

# Identifying the Risk Factors for Postoperative Sore Throat After Endotracheal Intubation for Oral and Maxillofacial Surgery

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**Objective:** To identify risk factors for postoperative sore throat (POST) after general anesthesia in oral and maxillofacial surgery.

**Material and Methods:** This study is a retrospective cohort design study. We enrolled patients with oral and maxillofacial surgery who underwent endotracheal intubation under general anesthesia in the Stomatology Hospital, Zhejiang University School Of Medicine between April 2020 and April 2021. They were divided into the POST group and the without POST group. The distribution Of various characteristics in the two groups was firstly analyzed. Then, logistic regression analysis was performed to explore the independent predictors for POST occurrence. Following this, logistic regression and random forest models were constructed and their performance was evaluated to predict POST occurrence.

**Results:** A total of 891 participants were enrolled in the study. Female gender and cough during extubation were significantly associated with increased POST occurrence in multivariate analysis (all  $P < 0.05$ ). Stratified logistic regression analysis results showed that the female gender was an independent predictor for POST occurrence in the  $4 \leq \text{age} \leq 14$  and  $14 < \text{age} \leq 60$  groups after adjusting all the covariates, while cough during extubation independently predicted POST in the  $\text{age} > 60$  group after adjusting American Society of Anesthesiologists status and throat and lung disease (all  $P < 0.05$ ). The logistic regression model had a similar effect to the random forest model in predicting POST occurrence. Interestingly, the female gender had a higher important weight compared to the cough during extubation.

**Conclusion:** This research reveals female gender and cough during extubation as potential risk factors for POST occurrence, which may provide guidance for the effective prevention of POST in oral and maxillofacial surgery.

**Keywords:** oral and maxillofacial surgery, postoperative sore throat, female gender, cough during extubation, predictors

## Introduction

In the case of oral and maxillofacial surgery, general anesthesia is commonly used for major surgical procedures and invasive surgical operations.<sup>1</sup> Endotracheal intubation is an essential operation to secure airway patency and reduce gastric reflux and pulmonary aspiration risk.<sup>2</sup> General anesthesia with endotracheal intubation is overall safe but has countless complications, which may affect the general condition of patients and prolong the postoperative hospital stay.<sup>3</sup> The incidence of postoperative complications might be related to surgical procedures and general physical health. People having serious medical conditions such as high blood pressure, smoking and stroke can be aggravating factors for anesthesia.<sup>4</sup> Currently, anesthetic risks have markedly reduced due to the discovery of advanced anesthetic techniques and sophisticated monitoring equipment.<sup>5</sup> However, the incidence of postoperative complications has not changed significantly.<sup>6</sup>

Postoperative sore throat (POST) is a common consequence of general anesthesia after endotracheal intubation with an incidence varying from 15% to 64%.<sup>7,8</sup> The symptoms of POST include pain and discomfort, cough, hoarseness, and laryngitis, which may be the result of inflammation caused by mucosal damage during airway fixation.<sup>9,10</sup> Its etiology is believed to involve mucosal dehydration, trauma from tracheal intubation, and mucosal erosion caused by tracheal tube cuff pressure.<sup>11</sup> Although clinicians often regarded POST as a relatively minor complication in the past, it leads to a prolonged hospital stay, decreased patient satisfaction, and an increased number of medical complaints.<sup>12</sup> Therefore, more and more attention has been paid to the prevention and treatment of POST. A variety of factors have been identified to be associated with POST, such as cuff pressure, surgical sites, operation duration, female gender, and the size of the endotracheal tube used.<sup>13</sup> In addition, multiple attempts at laryngoscopy and younger age were closely correlated with an increased risk of POST.<sup>14,15</sup> However, there is a lack of research on the risk factors predicting POST occurrence in patients undergoing oral and maxillofacial surgery.

This study aims to determine the possible risk factors associated with POST following oral and maxillofacial surgery to reduce POST occurrence, provide patients with more comfortable medical services, and improve patient satisfaction.

