differ significantly between the two groups at 6 and 24 hours postoperatively. This finding suggests that remimazolam does not exert a residual adverse effect on cognitive function. This is likely attributable to its rapid clearance and lack of drug accumulation. Furthermore, some studies have suggested that remimazolam may have a protective effect against POD compared with other sedatives; however, larger trials are needed to substantiate this observation [30–34]. Regarding safety, although a slightly higher incidence of transient respiratory depression was observed in Group R (5.13%), all cases were mild and easily managed with simple airway maneuvers. This finding underscores the importance of continuous monitoring even during light sedation with remimazolam in elderly patients[35, 36].

4.4 Limitations

Nevertheless, this study has several limitations. First, the sample size was relatively small and the study was conducted at a single center. Second, objective brain function monitoring tools, such as the Bispectral Index (BIS), were not used to quantify sedation depth, and sedation assessment relied instead on the clinical RASS scale. Third, long-term cognitive outcomes beyond 24 hours were not evaluated. Future multicenter studies with longer follow-up periods are warranted.

4.5 Conclusion

In conclusion, remimazolam tosylate is an effective and safe sedative for elderly patients undergoing PVP under local anesthesia. It provides stable hemodynamics and satisfactory sedation depth without

impairing early postoperative cognitive function, making it a viable option for promoting “comfortable medicine” in minimally invasive spinal surgery.

Declarations

Data availability statement

The original contributions presented in the study are included in the article, further inquiries can be directed to the corresponding author.

Ethics approval and consent to participate

The studies involving humans were approved by the Institutional Review Board of Jintang County First People's Hospital (NO: 20240912001). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent to participate was obtained from all participants or their legal representatives before enrollment.

Author contributions

YQ: Methodology, Writing – original draft, Data curation, Project administration. YH: Data curation, Writing – review & editing, Formal analysis. YH,DQ: Project administraion, Writing – review & editing. DYL: Writing – review & editing, Supervision.

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Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Figures

