Drug Design, Development and Therapy

Dovepress
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CLINICAL TRIAL REPORT

# Efficacy and Safety of Remimazolam versus Dexmedetomidine and Midazolam in Awake Endotracheal Intubation for Difficult Airway Patients: A Randomized Controlled Study

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**Objective:** To compare the safety and efficacy of remimazolam, dexmedetomidine, and midazolam in awake endotracheal intubation by flexible bronchoscopy for patients with difficult airways.

**Methods:** Ninety patients with difficult airways undergoing elective surgical procedures requiring awake endotracheal intubation under general anesthesia were randomly assigned to three groups, with 30 patients per group: Group M (midazolam), which received a 0.04 mg/kg intravenous (IV) bolus; Group D (dexmedetomidine), which was given via intravenous infusion pump at a rate of 1.0 μg/kg/min for 10 minutes; and Group R (remimazolam), which received a 0.15 mg/kg IV bolus. All patients first received 0.1μg/kg of sufentanil intravenously for basic analgesia. A 2-minute interval was allowed to ensure initial onset of the analgesic effect, followed by administration of the respective sedative agents for each group as detailed above. Upon achieving a Modified Observer's Assessment of Alertness/Sedation (MOAA/S) score of≤2, pharyngeal topical anesthesia was administered, followed by flexible fiberoptic endotracheal intubation. The primary outcome measure was the first-attempt intubation success rate. All other evaluated parameters were defined as secondary outcomes. Mean arterial pressure (MAP), heart rate (HR), and oxygen saturation ($SpO_2$) were recorded at four time points: baseline ($T_0$), immediately before intubation ($T_1$), immediately after intubation ($T_2$), and 3 minutes post-intubation ($T_3$). Additional outcomes assessed included the duration of anesthetic induction, the interval from induction to intubation, patient comfort levels, post-induction MOAA/S scores, and the incidence of adverse events.

**Results:** The first-attempt intubation success rates across the three groups were 70%, 93.3%, and 100%, respectively. Compared with the values at $T_1$, mean arterial pressure (MAP) and heart rate (HR) were significantly higher in Group M at $T_2$ and $T_3$ (both $P<0.05$). In Group D, HR at $T_1$ was significantly lower than that at $T_0$ ($P<0.05$). For inter-group comparisons, HR in Group D was significantly lower than in Group R at $T_1$ ($P<0.05$). Additionally, Group D had the longest duration of anesthetic induction and the longest interval from induction to intubation (both $P<0.05$). Compared with Group M, both Group D and Group R exhibited significantly higher first-attempt intubation success rates ($P<0.05$). Group R achieved the highest patient comfort scores, the highest success rate of sedation after a single induction dose, and the lowest incidence of adverse events (all $P<0.05$).

**Conclusion:** Remimazolam provides effective sedation for awake tracheal intubation in patients with difficult airways. It exerts minimal impact on respiratory and circulatory function, is associated with fewer adverse events, and yields a higher intubation success rate, making it a favorable option for this patient population.

**Keywords:** remimazolam, difficult airways, awake intubation, dexmedetomidine, midazolam

## Introduction

Airway management is a core component for the smooth progression of general anesthesia surgery and is directly related to patients' perioperative safety. Failure to effectively establish or maintain the airway can quickly lead to severe

Received: 30 August 2025
Accepted: 18 November 2025
Published: 1 December 2025

complications such as hypoxia and respiratory failure, and may even be life-threatening. According to the definition of the American Society of Anesthesiologists (ASA), a difficult airway refers to clinical situations where physicians trained in anesthetic care encounter anticipated or unanticipated difficulty or failure, including but not limited to obstacles in mask ventilation, laryngoscopy, use of supraglottic airway ventilation, tracheal intubation, extubation, or invasive airway establishment.[1] Its extreme form is "can't intubate, can't oxygenate" (CICO). Although the incidence of such cases is only 0.003%, it accounts for 25% to 28% of perioperative patient deaths.[2] Therefore, early identification and assessment of difficult airways before and during surgery are of crucial significance for optimizing airway management strategies and reducing perioperative risks.

