REVIEW

## Postoperative Sore Throat After Tracheal Intubation: An Updated Narrative Review and Call for Action

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**Background:** Postoperative sore throat (POST) represents a common airway complication closely related to endotracheal tube (ETT), exhibiting a higher incidence following tracheal intubation compared to other airway apparatuses. Nevertheless, considering its mild and self-limiting character, POST is often overlooked. This study provides an updated narrative review on the latest perspectives regarding POST, including a comprehensive summary of its mechanisms, risk factors, clinical assessment methods, prevention and treatment strategies. Additionally, directions for future research are proposed.

**Methods:** A comprehensive search was conducted using keywords such as "postoperative sore throat" and "tracheal intubation" in PubMed, Web of Science, and Cochrane databases from their inception to October 2024. Two groups of reviewers independently performed data search and cleaning after standard training. To address gaps in knowledge or potential biases, the literature was thoroughly screened based on established criteria, and a comprehensive synthesis, analysis, and summary of the relevant findings was conducted.

**Results:** The precise cause of POST remains unknown, and its potential mechanism is believed to involve secondary inflammation triggered by irritation, mechanical trauma, tracheal intubation, and cuff inflation. The risk factors for POST encompass preoperative, intraoperative, and postoperative factors. Currently, effective prevention methods for POST consist of pharmacological interventions, non-pharmacological interventions, and traditional Chinese medicine (TCM) therapy. In terms of pharmacological interventions, non-steroidal anti-inflammatory drugs (NSAIDs) and steroid can effectively prevent the occurrence of POST through their anti-inflammatory properties. However, given the unavoidable side effects of medications, non-pharmacological interventions and non-invasive methods may offer greater benefits for POST and related hoarseness. For example, proficient and gentle intubation techniques can prevent mechanical injury caused by repeated intubation attempts. Currently, several studies have demonstrated the potential role of TCM in managing POST. Nonetheless, the precise mechanisms underlying its effects remain to be elucidated, and the available clinical evidence is still limited.

**Conclusion:** Given that POST is prevalent following tracheal intubation but frequently overlooked, we advocate heightened awareness of its occurrence and progression, and recommend integrating the prevention and management of POST into routine clinical practice.

Keywords: postoperative sore throat, tracheal intubation, risk factor, prevention

Published: 6 May 2025

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## Introduction

Postoperative sore throat (POST) pertains to the throat pain or discomfort endured by patients after surgical operations carried out under general anesthesia (GA) or local anesthesia involving oral tracheal intubation or oropharyngeal airway.<sup>1,2</sup> POST is a common postoperative complication that frequently emerges following extubation of endotracheal tube (ETT) in patients undergoing GA.<sup>2,3</sup> Current research has demonstrated that the incidence of POST following GA varies from 12.1% to 70%.<sup>1,4</sup> Notably, POST may occur in more severe forms in patients undergoing head or neck surgery or when placed in the prone position.<sup>1,4,5</sup> The condition encompasses diverse disorders that occur in the early postoperative stage, such as pharyngitis, laryngitis, tracheitis, cough, hoarseness, and dysphagia.<sup>2</sup> Previous clinical studies have primarily defined POST and hoarseness as endpoints.<sup>6</sup> Patients frequently report POST following tracheal intubation, which may be accompanied by hoarseness.<sup>7–10</sup> The incidence of these two complications is particularly elevated in cases involving prolonged surgical duration or improper intubation techniques. POST can prolong patients' hospital stays, delay postoperative recovery, and potentially increase associated medical expenses.<sup>11,12</sup> Consequently, POST has emerged as a critical perioperative concern that anesthesiologists must address.

In most cases, POST can heal by itself and is often overlooked in clinical practice.<sup>13,14</sup> However, POST can cause a tonic spasm of the pharyngeal muscles. In severe cases, aspiration pneumonia may occur, significantly affecting the recovery of patients after anesthesia and the satisfaction of hospitalized patients.<sup>15–17</sup> This is particularly evident after tracheal intubation, especially double-lumen tracheal intubation.<sup>18,19</sup> Previous studies have demonstrated a significantly higher prevalence of POST following outpatient surgery with ETTs compared to patients with laryngeal masks (45.4% vs 17.5%).<sup>4</sup>

Mechanical injury, inflammatory responses, and procedural factors during tracheal intubation are associated with the occurrence of POST, but the precise molecular biological mechanisms remain incompletely understood.<sup>2,12</sup> For example, the detailed cascade of inflammatory mediators involved in the progression of POST remains obscure. At present, numerous prevention and treatment approaches have been proposed to minimize POST (Figure 1 and <u>Supplement Table 1</u>). However, their efficacy and safety are still controversial. Owing to demographic variations among previous studies, such as differences in gender, age, and comorbidities, as well as inconsistencies in the details of preventive strategies—particularly the timing of drug administration—controversial results have been reported.<sup>1,20</sup> This heterogeneity presents significant challenges in interpreting the clinical endpoints for preventing POST.

Considering the high incidence of POST after tracheal intubation, this review focuses on the occurrence mechanism of POST, the evaluation of POST, the risk factors, the current prevention and treatment methods, and future research trends. Given that POST has a high prevalence following endotracheal intubation and is frequently overlooked, this



Figure I Significant findings in prevention and treatment approaches for POST after tracheal intubation.

Note: Green indicates pharmacological interventions, and blue indicates non-pharmacological interventions.

Abbreviations: POST, Postoperative sore throat; PAS, Capsicum plaster applied at the Korean hand acupuncture point; HFJV, High-frequency jet ventilation; GVL, Glidescope video laryngoscopy; ETT, Endotracheal tube; AWS, AirWay scope; EZB, EZ-Blocker; RLGL, Light-guided laryngoscopy; PVC, Polyvinylchloride; BIS, Budesonide inhalation suspension; SLNB, Superior laryngeal nerve block; TTI, Tracheal-tube introducer; SGB, Stellate ganglion block; VDLT, Viva-sight double-lumen tube.

review emphasizes the importance of preventive measures and treatment of POST after tracheal intubation to improve medical care and promote enhanced recovery after surgery (ERAS).

