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Original Article

Effect of dexmedetomidine on stress and inflammatory responses in patients with nasotracheal intubation after oral and maxillofacial surgery

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Abstract: Objective: To investigate the effect of dexmedetomidine on stress and inflammatory responses in patients undergoing postoperative nasotracheal intubation after oral and maxillofacial surgery. Methods: We retrospectively analyzed 210 patients who underwent elective radical oral cancer resection at Hubei Province Hospital of Traditional Chinese Medicine between April 2023 and April 2025. Patients were divided into the dexmedetomidine group (n=105) and the control group (n=105). Both groups received general anesthesia with nasotracheal intubation and were admitted to the ICU postoperatively. The control group received intravenous midazolam (loading dose: 0.03-0.3 mg/kg; maintenance dose: 0.04-0.2 mg/(kg·h)), while the dexmedetomidine group received dexmedetomidine (loading dose: 0.6-1 μg/kg over 10 minutes; maintenance dose: 0.04-0.2 μg/(kg·h)). Outcomes included Ramsay Sedation Scores, Behavioral Pain Scale (BPS) scores, hemodynamic parameters (heart rate, mean arterial pressure [MAP]), stress markers (plasma cortisol), inflammatory cytokines (TNF-α, IL-6), and adverse drug reactions (ADRs) at multiple time points: before sedation (T0), 0.5 h (T1), 1 h (T2), 6 h (T3), 12 h (T4) post-sedation, and 10 minutes after extubation (T5). Results: Both groups achieved target Ramsay sedation scores of 2-4. BPS scores significantly decreased post-sedation in both groups (both $P<0.05$), with the dexmedetomidine group showing superior analgesia at T2-T5 (all $P<0.05$). HR and MAP decreased in both groups without significant intergroup differences (both $P>0.05$). Cortisol, TNF-α, and IL-6 levels increased postoperatively (all $P<0.05$) but were significantly lower after extubation in the dexmedetomidine group (all $P<0.05$). The dexmedetomidine group exhibited fewer ADRs (18.1% vs. 24.8%, $P>0.05$) and demonstrated superior suppression of IL-6 and cortisol across subgroups (all $P<0.05$). Conclusion: Dexmedetomidine provides effective sedation and superior analgesia postoperatively, significantly reducing the stress response and inflammation compared to midazolam, with a favorable safety profile for nasotracheal intubation.

Keywords: Dexmedetomidine, oral and maxillofacial surgery, trans-nasal endotracheal tube, stress response, inflammatory reaction

Introduction

In modern oral and maxillofacial surgery, the demand for tumor resection and functional reconstruction has increased, leading to more complex surgeries and higher risks associated with managing the postoperative airway [1]. Given that these surgeries are performed on the head, general anesthesia with endotracheal intubation is often the preferred method for ensuring airway patency [2]. Oral and maxillofacial tumor surgeries involve upper respiratory areas such as the oral cavity, tongue base, mandible, and neck. Postoperative edema in the surgical area, swelling of the reconstructed flap, lymphatic drainage issues, and the head and neck positioning required can increase the risk of upper airway obstruction [3]. With advances in ICU technology, the practice has shifted to retaining the nasotracheal tube postoperatively, which reduces complications associated with tracheostomy and accelerates patient recovery [4, 5]. However, trans-nasal endotracheal tubes (ETTs) can be irritating, causing adverse reactions such as cough, restlessness, increased blood pressure, and heart rate.

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Patients may struggle to tolerate these effects even without clear pain [6, 7]. These irritations not only adversely affect physiological functions but also delay recovery and may lead to serious complications [8]. Thus, the rational use of drugs and effective sedation and analgesia are crucial to mitigate these stress responses and physiological changes, improving patient comfort and outcomes, and reducing postoperative complications [9].

Midazolam and dexmedetomidine are commonly used sedative agents in perioperative and ICU settings, yet their clinical value in patients undergoing postoperative nasotracheal intubation after oral and maxillofacial surgery has not been systematically compared. Midazolam, a classic benzodiazepine, produces sedative, anxiolytic, and amnestic effects by enhancing γ-aminobutyric acid neurotransmission in the central nervous system. Although it is widely used for sedation in intubated patients due to its rapid onset and ease of titration, it lacks intrinsic analgesic properties, requiring combination with opioids (e.g., sufentanil) for adequate pain relief. This combination increases the risk of respiratory depression, hypotension, and nausea. Additionally, midazolam's limited ability to suppress postoperative stress responses (e.g., elevated plasma cortisol) and systemic inflammation can delay recovery in patients undergoing major surgeries like oral cancer resection.

In contrast, dexmedetomidine, a highly selective α_2-adrenergic receptor agonist, has gained attention for its "sedation with preserved arousal" profile and analgesic effects. It works by binding to α_2 receptors in the locus coeruleus, inhibiting norepinephrine release, reducing central nervous system excitability, and achieving stable sedation without significant respiratory depression. Studies have shown that dexmedetomidine can mitigate stress and inflammatory responses in patients undergoing various surgeries, including orthognathic surgery, dental implantation, and abdominal surgery. For example, a meta-analysis by Zhang et al. found that dexmedetomidine provided superior analgesia and lower delirium incidence compared to midazolam in dental surgery. However, most studies have focused on short-term sedation for minor procedures or non-intubated patients. Data on its efficacy in patients undergoing major surgeries, such as oral cancer resection with prolonged nasotracheal intubation (a high-risk group for airway obstruction and stress), are scarce. Furthermore, few studies have monitored dynamic stress (e.g., cortisol) and inflammatory markers (e.g., TNF-α, IL-6) over multiple time points, including post-extubation, or explored subgroup differences (e.g., elderly patients, ASA III patients, varying intubation durations), which are crucial for guiding individualized sedation in high-risk groups.