## Materials and Methods

### Study Population

Patients with oral and maxillofacial surgery who underwent endotracheal intubation under general anesthesia in the Stomatology Hospital, Zhejiang University School of Medicine between April 2020 and April 2021 were enrolled in the current retrospective research (n=908). Inclusion criteria: age between 4 and 80 years; in the American Society of Anesthesiologists (ASA) I and II physical status; in need of oral and maxillofacial surgery; with preoperative case data and anesthesia record sheet; the patients were evaluated in the postoperative period for the duration of their hospital stay. Exclusion criteria: patients with obstructive respiratory disease (n=3); patients with severe systemic disease (n=2); patients with acute upper respiratory tract infection (n=5); patients with severe drug dependence and mental disorder (n=4); patients with acute pharyngitis (n=3). The study was performed in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Stomatology Hospital, Zhejiang University School of Medicine [No.2021-28(R)]. Written informed consent was waived due to the study's retrospective design. All patients data were anonymized and maintained with confidentiality.

### Data Collection

Data were obtained from patient's hospitalization records, anesthesia records, postoperative follow-up records, and anesthesia quality control report forms. Information was collected on the factors that were thought to have influenced POST. Preoperative evaluation: gender, age, ASA, surgical site, and the presence or absence of throat and lung disease. Intraoperative evaluation: operative duration, catheter fixation types, cough during extubation, nasal intubation, difficult laryngeal exposure, use of non-steroidal analgesics, intubation frequency, cuff pressure, and catheter sliding distance. Postoperative evaluation: the presence or absence of sore throat was recorded during the first 24h after the operation.

### Anesthesia Methods

After entering the operating room, various vital signs of patients were routinely monitored, including heart rate, respiration, non-invasive blood pressure, pulse oxygen saturation, etc. Peripheral venous access was opened. Anesthesia was induced by intravenous injection of propofol 1.5–2.5 mg/kg, fentanyl 2µg/kg, cis-atracurium 0.15mg/kg, remifentanyl 1µg/kg and dexamethasone 0.1mg/kg. All intubations were performed by an anesthesiologist with at least 3 years of experience with a visual laryngoscope (UEScope, Zhejiang UE Medical Corp. China). The size of the blade was chosen based on the patient's size and the anesthesiologist's preference. Disposable PVC endotracheal tubes with high volume low-pressure cuffs were used for intubation. Immediately after intubation, the tracheal tube cuff was inflated with enough room air until no air leakage was audible. The endotracheal tube was fixed with adhesive tape, which could be divided into unilateral fixation and bilateral fixation. Unilateral fixation: the end of the adhesive tape is

located at the same side of the endotracheal tube; Bilateral fixation: the end of the adhesive tape is located on the left and right sides of the endotracheal tube.

Anesthesia was maintained with remifentanyl (0.1–0.2 µg/kg/min), nitrous oxide (40–50%), and sevoflurane (0.8–2%) at a minimum alveolar concentration value of 0.6–1.0, or with propofol (4–6mg/kg/h). Medication dosage was adjusted according to the change in vital signs, and the bispectral index (BIS) value was maintained between 40 and 60. At the end of the operation, anesthesia maintenance drugs were stopped, and cuff pressure was monitored. The endotracheal tube was removed when the patient showed stable vital signs and met the criteria of extubation. The patients were returned to the ward after complete resuscitation.

## Statistical Analysis

Statistical analysis was performed by SPSS software (version 23.0). Categorical variables were expressed as counts (percentages) and were analyzed by the chi-square test. The Kolmogorov–Smirnov test was used to check the distribution normality. Normally distributed continuous variables were expressed as mean ± SD, and non-normally distributed continuous variables were represented as the median and quartile [M (P25, P75)]. The comparisons of continuous variables were made using the Mann–Whitney *U*-test based on the data distribution. Logistic regression analysis was adopted to identify the independent predictors for POST. Then, the independent predictors of POST in different age groups (4≤age≤14; 14<age≤60; age >60) were analyzed after adjusting for relevant covariates such as gender, ASA, throat and lung disease, nasal intubation, and so on by logistic regression analysis. A *P*-value less than 0.05 was considered as statistically significant.

Based on the multivariate logistic regression analysis results, the independent predictors were included for logistic regression model construction. The random forest model was also constructed to compare the performance with the logistic regression model. The dataset was divided into 3 parts, 20% for testing, 70% for training, and 10% for validation. The performance of the model was evaluated using the AUC of ROC, accuracy, sensitivity, specificity, and F1. In addition, the importance of each feature was calculated using sklearn.