## Methodology

To ensure the inclusion of all potentially relevant articles, POST following tracheal intubation was discussed by reviewing published literature from PUBMED, Web of Science, and Cochrane. The keywords included "postoperative sore throat" and "tracheal intubation". Two groups of reviewers independently performed data search and cleaning after standard training. The articles that met the following criteria were included: (1) the studies were written in English; (2) the studies focused on POST after tracheal intubation; and (3) the document type was original article, meta-analysis, or literature review.

### Anatomical and Physiological Aspects of the Larynx and Pharynx

The larynx and pharynx are critical components of the respiratory system, with their structural and functional characteristics significantly influencing POST following tracheal intubation. The larynx is composed of several cartilages. The vocal cords, situated within the larynx, serve as the primary structures for sound production.<sup>21</sup> In addition, the mucous membrane lining the larynx is richly vascularized and innervated, rendering it susceptible to irritation. The pharynx is anatomically divided into the nasopharynx, oropharynx, and laryngopharynx, each serving distinct functions in swallowing and respiration.<sup>21,22</sup> The pharyngeal walls comprise muscular layers and smooth muscle that coordinate the mechanics of swallowing while providing a conduit for airflow.<sup>21,22</sup>

During the tracheal intubation process, the mucous membrane and neural structures of the larynx may sustain direct injury, resulting in a localized inflammatory response and subsequent pain. The vocal cords may also receive minor mechanical damage, leading to POST or hoarseness.<sup>23,24</sup> Consequently, the larynx and pharynx are particularly vulnerable to injury and stimulation during intubation due to their anatomical and physiological characteristics, thereby contributing to the occurrence of POST.<sup>12,23</sup>

#### Development and Mechanism of POST After Tracheal Intubation

POST is primarily caused by injury to the supraglottic structures (possibly induced by laryngoscope insertion) and injury to the subglottic structures (possibly caused by tracheal intubation or cuffs).<sup>25,26</sup> At present, the precise cause of POST remains unknown, and its potential mechanism is believed to involve secondary inflammation triggered by irritation, mechanical trauma, tracheal intubation, and cuff inflation.<sup>8,12</sup> The current research findings indicate that the mechanisms of POST after tracheal intubation can be categorized into the following several major aspects.

The primary mechanism underlying POST following tracheal intubation is the stimulation induced by the ETT. During the tracheal intubation process, the insertion of the laryngoscope, such as the Macintosh laryngoscope, can cause mechanical injury to the pharyngeal area (Figure 2).<sup>27–30</sup> The procedure of inserting an ETT can stimulate the glottis and the posterior pharyngeal wall, resulting in mucosal damage.<sup>31–33</sup> Additionally, tracheal extubation procedures may also affect POST, as the extraction force during the removal of the tracheal intubation stylet, the duration of extubation, and coughing during extubation may cause injury.<sup>34–36</sup> Moreover, the occurrence of POST may also be affected by the size, material of the ETT, and the pressure of the tracheal catheter cuff.<sup>37–42</sup>

In addition to tracheal intubation procedures, certain surgical operations can lead to direct injuries to laryngeal tissues, such as mucosal rupture and vascular rupture, thereby triggering inflammatory responses and pain and accelerating the occurrence of POST.<sup>43,44</sup> During thyroid surgery, traction may cause repeated movement of the ETT, resulting in laryngeal edema. During the surgery, the ETT can be compressed, elevating the pressure of the cuff and the probability of inflammation, thereby expediting the occurrence of POST.<sup>45–47</sup>

Some recent studies have reported that drugs associated with GA may contribute to the occurrence of POST. Some anesthetic drugs may, through neurally mediated mechanisms, give rise to excitement and inflammatory responses, resulting in POST. For instance, low concentrations of nitrous oxide can stimulate the laryngeal sensory nerves, increase the pressure of the tracheal intubation cuff, and induce pain and discomfort.<sup>48</sup> In addition, irritation caused by desflurane may result in coughing and POST.<sup>49,50</sup> Fentanyl and other analgesic drugs might enhance the inflammatory response by acting on immune cells and inflammatory mediators.<sup>51</sup>



Figure 2 The process of tracheal intubation.

In summary, the mechanism of POST is complex and involves multiple aspects.<sup>52</sup> POST typically results from a combination of various factors.<sup>52</sup> Hence, targeted treatment and prevention for the relevant mechanisms have been proposed.

## Risks Factors of POST After Tracheal Intubation

Several high-quality meta-analyses and clinical studies have conducted in-depth investigations into the risk factors of POST after tracheal intubation.<sup>1,4,20,23,40,50,53–62</sup> The risk factors were summarized, which can primarily be classified into preoperative, intraoperative, and postoperative factors (Figure 3).





Figure 3 Risk factors of POST after tracheal Intubation. Notes: Created in BioRender. Chen, Z (2024) <u>BioRender.com/w63m753</u>. Abbreviations: POST, Postoperative sore throat. Gender is a major determinant of POST. The incidence of POST following surgery in women is approximately 4%–11% higher compared to that in men. This could be attributed to the physiological characteristics of women. For instance, the laryngeal structure of women is narrower than that of men, thereby making them more vulnerable to the stimulation and injury caused by surgical procedures and tracheal intubation, increasing the occurrence of POST.<sup>63</sup> Moreover, gender may also have an impact on the severity and duration of POST. This observation is highly likely to be correlated with the physiological traits and physiological cycles of women. For example, estrogen levels in women decline during menstruation, which may exacerbate the occurrence and severity of POST. The menstrual cycle of women is accompanied by significant hormonal fluctuations, inducing mood changes and leading to premenstrual syndrome (PMS), influencing the pain tolerance threshold.<sup>64</sup> Furthermore, women react differently to opioid and non-opioid analgesics and typically require higher doses than men.<sup>65,66</sup>