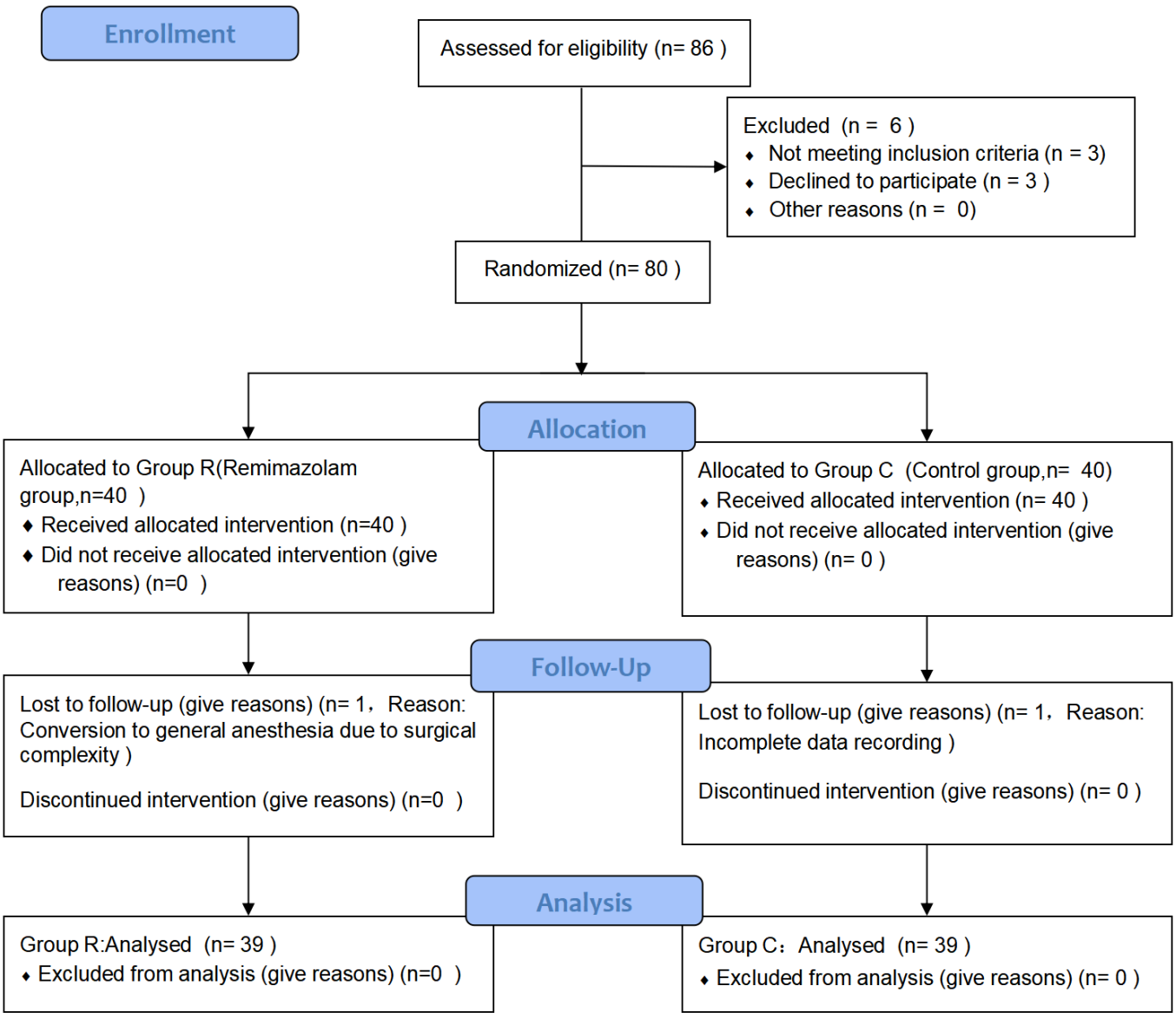


Figure 1

CONSORT flow diagram of the study participants.

The diagram illustrates the recruitment, randomization, and follow-up process. Initially, 80 patients were enrolled, and 78 completed the study after two cases were excluded (one due to conversion to general anesthesia and one due to incomplete data).