## Results

### Population Characteristics

A total of 891 participants (483 males and 408 females) of which 153 cases had postoperative sore throat were finally enrolled in the study. The mean age of patients was 26.019±17.467 years. About 5.882% of cases had a cough during extubation in patients with POST compared with that 2.304% in those without POST with a significant difference (*P* <0.05). There were 87 females in the POST group and 321 females in the without POST group accounting for 56.863% and 43.496, respectively (*P* <0.05). Besides, the significant distribution of surgical sites between those with and without POST was observed (*P* <0.05). However, there were no significant differences in throat and lung disease, nasal intubation, difficult laryngeal exposure, use of non-steroidal analgesics, catheter fixation types, intubation frequency, ASA, cuff pressure, catheter sliding distance, operation duration, and age between two groups (all *P* >0.05) (Table 1).

In detail, the without POST group consists of 417 males (56.5%) and 321 females (43.5%). The POST group included 66 males (43.1%) and 87 females (56.9%). In the without POST group, the distribution of age, ASA, catheter fixation types, use of non-steroidal analgesics, throat and lung disease, nasal intubation, surgical sites, and operation time were significantly different from the male and female groups (all *P* <0.05). However, no significant gender-specific differences were evident for all covariates in the POST group (all *P* >0.05) (Table S1).

### Cough During Extubation and Female Gender Independently Predicted POST

To investigate the risk factors associated with POST, univariate and multivariate logistic regression analyses were performed. Univariate analysis revealed that the cough during extubation and gender were significantly associated with POST (all *P* <0.05). Cough during extubation with an odds ratio (OR) of 2.983 and gender female (OR=1.833) were still independent predictors for POST (all *P* <0.05) (Table 2). These results indicated that a cough during extubation and female gender would increase the risk of POST occurrence.

**Table 1** Characteristics of Patients Without or with POST

Characteristics		Without POST (n=738)	With POST (n=153)	$\chi^2/U$	P
Cough during extubation	No	721 (97.696)	144 (94.118)	4.536	0.033
	Yes	17 (2.304)	9 (5.882)		
Throat and lung disease	No	729 (98.780)	149 (97.386)	0.882	0.348
	Yes	9 (1.220)	4 (2.614)		
Nasal intubation	No	562 (76.152)	119 (77.778)	0.186	0.666
	Yes	176 (23.848)	34 (22.222)		
Difficult laryngeal exposure	No	734 (99.458)	152 (99.346)	0.028	0.866
	Yes	4 (0.542)	1 (0.654)		
Use of non-steroidal analgesics	No	382 (51.762)	86 (56.209)	1.005	0.316
	Yes	356 (48.238)	67 (43.791)		
Catheter fixation types	Unilateral	514 (69.648)	110 (71.895)	0.305	0.581
	Bilateral	224 (30.352)	43 (28.105)		
Surgical sites	1	344 (46.612)	54 (35.294)	15.316	0.018
	2	183 (24.797)	47 (30.719)		
	3	133 (18.022)	32 (20.915)		
	4	30 (4.065)	13 (8.497)		
	5	12 (1.626)	4 (2.614)		
	6	29 (3.930)	3 (1.961)		
	7	7 (0.949)	0 (0.000)		
Intubation frequency	1	730 (98.9)	150 (98.0)	0.242	0.623
	2	8 (1.1)	3 (2.0)		
ASA	I	672 (91.057)	135 (88.235)	1.182	0.277
	II	66 (8.943)	18 (11.765)		
Gender	Male	417 (56.504)	66 (43.137)	9.122	0.003
	Female	321 (43.496)	87 (56.863)		
Cuff pressure (cm H <sub>2</sub> O)		35.000 [30.000, 43.000]	36.000 [30.000, 44.000]	-0.513	0.604
Catheter sliding distance (cm)		0.000 [0.000, 0.000]	0.000 [0.000, 0.000]	0.031	0.966
Operation duration (h)		1.000 [0.500, 1.500]	1.000 [0.500, 1.500]	0.606	0.525
Age		23.000 [10.000, 36.000]	24.000 [12.000, 39.000]	-1.554	0.12

**Notes:** Surgical sites: 1, maxillary-related surgery; 2, mandibular-related surgery; 3, maxillary-related surgery combined with mandibular-related surgery; 4, sublingual gland, lingual frenulum, and submandibular gland surgery; 5, tongue and cheek surgery; 6, surgery on external oral tissues such as parotid gland, condyle, zygomatic arch (extraoral incision); 7, malignant tumor and neck dissection.