This study aims to address these gap. We compare the sedative and analgesic effects of dexmedetomidine and midazolam, focusing on their impact on hemodynamic stability, dynamic stress and inflammatory indicators, and adverse reactions. Additionally, we assess the efficacy and safety of dexmedetomidine across subgroups (age, ASA classification, intubation duration) to provide targeted evidence for sedative drug selection in this clinical setting.

Materials and methods

Retrospective enrollment and data source

This retrospective study enrolled 210 patients who underwent elective radical surgery for oral cancer at Hubei Province Hospital of Traditional Chinese Medicine between April 2023 and April 2025. Data were collected by reviewing medical records, and patients were divided into the control group (n=105) and the dexmedetomidine group (n=105) based on their perioperative medication regimens. Data extraction covered demographic characteristics, surgical details, and medication records, with missing data addressed using standard retrospective imputation methods. The study was approved by the Ethics Committee of Hubei Province Hospital of Traditional Chinese Medicine, and all procedures involving human participants were conducted in accordance with the Declaration of Helsinki (2013 revision).

Inclusion criteria

(1) Undergoing radical surgery for oral cancer, which included resection of the primary tumor, repair of oral and maxillofacial tissue defects via forearm flap, neck lymph node dissection, and small vessel anastomosis; (2) 18 years or older; (3) an ASA classification of I or II; (4)

requiring sedation and analgesia with a nasotracheal tube postoperatively.

Exclusion criteria

(1) Neurological diseases, severe uncontrolled diabetes with complications; (2) severe heart failure or liver and kidney dysfunction; (3) pregnant or lactating women; (4) allergic to the drugs used in this study.

Retrospective reconstruction of perioperative protocols

Anesthesia and analgesia regimens were verified against anesthesia records and nursing notes to ensure accuracy of the retrospective data. Both groups of patients received general anesthesia and nasotracheal intubation during their treatment. As documented in the medical records, anesthesia induction was achieved with intravenous midazolam (0.05 mg/kg), sufentanil (0.5 μg/kg), atracurium cisenesulfonate (2 mg/kg), and propofol (1-2 mg/kg). After successful induction, a spring-loaded catheter (6-7 mm in diameter) was inserted through the nasal cavity for intubation. During the maintenance phase, patients inhaled sevoflurane and received intravenous remifentanil, with intermittent doses of cisatracurium besylate for muscle relaxation. Post-surgery, when spontaneous breathing was restored, both groups retained the trans-nasal endotracheal tube and were admitted to the ICU.

Postoperative sedation and analgesia protocol

All patients received a standardized postoperative analgesic regimen along with the study sedative medication. Analgesia was primarily provided via intravenous sufentanil, starting at 0.1 μg/(kg·h) and titrated by the attending ICU nurse to maintain a Behavioral Pain Scale (BPS) score of ≤5. The control group received intravenous midazolam for sedation (loading dose: 0.03-0.3 mg/kg, maintenance dose: 0.04-0.2 mg/(kg·h)), while the dexmedetomidine group received intravenous dexmedetomidine (loading dose: 0.6-1.0 μg/kg over 10 minutes, maintenance dose: 0.04-0.2 μg/(kg·h)). The infusion rate was adjusted to achieve a target Ramsay sedation scores of 2-4, and sufentanil consumption was recorded for both groups to ensure comparability of analgesic levels.

Outcome indicators

Sedation: In this study, patient sedation status was comprehensively assessed using both the Ramsay Sedation Scale (RSS) and the Sedation-Agitation Scale (SAS). The Ramsay score was recorded at the following time points: before sedation (T0), 0.5 h (T1), 1 h (T2), 6 h (T3), 12 h (T4) post-sedation, and 10 minutes after extubation (T5). The RSS ranges from 1 to 6, where a score of 1 indicates anxiety and restlessness, 2 denotes cooperation and calmness, and scores of 3-5 reflect varying degrees of sedation; a range of 2-4 is considered clinically optimal for adequate sedation. Additionally, the SAS was used to evaluate sedation-agitation status at 24 hours post-extubation. The SAS ranges from 1 to 7: a score of 1 indicates unarousability (no response to any stimulation), 2-3 reflects increasing levels of sedation (response only to strong or light stimulation, respectively), 4 represents a calm and cooperative state (awake, follows simple commands), and scores of 5-7 indicate progressively severe agitation - from mild restlessness to dangerous, combative behavior. Lower SAS scores signify better sedation control and fewer agitation-related complications.

Pain: Pain levels were assessed using the Behavioral Pain Scale (BPS) at the above time points. The total score is ranged from 3 to 12, with a higher score indicating greater pain.

Hemodynamic Indicators: Heart rate (HR) and mean arterial pressure (MAP), systolic blood pressure (SBP) and respiratory rate (RR) were compared between groups at the specified time points.