Awake tracheal intubation is widely regarded as the gold standard for managing anticipated difficult airways, as it allows for the preservation of spontaneous respiration and provides a safer margin against the risk of airway obstruction or hypoxemia.[3] Among various techniques, fiberoptic bronchoscopy has become the most commonly used method for awake intubation, given its flexibility, clear visualization, and high success rate, particularly in patients with limited mouth opening, cervical spine immobility, or other anatomical challenges.[4,5] However, the procedure is often associated with significant patient anxiety, discomfort, and reflex responses such as coughing or gagging, which may compromise intubation conditions and increase the risk of complications.[6]

To improve patient tolerance and optimize intubation success, surface anesthesia is typically combined with low-dose sedatives and opioids.[7,8] This balanced approach can provide adequate anxiolysis and comfort while minimizing the risk of respiratory depression. The core requirements for sedative drugs in awake patients with difficult airways are as follows: ① rapid onset of action to shorten the waiting time for the procedure; ② moderate sedation depth (maintaining a MOAA/S score of 2–3 points) to ensure the patient's spontaneous breathing function; ③ stable circulation, requiring the fluctuation range of mean arterial pressure to not exceed 20% of the baseline value; ④ rapid recovery to reduce the impact of residual sedative effects on the patient after surgery. Nevertheless, conventional sedatives such as midazolam and dexmedetomidine present limitations. Midazolam, while effective, may require higher doses that lead to prolonged sedation and potential respiratory depression.[9] Dexmedetomidine offers cooperative sedation with minimal respiratory suppression, but its slow onset and frequent occurrence of bradycardia or hypotension limit its clinical utility. In a study comparing dexmedetomidine and propofol for C-MAC® D-Blade video laryngoscope-guided awake nasotracheal intubation, Vishnoi et al[10] reported the following key findings: the time taken to reach the target bispectral index (BIS) value in the dexmedetomidine group was four times longer than that in the propofol group ($P < 0.05$). Additionally, compared with propofol, dexmedetomidine was more likely to induce bradycardia during awake intubation, resulting in inferior hemodynamic stability.[11] Therefore, there remains an unmet need for a sedative agent that provides rapid, predictable onset of sedation, hemodynamic stability, and quick recovery, while ensuring patient safety during awake intubation.

Remimazolam, a novel ultra-short-acting benzodiazepine, has emerged as a promising candidate. It combines the favorable pharmacodynamic profile of midazolam with a unique metabolic pathway that allows rapid clearance by tissue esterases, independent of hepatic or renal function.[12,13] This results in a fast onset, short duration of action, and low risk of drug accumulation, even in vulnerable patient populations. This was a single-center randomized controlled trial conducted at Tianjin Nankai Hospital, enrolling 518 patients undergoing elective ERCP who required deep sedation. It compared the efficacy of the remimazolam-alfentanil combination versus the propofol-alfentanil combination. Results showed that the remimazolam group had a lower hypoxia rate (9.6%), lower hypotension rate, and lower rate of airway maneuvers needed due to hypoxia than the propofol group, with higher patient satisfaction.[14] Ju et al[15] conducted a randomized controlled trial focusing on post-induction hypotension in patients undergoing coronary artery bypass grafting (CABG), comparing the effects of remimazolam and propofol. The study demonstrated that remimazolam could enhance hemodynamic stability in CABG patients during anesthetic induction. Moreover, remimazolam is associated with minimal cardiorespiratory depression and has an available antagonist (flumazenil), which further enhances its safety profile.[16] Preliminary studies have demonstrated its efficacy in procedural sedation, gastrointestinal endoscopy, and bronchoscopy, suggesting potential value in difficult airway management.[17,18] In the aforementioned scenarios, this drug has demonstrated strong sedation controllability and safety. It not only allows for precise regulation of sedation depth to align with procedural needs but also minimizes the risk of adverse events, providing crucial preliminary support for its expanded use in difficult airway management contexts.

Difficult airway management imposes more specific clinical requirements, such as higher standards for hemodynamic stability and precise control over the degree of airway reflex suppression. However, evidence regarding the use of remimazolam in awake tracheal intubation remains scarce. Given the clinical importance of achieving adequate sedation while maintaining spontaneous breathing and hemodynamic stability, further investigation is warranted. This study therefore aimed to evaluate and compare the efficacy and safety of remimazolam, midazolam, and dexmedetomidine in awake fiberoptic tracheal intubation in patients with difficult airways. Key outcomes included intubation success rate, depth of sedation, hemodynamic fluctuations, and the incidence of adverse reactions, thereby providing evidence to guide clinical practice and optimize sedation strategies for difficult airway management.

