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Emergency department airway management-2026: EMAT clinical policy guideline

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Abstract:

This clinical policy was developed by Emergency Medicine Association of Türkiye (EMAT) to evaluate current evidence on airway management in the emergency department (ED) and to provide clinicians with practical, evidence-based recommendations. Although rapid sequence intubation in the ED is a life-saving intervention in critically ill patients, the choice of techniques and medications during its implementation has a decisive impact on patient safety and clinical outcomes. This policy was developed by the research committee (RC) using the "*Grading of Recommendations, Assessment, Development, and Evaluations (GRADE)*" methodology, based on systematic literature reviews and expert opinion. Within the framework of five key clinical questions, the following topics were examined: preoxygenation strategies (noninvasive mechanical ventilation, high-flow nasal oxygen, face mask, and conventional techniques); the effectiveness and safety of apneic oxygenation; the use of a gum elastic bougie during intubation; the role of push-dose vasopressors in patients at high

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risk of hypotension; and the safety of ketamine use in patients at risk of increased intracranial pressure. This policy aims to reduce complications related to airway management and improve patient outcomes by providing emergency physicians with an evidence-based framework for preintubation preparation, medication selection, and equipment use.

Keywords:

Airway management, emergency medicine, intracranial pressure, intratracheal, intubation, ketamine, noninvasive ventilation, oxygen inhalation therapy, patient safety, preoxygenation, vasoconstrictor agents

Introduction

Airway management in the emergency department (ED), particularly rapid sequence intubation (RSI), is one of the most fundamental and highest-priority interventions in the evaluation and treatment of critically ill patients. Unlike the operating room and intensive care unit (ICU), the ED is a dynamic, high-stress environment that often lacks sufficient time for patient preparation, requiring rapid and accurate decision-making. Under these conditions, establishing an effective and safe airway is of vital importance to prevent serious complications such as hypoxemia, cardiac arrest, and mortality.[1,2] To this end, numerous studies conducted in recent years have evaluated preintubation preoxygenation strategies, apneic oxygenation techniques, the use of high-flow nasal oxygen (HFNO), the role of alternative induction agents, and the effectiveness of intubation adjuncts (rigid and flexible stylets, gum elastic bougie [GEB], etc.), generating ongoing debate regarding airway management practices in the ED.[3,4] However, most of these studies were conducted in different patient populations and under ICU or anesthesia conditions. Therefore, careful interpretation is required when applying these data directly to the ED setting.

This clinical policy guideline was developed during 2025–2026 by the Research Committee (RC) of the Emergency Medicine Association of Türkiye (EMAT) with the aim of providing evidence-based answers to clinically important questions in ED airway management and guiding physicians across different clinical scenarios. Rather than adopting a perspective that encompasses all aspects of airway management or revisits questions with well-established answers in the literature, this guideline focuses on emerging debates highlighted by recent studies.

Methods

This clinical policy guideline was developed based on the "Grading of Recommendations, Assessment, Development, and Evaluations" (GRADE) approach and through evaluation of the evidence available in the literature.[5] When preparing the recommendations in the guideline, the level of evidence in the literature was taken into consideration. In cases where the evidence was insufficient or conflicting, the relevant clinical questions were answered through voting by the advisory board members of the RC, based on the principle of majority decision. The resulting clinical policy guideline was initially published on the EMAT and EMAT-RC websites, announced through social media, and published by EMAT-affiliated outlets. It was decided that EMAT-RC clinical policy guidelines would be routinely updated every 3 years, while allowing for earlier updates in the event of major developments.

Identification of clinical questions

Priority clinical policy topics to be developed were identified by the advisory board of EMAT-RC. Clinical questions related to the selected topics were collected from the field. For this purpose, announcements were made using the EMAT and RC websites and social media tools. Clinical questions were collected using Google Forms. Within the specified period (60 days), the collected clinical questions were voted on by 11 members of the EMAT-RC advisory board using a 9-point Likert scale according to the priority of the need to address the outcome (1–3: noncritical and unimportant outcomes; 4–6: noncritical but important outcomes; and 7–9: critical outcomes). As a result of the voting, noncritical but important outcomes and critical outcomes were considered appropriate to be answered using an evidence-based approach.