Multiple studies have reported that the duration of anesthesia is also associated with POST, with prolonged anesthesia increasing the incidence of POST. Research has demonstrated that with an anesthesia duration of over 4 hours, cellulose within the tracheal lumen gradually seeps out and triggers a series of adverse reactions, such as submucosal congestion and the release of inflammatory substances, causing extensive damage to the laryngeal and airway epithelium.<sup>53,56,57,67,68</sup>

Among numerous risk factors, the utilization of succinylcholine remains controversial. Considering that succinylcholine can induce significant muscle fasciculation and striated muscle pain, succinylcholine was believed to heighten the risk of POST.<sup>4,69</sup> Nevertheless, the outcomes of several studies remain inconclusive. Other studies reported that under standardized airway management, succinylcholine does not augment the risk of POST.<sup>70,71</sup>

#### Clinical Assessment of POST After Tracheal Intubation

In order to assess the occurrence and severity of POST, a series of scales have been adopted in the existing studies for evaluation (Table 1).

One commonly used scale is the Visual Analog Scale (VAS), which is prevalently acknowledged and employed approach for evaluating pain intensities in patients encountering POST. It offers a distinct and measurable means to assess the severity of POST by enabling individuals to denote their degree of discomfort on a scale spanning from 0 (signifying no sore throat) to 10 (representing the most severe throat discomfort conceivable).<sup>72</sup>

Another important tool is the Numeric Rating Scale (NRS), where patients rate their pain on a numerical scale, typically ranging from 0 (signifying no sore throat) to 10 (representing the utmost severe throat discomfort conceivable).<sup>73</sup> In some studies, the NRS score is categorized into four levels—none, mild, moderate, and severe—to more precisely describe the severity of POST.

Type of Scale	Characteristics
VAS score	0–100 mm visual analog scale: 0 (no pain) to 10 (the worst pain imaginable);
NRS score	0 (signifying no sore throat) to 10 (representing the utmost severe throat discomfort conceivable)
	0 (None): 0;
	I (mild): I–3;
	2 (moderate): 4–6;
	3 (severe): 7–10;
4-grade scale	Grade I (None): absence of throat pain;
	Grade II (Mild): mild discomfort during swallowing;
	Grade III (Moderate): continuous throat pain that deteriorates upon swallowing;
	Grade IV (Severe): denotes intense throat pain that impedes eating and demands rescue medication;
TPS	0 (None): no throat pain;
	I (Mild): less than the common cold;
	2 (Moderate): similar to the common cold;
	3 (Severe): more than the common cold.

Table I Clinical Assessment Scales of POST After Tracheal Intubation

Abbreviations: VAS, Visual Analog Scale; NRS, Numerical Rating Scale; TPS, Throat Pain Scale.

In addition to the VAS score, another commonly utilized rating scale within the domain of POST research is employed to assess the severity of this condition. This alternative scale classifies POST into diverse grades based on the extent of throat pain. Grade I indicates the absence of throat pain, while Grade II suggests mild discomfort during swallowing. Progressing in severity, Grade III represents continuous throat pain that deteriorates upon swallowing, and Grade IV indicates intense throat pain that impedes eating and demands rescue medication.<sup>18,73,74</sup>

In the research of Calabrese et al<sup>8</sup> and Tazeh-Kand et al,<sup>75</sup> a verbal scale, namely the Throat Pain Scale (TPS), was used as a supplement to the VAS scale to evaluate POST. TPS: 0 no throat pain; 1 mild (less than the common cold); 2 moderate (similar to the common cold); and 3 severe (more than the common cold).<sup>8,76,77</sup>

In addition to the assessment methods, the timing and duration of the evaluation hold paramount significance. Given that swallowing movements may enhance the incidence and severity of POST, certain studies have separately evaluated POST in the non-swallowing resting state and the swallowing state, yielding more objective and dependable outcomes.<sup>78</sup> In clinical research, the follow-up and evaluation period of POST is mainly restricted to within 3 days after the surgery.<sup>18,79</sup> POST is more prevalent within 6 hours after the surgery, and its incidence and severity gradually decline as time progresses.<sup>74</sup> Thus, POST should be evaluated at multiple time points after the surgery.

## Non-Pharmacological Prevention and Treatment of POST After Tracheal Intubation Size and Type of ETT

The size and type of ETT can profoundly impact the incidence of POST. In airway management, the appropriate size and type of ETT should be selected, as a smaller ETT can mitigate the occurrence of POST. Specifically, for female patients, a 6.0 mm ETT is generally preferred over a 7.0 mm ETT; for male patients, a 7.0 mm ETT results in a lower POST occurrence compared to an 8.0 mm ETT.<sup>38,39,80–84</sup> For double-lumen tubes (DLT), airway complications such as POST can be mitigated by selecting a DLT in which the inner diameters of the trachea and bronchus measured on the chest CT slice match the outer diameters of the tracheal and bronchial cuffs when inflated.<sup>85</sup> Furthermore, the incidence of POST was significantly lower with the reinforced DLT made of silicone compared to that of the common DLT made of polyvinyl chloride (PVC).<sup>86</sup>

#### Cuff Pressure and Cuff Shape of ETT

A series of studies have been conducted to investigate the effects of cuff pressure on POST. Inflated endotracheal intubation cuffs can mitigate the risk of reflux and aspiration. However, excessive cuff pressure and prolonged hyperventilation may result in ischemic necrosis of the mucosa and elevate the risk of POST.<sup>1,87–89</sup> Ryu et al<sup>90</sup> indicated that maintaining the cuff pressure at approximately 25 cm H<sub>2</sub>O during thyroid surgery could prevent the occurrence of POST. In contrast, Lee et al<sup>55</sup> reported that the cuff pressure should be restricted to 17 cm H<sub>2</sub>O. The discrepancy in results may be attributed to the different populations and surgical procedures. In some surgeries, increased airway pressure and cuff pressure are observed due to surgical procedures and body positions, such as pneumoperitoneum and the Trendelenburg position in gynecological surgeries.<sup>41</sup> Hence, Zhu et al<sup>40</sup> proposed a method for continuous monitoring of the cuff pressure to control the occurrence of POST.