# Subjects and Methods

## Subjects

This prospective randomized controlled study was conducted in strict adherence to the ethical principles outlined in the 1964 Declaration of Helsinki and its subsequent revisions. The study protocol was reviewed and approved by the Institutional Review Board of the First Affiliated Hospital of Yangtze University (Approval Number: LL202287). Additionally, this study has been registered in the Chinese Clinical Trial Registry, with the registration number ChiCTR2500111193. Written informed consent was obtained from each participant or their legally authorized representatives prior to enrollment. All participants were fully informed of the study's objectives, procedures, potential risks, and benefits, and had the right to withdraw from the study at any time without prejudice to their subsequent medical care. Ninety patients undergoing elective fiberoptic awake tracheal intubation for general anesthesia were enrolled and randomly assigned to three groups (n=30 each): group M (midazolam), group D (dexmedetomidine), and group R (remimazolam). The inclusion and exclusion criteria were formulated in accordance with the criteria for difficult airway assessment established by the American Society of Anesthesiologists (ASA).[1]

Inclusion criteria: Age 1860 years; BMI 18.523.9 kg/m²; ASA class I–III; anticipated difficult airway (criteria: Mallampati grade III–IV, mouth opening <3 cm, thyromental distance <6 cm or less than three fingerbreadths, limited mandibular protrusion, ultrasound measurement of the skin-to-epiglottis distance> 2.54 cm, and skin-to-hyoid distance >1.28 cm or restricted atlantoaxial extension).

Exclusion criteria: Allergy to benzodiazepines or flumazenil; airway hyperresponsiveness; full stomach; reflux esophagitis; intestinal obstruction; clinically significant cardiovascular disease, neurologic or psychiatric disorders, or other contraindications.

## Sample Size Calculation

The sample size estimation was centered on the primary outcome measure—the first-attempt intubation success rate across the three groups—and was comprehensively determined by integrating statistical software analysis and consideration of potential clinical dropout risks. The detailed process is as follows:

For the three study groups (midazolam group [Group M], dexmedetomidine group [Group D], and remimazolam group [Group R]), the first-attempt intubation success rates were set based on relevant previous literature reports and preliminary pilot study results, with values of 71% for Group M, 94% for Group D, and 98% for Group R, respectively. Sample size estimation was performed using PASS15 software. The "Comparison of Proportions" analysis module was selected, and the aforementioned first-attempt intubation success rates were used as input parameters; this calculation yielded an effect size of 0.36 for the study.

A significance level (α) of 0.05 (two-tailed) and statistical power (1-β) of 0.80 were predefined. Using the aforementioned effect size, PASS software calculations determined the minimum initial sample size for statistical validity to be 74 patients. Accounting for potential dropouts (due to poor compliance, clinical condition changes, or unexpected events) and referencing dropout rates in similar anesthesiology studies, a 15% dropout rate was set. The adjusted sample size was thus 74 patients ÷ (1–15%) ≈ 87 patients. To ensure balanced group sizes and enhance result reliability, the final total sample size was set to 90 patients, evenly allocated to the three groups (30 patients each) via complete randomization.

## Randomization

A complete randomized block design was adopted in this study. For the three study groups (midazolam group, dexmedetomidine group, and remimazolam group), random numbers were generated using Microsoft Office Excel software to ensure that patients were evenly allocated to the three groups at a 1:1:1 ratio. All generated random numbers and corresponding patient grouping information were sealed in opaque envelopes, which were uniformly kept by an independent data manager who was not involved in patient enrollment, drug administration, or data collection. Only when a patient was enrolled would the designated drug administrator obtain the corresponding envelope from this manager.

## Blinding

To minimize subjective bias, a double-blinding design with multi-role information isolation was implemented. Specifically, since dexmedetomidine required intravenous infusion via a pump while the other two drugs were administered as intravenous boluses, an independent drug administrator was assigned. This administrator did not participate in the patient enrollment process and only administered the sedative corresponding to the patient's randomization number accurately during the intubation procedure. Throughout the study, the administrator was prohibited from communicating any grouping-related information with other research personnel.

Additionally, all intubation procedures for enrolled patients were performed by an anesthesiologist with extensive experience in awake fiberoptic bronchoscopic intubation, who remained unaware of the patients' grouping information throughout the study. Meanwhile, another researcher, also blinded to the grouping information, was assigned to independently collect and record baseline data before intubation, key indicators during intubation, and follow-up data after the procedure.

## Anesthesia Method

This study was designed as a double-blind prospective trial. All patients fasted preoperatively and received no premedication. Upon arrival, oxygen (6 L/min) was administered, intravenous access established, and MAP, HR, and $SpO_2$ were continuously monitored.