Oxygenation Indicator: Oxygen saturation (SpO_2, unit: %), an indicator reflecting the oxygenation status of the body, was monitored and compared between the two groups at each time point (T0-T5, as well as T6 [24h post-op] and T7 [48h post-op] for extended observation).

Stress and Inflammatory Indicators: Changes in plasma cortisol, C-reactive Protein (CRP), blood glucose, tumor necrosis factor-α (TNF-α), Interleukin-10 (IL-10), Superoxide Dismutase (SOD), Malondialdehyde (MDA), and interleukin-6 (IL-6) levels were compared before sur-

gery, after surgery, and post-extubation in the ICU.

Neurofunction and Subjective Experience Indicators: Postoperative Delirium: Assessed via the Confusion Assessment Method for the ICU (CAM-ICU) at 24 hours post-extubation; Cognitive Function: Evaluated via the Mini-Mental State Examination (MMSE) at 48 hours post-extubation (total score 30, higher = better cognitive function); Patient Satisfaction: Measured via the Visual Analog Scale (VAS) at discharge (score 0-10, higher = greater satisfaction).

Adverse Drug Reactions (ADRs): The incidence of ADRs was observed and compared between the two groups. Indicator data were extracted from ICU monitoring systems, laboratory test databases, and nursing assessment records, with time points standardized based on documentation timestamps.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics (version 29.0; IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test was used to assess the normality of continuous variables, with normally distributed continuous data presented as mean ± standard deviation (SD), non-normally distributed continuous data as median (interquartile range). Categorical data were presented as counts (percentages). For between-group comparisons, the independent samples t-test was applied to normally distributed continuous variables, the Mann-Whitney U test to non-normally distributed continuous variables, and the Chi-square test or Fisher's exact test (as appropriate) to categorical data. For repeated measures collected at multiple time points (e.g., hemodynamic parameters, biomarker levels), two-way repeated measures analysis of variance (ANOVA) was used to examine group, time, and group-by-time interaction effects. When a significant interaction effect was detected, simple effects analysis with Bonferroni correction was conducted as the post-hoc test to further compare differences between groups at each specific time point and differences within each group across different time points, ensuring the control of Type I error rate caused by multiple comparisons. Spearman's rank correlation coefficient was used to evaluate the relationship between dexmedetomidine concentration and clinical metrics. Pre-specified subgroup analyses were performed based on age, ASA classification, and intubation duration. A two-tailed *P*-value <0.05 was considered statistically significant for all analyses.

Results

Comparison of clinical data

The clinical data of the two groups were compared, showing no statistically significant differences in gender distribution, age, BMI, American Society of Anesthesiologists (ASA) classification, or duration of endotracheal intubation (all P>0.05) (**Table 1**).

Comparison of hemodynamic and oxygenation indices

Temporal changes in hemodynamic and oxygenation indices revealed distinct profiles between the two groups. For systolic blood pressure (SBP), the control group exhibited a sharp increase at T1 followed by a gradual decline, whereas the dexmedetomidine group showed more stable fluctuations, with significant differences (P<0.001) at multiple time points (**Figure 1A**). Heart rate (HR) and mean arterial pressure (MAP) followed similar trends, as the control group maintained higher HR and MAP values compared to the dexmedetomidine group, which displayed more gradual reductions, with consistent statistical significance (P<0.001) across most time points (**Figure 1B**, **1C**). For RR, the control group demonstrated slight fluctuations, while the dexmedetomidine group experienced an initial decline followed by stability, (P<0.001) at several time points (**Figure 1D**). Regarding SpO_2, both groups remained stable during early time points (T0-T3), but the control group exhibited a more pronounced decline in later phases (e.g., T6-T7), whereas the dexmedetomidine group retained higher SpO_2, with significant differences (P<0.001) emerging at later time points (**Figure 1E**).

Comparison of inflammatory, oxidative stress, and hormonal biomarkers

Temporal changes in biomarkers revealed that, compared to the control group, the dexmedetomidine group exhibited distinct profiles. Cortisol (**Figure 2A**) showed lower post-operative concentrations; pro-inflammatory cytokines TNF-α (**Figure 2B**) and IL-6 (**Figure 2C**) exhibited less pronounced increases after surgery; the anti-

Table 1. Comparison of clinical data between the two groups

Clinical data	Control (n=105)	Dexmedetomidine (n=105)	t/χ^2	P
Gender				
Male	42	55	0.388	0.534
Female	63	50		
Age (yd, $\bar{x}\pm s$)	56.4±7.1	58.4±8.1	-1.840	0.075
BMI (kg/m^2, $\bar{x}\pm s$)	24.42±3.52	24.11±3.08	0.445	0.658
ASA classification				
I	23	24	0.332	0.935
II	62	63		
III	20	18		
Endotracheal intubation time (h, $\bar{x}\pm s$)	15.29±5.48	15.90±5.26	-0.830	0.410
Operation time (min, $\bar{x}\pm s$)	58.4±12.3	59.1±11.8	-0.412	0.681
Intraoperative blood loss (ml, $\bar{x}\pm s$)	85.6±21.4	87.2±20.9	-0.476	0.635
Hospital stay (d, $\bar{x}\pm s$)	7.2±1.5	7.3±1.4	-0.512	0.610
History of hypertension [n (%)]	32 (30.5)	34 (32.4)	0.108	0.743
History of diabetes [n (%)]	21 (20.0)	23 (21.9)	0.125	0.723
Preoperative hemoglobin (g/L, $\bar{x}\pm s$)	135.2±12.6	136.5±11.8	-0.763	0.446
Preoperative white blood cell count ($\times10^9$/L, $\bar{x}\pm s$)	6.8±1.5	6.9±1.4	-0.503	0.616
Preoperative platelet count ($\times10^9$/L, $\bar{x}\pm s$)	225±42	228±40	-0.531	0.596
Preoperative ALT (U/L, $\bar{x}\pm s$)	32.5±8.4	33.2±7.9	-0.602	0.548
Preoperative AST (U/L, $\bar{x}\pm s$)	28.6±7.2	29.1±6.8	-0.489	0.625
Preoperative creatinine (μmol/L, $\bar{x}\pm s$)	68.5±10.2	69.2±9.8	-0.501	0.617