In addition to the cuff pressure of the ETT, the shape of the ETT cuff also influences POST. A prior study demonstrated that tapered cuffs were associated with a lower incidence of POST than traditional cylindrical cuffs and simultaneously reduced the incidence of postoperative hoarseness.<sup>42</sup> During anterior cervical surgery, the tapered cuff mitigates elevated pressure on the tracheal intubation cuff that may result from surgical procedures.<sup>91</sup> Furthermore, when the head and neck are extended during intubation, the pressure exerted by a tapered cuff is significantly lower compared to that of a cylindrical cuff.<sup>92</sup>

#### Two-Handed Jaw Thrust

The two-handed jaw thrust maneuver elevates the epiglottis and the base of the tongue away from the posterior pharyngeal wall and enlarges the laryngeal aperture, thereby effectively reducing the damage during intubation.<sup>32</sup> Several studies have demonstrated that the two-handed jaw thrust can effectively decrease the incidence and severity of POST within 24 hours after surgery in patients with ETT or DLT.<sup>32,33,93</sup> Moreover, the study by Yang et al<sup>93</sup> also indicates that the two-handed jaw thrust is more effective compared to the one-handed jaw thrust.

#### Thermal Softening

Thermal softening, achieved by heating, reduces the hardness of both ETT and DLT, effectively minimizing airway trauma during intubation. This approach was initially applied to DLT by Seo et al<sup>18</sup> in 2016, revealing that DLT thermally softened at 40°C for 10 minutes could lower the incidence of postoperative POST and vocal cord injury. Several subsequent studies indicated that this method was also applicable to ETT and could also alleviate the related POST after DLT intubation in patients with SARS-CoV-2 infection and smokers.<sup>77,94,95</sup> Similar to thermal softening, cold steam and ice cubes can decrease the occurrence of POST during the early postoperative stage; however, further studies are required to confirm these findings.<sup>96</sup>

#### 180° Rotation

The intubation process of DLT is challenging due to requiring a 90° rotation after its tip passes through the vocal cords to achieve a complete position. However, this procedure might increase the risk of glottic injury and raise the incidence of POST. Therefore, Seo et al<sup>97</sup> proposed a method of rotating 180° while passing through the glottis, which can effectively alleviate potential airway injuries. Rotating the DLT by 180° rather than 90° reduces the average intubation angle between DLT and the proximal trachea from an average of  $66.6 \pm 5.9$  to merely  $15.8 \pm 5.9$  degrees, leading to a decreased incidence of POST.<sup>98</sup>

# Pharmacological Prevention and Treatment of POST After Tracheal Intubation $\ensuremath{\mathsf{NSAIDs}}$

The pharmacological attributes of nonsteroidal anti-inflammatory drugs (NSAIDs) include anti-inflammatory and analgesic effects. Previous research has investigated the impacts of several NSAIDs on POST, including benzydamine hydrochloride, flurbiprofen, ketoprofen,<sup>99</sup> and others. Several clinical studies and meta-analyses have demonstrated the effectiveness of benzydamine hydrochloride in preventing POST, and its application has been recommended by a recent international Delphi-based consensus.<sup>11,45,100–104</sup> Benzydamine hydrochloride not only inhibits the synthesis of inflammatory mediators but also exhibits analgesic and local anesthetic effects.<sup>101</sup> Flurbiprofen is equally efficacious in preventing postoperative sore throat, which can be administered subglottically or orally.<sup>7,8</sup> However, the efficacy of diclofenac in POST significantly varies between different routes of administration. Studies have demonstrated that diclofenac patches are more effective than intravenous administration for POST.<sup>105,106</sup>

#### Steroid

A meta-analysis conducted by Zhang et al<sup>107</sup> revealed that corticosteroids may lower the incidence of postoperative POST and hoarseness. Furthermore, another meta-analysis indicated that corticosteroids were superior to lidocaine.<sup>108</sup> Several subsequent clinical studies have confirmed the efficacy of corticosteroids for POST, such as inhaled fluticasone propionate,<sup>75</sup> budesonide spray,<sup>109</sup> betamethasone gel,<sup>110</sup> etc. In addition, the meta-analysis conducted by Zhao et al<sup>111</sup> indicated that dexamethasone can reduce POST one hour after surgery. Both 2 mg/kg and 8 mg intravenous (IV) dexamethasone have shown promising potential in preventing POST.<sup>72,112,113</sup> However, corticosteroids are known to have significant side effects, especially when administered in high doses. Currently, further research is still necessary to ascertain their safety.

#### NMDA Receptor Antagonists

N-methyl-D-aspartic acid (NMDA) receptor antagonists have been extensively studied in recent years due to their favorable analgesic and anesthetic effects. Canbay et al<sup>114</sup> investigated the influence of ketamine gargle (40 mg of ketamine dissolved in 30 mL of normal saline) on POST in 46 patients undergoing tracheal intubation under GA, revealing positive effects in preventing POST due to EET intubation. For DLT intubation, a higher dose of esketamine gargle (50 mg dissolved in 30 mL of normal saline) was found to alleviate POST and hemodynamic fluctuations associated with intubation.<sup>73</sup> However, IV administration of a low dose of ketamine does not prevent EET-related POST.<sup>115</sup> Another NMDA receptor antagonist, magnesium, has also demonstrated considerable potential for the prevention of POST. Several studies have shown that preoperative oral administration of lozenges containing 610 mg magnesium citrate or 250 mg magnesium gargles is effective for POST.<sup>116,117</sup>