## Basic Analgesia and Sedation

Thirty patients were included in each of the three groups (n=30 per group). All patients first received basic analgesia via an intravenous (IV) bolus of sufentanil (Yichang Humanwell Pharmaceutical Co., Ltd., Batch No. 01A11141, Specification: 1 mL: 50 μg) at a dose of 0.1 μg/kg. Two minutes after sufentanil administration—allowing time for the drug to take initial effect and ensuring no significant pain or discomfort in patients—different sedative drugs were administered according to group allocation, as detailed below:

Midazolam Group:Midazolam (Jiangsu Nhwa Pharmaceutical Co., Ltd., Batch No.: MZ210608, Specification: 2 mL: 2 mg) was given as a single IV injection at a dose of 0.04 mg/kg, with the administration completed within 1 minute Dexmedetomidine Group: Dexmedetomidine (Jiangsu Nhwa Pharmaceutical Co., Ltd., Batch No.: D07-20180801, Specification: 2 mL: 200 μg) was administered via IV infusion pump at a constant rate of 1.0 μg/kg/min, and the infusion duration was set to 10 minutes. Remimazolam Group: Remimazolam (Yichang Humanwell Pharmaceutical Co., Ltd., Batch No. AC4090301, Specification: 25 mg/vial) was first diluted to 25 mL with normal saline, then administered as an IV bolus at a dose of 0.15 mg/kg, with the administration completed within 1 minute.

## MOAA/S Score Monitoring and Surface Anesthesia

After drug administration, different assessment time points were set based on the metabolic characteristics of each drug. The Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale was used to evaluate sedation depth; if the target sedation level was not achieved, medication was adjusted as follows:

Dexmedetomidine Group: MOAA/S score was assessed 2 minutes after the completion of initial administration. If the score was >2, dexmedetomidine infusion was continued via IV pump at a rate of 0.5 μg/kg/min, the midazolam group received a continuous IV bolus of midazolam at 2 μg/kg/min, while the remimazolam group received continuous IV infusion of

remimazolam via pump at 0.04 mg/kg/min. For all groups, MOAA/S score was re-evaluated every 3 minutes until the patient's corneal reflex disappeared and the MOAA/S score was ≤2. In cases of excessive sedation (MOAA/S score ≤1), sedative administration was stopped immediately. The anesthesiologist determined whether to use flumazenil for antagonism: an initial IV bolus of 0.2 mg flumazenil was given, and if the desired level of consciousness was not achieved (MOAA/S score still <1) after 1 minute, an additional dose was administered as appropriate.

All patients received topical pharyngeal and laryngeal anesthesia with 5 mL of 1% lidocaine, including supraglottic surface anesthesia, administered using an aerosol applicator (Huixin Nuo Medical Device Co., Ltd., Shenzhen, China; Production Registration No.: 20,220,095).

The usage of this new spray device is as follows: the front end of the device is equipped with two connectors—one for attaching to an oxygen source and the other for connecting to a lidocaine syringe—and these two connectors converge at the rear end of the device into a single common output channel. The spray device is shown in Figure 1.When in use, align the rear end with the patient's pharynx, first turn on the oxygen supply, then have an assistant push the lidocaine syringe. At this point, the device converts the lidocaine into a uniform aerosol, which is delivered to the patient's pharyngeal cavity and subglottic region along with oxygen. This achieves precise, rapid, and even surface anesthesia of the airway.

## Endotracheal Intubation and Anesthesia Management

All patients underwent orotracheal intubation using an electronic fiberoptic bronchoscope of the same model (UE PL-F520 Series Visual Electronic Flexible Scope, manufactured by Zhejiang Youyi Medical Device Co., Ltd., Zhejiang, China). For female patients, endotracheal tubes with an internal diameter of 6.5–7.0 mm were selected; for male patients, those with an internal diameter of 7.0–7.5 mm were used. All patients were placed in a supine position with slight hyperextension of the head and neck to optimize airway alignment. After the patient was sedated and received adequate topical anesthesia, the intubation procedure was performed by an anesthesiologist who met the following criteria: having at least 5 years of clinical experience in anesthesiology or emergency medicine, being familiar with airway anatomy and the management of complications related to awake intubation, having independently completed at least 500 cases of orotracheal awake intubation, and achieving an intubation success rate of ≥95% within the past year.

After successful intubation, all three groups immediately received an intravenous (IV) bolus of propofol at 1.5–2.5 mg/kg, sufentanil at 0.5 μg/kg, and rocuronium at 0.6–0.8 mg/kg. Tracheal intubation was performed when the train-of-four stimulation response showed a count of 0, and mechanical ventilation was initiated immediately after intubation to maintain respiration. For total intravenous anesthesia maintenance: All three groups received a continuous IV infusion of propofol at a