**Abbreviation:** POST, postoperative sore throat.

Further, we evaluated the value of cough during extubation and gender in predicting POST occurrence in different age groups. In the  $4 \leq \text{age} \leq 14$  and  $14 < \text{age} \leq 60$  groups, the female gender was associated with an increased risk of POST occurrence ( $P < 0.05$ ). After adjusting ASA and throat and lung disease, the gender female was still significantly related to POST ( $P < 0.05$ ). After adjusting all the other covariates, the female gender could also independently predict POST occurrence ( $P < 0.05$ ). However, cough during extubation was an independent risk factor for POST after adjusting ASA and throat and lung disease ( $P < 0.05$ ), while was not significantly linked to POST occurrence after adjusting all the other covariates ( $P > 0.05$ ) (Table 3). The above findings suggested that cough during extubation and female gender might play an essential role in predicting POST occurrence.

## Model Construction and Evaluation

Subsequently, cough during extubation and gender were enrolled for the logistic regression model and random forest model for comparison. The results showed that the random forest presented a slightly stronger effect on predicting POST occurrence than the logistic regression model in terms of AUC. The AUCs for the random forest model and logistic regression model were 0.627 and 0.625, respectively (Figure 1A). The random forest model had an accuracy of 0.832,

**Table 2** Association of POST Occurrence with Various Covariates Using Logistic Regression Analysis

Covariates	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	P	OR (95% CI)	P
Throat and lung disease (yes vs no)	2.174 (0.661–7.154)	0.201	1.779 (0.469–6.757)	0.397
Nasal intubation (yes vs no)	0.912 (0.601–1.384)	0.666	0.969 (0.579–1.623)	0.906
Difficult laryngeal exposure (yes vs no)	1.207 (0.134–10.876)	0.867	0.996 (0.102–9.729)	0.997
Use of non-steroidal analgesics (yes vs no)	0.836 (0.589–1.187)	0.316	0.74 (0.475–1.154)	0.184
Cuff pressure (cm H <sub>2</sub> O)	1.004 (0.990–1.018)	0.593	1.006 (0.992–1.020)	0.392
Catheter sliding distance (cm)	1.007 (0.773–1.311)	0.961	1.008 (0.767–1.323)	0.957
Catheter fixation types (bilateral vs unilateral)	0.897 (0.610–1.319)	0.581	0.893 (0.579–1.378)	0.61
Operation duration (h)	0.897 (0.738–1.089)	0.271	0.842 (0.660–1.074)	0.165
Surgical sites	1.076 (0.949–1.220)	0.254	1.113 (0.960–1.074)	0.842
Intubation frequency	1.825 (0.479–6.959)	0.378	1.514 (0.363–6.315)	0.569
Cough during extubation (yes vs no)	2.651 (1.159–6.064)	0.021	2.983 (1.223–7.277)	0.016
Gender (Female vs male)	1.712 (1.205–2.434)	0.003	1.833 (1.260–2.667)	0.002
Age	1.006 (0.996–1.016)	0.242	1.005 (0.991–1.018)	0.514
ASA (II vs I)	1.358 (0.781–2.360)	0.279	1.286 (0.635–2.603)	0.485