#### Local Anesthetics

A growing number of studies have investigated the role of local anesthetics (LA) such as lidocaine in preventing POST. The study conducted by Soltani et al<sup>118</sup> indicates that both inflating the ETT cuff with lidocaine or IV lidocaine can effectively reduce postoperative cough and POST, which is consistent with other studies.<sup>83,119–122</sup> Moreover, lidocaine spray on the laryngeal structure has also shown efficacy in preventing POST.<sup>123,124</sup> Early research findings revealed that lidocaine spray may increase the occurrence of POST rather than prevent it, which may be attributed to the function of the additives in the lidocaine spray rather than lidocaine itself.<sup>125</sup> The application of 5% EMLA (lidocaine-prilocaine) cream on the ETT cuff can equally reduce the incidence and severity of POST, cough, and hoarseness in adults after GA in the early postoperative stage.<sup>76</sup>

#### Ultrasound-Guided Block of the Internal Branch of the Superior Laryngeal Nerve

The superior laryngeal nerve (SLN) is a branch of the vagus nerve, and its internal branch governs the sensation of the larynx above the glottis and the laryngeal mucosa. Ultrasound-guided block of the internal branch of the superior laryngeal nerve (US-guided iSLNB) can be achieved by administering local anesthetics such as lidocaine, ropivacaine, and bupivacaine around the superior laryngeal nerve. This technique provides efficient laryngeal anesthesia for awake endotracheal intubation and pain management. While US-guided iSLNB is classified as a peripheral nerve block (PNB), its efficacy relies on the pharmacological properties of the LA used, representing a pharmacologically driven intervention. Several previous studies have investigated the efficacy of US-guided iSLNB at different timings, such as preoperatively and postoperatively, in reducing ETT-related POST; the results demonstrated that the incidence of POST could be mitigated.<sup>78,126,127</sup> Our previous study found that preoperative US-guided iSLNB, similar to the post-operative US-guided iSLNB, could alleviate DLT-related POST.<sup>74,128</sup> Our other recent study showed that the use of dexmedetomidine combined with ropivacaine for US-guided iSLNB significantly reduced the incidence of POST.<sup>129</sup> Although this approach has been proven effective for POST, this nerve block remains an invasive operation that inevitably causes damage.<sup>130</sup> Anesthesiologists need to carefully weigh the benefits and risks.

#### $\alpha_2$ -Adrenergic Receptor Agonists

Dexmedetomidine is an agonist of the  $\alpha_2$ -adrenergic receptor and is extensively utilized for sedation or adjunctive analgesia in the clinical setting. A meta-analysis conducted by Liu et al<sup>131</sup> revealed that the intravenous injection of dexmedetomidine exerts a positive impact on preventing POST. In contrast to the systemic application of dexmedetomidine, the combination of intratracheal dexmedetomidine and ropivacaine significantly decreases the incidence and severity of POST, reduces the consumption of opioids, and stabilizes hemodynamics.<sup>132</sup> Additionally, combining dexmedetomidine with the lidocaine gargle can effectively lower the VAS score associated with postoperative POST.<sup>133</sup> Conversely, oral administration of clonidine exacerbates POST.<sup>134</sup> Currently, studies on the systemic and local application of clonidine in POST are lacking.

#### Others

In addition to the aforementioned medications, a number of drug studies have recently been conducted to observe their efficacy on POST, including sodium azulene sulfonate gargle,<sup>135</sup> Strepsils® tablets,<sup>136</sup> chewing gum,<sup>137</sup> and so on. Azulene, a chamomile extract, has anti-inflammatory effects, and sodium azulene sulfonate has been used in the treatment of gastritis and pharyngitis.<sup>138</sup> Strepsils® tablets contain a variety of active ingredients, such as bactericidal ingredients and local anesthetics, which have antibacterial and pain-relieving effects and have been found to improve oral inflammatory diseases and oral mucosal damage in several previous studies.<sup>136</sup> Chewing gum can promote saliva secretion by regulating the neurally mediated saliva reflex, and a variety of bioactive substances in saliva have the effect of lubricating and protecting the throat mucosa, which can reduce damage during tracheal intubation.<sup>139</sup>

#### Traditional Chinese Medicine Therapy of POST After Tracheal Intubation Traditional Chinese Medicine

Licorice is a traditional Chinese medicine (TCM) that exhibits functions such as heat-clearing and detoxification, phlegm-eliminating, and cough-relieving. Glycyrrhizic acid, the primary constituent of licorice, exhibits a wide range

of pharmacological properties, such as inhibiting inflammatory mediator release and alleviating pharyngeal edema associated with inflammation.<sup>140</sup> The effect of licorice on POST has been extensively explored in previous studies. The meta-analysis carried out by Singh et al<sup>141</sup> and Kuriyama et al<sup>142</sup> suggested that licorice, similar to steroids and magnesium, is the most efficacious in preventing POST. Compared to rinsing the sugar-water gargle, licorice can halve the incidence rate of POST.<sup>140,143</sup>

#### Acupuncture Point Stimulation

Acupuncture point stimulation is a TCM technique. Some preclinical studies have conducted in-depth research on its mechanism and discovered that it can exert anti-inflammatory properties by activating specific signaling pathways.<sup>144,145</sup> Jau et al<sup>146</sup> conducted a meta-analysis to explore the potential of acupuncture stimulation in preventing POST, indicating that acupuncture stimulation could reduce the incidence of POST and demonstrated favorable safety. Similar outcomes were also found in several clinical investigations.<sup>147,148</sup> Nevertheless, additional studies are required to elucidate the mechanism of acupuncture point stimulation in the prevention of ETT-related POST.

