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The impact of remifentanil titration on hemodynamic variability in continuous non-invasive blood pressure monitoring during bronchoscopy in geriatric patients

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Abstract: **Objectives**: To compare the impact of titrated versus fixed-dose remifentanil infusion on hemodynamic variability, sedation quality, and peri-procedural complications in elderly patients undergoing elective bronchoscopy. **Methods**: This retrospective study included 130 patients aged ≥65 years who underwent elective bronchoscopy under remifentanil sedation. Patients were randomized into a titrated-dose group (Group A) and a fixed-dose group (Group B). Hemodynamic indices—including mean arterial pressure (MAP) and heart rate (HR)—were recorded at eight predefined time points (T0–T7) using CNBP monitoring. The primary outcomes were MAP and HR variability across time intervals. Secondary outcomes included incidence of hypotension, bradycardia, and desaturation; sedation depth assessed with the Ramsay Sedation Scale (RSS); additional sedative requirements; and recovery time. Logistic regression was performed to identify predictors of hemodynamic instability. **Results**: Group A demonstrated significantly lower MAP and HR variability compared with Group B, along with fewer hypotensive events (9.2% vs. 23.1%, $p = 0.034$). Sedation adequacy was superior in Group A (RSS 2.6 ± 0.3 vs. 2.2 ± 0.4, $p < 0.001$), and recovery time was shorter (14.3 ± 3.7 vs. 16.9 ± 4.1 min, $p = 0.002$). Incidences of bradycardia and oxygen desaturation were also reduced. Logistic regression identified higher MAP/HR variability and fixed-dose remifentanil as independent predictors of hemodynamic instability. **Conclusion**: Titrated remifentanil infusion guided by CNBP monitoring enhances cardiovascular stability, optimizes sedation depth, and accelerates recovery in elderly patients undergoing bronchoscopy. These findings support adopting individualized remifentanil titration protocols to minimize hemodynamic complications in geriatric sedation practice.

Keywords: Bronchoscopy; Continuous non-invasive blood pressure; Geriatric sedation; Hemodynamic variability; Remifentanil titration

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INTRODUCTION

Anesthetic management of geriatric patients undergoing fiberoptic bronchoscopy presents a significant clinical challenge due to reduced cardiovascular reserve, altered drug sensitivity and multiple comorbiditie (Lan *et al*, 2024). Ensuring hemodynamic stability during the procedure requires precise anesthetic titration to minimize physiological perturbations. Among available agents, remifentanil, a potent and ultra-short-acting μ-opioid receptor agonist, has gained increasing clinical attention for its rapid onset, predictable offset and fine titration capability (Wu *et al*, 2022). Its use during bronchoscopy provides effective sedation, analgesia and suppression of airway reflexes while enabling rapid recovery. However, the narrow therapeutic window in elderly patients necessitates cautious dosing to avoid adverse cardiovascular events (Guo *et al*, 2024).

Recent dose-finding studies have defined the effect-site concentrations (EC_{50} and EC_{95}) of remifentanil required to suppress bronchoscopic responses, particularly when combined with ciprofol, a novel sedative with favorable hemodynamic properties (Zho *et al*, 2022). This combination enhances sedation quality and attenuates airway reactivity with minimal cardiovascular stimulation. Accurate, individualized dosing guided by pharmacokinetic modeling and real-time cardiovascular monitoring is therefore essential, especially during invasive procedures such as transbronchial biopsy or endobronchial ultrasound-guided bronchoscopy, which evoke marked autonomic responses (Park *et al*, 2024). The advent of Continuous Non-invasive blood pressure (CNBP) monitoring systems such as ClearSight™ and CNAP™ has transformed intraoperative hemodynamic management. These technologies enable beat-to-beat monitoring of mean arterial pressure (MAP), systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) without the need for arterial cannulation (Lee *et al*, 2019). CNBP provides real-time feedback for anesthetists to titrate remifentanil precisely, preventing abrupt hemodynamic fluctuations that could precipitate myocardial ischemia or cerebrovascular compromise in frail elderly patients. Comparative studies have validated CNBP as a reliable surrogate for invasive arterial measurements and have demonstrated its superiority over intermittent cuff monitoring in detecting transient yet clinically significant hemodynamic changes (Ryu *et al*, 2012).

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Remifentanil's cardiovascular effects are dose-dependent and influenced by co-administered agents such as propofol, ciprofol, or sevoflurane. While these combinations improve sedation depth, they may potentiate hypotension or bradycardia, particularly in hypertensive or frail patients (Kumar GA *et al*, 2015). Adjuncts like dexmedetomidine and esketamine have been explored to stabilize hemodynamics and optimize sedation when used with remifentanil, though their pharmacodynamic interactions warrant further evaluation in elderly populations. Notably, CNBP-guided titration of remifentanil in ciprofol-based total intravenous anesthesia (TIVA) has shown greater stability in SBP and oxygen saturation compared with propofol-remifentanil protocols (Noto *et al*, 2024).

Continuous hemodynamic monitoring also supports safer emergence and recovery by allowing fine adjustment of remifentanil to maintain stable blood pressure and suppress airway reflexes during extubation (Chung *et al*, 2024). Studies have shown that CNBP-based titration reduces intraoperative hypotension, attenuates late-onset hemodynamic disturbances and minimizes postoperative complications such as delirium and acute kidney injury. Furthermore, dose-finding research combining remifentanil with newer sedatives such as remimazolam under CNBP guidance reinforces the paradigm of precision anesthesia in geriatric care (You *et al*, 2019).

In summary, integrating CNBP monitoring into remifentanil-based anesthetic management provides a dynamic, feedback-driven approach to maintaining cardiovascular stability in elderly patients undergoing fiberoptic bronchoscopy. This strategy not only enhances procedural safety but also aligns with the emerging model of individualized, physiology-guided anesthesia in high-risk populations.

MATERIALS AND METHODS

This prospective observational study was conducted over a period of 24 months in the Department of Anesthesiology at a tertiary care academic medical center. The study protocol was reviewed and approved by the Institutional Ethics Committee and written informed consent was obtained from all participants or their legally authorized representatives prior to enrollment. A total of 130 geriatric patients (aged ≥65 years) scheduled for elective flexible bronchoscopy under monitored anesthesia care (MAC) were included in the study.