Note: BMI, Body Mass Index; ASA, American Society of Anesthesiologists; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; yd, year old.

inflammatory cytokine IL-10 (**Figure 2D**) showed a more marked elevation; the acute-phase reactant CRP (**Figure 2E**) demonstrated a reduced post-operative surge. Oxidative stress markers showed that SOD (**Figure 2F**) declined less and MDA (**Figure 2G**) increased less in the dexmedetomidine group. All these seven indicators showed statistically significant intergroup differences at key postoperative time points (24h Post-op and 48h Post-op, **Figure 2**), with all P<0.001 (analyzed by two-way repeated measures analysis of variance [ANOVA] with simple effects analysis, as specified in the Statistical Analysis section). This indicates that dexmedetomidine modulates the inflammatory response, oxidative stress, and hormonal regulation better than the midazolam group.

Comparison of subjective experience and neurofunctional indicators

Comparison of subjective experience and neurofunctional indicators revealed significant differences between the groups. The SAS score at 24 hours post-extubation was significantly lower in the dexmedetomidine group (t=8.762, P<0.001), indicating better sedation control. Patient satisfaction, measured by the Visual Analogue Scale (VAS) at discharge, was higher in the dexmedetomidine group (t=9.143, P< 0.001). The incidence of postoperative delirium (assessed by CAM-ICU) at 24 hours post-extubation was lower in the dexmedetomidine group (χ^2=4.157, P=0.041); and the Mini-Mental State Examination (MMSE) score at 48 hours post-extubation was significantly higher in the dexmedetomidine group (t=6.725, P< 0.001) (**Table 2**).

Comparison of ADRs

In the control group, hypotension was the most common ADR (11 cases, 10.5%), followed by nausea (9 cases, 8.6%) and bradycardia (6 cases, 5.7%). The total ADR incidence in the

