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ORIGINAL RESEARCH

Comparison of Remimazolam versus Dexmedetomidine on Hemodynamics in Older Patients Under Lower Extremity Orthopedic Surgery with Spinal Anesthesia: A Randomized Controlled Trial

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Purpose: To compare the effects of remimazolam and dexmedetomidine on the hemodynamics in elderly patients undergoing orthopedic surgery under spinal anesthesia.

Methods: This study evaluated 126 patients aged ≥ 60 years undergoing lower-extremity orthopedic surgery under spinal anesthesia, randomizing them into remimazolam and dexmedetomidine groups. The primary outcome was the incidence of hemodynamic fluctuations, such as hypotension and bradycardia. The secondary endpoints included the cumulative dose vasoactive medication and the incidence of hypertension, tachycardia, postoperative nausea and vomiting (PONV), postoperative delirium (POD), and hypoxemia. Continuous hemodynamic variables including mean arterial pressure (MAP) and heart rate (HR) were recorded at baseline, every 5 min for the first 20 min after intravenous infusion of sedatives, every 10 min thereafter, up to one hour, at the end of the surgery, and in the post-anesthesia care unit (PACU).

Results: Compared to dexmedetomidine group, patients in the remimazolam group demonstrated significantly higher MAP at three specific time points (60 minutes after baseline, at the end of surgery, and in the PACU) and higher HR at all time points after T3 (15 minutes after baseline). The remimazolam group also reduced norepinephrine and atropine interventions. There were no statistically significant differences in other adverse events between the two groups.

Conclusion: Remimazolam demonstrated superior hemodynamic stability and fewer adverse cardiovascular events than dexmedetomidine, along with reduced requirements for vasoactive medications, making it an alternative to intraoperative sedation in older patients undergoing lower limb surgery under spinal anesthesia.

Keywords: benzodiazepines, hemodynamics, older adults, orthopedic surgery, dexmedetomidine, remimazolam

Introduction

Spinal anesthesia combined with intraoperative sedation is widely used as an important anesthesia method for lower-limb fracture surgery in older patients.[1] Compared to general anesthesia, spinal anesthesia is a cost-effective, physiologically less invasive alternative that promotes patient recovery, enhances comfort, and reduces postoperative complications.[2,3] During spinal anesthesia, sedatives are commonly administered to alleviate anxiety and tension in patients. Midazolam, propofol, and dexmedetomidine are the most commonly used medications for sedation. However, some studies have indicated that the use of sedatives may lead to intraoperative hypotension.[4] Hypotension can precipitate renal or myocardial injury; potentially

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prolonging intensive care unit stay and increasing the risk of perioperative complications and mortality.[5] This concern is particularly among older patients, whose physiological decline results in altered tolerance and responsiveness to anesthetic drugs compared with younger patients, intraoperative hypotension warrants heightened vigilance.

Remimazolam is a novel, ultra-short-acting γ-aminobutyric acid type A (GABA-A) receptor agonist belonging to the benzodiazepine class of drugs.[6–8] Notably, remimazolam is characterized by a consistent context-sensitive and rapid elimination half-life.[9] Furthermore, it exerts minimal respiratory and circulatory depressive effects, virtually eliminating injection pain, and administration of the specific antagonist flumazenil can achieve selective reversal of the sedative effects of remimazolam.[10–12] However, the hemodynamic effects of remimazolam remain inconclusive, particularly in older patients undergoing lower-extremity orthopedic surgery under spinal anesthesia.

This study aimed to compare the hemodynamics of remimazolam and dexmedetomidine in older patients undergoing lower-limb orthopedic surgery under spinal anesthesia. By evaluating the efficacy and safety of these sedative agents, we aimed to provide evidence-based guidance to clinicians in selecting the most appropriate adjunctive medication, thereby enhancing patient comfort and perioperative outcomes.

Materials and Methods

Study Design

This single-blind, randomized controlled trial was approved by the Ethics Committee of the Central Hospital of Dalian University of Technology (Dalian Municipal Central Hospital) (Liaoning, China; 2024–039-01; April 2024) and was registered prior to patient enrollment at https://www.chictr.org.cn (ChiCTR2400083380; principal investigator: Di Wang; registered on April 22, 2024). All experimental participants or their authorized representatives signed an informed consent form on the document outlining the details of the study. This study was conducted at the Central Hospital of Dalian University of Technology (Dalian Municipal Central Hospital) from April 2024 to September 2024.