**Abbreviations:** POST, postoperative sore throat; OR, odds ratio; 95% CI, 95% confidence interval.

**Table 3** The Value of Cough During Extubation and Gender in Predicting POST Occurrence Stratified by Age

Covariates	Model 1	P	Model 2	P	Model 3	P
	OR (95% CI)		OR (95% CI)		HR (95% CI)	
<b>4≤Age≤14</b>						
Cough during extubation	4.549 (0.722–28.659)	0.107	4.651 (0.736–29.380)	0.102	6.001 (0.785–45.874)	0.084
Gender (Female vs male)	1.944 (1.035–3.652)	0.039	1.999 (1.057–3.778)	0.033	2.086 (1.066–4.084)	0.032
<b>14&lt;Age≤60</b>						
Cough during extubation	1.802 (0.558–5.817)	0.325	1.736 (0.527–5.717)	0.365	2.137 (0.612–7.464)	0.234
Gender (Female vs male)	1.725 (1.096–2.714)	0.018	1.935 (1.201–3.118)	0.007	1.842 (1.126–3.014)	0.015
<b>Age &gt;60</b>						
Cough during extubation	14.231 (1.561–129.755)	0.019	14.024 (1.464–134.319)	0.022	191.304 (0.420–87164.932)	0.093
Gender (Female vs male)	0.439 (0.071–2.701)	0.374	0.438 (0.070–2.736)	0.377	0.449 (0.012–17.331)	0.667

**Notes:** Model 1: Cough during extubation and gender; Model 2: after adjusting ASA and throat and lung disease; Model 3: after adjusting all other covariates including throat and lung disease, nasal intubation, difficult laryngeal exposure, use of non-steroidal analgesics, cuff pressure (cm H<sub>2</sub>O), catheter sliding distance (cm), catheter fixation types, operation duration (h), surgical sites, intubation frequency, cough during extubation, gender, age, and ASA.

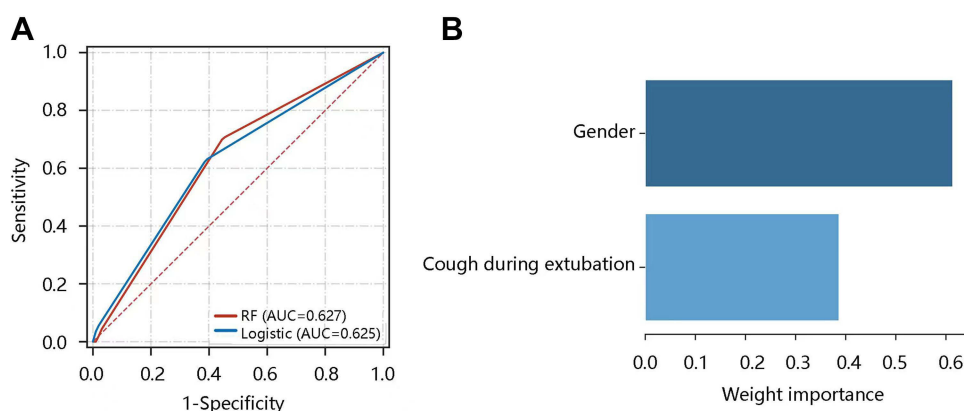
**Abbreviations:** POST, postoperative sore throat; OR, odds ratio; 95% CI, 95% confidence interval.

a sensitivity of 0.704, a specificity of 0.553, and an F1 of 0.311. The logistic regression model showed an accuracy of 0.799, a sensitivity of 0.629, a specificity of 0.611, and an F1 of 0.489 (Table 4).

Further, we identified the variable that had a higher contribution to the model predictive power by sklearn. The importance weights were obtained for each variable. As shown in Figure 1B, gender had a higher importance weight than cough during extubation. These results revealed that the model containing gender and cough during extubation had a certain performance in predicting POST occurrence. Of note, gender exhibited a superior ability to cough during extubation.

## Discussion

POST is a well-recognized complication after general anesthesia with endotracheal intubation.<sup>16</sup> While it is generally considered as a minor side effect, POST is a leading undesirable postoperative outcome and negatively affects patient satisfaction and recovery.<sup>17</sup> POST occurrence has been described in the literature in the context of various surgeries such as nasal surgery, lumbar or thoracic spine surgery, orthopedic lower extremity surgery, and total hip arthroplasty.<sup>18–22</sup>



**Figure 1** Random forest model and logistic regression model evaluation. **(A)** The receiver operating characteristic curves showing the random forest model had a slightly stronger effect in predicting postoperative sore throat (POST) occurrence. **(B)** Bar graph diagram showing the relative importance of predictors for POST.