Systematic literature search and article selection

For each identified clinical question, a systematic literature search was conducted in the SCOPUS, MEDLINE, and WOS databases using predefined keywords (search details are provided separately in the section corresponding to each clinical question).

Articles identified through the systematic literature search were uploaded separately into the Rayyan software for each clinical question.[6] Two independent, blinded reviewers evaluated whether the articles were relevant to the clinical question based on abstract review. Articles deemed appropriate were included for full-text assessment, while those considered inappropriate were excluded. Articles for which the two reviewers had conflicting decisions were evaluated by a third reviewer, who made the final decision.

When performing meta-analyses using data from primary studies, in cases where the reported effect size categories were not identical, the following approaches were preferred when possible: mathematical conversion of effect sizes, requesting the relevant effect size directly from the study authors, or using data from secondary publications in the form of systematic reviews that had previously used the primary studies and reported the relevant effect size.

Classification of evidence

For each critical question, critical appraisal of the studies included in the review was performed by at least two researchers, and evidence grading was conducted using the GRADEPro software in accordance with the GRADE approach (very low, low, moderate, and high level of evidence). Risk of bias assessment was performed using the RoB 2 tool for randomized controlled trials (RCTs), while observational studies were directly considered to be at high risk. Risk of bias assessment was carried out by two blinded reviewers; studies for which the reviewers had conflicting judgments were evaluated by a third reviewer, who made the final decision.

Determination of recommendation levels from levels of evidence

Recommendations were developed according to the appropriate levels of recommendation based on the evidence tables generated using the GRADE approach. Accordingly, the levels of recommendation are presented as shown in Table 1.

This clinical policy guideline is intended as a recommendation document for physicians working in EDs. The patient population includes adult patients presenting to EDs, while pediatric patients are excluded from the scope of the guideline. EMAT-RC clinical policy guidelines reflect the official position of EMAT-RC, as they provide evidence-based answers and recommendations derived from the current literature. However, they do not constitute definitive or absolute recommendations for physicians. EMAT-RC respects physicians' clinical experience and patients' preferences when final decisions are made.

As a result of the panel voting, all five clinical questions addressed in this guideline were categorized as "noncritical but important questions," and none were classified as a "critical question."

Noncritical But Important Clinical Questions

Noncritical but important clinical questions and their evidence-based answers are presented in detail below, along with a discussion of the literature. A summary of all the recommendations included in this clinical policy is shown in Supplementary File 1.

Scenario-1

During the preoxygenation phase of RSI in the ED, is there a difference in oxygenation success (incidence of severe hypoxia) among noninvasive mechanical ventilation (NIV), HFNO, face mask, and conventional techniques [Table 2]?

Rationale and background

In the RSI procedure in EDs, it is undesirable for patients to remain hypoxic during the period until a definitive airway is secured. To reduce this risk, administration of oxygen for several minutes before the procedure is recommended; this practice is referred to as preoxygenation. The aim of this intervention is to increase pulmonary oxygen reserves and subsequently reduce the development of hypoxia during procedural interventions. While the most common practice involves patients receiving oxygen therapy through nasal cannula or face mask, alternative methods such as NIV and HFNO have increasingly been used during the preoxygenation phase in recent years. In this guideline, the effectiveness and safety of preoxygenation methods used during the RSI procedure in critically ill patients with an indication for intubation in the ED are evaluated based on evidence, with the goal of providing recommendations to emergency physicians regarding which method is more effective and reliable.

Study selection

In studies comparing preoxygenation methods, highly heterogeneous scenarios exist due to methodological differences in the intervention arms. To answer the relevant clinical question, only well-defined clinical studies that compared different oxygen delivery methods specifically during the preoxygenation period were considered throughout the guideline development process. Nevertheless, studies with differing designs regarding oxygen administration are also present in the literature. In some studies, the oxygen delivery methods preferred during the preoxygenation process were not limited to the preoxygenation period and were also continued during the apneic oxygenation phase. In other studies, oxygen support was provided only during the preoxygenation phase or only during the apneic phase, with no oxygen administration during the other phase. To provide a clear answer to the relevant clinical question, studies that compared different oxygen delivery methods solely during the preoxygenation phase and did not apply any oxygenation during the apneic period were ultimately included for evaluation, and the data from these studies were used to perform meta-analyses and included in effect size pooling.