## Innovative Technologies for the Assessment and Monitoring of POST

With advancements in medical technology and artificial intelligence (AI), machine learning (ML) has been employed to predict postoperative complications and inform anesthesia management during the perioperative period. Currently, machine learning can be employed to evaluate postoperative delirium (POD), acute kidney injury (AKI), and other complications.<sup>149,150</sup> Additionally, ML has been developed within the realm of pain management to classify and quantify acute postoperative pain.<sup>151–153</sup> Facial recognition technology may also serve as a tool for assessing pain levels during surgery.<sup>154,155</sup> A prior study demonstrated that, in POST, the neural network (NN) outperformed extreme gradient boosting (XGBoost) and random forest (RF), achieving an area under the curve (AUC) of 0.81.<sup>156</sup> Additionally, the advent of wearable devices facilitates real-time monitoring of postoperative pain intensity, which holds potential applications in POST.<sup>157</sup>

## POST and Hoarseness

Hoarseness is defined as an alteration in voice quality, typically manifested as a rough, low-pitched, or monotone sound.<sup>158,159</sup> This condition is generally associated with vocal cord dysfunction. During intubation, the placement of the endotracheal tube may induce direct mechanical stimulation, compression, or trauma to the vocal cords.<sup>160–162</sup> Furthermore, variations in tracheal pressure, airflow dynamics, and localized inflammatory responses following prolonged intubation can further aggravate vocal cord injury.<sup>160</sup>

Research has demonstrated a significant correlation between POST and hoarseness.<sup>163</sup> The onset of POST is frequently associated with inflammation and edema of the laryngeal tissues, which can disrupt the normal vibration of the vocal cords, resulting in hoarseness.<sup>164</sup> This underscores the potential importance of managing POST to prevent subsequent hoarseness. Consequently, strategies aimed at preventing or managing POST may also prove effective in addressing postoperative hoarseness.<sup>8,72,110</sup>

## Controversies

There is an ongoing debate regarding the efficacy of some interventions in preventing POST. A key factor contributing to this controversy is the heterogeneity of research samples.<sup>1,4,53,165</sup> Different populations, including children, adults, and the elderly, exhibit varying tolerances to ETTs due to differences in their laryngeal physiological and anatomical structures and functions.<sup>166,167</sup> At the baseline characteristics of the patients, pre-existing conditions such as chronic respiratory diseases and prior surgical history can influence the effectiveness of POST prevention, which are often overlooked.<sup>53,129,162</sup> Preoperative psychological factors, including anxiety, depression, and sleep quality, have also been increasingly recognized as significant determinants of clinical outcomes.<sup>129,168,169</sup> Moreover, variations in control group settings across studies, such as the use of blank controls versus alternative interventions, may complicate the interpretation of results. Considering that most significant POST studies have been single-center trials with varying conditions, future multi-center studies with larger sample sizes are required to validate the efficacy of these interventions.

## Potential Conflict of Interest Bias

In this review, we systematically analyzed the funding sources of the included studies and found that the majority were predominantly supported by intramural departmental sources, such as hospitals, with only a minority receiving funding from government or non-profit organizations (Table 2). Additionally, in some studies, researchers reported that specific new equipment, such as ETT, was funded by companies.<sup>170,171</sup> Despite these findings, none of the articles explicitly disclosed potential conflicts of interest that might influence study outcomes.

Given that the involvement of pharmaceutical companies in sponsoring trials or reviews may raise concerns about bias in result reporting, particularly in systematic reviews and meta-analyses where the inclusion or exclusion of certain studies can affect overall conclusions, we observed that only a limited number of systematic reviews and meta-analyses received funding from intramural departmental sources or the government.<sup>175,189</sup>

## Future Research Trends

Currently, several preventive measures have been developed to reduce POST (Table 3). Undoubtedly, considering the side effects of drugs, non-pharmacological treatments offer superior prospects and safety. A previous meta-analysis revealed that providing non-pharmacological treatment prior to intubation was the most effective in reducing POST.<sup>190</sup> Based on the relevant literature, several issues have been identified that urgently require attention.

Title	Research Type	Funding	Potential Conflicts of Interest	Intervening Measure	Positive or Negative Results*	Reference
Controlled comparison between betamethasone gel and lidocaine jelly applied over tracheal tube to reduce postoperative sore throat, cough, and hoarseness of voice	RCT	Intramural departmental sources	None	Betamethasone gel	Positive	[110]
Prophylactic dexamethasone decreases the incidence of sore throat and hoarseness after tracheal extubation with a double- lumen endobronchial tube	RCT	Intramural departmental sources	None	Dexamethasone	Positive	[72]
Laryngeal injuries and intubating conditions with or without muscular relaxation: an equivalence study	Equivalence study	Intramural departmental sources	None	Cisatracurium	Negative	[172]
Propofol causes less postoperative pharyngeal morbidity than thiopental after the use of a laryngeal mask airway	RCT	VGHKS95-055 and The CY Foundation for Advancement of Education, Sciences and Medicine	None	Propofol	Positive	[173]
Randomised comparison of Pentax AirwayScope and Glidescope for tracheal intubation in patients with normal airway anatomy	RCT	Intramural departmental sources	None	Pentax airway scope	Positive	[174]
Lidocaine for preventing postoperative sore throat	Meta	Intramural departmental sources	None	Lidocaine	Positive	[175]
Effect on postoperative sore throat of spraying the endotracheal tube cuff with benzydamine hydrochloride, 10% lidocaine, and 2% lidocaine	RCT	Intramural departmental sources	None	Benzydamine hydrochloride	Positive	[102]

Table 2 Funding Sources and Related Information for Included Studies with Conflicts of Interest

(Continued)