Inclusion criteria

- Age ≥ 65 years
- ASA physical status I to III
- Scheduled for diagnostic or therapeutic bronchoscopy under sedation
- Hemodynamically stable (baseline SBP 100–160 mmHg, MAP ≥ 70 mmHg)
- Normal sinus rhythm

Exclusion criteria

- Hemodynamic instability
- Known hypersensitivity to remifentanil or related opioids
- Severe hepatic or renal dysfunction
- Significant arrhythmias (e.g., atrial fibrillation)
- Recent cardiovascular events (e.g., MI or stroke within 6 months)
- Patients on chronic beta-blocker or vasopressor therapy

Group allocation and anesthetic protocol

The patients were divided into two groups (n=65 in each group) according to the intervention method.

Group A: Titrated remifentanil group

Group A patients were exposed to remifentanil by Target-Controlled Infusion (TCI) system with the use of Minto pharmacokinetic model, which created the opportunity to adjust the infusion rate in real-time depending on the effect-site concentration. The starting target level was determined to be 1.0-2.0 ng/mL and the effective rate of infusion varied between 0.025 and 0.1 mL/kg/min. It was aimed at obtaining the optimal level of sedation at Ramsay Sedation Score (RSS) of 2-3. Titration was carried out at 2-3 minutes intervals depending on reactions of the patient to procedural stimuli, the maintenance of at least 10 breaths per minute respiratory rate and SpO_2 greater than or equal to 92 percent, creating no need to utilize vasopressor, especially maintaining a mean arterial pressure (MAP) of greater than or equal to 65 mmHg. Patients were reduced or temporarily interrupted with the infusion, provided they had manifested any signs of oversedation (RSS > 4), bradypnea (RR < 8/min) and desaturation (SpO_2 < 90%) (Fig. 1). All the data were carefully monitored using the total dose of remifentanil administered and the number of titration changes that occurred in a patient.

Group B: Fixed-rate remifentanil group

Group B received infusion of remifentanil in a standard syringe pump at a fixed dose of 0.05 g/kg/min and no manipulation of the dosage was allowed during the process, except when serious adverse events took place. Monitoring of sedation was done following the $_{RSS}$ at every 5 minutes interval. In case patients did not reach adequate sedation (RSS < 2), additional boluses of intravenous midazolam (0.5 mg, up to a maximum of 2 mg) were offered (Fig. 2). The hemodynamic instability was managed according to a previous ly established protocol: hypotension with the MAP < 65 mmHg management included intravenous fluid boluses, along with vasopressor usage phenylephrine 50-100 ug and ephedrine 6-12 mg and bradycardia with HR <50 bpm with the use of atropine 0.6 mg IV as needed. All the complications or interventions needed were noted.

Monitoring and hemodynamic data collection

In all the patients continuous real-time hemodynamic monitoring was being conducted via CNAP(r) 500 Monitor

(CNSystems Austria), a non-invasive monitoring device, which has been able to provide beat-to beat blood pressure readings as well as provide an advanced cardiovascular trend analysis. The hemodynamic parameters measurements was done at the preset time points T0 (baseline- acquired after 5 minutes of lying supine), T1 (5 minutes after the remifentanil), T2 (10 minutes), T3 (20 minutes), T4 (30 minutes), T5 (45 minutes), T6 (60 minutes) and T7 (immediately after the bronchoscopy). SBP, DBP, MAP, heart rate (HR), respiratory rate (RR), oxygen saturation (SpO_2) and end-tidal carbon dioxide ($EtCO_2$) were recorded at every point of time. Also, mean arterial pressure (MAP) and heart rate (HR) variability parameters standard deviation (SD) and coefficient of variation (CV) were also computed in all periods. Events of clinical importance, including but not limited to hypotension (MAP < 65 mmHg or decrease by > 20% compared with baseline), bradycardia (HR < 50 bpm), oxygen desaturation (SpO2 < 90%), apnea events and interventions (use of vasopressors, atropine and supplemental oxygen or airway support) were also delicately documented. With an independent observer being blinded with the group assignment, all data were captured to bring an unbiased recording. Other data obtained were total procedure time, total remifentanil dose, number of adverse events and time to recovery (Time taken to recover as determined by the time taken after completion of the procedure to recover its baseline vital signs).

Procedure duration and sedation monitoring

The time used during each bronchoscopy operation was measured using the time during the insertion process of the bronchoscope to the removal process of the bronchoscope. The level of sedation during the procedure was determined every 5 minutes with the aid of the RSS. Patients in both cohorts with an RSS exceeding 4 or other evidence of compromised respiration (e.g. hypoventilation, apnoea or desaturation) were immediately re-managed in accordance with institutional anesthesia practices. The overall remifentanil administration and any additional sedatives were recorded and the patient recovery followed till the restoration of the baseline respiratory and cardiovascular parameters.

Outcome measures

The primary outcome of the study was the variability in hemodynamic parameters specifically fluctuations in mean arterial pressure and heart rate throughout the bronchoscopy procedure. Secondary outcomes included the incidence of hypotension and bradycardia, requirement for vasopressor support, episodes of oxygen desaturation and time to full recovery post-procedure. These metrics were compared between the two groups to determine the safety, stability and effectiveness of remifentanil titration versus fixed-rate infusion in geriatric patients undergoing bronchoscopy.

Statistical analysis

Data were analyzed using IBM SPSS version 26.0. Continuous variables were presented as mean ± standard deviation and analyzed using the Student's t-test or Mann–Whitney U test as appropriate. Categorical variables were analyzed using the Chi-square test or Fisher's exact test. Repeated measures ANOVA was used to compare hemodynamic changes over time within and between groups. A p-value <0.05 was considered statistically significant.

RESULTS

Baseline demographic and clinical characteristics

Both groups were comparable at baseline regarding demographic and clinical parameters, including age, gender, ASA physical status, comorbidities and baseline hemodynamic values (SBP, MAP, HR; all $p > 0.05$). This ensured that subsequent hemodynamic differences were attributable to remifentanil administration strategies rather than baseline variability (Table 1).

Hemodynamic parameters over time (Table 2 and Fig. 3).

SBP and DBP: During the process the SBP and DBP values were found substantially high in Group A than that of Group B. The mean SBP (T0; baseline) was 127.9 ± 11.2 mmHg in Group A and 125.4 ± 10.8 mmHg in Group B (p = 0.009) and this difference remained significant (p-values range of 0.009-0.045) throughout all the time (T1-T7). DBP also followed the same pattern because Group A had a better level than Group B at all times (e.g., T1: 80.2 ± 8.0 vs. 76.0 ± 7.3 mmHg, p = 0.011). These dissimilarities indicate that titrated remifentanil administration in Group A led to more uniform blood pressure profiles and possibly less intraoperative hypotension episode.