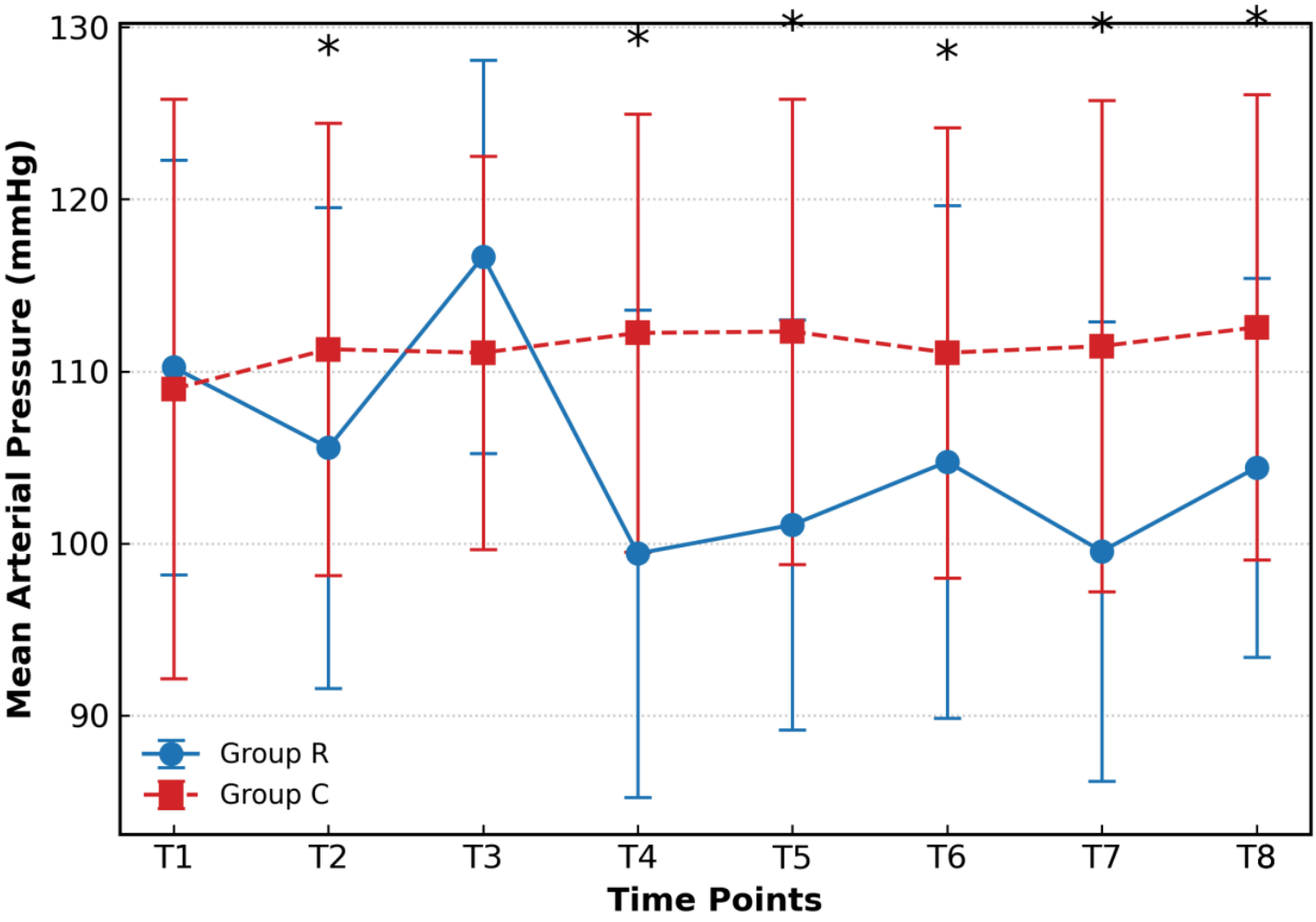


Figure 2

Trends in MAP at different time points. Data are shown as mean ± SD. $^{*}P$ 0.05 compared with Group C.

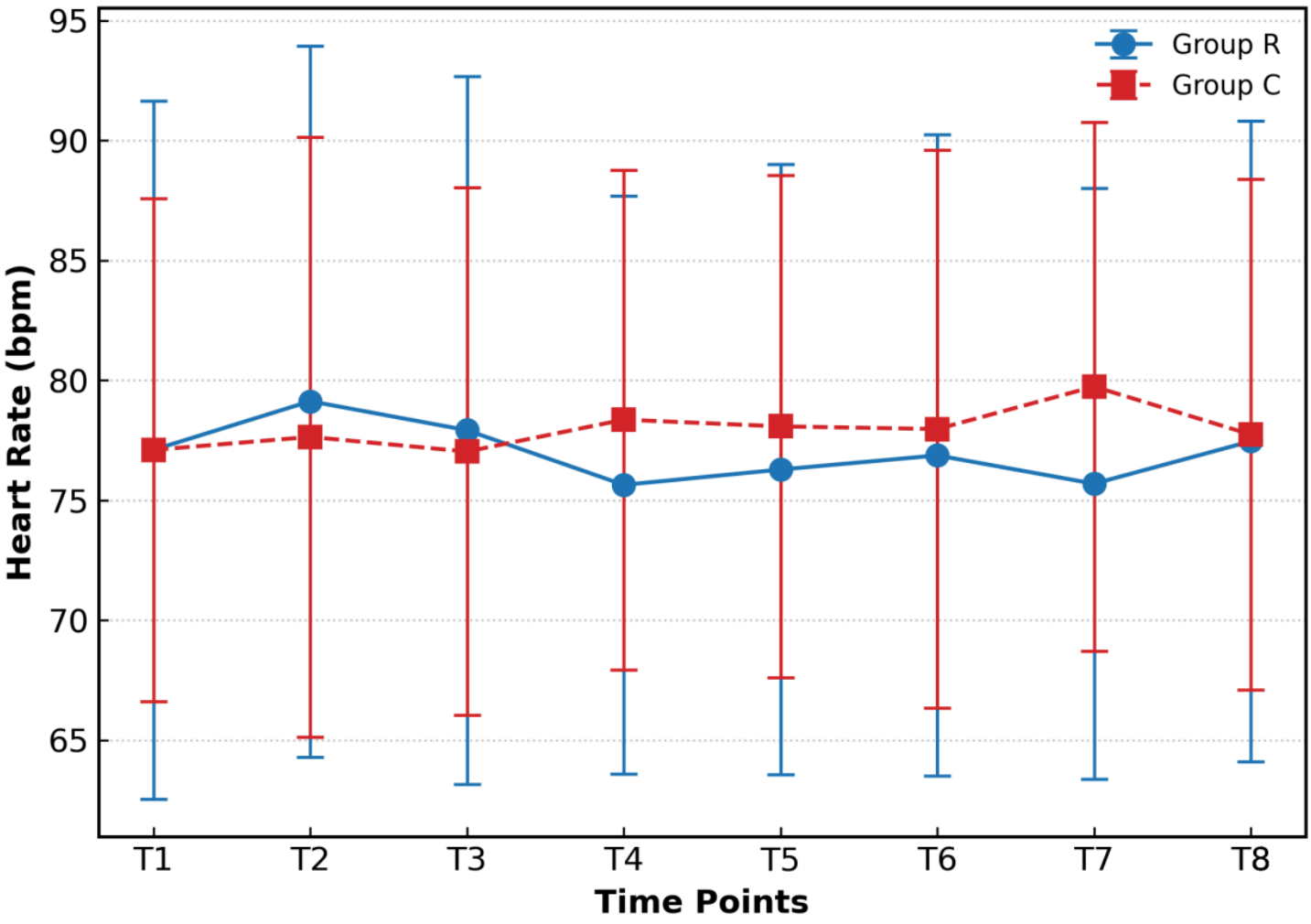


Figure 3

Trends in HR at different time points. Data are shown as mean ± SD. No significant differences were observed between groups.