Table 1: Levels of recommendation

Level of recommendation	Recommendation
Strong	Recommendations supported by moderate or high levels of evidence in which the benefit of the intervention clearly outweighs its harm, as well as recommendations – particularly in the context of critical outcomes – where, despite low levels of evidence, the majority of panel members consider the investigated intervention to be clearly beneficial
Moderate	Topics for which there is conflicting moderate- or high-level evidence regarding whether the benefit of the intervention outweighs its harm, or for which the evidence supporting that the benefit outweighs the harm is of low or very low level
Weak	Recommendations for which there is conflicting low- or very low-level evidence regarding whether the benefit of the intervention outweighs its harm
	Recommendations for which there is disagreement among panel members regarding the benefit of the intervention
Level of recommendation against	**Recommendation against**
Strong against	Recommendations supported by moderate or high levels of evidence indicate that the harm of the intervention clearly outweighs its benefit
	Recommendations for which, particularly in the context of critical outcomes, the majority of panel members consider the investigated intervention to be clearly harmful despite low levels of evidence
Moderate against	Recommendations for which there is conflicting moderate- or high-level evidence regarding whether the harm of the intervention outweighs its benefit
	Recommendations for which the evidence supporting that the harm outweighs the benefit is of low or very low level
Weak against	Recommendations for which there is conflicting low- or very low-level evidence indicating that the harm of the intervention outweighs its benefit
	Recommendations for which there is disagreement among panel members regarding the harm of the intervention

Table 2: Scenario-1

Scenario-1 Comparison of NIV, HFNO, and conventional techniques for preoxygenation	
During the preoxygenation phase of rapid sequence intubation in the emergency department, is there a difference in oxygenation success (incidence of severe hypoxia) among noninvasive mechanical ventilation, high-flow nasal oxygen, face mask, and conventional techniques?	
Levels of recommendation and recommendations	**Level of evidence**
Moderate	
For adult patients in the emergency department with severe hypoxemia or a high risk of hypoxia, preoxygenation with noninvasive mechanical ventilation is recommended during rapid sequence intubation instead of a standard face mask or bag-valve mask	Moderate
Weak	
In the emergency department, for patients with severe hypoxemia or a high risk of hypoxia undergoing rapid sequence intubation, high-flow nasal oxygen therapy may be used as an alternative for preoxygenation when noninvasive mechanical ventilation is not feasible	Very low

HFNO: High-flow nasal oxygen, NIV: Noninvasive mechanical ventilation

Because the keywords of studies comparing preoxygenation methods and those comparing apneic oxygenation are very similar, and due to a lack of conceptual clarity in the existing literature, a common literature search was performed for both topics, and the articles were subsequently classified into two main categories through rapid abstract screening. Accordingly, a total of 119 articles were identified as a result of the systematic literature search conducted using the relevant keywords [Supplementary File 2; located at the end of the document]. From these articles, observational studies, studies not related to the clinical question, pediatric studies, and – as mentioned above – studies in which different oxygen therapy modalities were applied not only during the preoxygenation phase but also thereafter (during the apneic period) were excluded. The remaining five RCTs were included in the final evaluation. All of these RCTs were studies that compared methods providing oxygen therapy exclusively during the preoxygenation phase [Supplementary File 3].[7-11]

Four RCTs that provided oxygen support during both the preoxygenation and apneic oxygenation phases and did not meet the inclusion criteria specified above, but were considered to be indirectly related to the topic, were additionally discussed at the end of this section under the heading *"Other relevant articles"*.

In the risk of bias assessment performed using the Cochrane RoB 2 tool for studies with a randomized clinical trial design, a moderate-risk-of-bias was identified in four articles,[7-10] while a high-risk-of-bias was identified in one article[11] [Figure 1]. Summaries of the studies are presented in Supplementary File 4.