Participants, Study Design, and Randomization

The study population comprised older patients aged ≥60 years who were scheduled to undergo lower limb orthopedic surgery involving spinal anesthesia. We included patients who met the American Society of Anesthesiologists physical status (ASA) I–III. Exclusion criteria included deviation from the designated anesthetic plan, such as patients intending to undergo general anesthesia, or those presenting with contraindications to spinal anesthesia. Additional exclusion criteria included chronic use of opioids or benzodiazepines (defined as use exceeding three months). Furthermore, patients with severe heart failure, characterized by a left ventricular ejection fraction (EF) < 30%, were excluded because pre-existing conditions could potentially impact hemodynamics. Communication impediments such as severe hearing disorders or diminished communicative abilities were also excluded from the study.

This study was a randomized parallel-group trial with equal group sizes. Randomization sequences were generated using SPSS version 25.0 to ensure a 1:1 allocation ratio. Anesthesiologists were responsible for executing randomization and preparing individual opaque sealed envelopes containing computer-generated group assignments for each participant. On the day of surgery, prior to entering the operating room, patients were randomly assigned to either remimazolam or dexmedetomidine group. The patients were blinded to the group allocation and the medications administered.

Preoperative Baseline Characteristics and Comorbidities

The baseline characteristics and comorbidities of each patient were recorded before surgery. This mainly included weight, sex, age, blood pressure, heart rate, ASA physical status classification, and relevant medical comorbidities.

Intervention and Control

No patients received pre-anesthetic medication. Upon arrival in the operating room, venous access was established and 500 mL of crystalloid (Ringer lactate) was administered at a rate 5–7 $mL \cdot kg^{-1} \cdot h^{-1}$. Standard monitoring included electrocardiography, percutaneous arterial oxygen saturation monitoring, and invasive arterial pressure monitoring were implemented. Supplemental oxygen was delivered via face mask at a flow rate of 2–3 L/min under medical supervision. After positioning the patient

appropriately, a midline approach was utilized to insert a Quincke needle with the bevel oriented cephalad into the L2-L3 or L3-L4 interspace. Upon confirmation of cerebrospinal fluid return, 2–2.5 mL of 0.5% hyperbaric bupivacaine was administered intrathecally. Patients in whom the neuraxial anesthesia level extends above the T8 level were excluded.

After confirming the appropriate neuraxial anesthesia level, remimazolam or dexmedetomidine was intravenously administered for intraoperative sedation until the end of surgery. Given the original development of the Bispectral Index (BIS) for propofol and the weaker correlation between the BIS and depth of sedation with remimazolam and dexmedetomidine, as demonstrated in studies,[13–16] we opted to solely utilize the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale for assessing sedation depth in this study.

In the dexmedetomidine group, an intravenous infusion of dexmedetomidine was initiated at a loading dose of 0.5 μg· kg^{-1} over the first 10 minutes, followed by a maintenance infusion rate ranging from 0.2 to 0.6 $\mu g \cdot kg^{-1} \cdot h^{-1}$. In the remimazolam group, the loading dose was 0.1 $mg \cdot kg^{-1}$ for the remimazolam group for the first 10 min, followed by a maintenance rate of 0.1 to 0.3 $mg \cdot kg^{-1} \cdot h^{-1}$. Adjustments to the dosage were made to maintain a moderate level of sedation (MOAA/S score of 2–3).

The baseline point (T0) was defined as the initiation of loading sedation. Mean Arterial Pressure (MAP) and Heart Rate (HR) were recorded at 5, 10, 15, 20, 30, 40, 50, and 60 min after baseline (T1-T8), at the end of surgery (T9), and in the post-anesthesia care unit (PACU) (T10). Hypotension was defined as systolic blood pressure < 70% of baseline or < 90 mmHg, received intravenous norepinephrine for treatment. Intraoperative bradycardia was identified when the patient's HR < 55 beats·min^{-1}. Considering the advanced age of the patients, the anesthesiologist administered intravenous atropine (0.5 mg) only when the HR < 40 beats·min^{-1}. If hypertension (systolic arterial pressure > 180 mm Hg or diastolic arterial pressure > 110 mm Hg) occurred, 0.5–1 mg of nicardipine hydrochloride was administered intravenously. In the event of tachycardia, defined as a heart rate exceeding 110 beats·min^{-1}, patients were administered 5–10 mg of esmolol intravenously. For cases of respiratory depression or hypoxia, indicated by SpO_2 < 90%, patients received jaw-thrust assistance. If additional intraoperative blood loss occurred, an estimated equivalent volume of colloid solution (Hydroxyethyl Starch 130/0.4 in Sodium Chloride Injection) was administered to maintain hemodynamic stability.