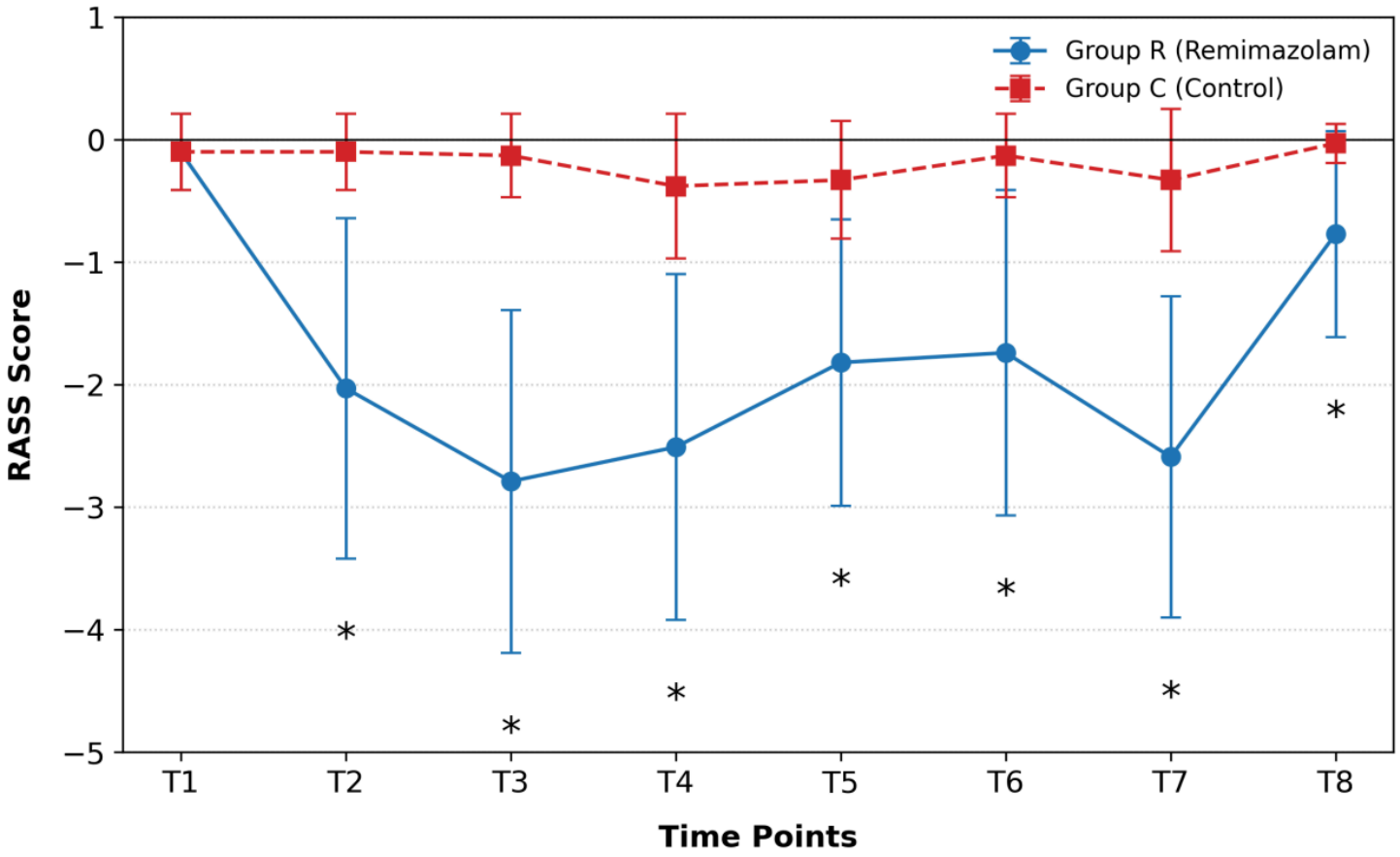


Figure 4

RASS scores were recorded as negative values in accordance with international standards. Group R (blue) maintained a consistent light-to-moderate sedation level (−1.74 to −2.79) throughout the procedure (T2–T8), whereas Group C (red) remained close to baseline. The horizontal line at 0 represents the alert/calm state. Error bars represent SD.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- CONSORT2025editablechecklist.docx