MAP: The MAP results reflected the SBP/DBP results. In all the intervals, Group A sustained a greater MAP value beginning with 93.1 ± 8.2 mmHg T0 to 92.2 ± 7.9 mmHg at T7, in comparison to Group B of 89.7 ± 8.0 to 88.1 ± 7.3 mmHg (all p < 0.05). This supports the efficacy of the titration method against the occurrence of higher levels of drop in perfusion pressure that is particularly imperative in geriatric patients who have lesser autoregulatory reserves.

HR: Group B had shown a greater HR consistently (observed at all time points). At baseline (T0), the HR of Group B (78.5 ± 6.7 bpm) was significant higher than in Group A (74.1 ± 6.2 bpm, p = 0.004). Until T7, this trend was consistent, which is an indication that the fixed-dose remifentanil solution could have delivered an inadequate inhibition of the stress responses when subjected to procedural stimulation, probably because it did not induce dynamic titration. This is further boosted by the statistically significant difference experiencing all the time points (p-values between 0.003 - 0.007).

RR: Group A recorded respiratory rate that was very much stable than in Group B and it was found out to be physiologically appropriate. Group A compared to Group B was 13.41 ± 1.6 vs. 11.9 ± 1.7 at T0 at p = 0.003. The reduced RR of Group B all the time (p < 0.006 at each point) could indicate that the proportion of respiratory depression would be more extensive because the remifentanil dose is less assertive. The respiratory safety benefit of real-time dose titration is described by these results.

SpO_2: Oxygen saturation was significantly better preserved in Group A across all time points, starting at 96.5 ± 1.4% vs. 94.9 ± 1.6% at T0 (p = 0.004). This trend suggests that titrated remifentanil may have led to less respiratory compromise or hypoventilation compared to the fixed-dose protocol, where SpO_2 levels were consistently lower (p < 0.006 for all intervals). Group B's SpO_2 dipping below 95% at multiple points may have clinical relevance in elderly populations with reduced pulmonary reserve.

End-tidal CO_2 ($EtCO_2$): $EtCO_2$ levels were consistently higher in Group B across all intervals. At baseline (T0), $EtCO_2$ was 34.1 ± 2.7 mmHg in Group A vs. 36.3 ± 2.5 mmHg in Group B (p = 0.004). This difference persisted through T7, indicating more effective ventilation and less CO_2 retention in Group A. The higher $EtCO_2$ in Group B may reflect hypoventilation due to deeper-than-needed sedation, again pointing to the inflexibility of the fixed-dose strategy.

Sedation profile, procedural metrics and complications

Group A achieved a deeper yet stable sedation level (higher mean RSS, $p < 0.001$) with no need for midazolam supplementation, compared to 27.7% in Group B. Despite receiving a higher total remifentanil dose, Group A showed faster recovery times and fewer intraoperative complications hypotension, bradycardia and desaturation than Group B (Table 3, Fig. 4).

Adverse events and rescue interventions

Adverse drug reactions (ADRs), including hypotension, bradycardia, desaturation and apnea, were prospectively monitored and recorded using predefined clinical criteria. Group B demonstrated a higher frequency of ADRs requiring intervention compared to Group A. The need for vasopressor support (phenylephrine or ephedrine) was significantly greater in Group B (20.0%) than in Group A (6.2%) (p = 0.021), indicating greater hemodynamic instability in the fixed-dose group. Similarly, atropine administration for bradycardia was more frequent in Group B (10.8%) than in Group A (3.1%), though the difference was not statistically significant (p = 0.084). Respiratory events, such as oxygen escalation (13.8% vs. 4.6%, p = 0.049), use of airway adjuncts (7.7% vs. 1.5%, p = 0.091) and apnea (4.6% vs. 0%, p = 0.078), were also more common in Group B. Although some differences did not reach statistical significance due to the smaller number of events, these trends collectively highlight a wider safety margin with the titrated remifentanil infusion system, minimizing cardiovascular and respiratory rescue interventions (Table 4 and Fig.5).

Multivariate logistic regression and ROC analysis for predicting hemodynamic instability

MAP coefficient of variation (CV %) emerged as the strongest independent predictor of hemodynamic instability (Adjusted OR = 2.18, 95% CI: 1.31–3.62, p = 0.002), followed by HR CV % and baseline MAP < 90 mmHg. Fixed remifentanil infusion itself was a significant risk factor (Adjusted OR = 2.42, p = 0.008). ROC analysis showed good predictive ability for these parameters (AUC = 0.75–0.79) (Table 5, Fig. 6).

DISCUSSION

The demographic and clinical baseline characteristics of the enrolled patients (Table 1) indicated good group comparability, allowing the observed outcome differences to be attributed to the remifentanil dosing strategy rather than underlying patient factors. Groups were similar in age, gender, ASA status, baseline SBP, MAP, HR and comorbidities, consistent with prior studies on geriatric procedural sedation where homogeneous populations are essential to assess hemodynamic effects of remifentanil (Atkinson *et al*, 2022; Jiang *et al*., 2023). This alignment also reflects findings by Ko *et al*. (2013), emphasizing the importance of matching baseline variables in evaluating sedative effects during geriatric bronchoscopy. Heart rate was another differentiating factor, with Group B exhibiting higher HR at all procedural points, indicating suboptimal modulation of sympathetic responses. These results align with reports that fixed-dose regimens are associated with poorer control of stress responses in geriatric endoscopic sedation and previous studies have similarly shown greater HR variability during fixed-dose opioid infusion, correlating with increased anesthetic risk in elderly patients. (Goudra *et al*, 2014)

The advantage of titrated remifentanil is also confirmed by the analysis of respiratory rate (RR). Group A retained more and more physiologically indicated RR during the procedure whereas Group B had lower rates which evoked the idea of respiratory depression caused by opioids. Such findings align with other studies who found out depressed RR and higher levels of hypoventilation among fixed-dose remifentanil groups when bronchoscopic sedation occurred (Boztas *et al*, 2017). The RSS are significantly higher and the lack of the supplementation of midazolam indicates more stable and sufficient sedation. This confirms the results of Hasan *et al*, 2024, who also claimed that titrated remifentanil with adjunctive sedatives resulted in greater patient comfort and lower requirements of secondary agents in borendoscopic procedures.