After the surgical procedure, patients underwent a femoral nerve block, lumbar plexus block, or sciatic nerve block using 20–30 mL of ropivacaine 0.375% for postoperative analgesia. Subsequently, all patients were observed in the PACU for 20 minutes.

Outcome Measures

The primary endpoint was to determine whether there was a significant difference in the occurrence of hemodynamic fluctuations, specifically hypotension and bradycardia, between groups.

Secondary endpoints included the total doses of norepinephrine, atropine and the incidence of hypertension, tachycardia, postoperative nausea and vomiting (PONV), postoperative delirium (POD), and hypoxemia requiring treatment. Additionally, we analyzed continuous hemodynamic variables, including MAP and heart rate. Measurements were recorded at baseline, every 5 minutes during the first 20 minutes after sedative infusion, every 10 minutes thereafter up to 60 minutes, at the end of surgery, and in the PACU.

Sample Size

This randomized controlled trial compared remimazolam with dexmedetomidine. The primary outcome used for sample size estimation was the incidence of intraoperative hypotension. Based on our pre-test results, the incidence of intraoperative hypotension was 31% in the remimazolam group and 56% in the dexmedetomidine group. With a two-sided α of 0.05 and power of 80% (β = 0.20), a sample size of 60 patients per group was calculated. Allowing for a 10% dropout rate, at least 66 patients were required in each group, resulting in a total sample size of 132 patients.

Statistical Analysis

Quantitative data were assessed for normality using the Shapiro–Wilk test. Normally distributed continuous variables were analyzed using the independent samples *t*-test and reported as mean ± standard deviation (SD). Non-normally distributed variables were summarized as median (interquartile range, IQR: 25th–75th percentile) and compared using the Mann–Whitney *U*-test. Categorical variables were described using frequencies (percentages) and analyzed with chi-

square tests or Fisher's exact tests. Repeated-measures ANOVA was used to assess the differences in variables measured multiple times, conducting both between- and within-group statistical comparisons. Mauchly's sphericity test was performed. If the sphericity assumption was violated, the modified statistic tests as Greenhouse-Geisser and Huynh-Feldt were used. If there was a significant interaction with time and group, post hoc Bonferroni corrections were used to correct the type I error. Results of missing data were excluded from the analysis. All statistical analyses were performed using SPSS version 25.0 (IBM, Armonk, NY, USA), with two-tailed P-values < 0.05 considered statistically significant.

Results

Our clinical trial entailed screening of 144 patients to assess their eligibility. Among these individuals, eight were deemed ineligible for participation and four met the exclusion criteria. The remaining 132 patients were randomly allocated in a 1:1 ratio to receive either remimazolam or dexmedetomidine After excluding 3 patients in remimazolam group and 3 patients in dexmedetomidine group, due to sedation failure or surgery cancellation. A total of 126 patients were included in the intention-to-treat analysis. We recruited participants until the target was reached and recruitment was stopped (Figure 1).

Patient characteristics and procedural data in both groups are presented in Table 1, and no statistically significant differences were observed between the two groups.

For the primary outcome, the remimazolam group had a significantly reduced frequency of hypotension (22.4% vs 52.4%, p <0.001) and bradycardia (9.5% vs 61.9%, p <0.001) compared to the control group. Additionally, the secondary endpoint, which included the application of atropine (p = 0.012) and the total administered dose of norepinephrine (p=0.001), was significantly lower in the remimazolam group.