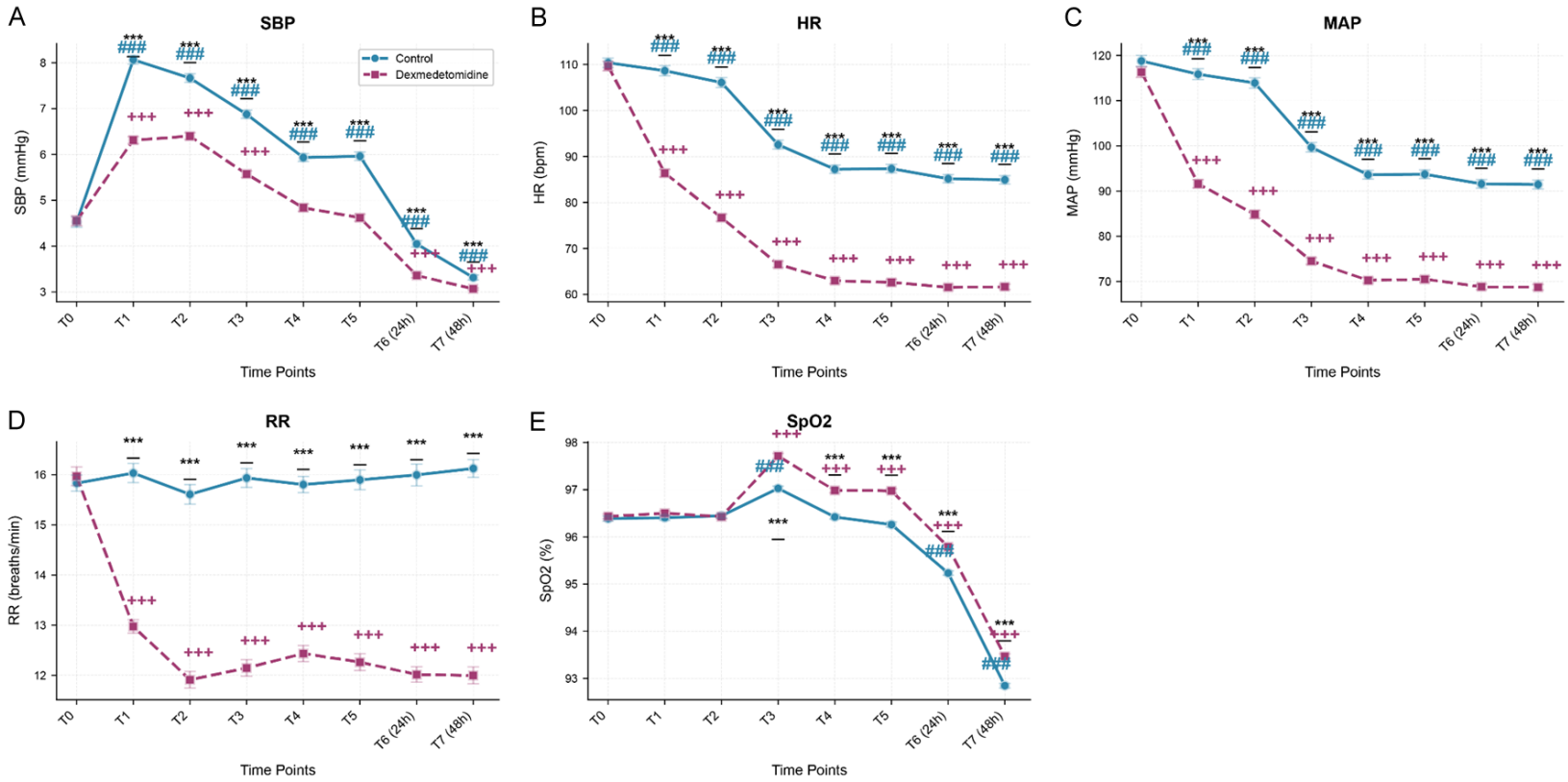

Figure 1. Temporal changes in hemodynamic and oxygenation indices: control vs. dexmedetomidine group. A. Temporal changes in systolic blood pressure (SBP, unit: mmHg); B. Temporal changes in heart rate (HR, unit: beats per minute); C. Temporal changes in mean arterial pressure (MAP, unit: mmHg); D. Temporal changes in respiratory rate (RR, unit: breaths per minute); E. Temporal changes in oxygen saturation (SpO_2, unit: %). Note: SBP, Systolic Blood Pressure; HR, Heart Rate; MAP, Mean Arterial Pressure; RR, Respiratory Rate; SpO_2, Oxygen Saturation. ***P<0.001 (between groups); ###P<0.001 (Control vs. T0); +++P<0.001 (Dex vs. T0).