Overview of the studies and outcome measures

When the clinical settings of the studies are examined, the majority are noted to have been conducted in ICUs; four studies were performed in the ICU, while one study was conducted in both the ICU and the ED. The two studies by Baillard *et al*.[7,10] published in 2006 and 2018 were conducted in hypoxic patients, whereas the study by Guitton *et al*.[8] was conducted in patients without severe hypoxemia. The study by Gibbs *et al*.[9] was conducted in

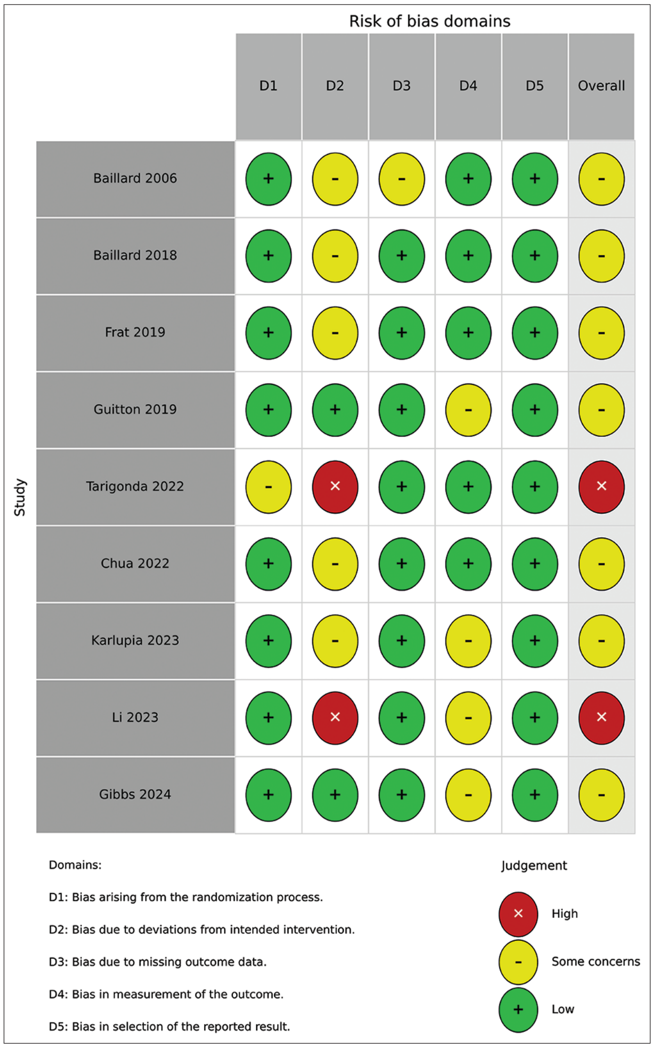

Figure 1: Traffic light plots of randomized clinical trials comparing preoxygenation methods during rapid sequence intubation in the emergency department (RoB 2 risk of bias assessment)

patients described as severely ill; however, the definition of "severely ill patient" was not explained in detail in the article. Among the included studies, only the study by Li *et al*.[11] was conducted in a patient population requiring emergency surgery.

In the studies, the standard treatment arms included oxygen support delivered through face mask (nonrebreather face mask in one study) and bag-valve mask (BVM). In the study by Li *et al*.,[11] the standard treatment arm did not include a BVM, and oxygen was administered using a face mask only. In three of the five RCTs, NIV was used in the intervention arm, while HFNO was used in the remaining two studies.[7-11]

A wide variety of outcomes, often differing substantially from one another, were addressed across the studies. In many studies, mean/median SpO_2 values at the end of the RSI procedure in both arms, the lowest SpO_2 values, or oxygen values before and after preoxygenation were compared. However, the clinical significance of these outcomes is limited. When supplemental oxygen is administered to any patient, an increase in postintervention values compared with baseline is already expected; therefore, pre–post comparisons have very limited clinical value in this context. Similarly, comparing mean/median SpO_2 values between the two arms at the end of intubation carries limited clinical relevance. Small differences that may be statistically significant but clinically insignificant can be negligible for clinicians. For example, a mean SpO_2 value of 96% in one arm versus 94% in the other, even if statistically significant, may be considered to have a negligible impact on clinical decision-making and patient-centered outcomes. In this context, the incidence of severe hypoxia in the treatment arms was considered the primary clinically meaningful outcome, and the meta-analysis focused on this endpoint. As many studies defined severe hypoxia as SpO_2 <80% or 85%, this threshold was adopted in the clinical policy. Although of limited clinical significance, the lowest SpO_2 values during intubation were also included as a secondary outcome for the meta-analysis.