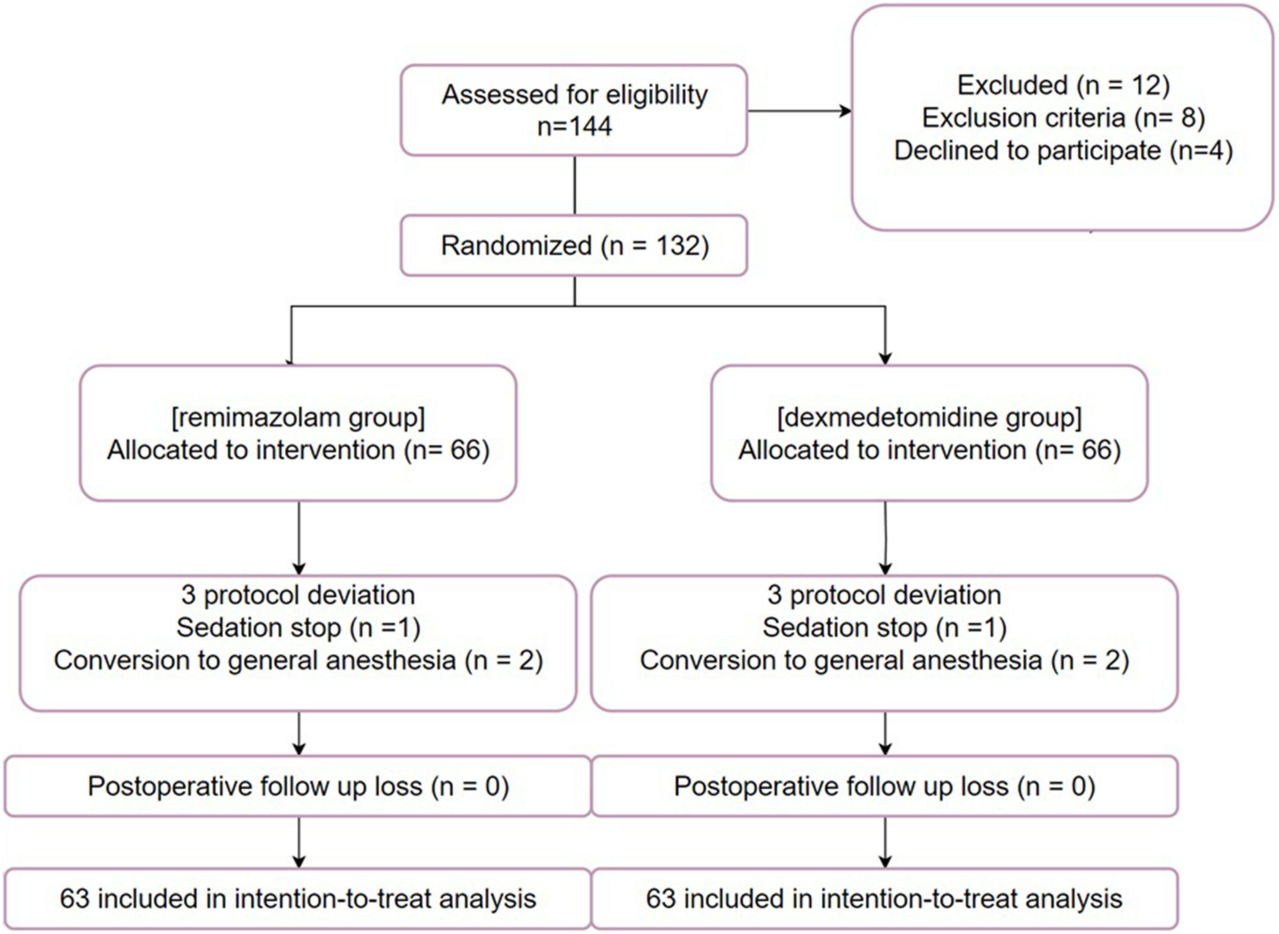

Figure 1 Trials diagram.

Table 1 Patient Characteristics and Procedural Data

	Remimazolam Sedation (n=63)	Dexmedetomidine Sedation (n=63)	p-value
Age (yr)	71 (67–77)	71 (66–78)	0.664
Sex			
Male	16 (52.4)	24 (66.6)	0.081
Female	48 (47.6)	39 (33.3)	
Height (cm)	162 (160–168.5)	165 (160–170)	0.056
Weight (kg)	65 (59–70)	65 (60–73)	0.199
SBP	152 (141–162.5)	132 (160–165)	0.393
DBP	87 (80.5–93)	90 (80–95)	0.598
HR	81.70±10.45	81.49±10.80	0.913
ASA Physical Status classification			
I/II/III;	0/33/30	0/42/21	0.104
Underlying disease			
Hypertension	26 (41.3%)	31 (49.2%)	0.411
Coronary heart disease	5 (6.3%)	4 (7.9%)	0.744
Type of surgery			
Total hip arthroplasty	5	5	0.454
Femoral open reduction and internal fixation	14	10	
Femoral intramedullary nailing	18	15	
Total knee arthroplasty	18	25	
Tibial open reduction and internal fixation	4	7	
Others	4	1	
Surgery time (min)	99.5 (78.75–125)	99.5 (78.75–125)	0.805
Estimated blood loss (mL)	50 (50–100)	100 (50–150)	0.909
Crystalloid (mL)	1000 (500–1500)	1000 (500–1500)	0.581
Colloid (mL)	0 (0–500)	0 (0–500)	0.106
Spinal anesthesia level (T8/T10/T12)	21/38/4	22/41/0	0.126

Note: Data expressed as mean (±SD), median (interquartile range) or n (%).