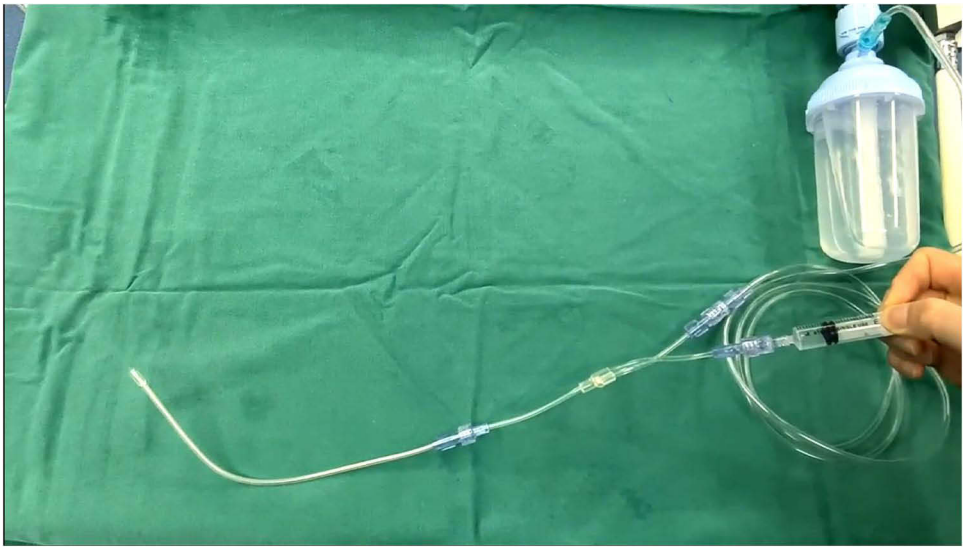

**Figure 1** A display diagram of a new spraying device.


https://doi.org/10.2147/DDDT.S564228

rate of 4–12 mg/kg/h. Throughout the procedure, the infusion rate of the corresponding drug in each group was adjusted via dose titration to ensure that the bispectral index (BIS) value was stably controlled between 40 and 60, thus maintaining an appropriate depth of anesthesia. Remifentanil was administered via manual adjustment, with the target plasma concentration controlled within the range of 2–8 ng/mL. The concentration was adjusted in increments/decrements of 0.5 ng/mL each time to maintain the patient's intraoperative blood pressure fluctuation within ±20% of the baseline blood pressure. Neuromuscular blockade was maintained with intermittent IV boluses of rocuronium. At the end of the surgery, the anesthetic maintenance drugs were discontinued, and the patients were transferred to the post-anesthesia care unit (PACU).

## Outcome Measures

The mean arterial pressure (MAP), heart rate (HR), and oxygen saturation ($SpO_2$) of patients at each time point before induction ($T_0$), before intubation ($T_1$), immediately after intubation ($T_2$), and 3 min after intubation ($T_3$) were recorded; The duration of anesthetic induction, induction-to-intubation interval, first-attempt success rate were recorded; The comfort level and MOAA/S scores of the three groups after induction were recorded; The incidence of adverse reactions, such as respiratory depression, hypotension, and bradycardia were observed.

Comfort level score: 1=mild discomfort but tolerable; 2=moderate discomfort with mild resistance; 3=severe discomfort with irritability, limb movement, or significant resistance.

MOAA/S score: 0=no response to painful stimulus; 1=response to pain only; 2=response to mild physical stimulus; 3=response only after loud or repeated calling; 4=delayed response to normal voice; 5=alert and responsive to normal voice.

## Statistical Analysis

All data were analyzed using SPSS 27.0. For continuous variables, normality (Shapiro–Wilk test) and homogeneity of variance (Levene test) were first assessed: data with normal distribution and homogeneous variance were expressed as mean±standard deviation (mean±SD), with one-way ANOVA for multi-group comparisons and LSD-*t* test for pairwise comparisons; non-normally distributed data were presented as median (25th percentile, 75th percentile) [M(P25, P75)] and analyzed via Kruska–Wallis *H*-test for multi-group comparisons. Categorical variables were expressed as number (percentage) [n (%)], with Pearson chi-square test for inter-group comparisons; Bonferroni correction was used to control Type I errors if pairwise multi-group comparisons were needed. Repeated-measures ANOVA was applied for repeated measurement data at different time points before and after intubation. A $P$-value $< 0.05$ was considered statistically significant.

# Results

From June 1, 2024, to June 30, 2025, 114 patients were assessed for eligibility. Among them, 24 patients were excluded: 20 did not meet the inclusion criteria, and 4 were excluded for other reasons. Subsequently, 90 patients were randomly assigned to three groups, with 30 patients in each group: Group M (the midazolam group), Group D (the dexmedetomidine group), and Group R (the remimazolam group). During the study, there were no patients lost to follow-up. Finally, all 90 patients (30 in each group) were included in the analysis (Figure 2).