**Abbreviations:** RF, random forest; AUC, area under the curve.

However, there is a lack of research on the targeting factors related to POST in patients undergoing oral and maxillofacial surgeries with general anesthesia. Our study revealed female gender and cough during extubation as the independent predictors for POST occurrence in oral and maxillofacial surgery after general anesthesia.

In this study, POST occurred in 17.2% (153/891) of patients who underwent oral and maxillofacial surgeries under general anesthesia. A variety of factors have been identified to be associated with POST incidence. Hohlrieder et al reported that the use of a 7.5–8 mm endotracheal tube for men and 6.5–7 mm for women contributed to lower POST rates compared with larger sizes of the endotracheal tube.<sup>23</sup> Besides, limiting cuff pressures might reduce POST occurrence.<sup>24</sup> Decreased blood flow to the tracheal mucosa might cause ischemic damage ranging from minor irritation to tracheal stenosis when the cuff pressure is above 30 cm H<sub>2</sub>O.<sup>25,26</sup> However, Phillip et al<sup>14</sup> observed no significant correlation between cuff pressure and POST, which was similar to the result of our study. This indicated that POST is more likely to occur when several factors overlap. Interestingly, previous studies have well documented the presence of racial differences in the POST incidence. There is a study in Iran showed that POST occurred in 13.7% of all patients who received general anesthesia,<sup>27</sup> while another study in the UK showed the incidence to be 63.9%.<sup>28</sup> We found that there were significant distributions of cough during extubation, surgical sites, and gender in patients with/without POST. Logistic regression analysis results showed that cough during extubation and female gender could independently predict the POST occurrence. Of note, the female gender was an independent predictor for POST occurrence after adjusting all covariates in patients at 4≤age≤14 and 14<age≤60 groups. In those at age >60 years, cough during extubation was notably related to POST occurrence after adjusting ASA and throat and lung disease. By integrating the two independent predictors into model construction, we found that the model exhibited certain performance in predicting POST occurrence.

POST is thought to be caused by chronic inflammatory stimulation of the airway (device factors), leading to abrasion of the airway mucosa and the release of neurotransmitters.<sup>29</sup> When men and women were exposed to the same pain stimulus, women assessed the level of pain more strongly.<sup>30</sup> Additionally, women tended to have a lower pain tolerance threshold than men, suggesting that female gender was a factor influencing POST recognizing and expressing POST.<sup>31</sup> Of note, anxiety and psychological stress would increase pain.<sup>32</sup> Therefore, the authors speculated that preoperative emotional intervention for women might help reduce or alleviate POST occurrence. Dryness in the mouth and throat

**Table 4** Machine Learning Algorithms and Accuracy in Predicting POST

Model	AUC	Accuracy	Sensitivity	Specificity	FI
Random forest	0.627	0.832	0.704	0.553	0.311
Logistic regression	0.625	0.799	0.629	0.611	0.489



was more common in females compared to males, which might be an explanation for the female gender with higher POST incidence.<sup>33</sup> Moreover, polymorphonuclear cells (PMNs) can be recruited to an inflammatory site by locally secreted pro-inflammatory cytokines during endotracheal intubation. These cytokines including IL-1 $\beta$ , TNF, and IL-8 may also delay PMN apoptosis, resulting in the production of more cytokines and chemokines to maintain local inflammation.<sup>34</sup> Hence, it is reasonable to infer that the cough during extubation might lead to the initial stimulus for the inflammation, promoting POST.

Although we failed to obtain NRS scores to analyze the POST severity since participants in our study involved many children who might reflect inaccurate scores, this research explored the potential risk factors for POST and might provide guidance for the effective prevention of POST occurrence in oral and maxillofacial surgery.

In conclusion, female gender and cough during extubation were independent predictors for POST after oral and maxillofacial surgery with general anesthesia. Careful attention should be paid to these two aspects and effective preventive strategies should be taken against POST to improve clinical outcomes and patient satisfaction degree.

## Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding authors upon reasonable request.

## Ethics Approval and Consent to Participate

The study was performed in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Stomatology Hospital, Zhejiang University School of Medicine. Written informed consent was waived due to the study's retrospective design. All patients data were anonymized and maintained with confidentiality.

## Disclosure

The authors report no conflicts of interest in this work.

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