The incidence of hypertension (41.3% vs 41.3%, p = 1.000), tachycardia (6.3% vs 3.2%, p = 0.403), or hypoxemia (6.3% vs 3.2%, p = 0.409) was comparable between the two groups. The incidences of PONV (19.4% vs 28.4%, p = 0.156) and POD (6.3% vs 3.2%, p = 0.51) did not differ significantly between the two groups (Table 2).

Analysis of hemodynamic variables using linear mixed-effects models showed that the between - group effect on MAP not statistically significant (p=0.092, Figure 2A), while that on HR was significant (p=0.001, Figure 2B). In the

Table 2 Primary and Secondary Endpoint

	Remimazolam Sedation (n=63)	Dexmedetomidine Sedation (n=63)	p-value
Hypotension, n (%)	14 (22.2%)	33 (52.4%)	< 0.001
Bradycardia, n (%)	6 (9.5%)	39 (61.9%)	< 0.001
Application of Atropine, n (%)	0	6 (9.5%)	0.012
Norepinephrine, total (μg)	0 (0–0)	8 (0–64)	0.001
Hypertension, n (%)	26 (41.3%)	26 (41.3%)	1.000
Tachycardia, n (%)	4 (6.3%)	2 (3.2%)	0.403
Hypertension, n (%)	26 (41.3%)	31 (49.2%)	0.411
Hypoxemia, n (%)	9 (6.8%)	6 (12.7%)	0.409
Delirium, n (%)	4 (6.8%)	6 (10.8%)	0.510
Nausea or vomiting, n (%)	13 (19.4%)	20 (28.4%)	0.156

Note: Data expressed as median (interquartile range) or n (%).

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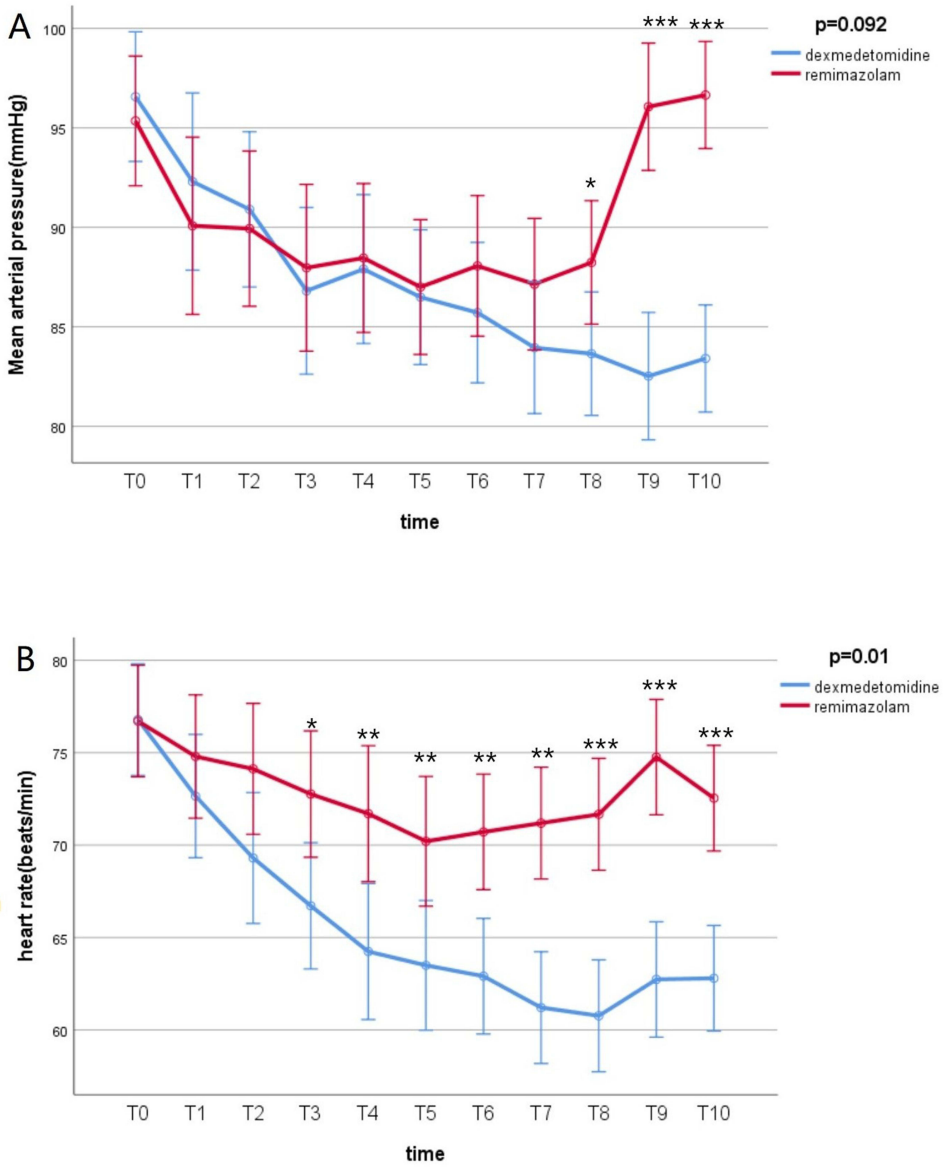