#### Table 2 (Continued).

Title	Research Type	Funding	Potential Conflicts of Interest	Intervening Measure	Positive or Negative Results*	Reference
Strepsils® tablets reduce sore throat and hoarseness after tracheal intubation	RCT	Intramural departmental sources	None	Strepsils® tablets	Positive	[136]
Endotracheal tube size and sore throat following surgery: a randomized-controlled study	RCT	The Centre for Health Care Sciences	None	Endotracheal tube size	Positive	[82]
GlideScope video laryngoscope vs Macintosh direct laryngoscope for intubation of morbidly obese patients: a randomized trial	RCT	Intramural departmental sources	None	GlideScope video laryngoscope	Negative	[176]
The Flex-Tip <sup>TM</sup> tracheal tube does not reduce the incidence of postoperative sore throat: a randomized controlled trial	RCT	Intramural departmental sources and all evaluated devices were purchased by the University of Western Ontario, Department of Anesthesia	None	Flex-Tip <sup>™</sup> tracheal tube	Negative	[177]
Comparison of techniques for double-lumen endobronchial intubation: 90° or 180° rotation during advancement through the glottis	RCT	Intramural departmental sources	None	180° rotation	Positive	[97]
Comparison of the Airtraq and the Macintosh laryngoscope for double-lumen tube intubation: a randomised clinical trial	RCT	Intramural departmental sources. The manufacturer, Prodol Limited, Viscaya, Spain, provided the Airtraq devices free of charge	None	Airtraq laryngoscope	Negative	[170]
The effects of lidocaine spray and intracuff alkalinized lidocaine on the occurrence of cough at extubation: a double-blind: randomized controlled trial	RCT	Intramural departmental sources dedicated to research projects and a department stipend held by two authors	None	Lidocaine spray	Positive	[178]
Dexamethasone for the prevention of postoperative sore throat: a systematic review and meta-analysis	Meta	Intramural departmental sources	None	Dexamethasone	Positive	[11]
Effect of intracuff lidocaine on postoperative sore throat and the emergence phenomenon: a systematic review and meta- analysis of randomized controlled trials	Meta	Intramural departmental sources	None	Intracuff lidocaine	Positive	[179]
Does the incidence of sore throat postoperatively increase with the use of a traditional intubation blade or the GlideScope?	Prospective cohort study	Intramural departmental sources	None	GlideScope	Negative	[30]
The effects of thermal softening of double-lumen endobronchial tubes on postoperative sore throat, hoarseness and vocal cord injuries: a prospective double- blind randomized trial	RCT	Intramural departmental sources	None	Thermal softening of DLTs	Positive	[18]

(Continued)

### Table 2 (Continued).

Title	Research Type	Funding	Potential Conflicts of Interest	Intervening Measure	Positive or Negative Results*	Reference
Early endotracheal tube insertion with the GlideScope: a randomized controlled trial	RCT	Intramural departmental sources and all devices evaluated were purchased by the London Health Sciences Centre or the Western University, Department of Anesthesia	None	GlideScope	Negative	[171]
Ketorolac tromethamine spray prevents postendotracheal- intubation-induced sore throat after general anesthesia	RCT	Intramural departmental sources	None	Ketorolac tromethamine spray	Positive	[180]
The effect of lidocaine jelly on a taper-shaped cuff of an endotracheal tube on the postoperative sore throat: a prospective randomized study: A CONSORT compliant article	RCT	Intramural departmental sources	None	Lidocaine jelly	Positive	[181]
Combined intraoperative paracetamol and preoperative dexamethasone reduces postoperative sore throat: a prospective randomized study	RCT	Intramural departmental sources	None	Combined intraoperative paracetamol and preoperative dexamethasone	Positive	[182]
The influence of high-dose intraoperative remifentanil on postoperative sore throat: a prospective randomized study: A CONSORT compliant article	RCT	Intramural departmental sources	None	High-dose intraoperative remifentanil	Positive	[183]
Maintaining endotracheal tube cuff pressure at 20 mmHg: during anterior cervical spine surgery to prevent dysphagia: a double-blind randomized controlled trial	RCT	Intramural departmental sources	None	Maintaining ETT cuff pressure at 20 mmHg	Positive	[87]
Effect of topical ropivacaine on the response to endotracheal tube during emergence from general anesthesia: a prospective randomized double-blind controlled study	RCT	NSFC and Scientific Research Foundation of the Institute for Translational Medicine of Anhui Province	None	Topical ropivacaine	Positive	[184]
Lidocaine lubricants for intubation-related complications: a systematic review and meta- analysis	Meta	Intramural departmental sources	None	Lidocaine	Positive	[185]
The effect of zinc lozenge on postoperative sore throat: a prospective randomized, double-blinded, placebo- controlled study	RCT	Intramural departmental sources	None	Zinc lozenge	Positive	[186]
Influence of intraoperative sevoflurane or desflurane on postoperative sore throat: a prospective randomized study	RCT	Intramural departmental sources	None	Intraoperative sevoflurane	Positive	[50]
Effects of benzydamine hydrochloride on postoperative sore throat after extubation in children: a randomized controlled trial	RCT	Intramural departmental sources	None	Benzydamine hydrochloride	Positive	[187]

(Continued)

#### Table 2 (Continued).

Title	Research Type	Funding	Potential Conflicts of Interest	Intervening Measure	Positive or Negative Results*	Reference
Lidocaine for postoperative sore throat: a meta-analysis of randomized controlled trials	Meta	NSFC, national Key research and Development Program of China, the Ministry of Education of China, the Science and Technology Bureau of Sichuan Province, and clinical discipline pro-gram (neonatology) from the Ministry of Health of China	None	Lidocaine	Positive	[121]
Two-handed jaw thrust decreases postoperative sore throat in patients undergoing double-lumen endobronchial intubation: A prospective randomised study	RCT	The Medical K Corp.	None	Two-handed jaw thrust	Positive	[33]
Effect of 5% EMLA cream on postoperative sore throat in adults following general endotracheal anesthesia: a randomized placebo-controlled study	RCT	Intramural departmental sources	None	5% EMLA cream	Positive	[76]
Standard and flexible tip bougie for tracheal intubation using a non-channelled hyperangulated videolaryngoscope: a randomised comparison	RCT	Guy' Airway Management Course	None	Flexible tip bougie	Negative	[188]
Effect of intratracheal dexmedetomidine combined with ropivacaine on postoperative sore throat: a prospective randomised double-blinded controlled trial	RCT	Anhui Medical University Foundation for Clinical Science	None	Intratracheal dexmedetomidine	Positive	[132]
Effect of postoperative ultrasound-guided internal superior laryngeal nerve block on sore throat after intubation of double-lumen bronchial tube: a randomized controlled double- blind trial	RCT	University-level funding from Anhui Medical University	None	US-guide iSLNB	Positive	[128]
Effect of esketamine gargle on postoperative sore throat in patients undergoing double-lumen endobronchial intubation: a randomised controlled trial	RCT	Basic and Applied Basic Research Foundation of Guangdong Province, the Science and Technology Program of Guangzhou and the Precision Medicine Foundation of Guangdong Province Hospital Association	None	Esketamine gargle	Positive	[73]
Effect of continuous measurement and adjustment of endotracheal tube cuff pressure on postoperative sore throat in patients undergoing gynecological laparoscopic surgery: a randomized controlled trial	RCT	Intramural departmental sources	None	ETT cuff pressure	Positive	[37]
Preoperative ketamine gargle for prevention of postoperative sore throat after tracheal intubation in adults: a meta-analysis	Meta	NSFC	None	Ketamine gargle	Positive	[189]