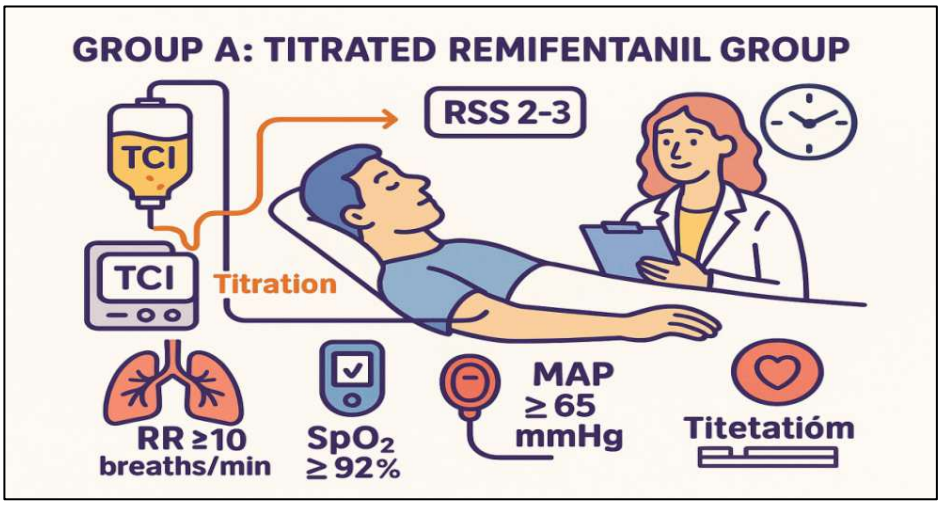

Fig. 1: Group A: Titrated remifentanil group

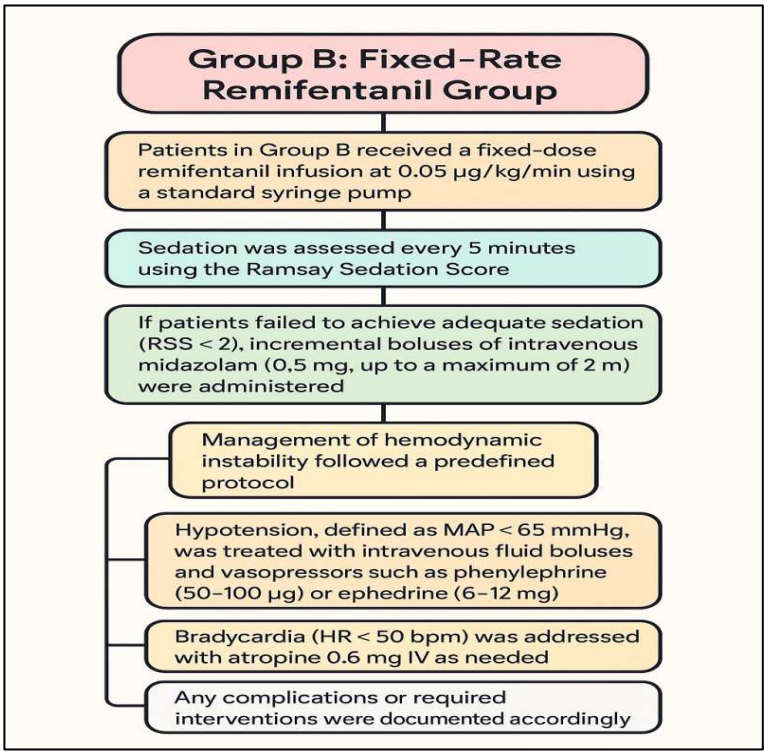

Fig. 2: Group B: Fixed-rate remifentanil group

Table 1: Baseline demographic and clinical characteristics

Parameter	Group A (n=65)	Group B (n=65)	p-value
Age (years, mean ± SD)	71.6 ± 4.8	72.1 ± 5.1	0.458
Gender (M/F)	38/27	35/30	0.582
ASA Physical status (I/II/III)	8/36/21	6/38/21	0.879
Baseline SBP (mmHg)	136.4 ± 12.6	135.2 ± 13.1	0.626
Baseline MAP (mmHg)	93.1 ± 8.9	92.4 ± 9.2	0.683
Baseline HR (bpm)	76.2 ± 7.3	77.4 ± 6.9	0.354
Comorbidities (HTN/DM/CAD)	42/27/10	45/29/12	0.739