Figure 2 Hemodynamic variables across ten time periods, compared between the two study groups. (**A**) Mean arterial pressure and (**B**) heart rate, measured at eleven time points: (1) starting the loading dose of sedative (T0); (2) 5 min after the infusion of sedative (T1); (3) 10 min after the infusion of sedative (T2); (4) 15 min after the infusion of sedative (T3); (5) 20 min after the infusion of sedative (T4); (6) 30 min after the infusion of sedative (T5); (7) 40 min after the infusion of sedative (T6); (8) 50 min after the infusion of sedative (T7); (9) 60 min after the infusion of sedative (T8); (10) at the end of the surgery (T9). (11) at PACU (T10). *p < 0.05. **p< 0.01 ***< 0.001.

dexmedetomidine group, MAP was decreased at all time points except at 5 min compared to baseline ($p < 0.05$ for all time points). In contrast, in the remimazolam group, MAP decreased at 10 min time points (all time points $p < 0.05$) but returned to the baseline level by T9 and T10 ($p > 0.05$).

The serially assessed HR showed significant differences at from 15 minutes after the initiation of sedation onward ($p < 0.01$, for all time). In contrast, MAP showed significant differences only 60 minutes after dosing ($p=0.041$), at the end of the procedure ($p < 0.001$), and in the PACU ($p<0.001$). At all other time points, HR (baseline $p = 0.971$, 5 min $p = 0.370$, 10 min $p = 0.059$) and MAP (baseline $p=0.601$; 5 min $p=0.486$; 10 min $p=0.729$; 15 min $p=0.699$; 20 min $p=0.836$; 30 min $p=0.834$; 40 min $p=0.354$; 50 min $p=0.180$) did not show any significant intergroup difference.

Discussion

Our findings indicate that older patients undergoing spinal anesthesia for lower-extremity orthopedic procedures in the remimazolam group exhibited a significantly lower incidence of hypotension and bradycardia, along with reduced requirements for norepinephrine and atropine, than those in the dexmedetomidine group. These results suggested that remimazolam may provide superior hemodynamic stability during spinal anesthesia in orthopedic procedures.

In our study, remimazolam demonstrated significant hemodynamic advantages over dexmedetomidine, manifesting as a lower incidence of hypotension and bradycardia, alongside a reduced total requirement for norepinephrine and atropine. Importantly, the comparable MAP values observed at multiple time points must be interpreted in the context of substantially higher vasopressor requirements in the dexmedetomidine group; this pharmacological compensation potentially masked underlying hemodynamic differences, further underscoring the stability advantage of remimazolam. Compared to dexmedetomidine, remimazolam was associated with a higher HR from T3 to T10 and significantly higher MAP from T8 to T10. The dexmedetomidine group exhibited persistently lower MAP and HR, extending into the PACU, likely attributable to its longer half-life. This prolonged effect, coupled with the greater need for vasopressors to maintain perfusion, poses potential risks for older patients with limited cardiovascular reserve. Conversely, the faster offset of remimazolam facilitates a swifter return to baseline hemodynamics, reducing complication risks and reliance on pharmacological support, positioning it as a potentially safer option for procedural sedation in vulnerable populations.