Compared with $T_1$, MAP was significantly higher in group M at the $T_2$-$T_3$ time point, and the difference was statistically significant, and the difference between groups D and R was not statistically significant. Compared with $T_0$, HR was significantly lower in group D at $T_1$, and the difference was statistically significant; compared with $T_0$, the difference between groups R at each time point $T_1$-$T_3$ was not statistically significant (Table 1). Among the three groups, the disappearance time of eyelash and the time from induction to tracheal intubation were the longest in group D, and the difference was statistically significant with the remaining two groups. Compared with group M, the success rate of one-time intubation was high in groups D and R, and the difference was statistically significant, and there was no statistically significant difference between groups D and R (Table 2). Group R achieved the highest comfort scores and the highest sedation success after a single induction. Differences between groups M and D were not statistically significant (Table 3). The highest rate of adverse reactions in group M, one case of hypotension and one case of respiratory depression in group R. The two cases were the same patient, symptoms resolved with supportive treatment (Table 4).

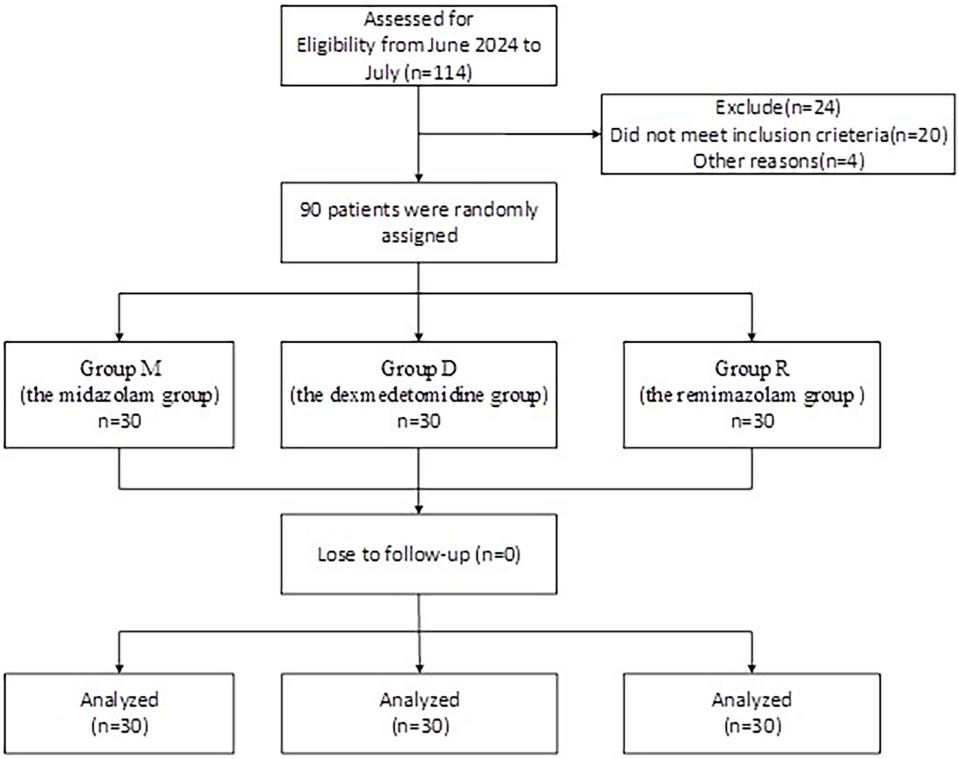


**Figure 2** Patient flowchart with CONSORT guidelines.

## Discussion

A difficult airway is defined as difficulty with ventilation or intubation despite the presence of an experienced anesthesiologist. Unexpected difficult airways can lead to severe hypoxia, hypercapnia, emergency tracheotomy, brain injury, or even death.[19,20] Currently, patients with an anticipated difficult airway can be intubated with the help of light bars, laryngeal masks, fiberoptic bronchoscopes, visual laryngoscopes, retrograde guidewires, and tracheotomies, and conscious tracheal intubation is chosen as much as possible to preserve voluntary breathing and prevent a predictable difficult airway from becoming an acute airway.[21] Adequate topical anesthesia is critical for successful awake tracheal intubation. In this study, we utilized a novel local anesthetic spray device to optimize this process. Compared with