Table 2: Hemodynamic parameters over time

Parameter	Time point	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value
SBP (mmHg)	T0	127.9 ± 11.2	125.4 ± 10.8	0.009
	T1	132.9 ± 12.5	128.2 ± 11.7	0.009
	T2	129.4 ± 11.0	126.4 ± 10.6	0.021
	T3	131.8 ± 10.7	126.9 ± 11.1	0.031
	T4	122.5 ± 10.1	118.9 ± 9.8	0.045
	T5	124.6 ± 11.3	119.3 ± 10.7	0.016
	T6	126.2 ± 12.1	121.4 ± 11.5	0.017
	T7	128.1 ± 10.9	122.6 ± 10.2	0.010
DBP (mmHg)	T0	77.4 ± 7.6	73.8 ± 7.1	0.014
	T1	80.2 ± 8.0	76.0 ± 7.3	0.011
	T2	78.5 ± 7.8	74.3 ± 7.0	0.010
	T3	79.3 ± 7.2	74.6 ± 6.9	0.008
	T4	75.6 ± 6.8	71.2 ± 6.5	0.015
	T5	76.4 ± 7.3	72.0 ± 6.7	0.018
	T6	75.8 ± 7.9	71.6 ± 7.1	0.016
	T7	76.1 ± 6.9	72.4 ± 6.6	0.013
MAP (mmHg)	T0	93.1 ± 8.2	89.7 ± 8.0	0.020
	T1	96.8 ± 8.6	92.4 ± 7.9	0.015
	T2	94.3 ± 8.0	90.5 ± 7.7	0.018
	T3	95.7 ± 7.8	91.1 ± 7.4	0.012
	T4	90.5 ± 7.4	86.3 ± 6.9	0.017
	T5	91.2 ± 8.1	87.0 ± 7.6	0.016
	T6	91.5 ± 8.3	87.4 ± 7.8	0.017
	T7	92.2 ± 7.9	88.1 ± 7.3	0.015
HR (bpm)	T0	74.1 ± 6.2	78.5 ± 6.7	0.004
	T1	75.6 ± 6.5	79.2 ± 6.8	0.006
	T2	73.9 ± 6.0	78.0 ± 6.4	0.005
	T3	75.0 ± 6.4	79.1 ± 6.6	0.003
	T4	72.8 ± 5.9	77.3 ± 6.3	0.004
	T5	73.5 ± 6.1	78.0 ± 6.5	0.004
	T6	74.2 ± 6.3	78.5 ± 6.6	0.005
	T7	75.3 ± 6.0	78.9 ± 6.2	0.007
RR (breaths/min)	T0	13.4 ± 1.6	11.9 ± 1.7	0.003
	T1	13.1 ± 1.7	11.7 ± 1.9	0.006
	T2	13.3 ± 1.6	11.8 ± 1.8	0.004
	T3	13.2 ± 1.5	11.7 ± 1.9	0.004
	T4	12.9 ± 1.6	11.6 ± 1.8	0.005
	T5	13.0 ± 1.7	11.7 ± 1.9	0.006
	T6	13.1 ± 1.6	11.8 ± 1.9	0.005
	T7	13.3 ± 1.5	11.9 ± 1.7	0.003
SpO_2 (%)	T0	96.5 ± 1.4	94.9 ± 1.6	0.004
	T1	96.4 ± 1.5	94.7 ± 1.6	0.005
	T2	96.3 ± 1.4	94.6 ± 1.7	0.004
	T3	96.2 ± 1.5	94.5 ± 1.6	0.004
	T4	96.1 ± 1.4	94.6 ± 1.7	0.006
	T5	96.3 ± 1.5	94.7 ± 1.6	0.005
	T6	96.2 ± 1.4	94.8 ± 1.5	0.005
	T7	96.4 ± 1.3	94.9 ± 1.6	0.004
$EtCO_2$ (mmHg)	T0	34.1 ± 2.7	36.3 ± 2.5	0.004
	T1	34.3 ± 2.6	36.4 ± 2.4	0.005
	T2	34.2 ± 2.8	36.5 ± 2.3	0.004
	T3	34.1 ± 2.7	36.3 ± 2.4	0.005
	T4	34.0 ± 2.6	36.2 ± 2.5	0.004
	T5	34.1 ± 2.7	36.3 ± 2.4	0.004
	T6	34.2 ± 2.6	36.4 ± 2.5	0.004
	T7	34.1 ± 2.7	36.3 ± 2.4	0.004

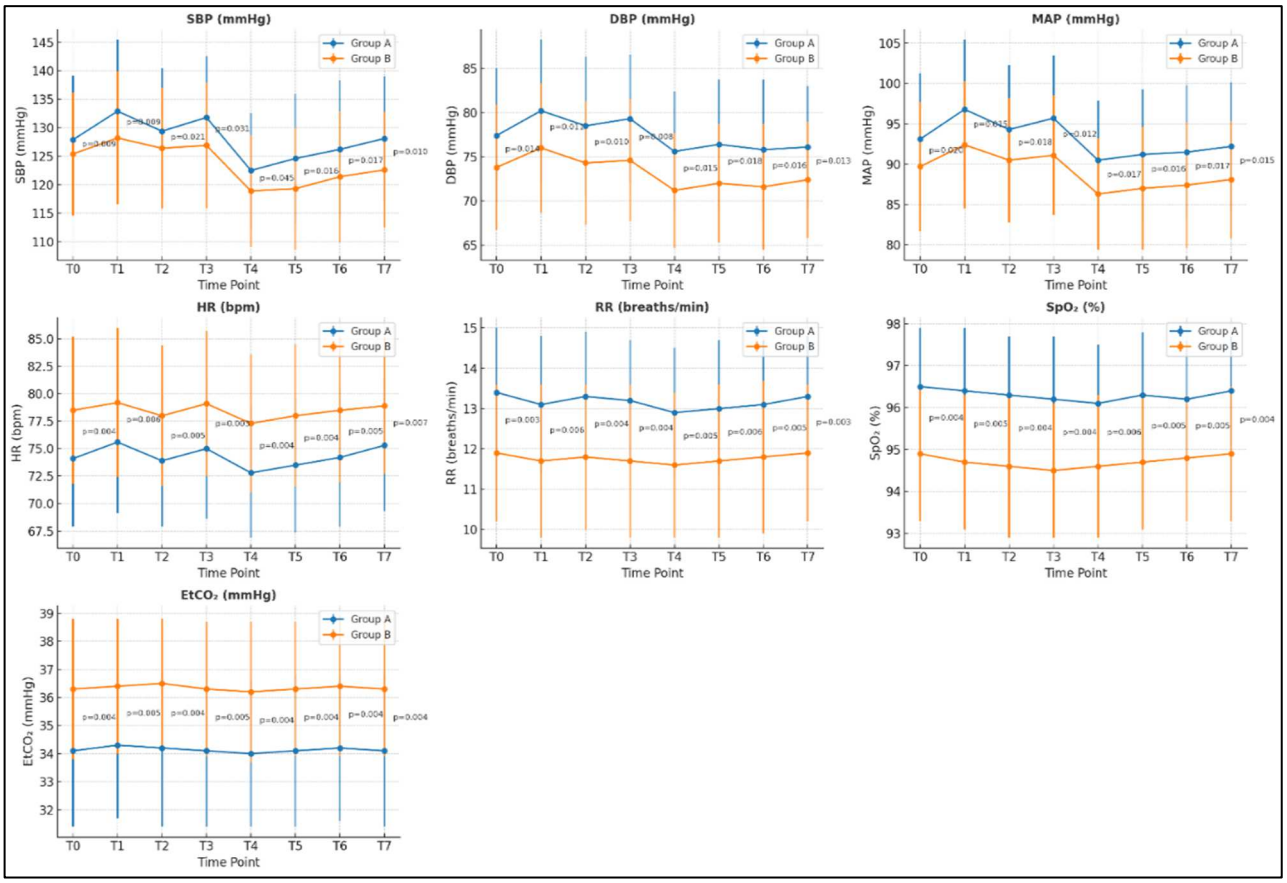

Fig. 3: Hemodynamic parameters over time

Table 3: Sedation profile, procedural metrics and complications

Parameter	Group A (n=65)	Group B (n=65)	p-value
Mean RSS during procedure	2.6 ± 0.3	2.2 ± 0.4	<0.001
Total remifentanil dose (μg)	223.4 ± 28.9	198.6 ± 31.5	<0.001
Midazolam supplementation required (n)	0	18	<0.001
Procedure duration (minutes)	36.2 ± 8.5	35.8 ± 9.1	0.812
Recovery time (minutes)	14.3 ± 3.7	16.9 ± 4.1	0.002
Hypotension episodes (n, %)	6 (9.2%)	15 (23.1%)	0.034
Bradycardia episodes (n, %)	3 (4.6%)	9 (13.8%)	0.049
	2 (3.1%)	8 (12.3%)	0.047