Many studies have showed that intraoperative use of remimazolam to maintain sedation was associated with more stable hemodynamic parameters in general anesthesia. In a randomized controlled trial, the researchers assigned 60 patients undergoing hip replacement surgery receiving general anesthesia to receive either remimazolam (initiated with a loading dose of 0.2–0.4 $mg \cdot kg^{-1}$, followed by a maintenance infusion of 0.3–0.5 $mg \cdot kg^{-1} \cdot h^{-1}$) or propofol (starting with a loading dose of 1.5–2 $mg \cdot kg^{-1}$, then maintained with 4–8 $mg \cdot kg^{-1} \cdot h^{-1}$).[17] The study revealed that patients in the remimazolam group experienced reduced respiratory and circulatory suppression, attenuated stress responses, and lower rates of cognitive dysfunction than those in the propofol group did. Similarly, patients undergoing general anesthesia for laparoscopic radical resection for gastric cancer, the intraoperative administration of remimazolam (with a loading dose of 0.2$mg \cdot kg^{-1}$, followed by a maintenance dose of 0.3–0.5 $mg \cdot kg^{-1} \cdot h^{-1}$) was linked to more stable hemodynamic parameters and a lower prevalence of early POCD compared to dexmedetomidine.[18] In our study, for intraoperative sedation during spinal anesthesia, remimazolam (with a loading dose of 0.1 $mg \cdot kg^{-1}$, and a maintenance dose of 0.1–0.3 $mg \cdot kg^{-1} \cdot h^{-1}$) exhibited more stable perioperative hemodynamics than dexmedetomidine (with a loading dose of 0.5 $\mu g \cdot kg^{-1}$, and a maintenance dose of 0.2–0.6 $\mu g \cdot kg^{-1} \cdot h^{-1}$). The loading doses and maintenance rates of dexmedetomidine and remimazolam used in our study were aligned with the sedative dosing regimens utilized in other studies and were appropriate for older patients.[19,20]

While our results underscore the hemodynamic advantages of remimazolam, particularly in reducing hypotension incidence compared to dexmedetomidine, some studies report comparable hypotension rates between the two drugs. These discrepancies likely stem from significant methodological heterogeneity across trials. Notably, studies employing higher maintenance doses—often necessary for deeper sedation in complex procedures—observed attenuated hemodynamic divergence. For instance, one study involving continuous intravenous infusion during regional anesthesia found no difference in hypotension between remimazolam (loading: 6 $mg \cdot kg^{-1} \cdot h^{-1}$ for 10 min, maintenance: 1 $mg \cdot kg^{-1} \cdot h^{-1}$) and dexmedetomidine (loading: 6 $\mu g \cdot kg^{-1} \cdot h^{-1}$ for 10 min, maintenance: 1 $\mu g \cdot kg^{-1} \cdot h^{-1}$).[21] Similarly, in patients undergoing fiberoptic bronchoscopy, remimazolam (loading: 6 $mg \cdot kg^{-1} \cdot h^{-1}$ for 10 min, maintenance: 1–2 $mg \cdot kg^{-1} \cdot h^{-1}$) did not significantly reduce hypotension incidence compared to dexmedetomidine (loading: 0.5 $\mu g \cdot kg^{-1}$ for 10 min, maintenance: 0.2–0.7 $\mu g \cdot kg^{-1} \cdot h^{-1}$).[22] In contrast, our weight-adjusted titration protocol utilized significantly lower maintenance doses (remimazolam: 0.1–0.3 $mg \cdot kg^{-1} \cdot h^{-1}$; dexmedetomidine: 0.2–0.6 $\mu g \cdot kg^{-1} \cdot h^{-1}$) targeting moderate sedation (MOAA/S 2–3), consistent with guideline-recommended dosing for older adults. Crucially, equipotent sedation was confirmed by identical MOAA/S targets, suggesting that observed hemodynamic differences are attributable to pharmacological profiles rather than sedation depth disparities. Furthermore, procedural and population differences are critical factors. Studies involving younger cohorts or general anesthesia settings may obscure age-related pharmacodynamic

vulnerabilities. Our cohort's advanced age (median 71 years) and standardized spinal anesthesia (sensory block lower than T8) heightened sensitivity to hemodynamic perturbations,[23] thereby amplifying the observed hemodynamic advantages of remimazolam in our setting.