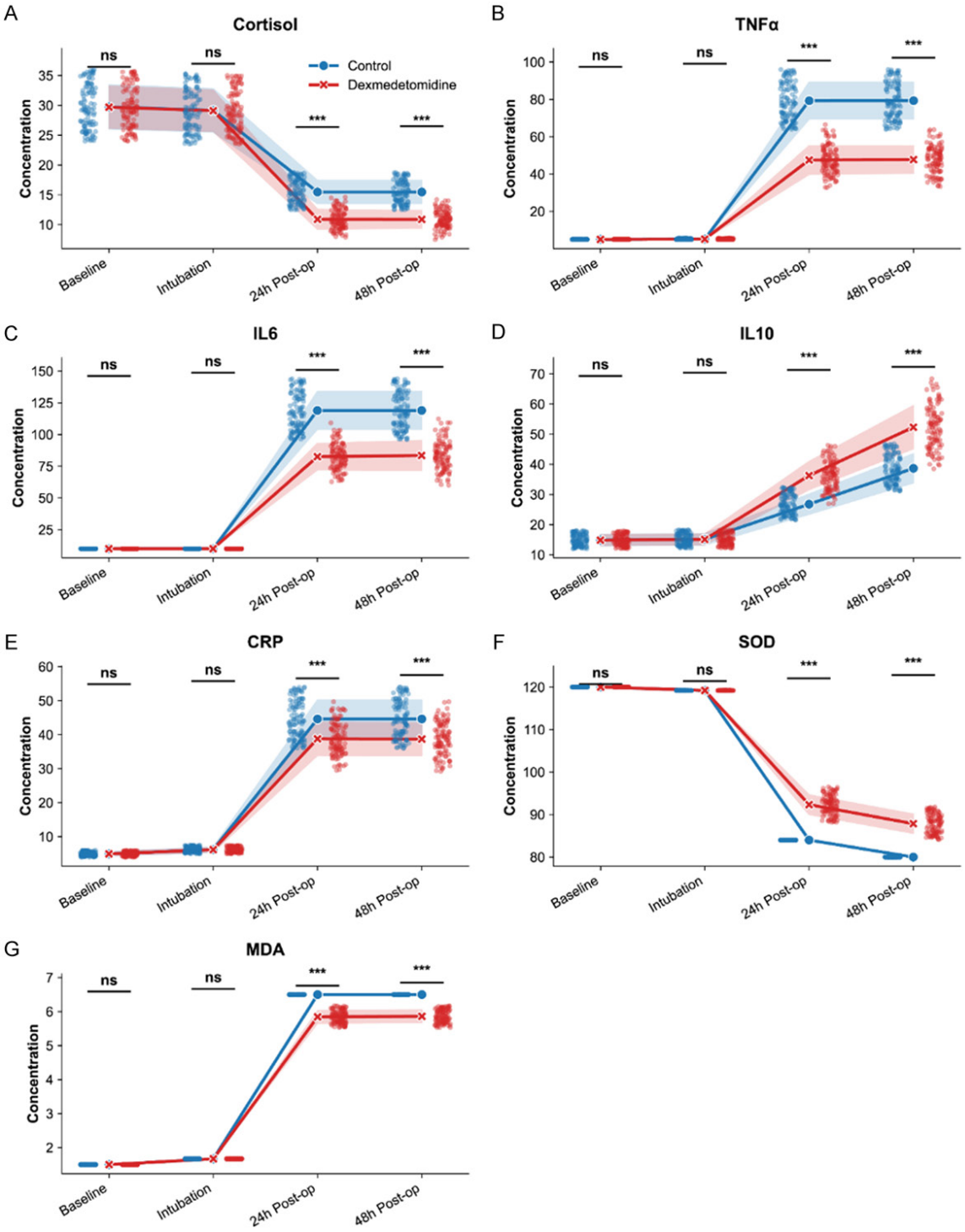

Figure 2. Temporal changes in inflammatory, oxidative stress, and hormonal biomarkers: control vs. dexmedetomidine group. A. Temporal changes in cortisol concentration; B. Temporal changes in tumor necrosis factor-α (TNF-α) concentration; C. Temporal changes in interleukin-6 (IL-6) concentration; D. Temporal changes in interleukin-10 (IL-10) concentration; E. Temporal changes in C-reactive protein (CRP) concentration; F. Temporal changes in superoxide dismutase (SOD) concentration; G. Temporal changes in malondialdehyde (MDA) concentration (*** P<0.001). Note: TNFα, Tumor Necrosis Factor α; IL6, Interleukin 6; IL10, Interleukin 10; CRP, C-reactive Protein; SOD, Superoxide Dismutase; MDA, Malondialdehyde. ***P<0.001, ns: not significant by Welch's t-test.

Table 2. Comparison of subjective experience and neurofunctional indicators between the two groups

Indicator	Time Point	Control (n=105)	Dexmedetomidine (n=105)	t/χ^2	P
Sedation-Agitation Scale (SAS)	24 h after extubation	4.25±1.03	3.12±0.85	8.762	<0.001
Patient Satisfaction VAS (points)	At discharge	6.5±1.5	8.2±1.3	9.143	<0.001
Postoperative Delirium (CAM-ICU)	24 h after extubation (positive rate)	12 (11.4%)	4 (3.8%)	4.157	0.041
MMSE Score (points)	48 h after extubation	25.3±2.8	27.5±2.1	6.725	<0.001

Note: SAS, Sedation-Agitation Scale; VAS, Visual Analog Scale; CAM-ICU, Confusion Assessment Method for the Intensive Care Unit; MMSE, Mini-Mental State Examination.

Table 3. Adverse Drug Reactions (ADRs) comparison

Adverse Reaction	Control (n=105)	Dexmedetomidine (n=105)	*P*-value
Bradycardia	6 (5.7%)	11 (10.5%)	0.312
Dry Mouth	0 (0.0%)	8 (7.6%)	0.007
Hypotension	11 (10.5%)	0 (0.0%)	<0.001
Nausea	9 (8.6%)	0 (0.0%)	0.003
Any ADR	26 (24.8%)	19 (18.1%)	0.313

Note: ADRs, Adverse Drug Reactions.

control group was 24.8% (26 cases). In the dexmedetomidine group (n=105), bradycardia was the primary ADR (11 cases, 10.5%), followed by dry mouth (8 cases, 7.6%). Notably, no cases of hypotension or nausea were reported in the dexmedetomidine group. The total ADR incidence in the dexmedetomidine group was 18.1% (19 cases). Hypotension (P<0.001) and nausea (P=0.003) were more frequent in the control group, while dry mouth was more common in the dexmedetomidine group (P=0.007). No significant difference in bradycardia incidence (P=0.312) or total ADR incidence (P=0.313) was found between the two groups (**Table 3**).

Analysis of spearman correlation: dexmedetomidine vs. key metrics

The heatmap quantifies Spearman correlations between dexmedetomidine concentration and key clinical metrics (BPS, IL-6, MAP) using 840 samples (8 time points per patient). Dexmedetomidine concentration showed perfect self-correlation (1.00, as expected). It exhibited weak-to-moderate positive correlations with BPS (0.35) and IL-6 (0.22), suggesting higher dexmedetomidine levels weakly correlate with increased pain behavior and pro-inflammatory signaling, potentially reflecting complex interactions between sedation, pain perception, and early-phase inflammatory trends. A weak negative correlation (-0.31) with MAP aligns with dexmedetomidine's α_2-adrenergic agonism, which can induce mild hypotension. Cross-metric analyses revealed moderate negative correlations between BPS & IL-6 (-0.59, indicating pain-induced immunosuppression) and IL-6 & MAP (-0.69, consistent with cytokine-mediated vasodilation), plus a weak-to-moderate positive correlation between BPS & MAP (0.39, reflecting pain-driven sympathetic activation). These relationships highlight dexmedetomidine's multifaceted impact on pain, inflammation, and hemodynamics, underscoring the need for context-specific dose optimization in clinical settings (**Figure 3**).