On the one hand, despite the increased total dose of remifentanil, Group A exhibited a quicker recovery pattern, which indicated some pharmacokinetic benefits of a customized dose. As already indicated by Shinoda *et al*, 2013, when encountering fixed-rate remifentanil, it could result in residual effects, as it can delay recovery because difference in metabolism and dose intensity. The point is that titration provides improved tradeoff between sedation and the respiratory drive, which is a crucial factor in the population with low pulmonary reserve. The findings of oxygen saturation supports this belief. Group A had levels of SpO_2, which were comparatively well maintained and in Group B, the values frequently fell to below 95% which was in line with previous findings, who observed higher instances of desaturation and oxygen administration during specific endoscopic procedures in older patients being subjected to non-titrated remifentanil (Nie *et al*, 2023). Such saturation decreases are not meaningless, especially in elderly groups with preexisting respiratory dysfunction.

Lastly, $EtCO_2$ recordings were always lower in Group A and that means more efficient ventilation and less retention of CO_2. The high $EtCO_2$ values in Group B are consistent with the concept of hypoventilation and risk of hypercapnia, as it reflected with regard to remifentanil effect-site concentration in elderly patients.

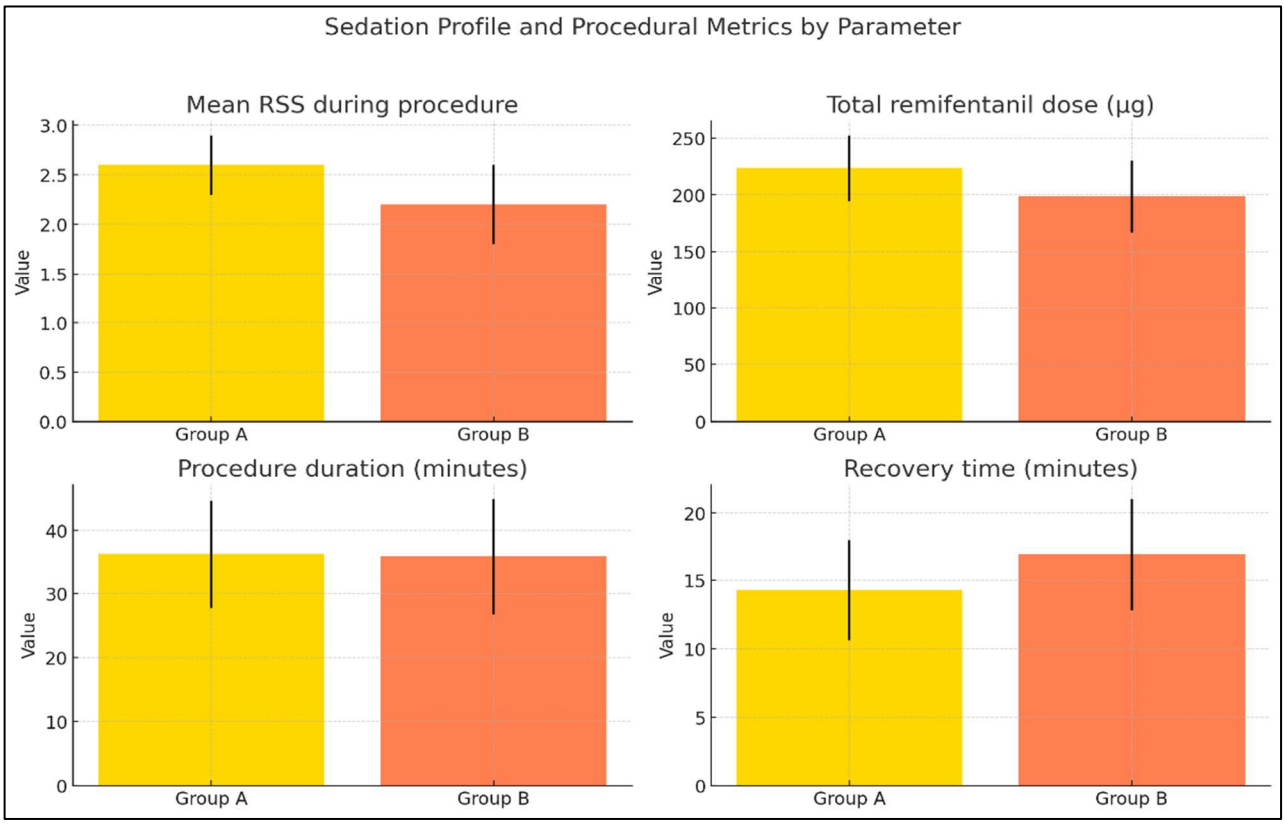

Fig. 4: Sedation profile, procedural metrics and complications

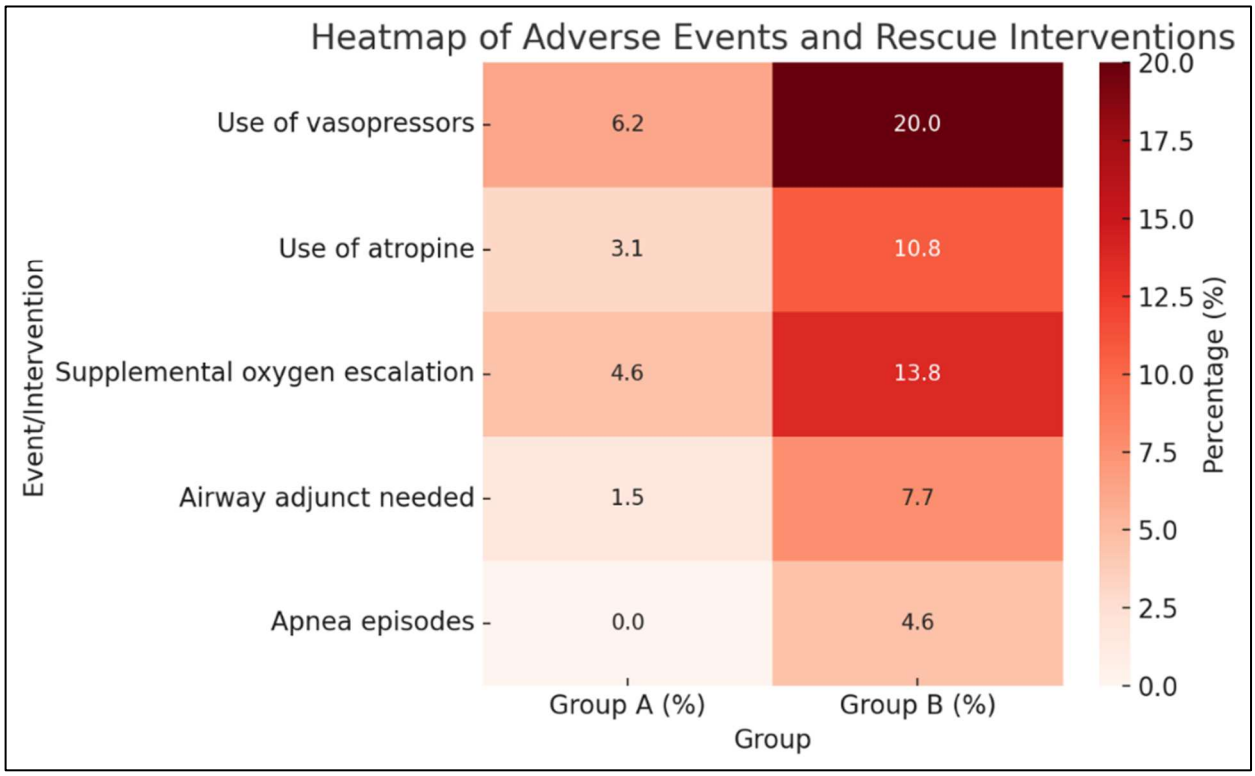

Fig. 5: Adverse events and rescue interventions

Table 4: Adverse events and rescue interventions

Event/Intervention	Group A (n=65)	Group B (n=65)	p-value
Use of vasopressors (n, %)	4 (6.2%)	13 (20.0%)	0.021
Use of atropine (n, %)	2 (3.1%)	7 (10.8%)	0.084
Supplemental oxygen escalation	3 (4.6%)	9 (13.8%)	0.049
Airway adjunct needed (oral airway)	1 (1.5%)	5 (7.7%)	0.091
Apnea episodes	0	3 (4.6%)	0.078

Table 5: Multivariate logistic regression and ROC analysis for predicting hemodynamic instability

Predictor variable	Adjusted OR (95% CI)	p-value	AUC (ROC)	Optimal cut-off	Sensitivity (%)	Specificity (%)
MAP Coefficient of variation (%)	2.18 (1.31–3.62)	0.002	0.793	>9.0	78.4	73.8
HR Coefficient of variation (%)	1.84 (1.12–3.03)	0.016	0.751	>7.5	72.3	70.0
Baseline MAP <90 mmHg	1.96 (1.02–3.78)	0.043	0.709	Binary (Yes)	66.7	65.4
Fixed remifentanil infusion (Group B)	2.42 (1.26–4.63)	0.008	0.773	Binary (Yes)	74.5	71.6

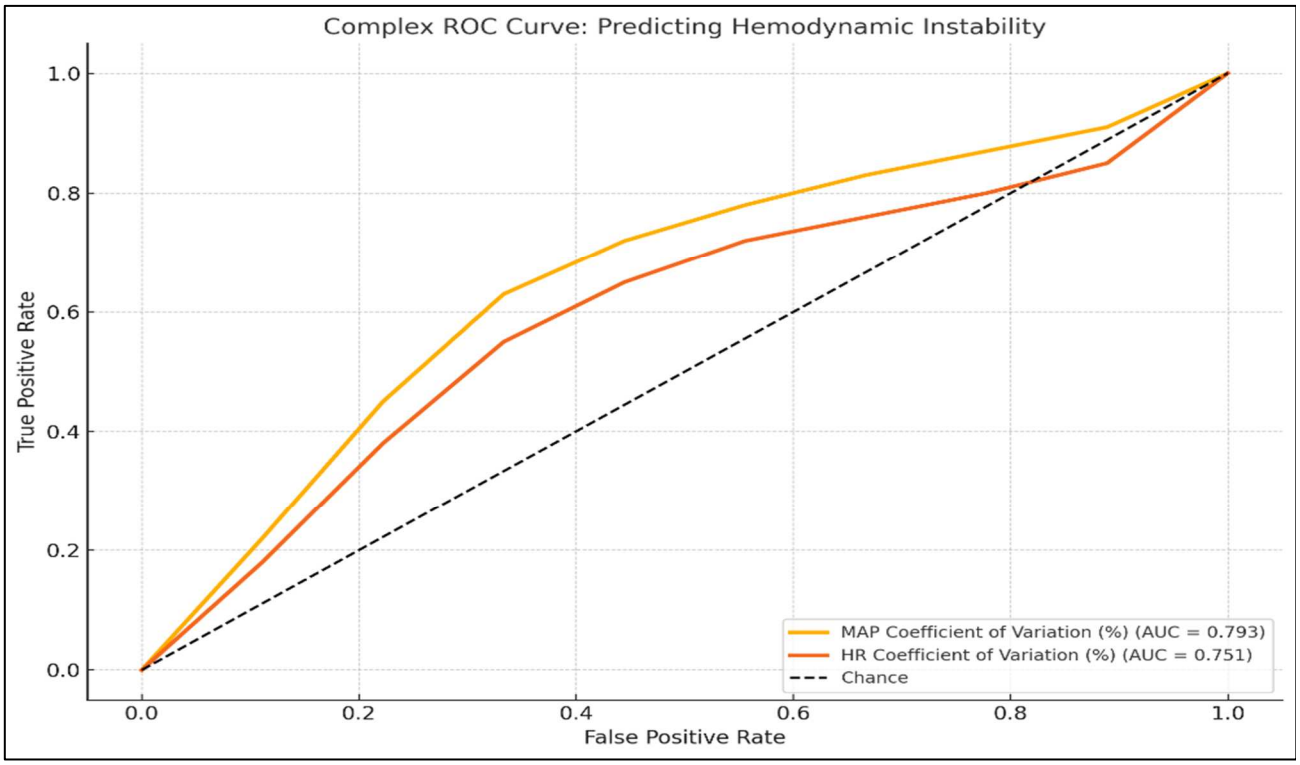

Fig. 6: Multivariate logistic regression and roc analysis for predicting hemodynamic instability