Other outcomes were not included in the meta-analyses either because they were not considered clinically meaningful or because they could not be analyzed in a poolable manner across studies. Outcomes that were not suitable for pooling but were considered clinically relevant were additionally discussed on a study-by-study basis.

Occurrence of severe hypoxia (SpO_2 <80%/85%) during intubation

In this guideline, the occurrence of severe hypoxia during the procedure, rather than clinically negligible decreases in oxygen saturation, was accepted as the most critical and clinically meaningful outcome. Of the four studies reporting this outcome, three compared NIV with a face mask (standard oxygen therapy) or face mask + BVM,[7,9,11] while one study compared HFNO with standard oxygen therapy.[8] In two of the three studies in which NIV was used in the intervention arm,[7,11] the control group included a nonrebreather mask + BVM, whereas in one study, the control group included either BVM or face mask alone, and it was emphasized that even in patients who received BVM, no active ventilation was performed.[9] Due to differences between the treatment arms, the meta-analysis was performed using stratification: in the subgroup analysis comparing the NIV intervention arm with the standard treatment arm and including three studies, a significantly lower incidence of severe hypoxia was observed in favor of NIV, with a notably large effect size (odds ratio [OR]: 0.40, 95% confidence interval [CI]: 0.28–0.59). Preoxygenation with NIV reduces the odds of severe desaturation by approximately 60% compared with a standard face mask. The absolute benefit was approximately 7%, meaning that one episode of severe hypoxia is prevented in 1 of every 14 patients.

Only one study, by Guitton *et al.*,[8] compared HFNO with standard therapy, and although a marked benefit in favor of HFNO was mathematically apparent in this study, it was not statistically significant (OR: 0.25, 95% CI: 0.05–1.25). Due to the presence of a single study and a small sample size, statistical confidence regarding the isolated effect of HFNO could not be established.

When the pooled overall effect of the four studies was examined, a significantly lower incidence of severe hypoxia during preoxygenation was observed in favor of the intervention arm (NIV or HFNO) (OR: 0.39, 95% CI: 0.20–0.57). The low-to-moderate heterogeneity ($I^2 \leq 39\%$) suggests that the results are consistent [Figure 2].

Lowest SpO_2 level during intubation

In three RCTs, the lowest SpO_2 levels during intubation were reported and were considered suitable for pooled analysis. Among these, the studies by Baillard *et al.*[7,10] and Gibbs *et al.*[9] compared NIV with face mask, while the study by Guitton *et al.*[8] compared HFNO with face mask.[6-10] In the study by Gibbs *et al.*,[9] the data were reported as median and interquartile range (IQR); therefore, these data were converted to mean and standard deviation according to the formula proposed by Luo *et al.*[12] and included in the analysis.

All three RCTs had a moderate-risk-of-bias. Although there was a mathematical trend in favor of the intervention arm (NIV/HFNO) in both the comparison of NIV versus face mask (mean difference: 6.76, 95% CI: 2.28–15.81) and the comparison of HFNO versus face mask (mean difference: 2.0, 95% CI: 0.69–4.69), no statistically significant difference was observed. However, when the pooled effect of both intervention arms was examined, a statistically significant benefit in favor of the intervention arm was identified (mean difference: 3.92, 95% CI: 0.78–7.05). Based on this, it can be considered that the lack of statistical significance in subgroup analyses according to treatment arms may be attributable to small sample sizes [Figure 3].

Inhospital mortality, aspiration, regurgitation, and risk of reflux

Among the preoxygenation studies, no study reported periresuscitative mortality. Instead, because the studies were predominantly conducted in intensive care settings, inhospital mortality was reported, and we consider this outcome to be not clinically meaningful with respect to NIV/HFNO therapies. This is because it is difficult to attribute a mortality occurring perhaps days after the intubation procedure to the treatment arms. Nevertheless, in all three RCTs that reported inhospital mortality, no significant difference between the treatment groups was reported.[8-10]

When comparisons were attempted in terms of aspiration risk, it was observed that the studies did not provide poolable data. The intervention groups were compared with respect to aspiration outcomes in two studies, regurgitation risk in two studies, and reflux risk in one study. Although these outcomes are similar, they do not reflect exactly the same clinical condition and therefore were not considered as composite outcomes. In addition, considering the methodological differences between the intervention arms, the existing literature was not suitable for meta-analysis with respect to these outcomes, and the studies were evaluated individually for these adverse effect outcomes.