Subgroup analyses of dexmedetomidine on stress (cortisol) and inflammatory (IL-6) responses

Subgroup analyses were conducted to explore the effects of dexmedetomidine on stress and inflammatory responses in patients with nasotracheal intubation after oral and maxillofacial surgery. The analysis focused on cortisol change (for stress) and IL-6 change (for inflammation). In the stress response (cortisol change, represented by blue markers), dexmedetomidine significantly decreased cortisol levels in the subgroup with intubation duration ≤24 hours, as evidenced by a negative mean difference whose 95% confidence interval (CI) did not cross zero. No valid data were available for the subgroup with intubation duration >24 hours. Regarding the inflammatory response (IL-6 change, represented by red markers), dexmedetomidine showed consistent inhibition of IL-6 across all subgroups. In ASA III patients, non-elderly patients (<65 years) and elderly patients (≥65 years), the mean differences in IL-6

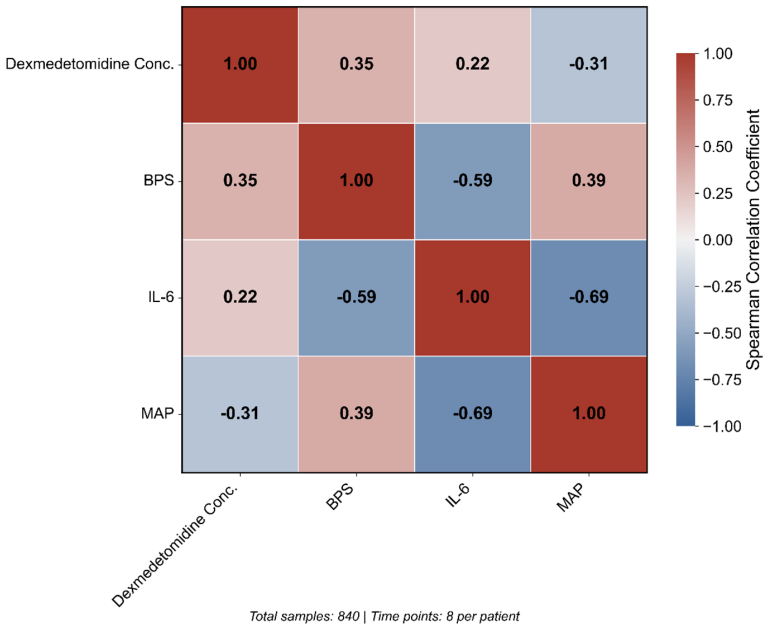

Figure 3. Spearman correlation heatmap: dexmedetomidine concentration and clinical/inflammatory metrics. Note: BPS, Behavioral Pain Scale; IL-6, Interleukin-6; MAP, Mean Arterial Pressure.

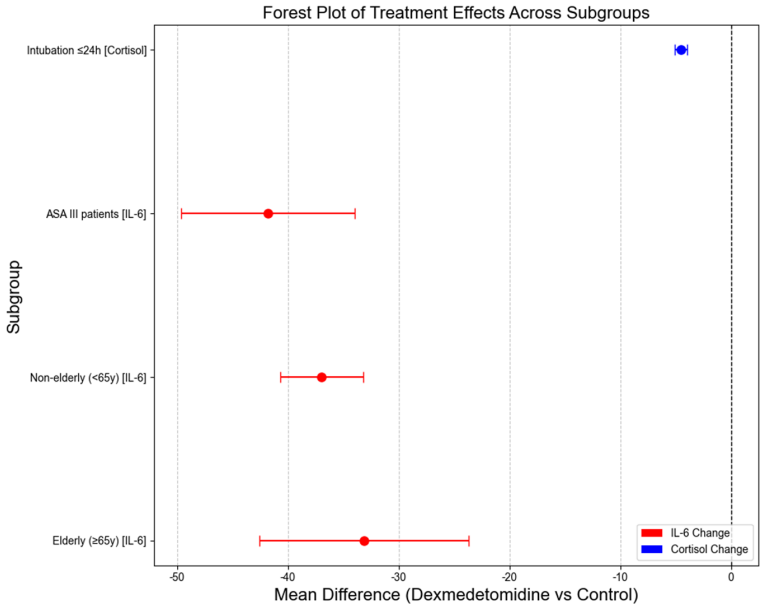

Figure 4. Forest Plot of treatment effects of dexmedetomidine on stress (Cortisol) and inflammatory (IL-6) responses across subgroups in patients with nasotracheal intubation after oral and maxillofacial surgery. Note: ASA, American Society of Anesthesiologists; IL-6, Interleukin-6.

levels between the dexmedetomidine and control groups were all negative, with 95% CIs not overlapping zero, indicating that dexmedetomidine effectively reduced IL-6 levels in these subgroups (**Figure 4**).

Discussion

Most oral and maxillofacial surgeries involve procedures on body surface and bone tissues, which are richly innervated and vascularized, resulting in significant postoperative swelling [10-13]. Due to the risks associated with removing the endotracheal tube immediately after surgery, it is often necessary to retain it until the swelling subsides [14-16]. However, the indwelling endotracheal tube exacerbates patient discomfort, hindering communication and interaction with medical staff, and causing anxiety, restlessness, and even helplessness [17]. This not only negatively impacts physiological functions but also significantly delays recovery and can lead to more severe complications [18]. Therefore, effective sedation is crucial for patients with indwelling tracheal tubes after oral and maxillofacial surgery [19-22]. Proper sedation allows patients to remain calm, increasing their tolerance to endotracheal intubation, which facilitates treatment and monitoring [23].