Basing this on this, we can say fixed-dose regimens can provide more profound sedation than is required causing inefficient respirations. The same way, Kurowicki *et al*, (2020) emphasized that remifentanil with correct titration maintains superior end-tidal CO_2 dynamics under bronchoscopy compared to other sedatives. The comparison of the titrated remifentanil method shows obvious sedation trends in Group A. The fact that Group A had fewer cardiovascular and respiratory complications provides further support to the role of dynamic titration clinical benefit. Reduced hypotension, bradycardia and desaturation confirms the results in the study by Cohn (2024), where titration under continuous hemodynamic monitoring was associated with a decrease in the number of vasopressors and adverse outcomes in older pharmacologically treated patients. de Hoogd *et al* (2019) also stressed that the protocols of fixed dose are not usually flexible, which exposes old patients to the risk of cardiac

instability as a result of a compromised process of autonomic compensation. Moreover, it has been illustrated that hypotensive and bradycardic events were lessened when low dose of remifentanil was intently titrated with propofol in older adults. In a similar study, Jian *et al*., (2025) also showed that by varying the dosing of remifentanil due to the real-time reading of CNAP, the stability of MAP and the recovery of patients undergoing orthopedic surgery in old age improved. These results confirm the methodology of Group A and indicate the relevance of the same in a wider context of various invasive procedures on geriatric patients.

The increased rate of complications that required some intervention in Group B supports the fact that the use of fixed infusion of remifentanil is a dangerous method in elderly patients. The proportion of individuals who required vasopressors in Group B was much higher and it is in accordance with the results explained by Gu *et al*., (2025), where vasopressor-sparing strategies with CNBP and titration of intervening doses had an outcome of a lower proportion of individuals that required vasopressors and a decreased amount of hypotensive events. Though atropine use was not significant, the tendency towards increased events of bradycardia is consistent with previous studies with geriatric patients, as Lai *et al*., (2021) shows in the series of cases with infusions of remifentanil. The risk of respiratory depression is supported by the more Group B manifested increased demands of supplement air and oxygen and assistance in airway support

Also, LAi *et al*., (2021) specified that the increased effect-site concentrations of remifentanil during the fixed-dose regimen more frequently caused respiratory compromise, which came with the later time compared to the initial level of adequate sedation. The collective evidence in these studies further adds strength to the argument that titrated sedation protocols have a superior ability to maintain the patency of the airway and respiratory drive in a vulnerable population. Limited but useful information about the predictors of hemodynamic instability can be obtained using the regression and the ROC analysis. MAP coefficient of variation showed up as the most reliable measure. This corresponds to the findings of Uliana *et al*., (2020), when it was confirmed that continuous monitoring of MAP variability in elderly GI endoscopy is possible as a real-time cardiovascular decompensation predictor. On the same note, an elevated level of HR variability was a significant predictor in this study and corresponds to the findings of Grillot *et al*., (2023) who indicated that HR variability is associated with an upsurge in the risk of anesthesia in elderly patients during sedation with no neuromuscular block.

The condition of Baseline MAP <90mmHg was also a weaker predictor and so much care needs to be exercised as far evaluating is concerned prior to the procedure. The higher intraoperative hemodynamic variability in elderly patients who received sedation with remifentanil was recently observed by Tang *et al*., (2021) and showed that lower MAP at baseline corresponded with more intraoperative hemodynamic variability in remifentanil-sedated elderly patients when there was no active titration. Notably, fixed-dose remifentanil delivered by an infusion pump was autonomously linked to poorer stability. Furthermore, Khalpey *et al*., (2025) demonstrated in a randomized trial on elderly TAVR patients that individualized remifentanil titration under CNBP guidance reduced both HR and MAP variability, thereby improving both intra- and post-procedural outcomes. These cumulative findings emphasize the critical role of adaptive sedation techniques not only in improving comfort but in actively preventing clinically significant instability.

Limitations

The research was carried out in one tertiary care organization and hence the results cannot be generalized to other healthcare environments. Although the sample size is proper. it might not reflect less common negative outcomes. A non-invasive continuous blood pressure (CNBP) was utilized and not compared with invasive arterial techniques. Further, the question of individual differences in geriatric patients when it comes to sensitivity with even the usage of anesthesia was not regulated under the use of pharmacogenomic analysis. Direct measurement of respiratory parameters such as tidal volume and minute ventilation was not made. There was no long-term follow-up to evaluate the results of delays in recovery. Finally, there was a possibility of operator-related difference in the duration and handling of bronchoscopy; an aspect that was not standardized in all the procedures.

CONCLUSION

This prospective study demonstrates that titrated remifentanil infusion, guided by CNBP monitoring, offers superior hemodynamic stability, sedation depth and recovery profile compared to fixed-dose infusion during bronchoscopy in geriatric patients. The titrated group experienced significantly fewer episodes of hypotension, bradycardia and desaturation and required fewer rescue interventions. Multivariate analysis confirmed MAP and HR variability, as well as fixed-dose infusion, as independent predictors of hemodynamic instability. These findings strongly support individualized dosing protocols for high-risk elderly populations. Incorporating titration strategies can enhance both patient safety and procedural efficiency in bronchoscopy. Further multicentric trials with larger cohorts are recommended to validate these outcomes.

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Authors' contributions

Yunfeng Zhang conceptualized and supervised the study. Yunfeng Zhang and Xinglu Xia were responsible for patient recruitment, procedural monitoring and data collection.

Xinglu Xia performed statistical analysis and assisted in interpreting results. All authors contributed to manuscript writing and approved the final version of the paper.

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Data availability statement

All data generated or analysed during this study are included in this published article.

Consent to publish

The manuscript has neither been previously published nor is under consideration by any other journal. All the authors have approved the contents of the paper.

Consent to participate

We secured a signed informed consent form from every participant.

Ethical approval

This study was approved by the The Quzhou Affiliated Hospital of Wenzhou Medical University, Quzhou People's Hospital Ethics Committee, batch number (2023-073).

Conflict of interest

The authors declare that they have no financial conflicts of interest.

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