In the study by Baillard *et al.*[10] published in 2006, no significant difference in regurgitation was detected between the intervention groups (NIV vs. BVM + face mask) (1 [4%] vs. 2 [8%], $P = 1$). In the 2018 study by the same authors comparing the same treatment arms, both groups were again reported to be similar in terms of regurgitation risk (NIV: 0 [0%], control group: 1 [2.2%]).[7] In the study by Gibbs *et al.*,[9] some patients in the control group received a face mask alone, while others additionally received BVM; however, no active ventilation was performed. In this study, no statistically significant difference in aspiration was detected between the treatment arms (NIV: 6 [0.9%], control group: 9 [1.4%], risk difference: 0.4, 95% CI: 1.6–0.7). In the study by Guitton *et al.*,[8] which compared HFNO with face mask, no aspiration was reported in the HFNO group, whereas aspiration was reported in two patients in the control group ($P = 0.15$). Finally, in the study by Li *et al.*[11] (HFNO vs. face mask), no reflux was reported in either treatment arm.

The lack of statistically significant differences between groups in terms of mortality as well as aspiration, regurgitation, or reflux outcomes may be due to small sample sizes; alternatively, particularly for mortality, which is a multifactorial outcome, it is also possible that despite reducing severe hypoxia, these interventions did not demonstrate an effect on mortality. While these results may be interpreted as indicating no meaningful benefit in secondary outcomes, they may also be interpreted as showing that the intervention arms were at least not harmful with respect to these outcomes.

Other safety outcomes

Although other adverse event–complication outcomes were reported in the studies, most were not suitable for

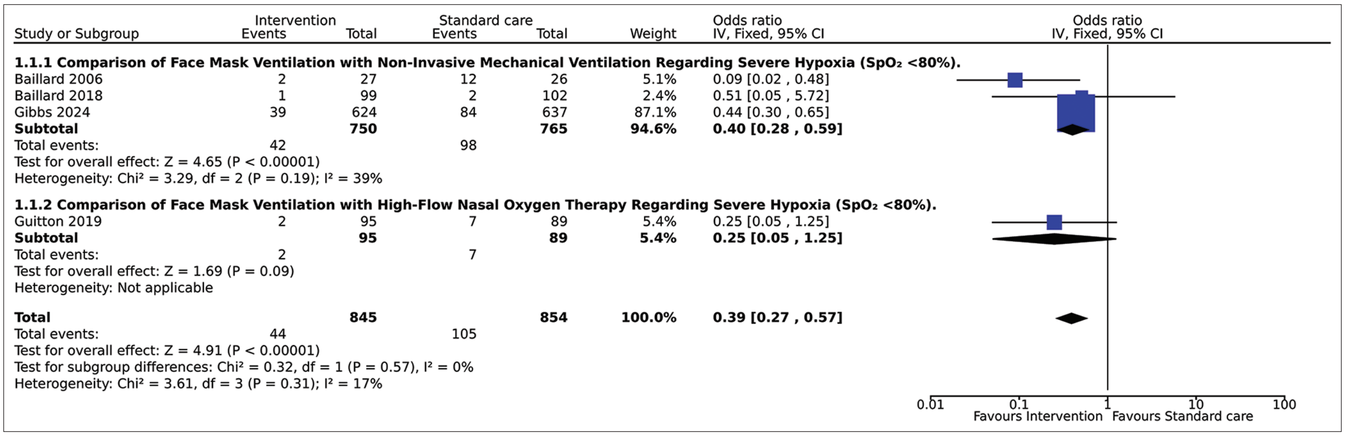

Figure 2: Forest plot showing the results of the meta-analysis of randomized clinical trials comparing the incidence of severe hypoxia (SpO_2 <80%/85%) with different preoxygenation methods during rapid sequence intubation in the emergency department. IV: Inverse variance, CI: Confidence interval