**Table 1** Changes in MAP, HR, and $SpO_2$ in the 3 Groups of Patients at Each Time Point ($\bar{x} \pm s$, n=30)

| Indicator | Group | $T_0$ | $T_1$ | $T_2$ | $T_3$ |
|---|---|---|---|---|---|
| MAP/ | Group M | 95.3±8.4 | 78.1±7.3[a] | 122.7±9.1[a] | 100.1±9.5[a] |
| (mmHg) | Group D | 93.5±8.8 | 77. 5±7.2[a] | 87.1±8.6[a] | 89.6±8.3 |
| | Group R | 94.8±8.7 | 72.6±6.0[a] | 85.2±7.9[a] | 86.7±7.2 |
| HR/ | Group M | 100.4±12.3 | 83.6±10.5[ab] | 110.0±12.5[ab] | 105±12.6[ab] |
| (beats/min) | Group D | 99.7±8.8 | 59.0±9.4[a] | 79.7±6.5[a] | 74.1±6.0[a] |
| | Group R | 98.4±8.9 | 70.2±8.0ab | 77.4±6.6[a] | 73.2±6.7[a] |
| SpO2 (%) | Group M | 99.4±0.3 | 99.4±0.5 | 97.2±1.7 | 96.1±3.0 |
| | Group D | 99.3±0.4 | 99.4±0.2 | 98.7±1.5 | 95.5±2.6 |
| | Group R | 99.6±0.3 | 99.2±0.1 | 98.4±1.6 | 95.5±2.9 |

**Note**: Group M (midazolam 0.04 mg/kg IV bolus), Group D (dexmedetomidine 1.0 μg/kg/min intravenous pump infusion), and Group R (remimazolam 0.15 mg/kg IV bolus). [a]$P<0.05$ indicates a statistically significant difference compared with $T_0$; [b]$P<0.05$ indicates a statistically significant difference compared with Group D.


https://doi.org/10.2147/DDDT.S564228

**Table 2** Comparison of Induction Time and Intubation Success Rate Among Patients in 3 Groups ($\bar{x} \pm s$, n=30)

| Group | The Induction-to-Intubation Interval (S) | Start of Induction to Intubation Time (S) | One-Time Intubation Success Rate [n(%)] |
|---|---|---|---|
| Group M | 150±38 | 174±45 | 21 (70) |
| Group D | 600±150 | 712±173 | 28 (93.3) |
| Group R | 120±29 | 138±36 | 30 (100) |

**Table 3** Comparison of patient comfort and MOAA/S scores after the first dose in 3 groups ($\overline{x} \pm s$, n=30)

| Group | Level of Comfort | MOAA/S Score After the First Dose |
|---|---|---|
| Group M | 2.56±0.7 | 3.49±1.0 |
| Group D | 2.01±0.5[a] | 2.65±0.8[a] |
| Group R | 1.33±0.3[ab] | 1.2±0.4[ab] |

**Note**: Compared with group M, [a]$P<0.05$, compared with group D, [b]$P<0.05$.

**Table 4** Incidence of Adverse Reactions in Patients in the 3 Groups [n(%)]

| Group | Choking Cough | Body Movement | Hypertension | Hypotension | Bradycardia | Respiratory Depression |
|---|---|---|---|---|---|---|
| Group M | 3 (10) | 5 (16.67) | 6 (20) | 0 (0) | 0 (0) | 0 (0) |
| Group D | 2 (6.67) | 3 (10) | 0 (0) | 0 (0) | 8 (26.67) | 0 (0) |
| Group R | 0 (0) | 1 (3.33) | 0 (3.33) | 1 (3.33) | 0 (0) | 1 (3.33) |

traditional hand-held pressurized sprayers, this new device offers key advantages: it delivers finer, more uniform atomization to expand anesthetic coverage and enhance efficacy, while its controlled low-pressure mechanism significantly reduces pharyngeal irritation—beneficial for maintaining patient tolerance during procedures such as tracheal intubation and gastroscopy. However, alongside adequate topical anesthesia, effective sedation and analgesia remain critical. The core challenge lies in identifying an induction approach that achieves the optimal sedation level required for intubation while avoiding respiratory and circulatory depression.[22] Suboptimal sedation or analgesia—characterized by inadequate muscle relaxation, persistent laryngeal reflexes, increased risk of vocal cord injury, accidental esophageal intubation, or exaggerated stress responses—may exacerbate underlying conditions such as coronary artery disease, asthma, or elevated intracranial pressure, and could even precipitate serious adverse events.[23,24]

Remimazolam is a new benzodiazepine sedative/anesthetic drug, which is an ultra-short-acting sedative-hypnotic drug modified from the structure of midazolam, combining the safety of midazolam with the effectiveness of propofol.[25] Its incidence of hypotension and respiratory depression is significantly lower than that of propofol, and it is especially suitable for hemodynamically unstable patients.[26] This new benzodiazepine is close to the ideal sedation requirements, and it has promising applications in clinical sedation, general anesthesia, ICU sedation, and adjunctive sedation for regional blocks.[27–29]