**Note**: \*Represents a negative or positive result regarding POST.

Abbreviations: RCT, Randomized controlled trial; ETT, Endotracheal tube; DLT, Double-lumen tube; US-guided iSLNB, Ultrasound-guided block of the internal branch of the superior laryngeal nerve; NSFC, National Natural Science Foundation of China.

Туре	Methods	Interventions	Reference
ETT	Non-pharmacological	Size and type of ETT	
	Interventions	Male 7.0 mm; Female 6.0 mm	[38,39,80–84]
		Cuff pressure and cuff shape of ETT	
		<17–25 cm H <sub>2</sub> O	[55,87–90]
		Continuous monitoring of the cuff pressure	[40]
		Tapered cuff	[42,91,191]
		ETT with pressure indicator	[192]
		• Two-handed jaw thrust	[32,93]
		Video laryngoscopy	[193]
		Thermal softening	
		• Transitioning patients' head position from the sniffing position to a head elevation position	[194]
	Pharmacological Interventions	• NSAID	
		Benzydamine hydrochloride	[11,45,100–104]
		Flurbiprofen	[7,8]
		Ketoprofen	[99]
		• Steroid	[107,108]
		Fluticasone propionate	[75]
		Budesonide spray	[109]
		Betamethasone gel	[110]
		Dexamethasone	[72,111–113]
		NMDA receptor antagonists	
		Ketamine gargle	[114]
		Esketamine gargle	[73]
		Magnesium gargles	[116,117]
		• LA	
		Lidocaine (IV; inflate the ETT cuff; spray)	[83,118–125]
		5% EMLA cream	[76]
		Topical ropivacaine	
		US-guided iSLNB (eg, lidocaine, ropivacaine, and bupivacaine)	[78,126,127]
		• $a_2$ -adrenergic receptor agonists	[131–133]
		Dexmedetomidine (IV; intratracheal; add into lidocaine gargle)	
	Others	Sodium azulene sulfonate gargle	[135]
		Strepsils® tablets	[136]
		Chewing gum	[137]
		• Liquorice	[141–143]
		Acupuncture point stimulation	[146–148]
DLT	Non-pharmacological	Size and type of ETT	
	Interventions	Inner diameters of trachea and bronchus matched the outer diameters of trachea and bronchus cuffs by CT	[85]
		Silicone	[86]
		Video double-lumen tubes	[195,196]
		Two-handed jaw thrust	[33]
		Thermal softening	[18,77,94,95]
		• 180° rotation	[97]
	Pharmacological Interventions	• NSAID	
		• Steroid	
		NMDA receptor antagonists	
		·LA	
		• $\alpha_2$ -adrenergic receptor agonists	
		• US-guided iSLNB	[74,128,129]
		• Liquorice	[139]

Table 3 Potential Prevention and Treatment of POST After Tracheal Intubation

Abbreviations: ETT, Endotracheal tube; DLT, Double-lumen tube; LA, Local anesthetics; IV, Intravenous; NSAID, Non-steroidal anti-inflammatory drugs; US-guided iSLNB, Ultrasound-guided block of the internal branch of the superior laryngeal nerve.

Firstly, new intervention measures are being developed to prevent POST, but their safety and efficacy require further verification. New advances in POST prevention methods, such as new endotracheal intubation technology and new cuff pressure monitoring devices, have greatly reduced the occurrence of POST. Secondly, the specific mechanism underlying POST requires further exploration, and the functional mechanisms of various drugs and intervention approaches remain elusive. Thirdly, the assessment methods for POST are simplistic, lacking objective assessment criteria and large-sample and multi-center clinical studies. Finally, while a specific variable was controlled in clinical research to assess its impact on POST, these methods are often employed in conjunction in actual clinical practice. For instance, the efficacy of US-guided iSLNB relies not only on the function of LA but also on the administration of PNB. Adjuncts such as corticosteroids can be incorporated into cuff pressure monitoring to enhance therapeutic outcomes; similarly, combining multiple agents, such as paracetamol and dexamethasone, could prove beneficial. Therefore, further studies are warranted to evaluate the advantages of combination therapy and to identify the most appropriate regimens for different patient populations, thereby optimizing clinical practice.

## Conclusion

This review updates the prevailing viewpoints and elaborates on the mechanisms, risk factors, assessment approaches, and preventive measures related to POST after tracheal intubation. POST is a self-limiting disorder that is often disregarded; however, its incidence remains high and significantly affects postoperative recovery. Due to the unavoidable side effects of medications, some non-medicinal and non-invasive methods may be more beneficial for POST and related hoarseness. Resolving the existing controversies surrounding POST is essential for the development of comprehensive guidelines and consensus, which will aid in the prevention of POST and enhance patient quality of recovery and satisfaction. In line with the notions of ERAS and comfortable medical care, we advocate heightened awareness of its occurrence and progression, and recommend integrating the prevention and management of POST into routine clinical practice.

## Acknowledgments

The authors thank all the research assistants for their time and efforts in this review. We thank biorender (<u>www.biorender.com</u>) for expert assistance in Figure 3. The authors also thank Home for Researchers editorial team (<u>www.home-for-researchers.com</u>) for language editing service.

## **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

This work was supported by 2023 Qilu medical characteristics undergraduate education teaching research project-Shandong University (No. qlyxjy-202367) and Shandong Provincial Natural Science Foundation (ZR2022QH328).

## Disclosure

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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