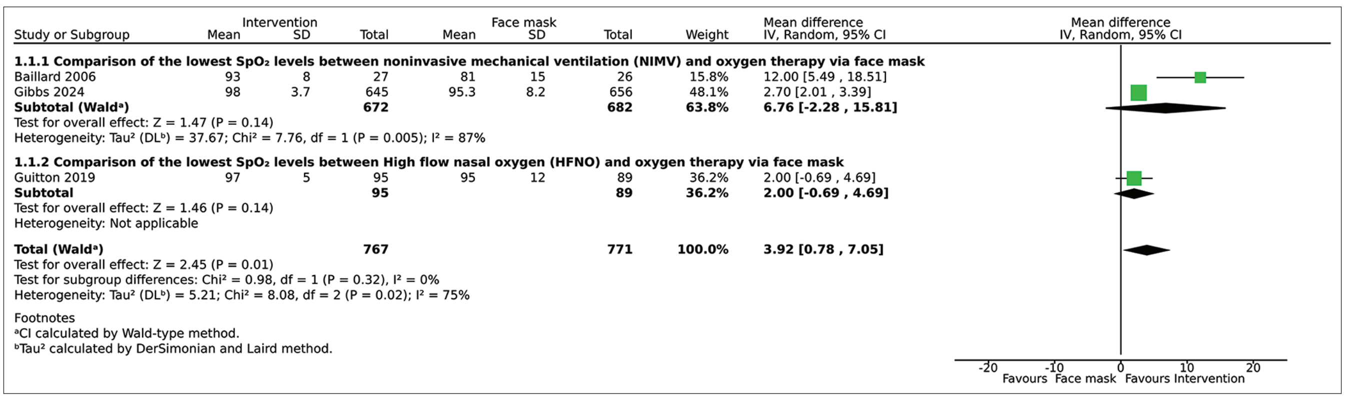

Figure 3: Forest plot showing the meta-analysis of the lowest SpO_2 values reported in three randomized clinical trials comparing intervention arms using NIV or HFNO for preoxygenation with a standard face mask during rapid sequence intubation in the emergency department, demonstrating a trend toward higher lowest SpO_2 levels in favor of the intervention arm in the combined analysis. IV: Inverse variance, CI: Confidence interval, SD: Standard deviation

pooling and were therefore discussed separately on a study-by-study basis.

In the study by Baillard *et al*.[10] published in 2006 comparing NIV and standard face mask, no differences were found between groups in terms of new infiltrates on postprocedure chest radiography, duration of mechanical ventilation, length of ICU stay, or ICU mortality. In a similar study by Baillard *et al*.[7] published in 2018, the incidence of adverse events was reported as 21.4% in the NIV group and 28.7% in the face mask group, with no significant difference (P = 0.24). In the same study, no significant difference was observed between groups in terms of the number of ventilator-free days within 28 days after intubation. Likewise, the number of days spent outside the ICU was also reported to be similar between groups.

Similarly, in the study by Gibbs *et al*.[9] that compared NIV and face mask, the incidence of new opacities on chest radiography and the incidence of pneumothorax were reported to be similar between the two study groups. No differences were detected between groups in SpO_2 and FiO_2 levels measured 24 h after intubation.

In the study by Guitton *et al*.[8] that compared HFNO and face mask, the duration of mechanical ventilation was found to be similar between the HFNO and standard face mask groups (3 [2–6] days and 3 [2–7] days, respectively; P = 0.80). During intubation, at least one intubation-related complication occurred in 6 patients (6%) in the HFNO group and in 17 patients (19%) in the standard treatment group, with the HFNO group found to be more favorable in terms of complications (relative risk (RR): 0.31, 95% CI: 0.13–0.76; P = 0.007).[8]

In the study by Li *et al*.,[11] which was the only RCT among the included trials with a high-risk-of-bias, the groups were reported to show no differences in other complications such as nasopharyngeal bleeding, postoperative pulmonary infection, postoperative nausea and vomiting, and postoperative nasopharyngeal pain.

In conclusion, across nearly all safety outcomes, neither NIV nor HFNO therapies, were reported to have adverse effects compared with standard treatment, and both methods can be considered safe with respect to these outcomes.