It has been demonstrated that remimazolam can produce good sedation in painless gastroscopy and treatment.[30,31] A systematic review on pharmacological strategies for sedation concluded that although no single approach demonstrated absolute superiority, remimazolam's rapid onset, fast recovery, and favorable hemodynamic profile suggest distinct advantages.[32] Similarly, randomized trials comparing remimazolam with propofol during gastrointestinal endoscopy revealed that remimazolam significantly reduced the incidence of hypotension and better preserved cardiac output. Furthermore, a controlled study

published in *Drug Design, Development and Therapy* found that in elderly patients, remimazolam provided greater hemodynamic stability with fewer episodes of hypotension and heart rate abnormalities compared with propofol.[33]

In this study, there were 30 cases in the remimazolam group, and all patients were successfully intubated under remimazolam-assisted low-dose sufentanil deep sedation, demonstrating its safety and efficacy in preserving spontaneous breathing for electronically soft microscopic tracheal intubation. In this experiment, the mean arterial pressure of midazolam was significantly higher at $T_2$ and $T_3$ compared with $T_1$, while there was no significant change in the dexmedetomidine and remimazolam groups, indicating that remimazolam can reduce the stress response and effectively maintain relative hemodynamic stability, which is consistent with the findings of Barbosa EC et al[17] on remimazolam in gastrointestinal microscopy. Compared with $T_0$, the heart rate was significantly lower in group D at $T_1$, and there was no significant change in group R, indicating that the effect of remimazolam on the heart rate of patients was not significant. The induction rate of group D was slow, and the time from the beginning of induction to the start of tracheal intubation was long, while the effect of remimazolam was rapid and the patient was comfortable, and the patient whose respiratory depression and blood pressure decreased was the same patient, and respiration slowly recovered after jaw-resting treatment before the decrease in blood oxygen saturation, and blood pressure returned to normal after the administration of ephedrine, which was considered to be related to the patient's light weight, posterior tongue drop or the speed of pushing the drug too fast. The aforementioned factors are merely preliminary speculations derived from clinical observations. Currently, direct pharmacokinetic data—including monitoring results of the patient's remimazolam plasma concentration at the time of the event—and airway imaging evidence are lacking to substantiate these speculations. Therefore, the specific causal relationship underlying this adverse event warrants further verification. Several studies have investigated the application of remimazolam in awake tracheal intubation. Zhou et al[34] reported in a randomized controlled trial that remimazolam combined with remifentanil achieved a high intubation success rate and demonstrated superior safety, which is consistent with our findings of rapid onset and stable cardiopulmonary function. Another retrospective study comparing remimazolam with dexmedetomidine in patients undergoing awake tracheal intubation for scoliosis surgery showed that remimazolam was associated with smaller changes in mean arterial pressure and heart rate, indicating more stable hemodynamic responses.[35] In addition, a systematic review on pharmacological strategies for sedation suggested that, although no single approach demonstrated clear superiority, remimazolam's rapid onset, prompt recovery, and favorable hemodynamic profile confer potential advantages.[36]

## Limitations

This study has certain limitations. The relatively small sample size and single-center design may restrict the generalizability of the findings. In addition, the absence of blinding could have introduced potential bias in assessment. Therefore, larger multicenter randomized controlled trials with extended follow-up are needed to further confirm the efficacy and safety of remimazolam in awake tracheal intubation.

## Conclusion

In patients with difficult airways, remimazolam combined with low-dose sufentanil achieves effective sedation during fiberoptic awake intubation, with minimal impact on respiratory and circulatory function. This combination reduces the incidence of adverse reactions, improves first-attempt intubation success rates, and thus represents a safe and reliable option in clinical practice.

## Abbreviations

MAP, Mean Arterial Pressure; HR, Heart Rate; $SpO_2$, Peripheral capillary oxygen saturation; BMI, body mass index; ASA, American Society of Anesthesiologists.

## Data Sharing Statement

The datasets generated and analyzed in this study are not publicly available due to containing sensitive information protected by data security regulations, but qualified researchers can obtain them by contacting the corresponding author (Dr. Rui Xia) upon stating a legitimate research purpose and signing relevant data usage agreements.

## Ethics Approval and Informed Consent

All patient-related procedures in this study complied with the 1964 Declaration of Helsinki and its subsequent revisions. The study was approved by the Institutional Review Board (IRB) of the First Affiliated Hospital of Yangtze University. Written informed consent was also obtained from each participant or their legally authorized representatives, who fully understood the study's objectives, procedures, risks, and benefits before consenting.

## 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.

## Funding

United Scientific Research Fund Project of Jingzhou City, Hubei Province, China, Grant Number: 2024LHY30.

## Disclosure

The authors declare that there are no conflicts of interest associated with this research.

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