Studies indicate that pain and discomfort are primary causes of restlessness in patients, making adequate analgesia a priority. Intravenous opioids are considered the first-line option for managing pain [24]. Compared to traditional sedative plans, this therapeutic approach reduces ICU stay and the need for mechanical ventilation [25]. Midazolam, a benzodiazepine, is commonly used in clinical sedation [26, 27]. It enhances γ-aminobutyric acid neurotransmitter function, inhibits the arousal of the mesencephalic network on the cortex, and reduces activity in the limbic system, producing hypnotic, amnestic, and anti-anxiety effects

[28]. Dexmedetomidine, a highly selective α2 adrenergic receptor agonist, acts at the locus coeruleus to inhibit norepinephrine release and reduce central nervous system excitability, providing sedative, hypnotic, and anti-anxiety effects [29].

This study compared the effects of dexmedetomidine and midazolam in sedated patients with trans-nasal endotracheal tubes after oral and maxillofacial surgery. Results showed that after sedation, Ramsay Sedation Scores in both groups were between 2-4 at all time points, with no significant differences between the groups. This suggests that both drugs provide similar sedative effects for patients with trans-nasal ETT. In terms of hemodynamics, heart rate and MAP levels during sedation were lower than pre-sedation levels in both groups, but comparisons at each time point showed no statistically significant differences. This indicates that dexmedetomidine and midazolam have comparable effects on the hemodynamics of ICU patients with trans-nasal ETT, consistent with previous studies [18]. Additionally, the incidence of ADRs was significantly lower in the dexmedetomidine group compared to the control group, which is in line with previous reports [20]. This suggests that while midazolam offers no intrinsic analgesic effect, dexmedetomidine provides mild analgesia. To achieve similar sedative effects, patients in the midazolam group required higher doses of the opioid analgesic sufentanil, which can lead to side effects [30]. Furthermore, midazolam is primarily metabolized by the liver and produces metabolites, which can cause respiratory depression and hypotension [31].

Surgical procedures themselves trigger a classic stress response, activating the peripheral immune system and releasing cytokines and inflammation-related mediators, thereby stimulating the central nervous system's inflammatory response [32-35]. Postoperatively, ICU-related stressors such as mechanical ventilation, movement restriction, noise, and communication barriers can further exacerbate this reaction [36-38]. Studies suggest that effective sedation can help reduce both stress and inflammation in patients [39-42]. The results showed that plasma cortisol, TNF-α, and IL-6 levels in both groups increased significantly after surgery and extubation, compared to pre-surgery levels. These markers were lower after extubation than post-surgery levels, with the dexmedetomidine group exhibiting significantly lower levels than the control group. This suggests that surgery activates the stress and inflammatory responses, and that effective sedation in the ICU can significantly mitigate these reactions. Furthermore, compared to midazolam, dexmedetomidine demonstrated a more pronounced inhibitory effect on these responses. Previous studies have suggested that dexmedetomidine's anti-inflammatory effects may be linked to the down-regulation of NF-κB expression and activation of cholinergic pathways in the anti-inflammatory process [43-46].

This study has several limitations. First, as a retrospective analysis, and is prone to selection bias and unmeasured confounding - patient grouping relied on historical medication records rather than randomization, and factors such as disease severity beyond ASA classification or variations in perioperative care may have influenced outcomes. Second, the cohort was limited to elective oral cancer resection patients at a single center (Hubei Province Hospital of Traditional Chinese Medicine), predominantly ASA I-II classification with intubation durations ≤24 h, limiting generalizability to more critically ill, emergency, or ethnically diverse populations. Third, stress and inflammatory markers were assessed only during the early perioperative period (within 48 h postoperatively), without evaluating longer-term outcomes such as ICU/hospital length of stay or cognitive recovery. Finally, real-time plasma dexmedetomidine concentrations were not monitored; although Spearman correlation analyses were performed, the absence of precise pharmacokinetic data constrains a definitive dose-response assessment.

Future studies should address the current limitations and further elucidate the clinical value of dexmedetomidine in oral and maxillofacial surgery. First, multicenter, large-sample randomized controlled trials are needed to minimize selection bias and enhance external validity by randomly assigning patients to dexmedetomidine or midazolam groups. Second, the study population should be broadened to include more diverse subgroups - such as elderly patients (≥75 years), those with ASA III-IV

status, and individuals undergoing varied procedures (e.g., trauma reconstruction or benign tumor resection) - to assess the drug's efficacy and safety across broader clinical contexts. Third, long-term follow-up (e.g., 1-3 months post-discharge) should be incorporated to evaluate impacts on quality of life, cognitive function, and late complications. Fourth, real-time monitoring of plasma dexmedetomidine concentrations, combined with patient-specific factors (e.g., age, weight, renal function), could enable personalized dosing to optimize sedation and reduce adverse effects. Finally, integrating molecular techniques - such as assessing NF-κB activation or cholinergic pathway-related proteins - may help clarify the anti-inflammatory and stress-modulating mechanisms of dexmedetomidine, strengthening the theoretical foundation for its clinical use.

In conclusion, dexmedetomidine is an effective sedative with a low ADR profile for patients with trans-nasal ETT after oral and maxillofacial surgery. It effectively inhibits the stress response and inflammatory reactions in these patients.

Disclosure of conflict of interest

None.

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