Hypotension is a prevalent adverse event in orthopedic surgery, and its incidence is further increased by spinal anesthesia.[24,25] The vasodilation of arteries and veins due to sympathetic blockage along with paradoxical activation of cardioinhibitory receptors is a primary cause of spinal anesthesia-induced hypotension.[26] Hypotension in older patients is a significant predictor of organ damage, cardiovascular condition, and postoperative cognitive decline. This condition not only increases the risk of 30-day mortality, but also correlates with acute kidney injury (AKI) and major adverse cardiac events, such as myocardial injury or infarction. Additionally, hypotension can extend hospital stays and increase healthcare costs, placing a substantial burden on both patients and the healthcare system.[27–29]

The divergent hemodynamic outcomes fundamentally stem from distinct pharmacological mechanisms, rather than disparities in sedative potency or dosing. Dexmedetomidine, an α_2-adrenoceptor agonist, centrally inhibits sympathetic outflow while potentiating vagal activity—inherently predisposing to dose-dependent hypotension and bradycardia, which could lead to an increased risk of hemodynamic instability.[24,30] Conversely, remimazolam's ultra-short-acting GABA-A receptor modulation, characterized by rapid esterase metabolism and context-independent half-life, minimizes cardiovascular depression while reducing drug accumulation.[9,31,32] By strictly adhering to guideline-recommended geriatric dosing and achieving equivalent MOAA/S-targeted sedation depth (scores of 2–3) between groups, our methodology ensured that sedation depth and pharmacological exposure were comparable.[33,34] Despite this rigorous control, dexmedetomidine was associated with a significantly higher incidence of hypotension (52.4% vs 22.2%) and bradycardia (61.9% vs 9.5%) than remimazolam. This finding confirms that the divergent hemodynamic profiles are directly attributable to dexmedetomidine's intrinsic pharmacological properties,[30] rather than pharmacological overexposure or inadequate sedation. Additionally, standardized 10-minute infusions were implemented to preclude rapid hemodynamic fluctuations potentially arising from differential onset kinetics between remimazolam and dexmedetomidine. Notably, studies reporting non-significant hemodynamic differences[21,22] were conducted in distinct clinical contexts—involving procedures requiring deeper sedation (eg, fiberoptic bronchoscopy[22]) or complex analgesic regimens—that necessitated higher dosing. Such regimens may obscure intrinsic pharmacologic differences, whereas our optimized protocol in spinal anesthesia clearly demonstrates the inherent hemodynamic advantage of remimazolam.

In our study, remimazolam not only effectively maintained the hemodynamic stability of the patient, but also demonstrated non-inferiority to dexmedetomidine in terms of POD, respiratory depression, and PONV. These effects are associated with the capacity of remimazolam to modulate microglial activity in a beneficial manner similar to dexmedetomidine, and its impact on the GABA-BDZ receptor complex, which reduces the activity of dopaminergic neurons and the release of serotonin like midazolam.[35–37] This finding is corroborated by a wealth of literature highlighting the multifaceted benefits of remimazolam in various surgical settings.[38–41]

However, our study has some limitations. First, it was conducted at a single center with a limited sample size. Second, the study only enrolled patients classified as ASA I–III, which necessitates further investigation of the effect of remimazolam on hemodynamic stability in high-risk populations. Future multi-center trials should validate these findings in broader populations, including those with significant cardiopulmonary comorbidities. Additionally, dose-response studies could optimize remimazolam dosing for specific surgical contexts.

Conclusion

Our findings show that remimazolam is a safe and effective alternative to dexmedetomidine for sedation in patients undergoing lower-extremity orthopedic surgery with spinal anesthesia own to its lower incidence of hypotension and bradycardia. In this context, remimazolam is a promising alternative to dexmedetomidine in minimizing the risk of cardiac-related adverse events.

Data Sharing Statement

The datasets for this study are available from the corresponding author (email: bcj0411@126.com) upon reasonable request.

Ethical Approval Statement

This study was approved by the Ethics Committee of the Central Hospital of Dalian University of Technology (Dalian Municipal Central Hospital) (Liaoning, China; 2024-039-01; April 2024). Informed consent was obtained from the study participants prior to the commencement of the study.

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Disclosure

The authors have no relevant financial or non-financial interests to disclose.

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