Articles indirectly related to the clinical question

Because oxygen support was provided during both the preoxygenation and apneic periods, four RCTs could not be evaluated for their isolated effect under either heading and were therefore not included in the meta-analyses. Nevertheless, as they applied treatments similar to the other studies during both phases and thus provide indirect evidence, they are discussed separately below. Of these studies, two were assessed as having a low-risk-of-bias, one a moderate-risk-of-bias, and one a high-risk-of-bias.[13-16]

The study by Chua *et al*.[13] was conducted in the ED on 192 patients with an indication for RSI for any reason, comparing oxygenation with HFNO and a nonrebreather face mask. The median lowest SpO_2 was calculated to be similar in both groups (100%). The incidence of SpO_2 dropping below 90% (incidence of hypoxia) was lower in the intervention group compared with the control group (15.5% vs. 22.6%, RR: 0.68, 95% CI: 0.37–1.25). The incidence of ventilator-associated pneumonia and aspiration pneumonia was reported to be similar in both groups. Overall, the groups were found to be comparable with respect to all complications.[13]

The study by Frat *et al*.,[14] conducted in ICU patients with acute hypoxemic respiratory failure, provided highly valuable data in terms of comparing HFNO and NIV interventions used in the intervention arms of other studies. In this multicenter study, including 313 cases from 28 centers, analysis of the entire patient cohort showed that the incidence of severe hypoxemia (SpO_2 <80%) was similar between the HFNO and NIV groups. However, according to subgroup analysis of 242 patients with moderate-to-severe hypoxemia (PaO_2/FiO_2 ≤200 mmHg), severe hypoxemia occurred less frequently in the NIV group compared with the HFNO group (24% vs. 35%, OR: 0.56, 95% CI: 0.32–0.99; $P = 0.046$). Serious adverse events did not differ between the treatment groups.[14]

In the study by Karlupia *et al*.,[15] which included patients who underwent RSI for abdominopelvic emergency surgery, oxygenation with HFNO was compared with face mask oxygenation. No statistically significant differences were identified between the two groups in terms of postintubation PaO_2 values, lowest SpO_2, apnea duration, number of laryngoscopy attempts, use of any rescue maneuvers, or adverse effects ($P > 0.05$). The study authors emphasized that the two methods were similar across all outcomes and highlighted that HFNO was at least as safe as face mask oxygenation.[15]

In the study by Tarigonda *et al*.,[16] which was the only RCT among the four articles with a high-risk-of-bias, the effectiveness of NIV (continuous positive airway pressure) and nasal cannula oxygen administration was compared in ICU patients with hypoxemic type 1 respiratory failure. The lowest SpO_2 values observed during intubation were found to be similar between groups. However, the degree of desaturation (the difference between SpO_2 after preoxygenation and SpO_2 during intubation) was calculated to be worse in favor of the nasal cannula group (nasal cannula: 4.24 ± 3.67 vs. NIV: 2.10 ± 3.50, $P = 0.007$). Intubation duration and complication rates were reported to be similar between the two groups.[16]

In summary, these four studies yield results that are largely consistent with those of the other studies. Both HFNO and NIV demonstrate outcomes that are either comparable to or superior to oxygen delivery through face mask or nasal oxygen. In addition, all methods appear to be similar in terms of adverse effects, indicating that they are safe. Although it is difficult to conclude, based on the available evidence, that NIV and HFNO have a clear superiority over one another in the intervention arms, NIV appears to be slightly more advantageous, particularly in patients with severe hypoxemia.

Conclusion

Considering the available results, the use of NIV instead of a standard face mask for preoxygenation is associated with a reduced risk of severe hypoxia. Given that no differences were observed in safety outcomes such as mortality and aspiration, preferring NIV over a standard face mask or BVM for preoxygenation – particularly in critically ill patients – appears reasonable in terms of reducing the incidence of severe hypoxemia.

Although the evidence is insufficient to draw definitive conclusions regarding the use of HFNO instead of a standard face mask/BVM for preoxygenation, HFNO therapy may provide a potential benefit. When the study by Frat *et al*.[14] that compared NIV and HFNO is considered, the possibility that HFNO may be at least as effective as NIV is increased. There is also no difference in safety outcomes compared with a standard face mask. In addition, because HFNO technically allows continuation of oxygenation during the apneic period, it may be considered as an alternative option for preoxygenation.

In conclusion, the overall body of evidence indicates that in patients at high risk of hypoxia, preoxygenation with NIV before emergency RSI significantly and clinically meaningfully reduces the incidence of severe hypoxia and is safe with respect to adverse effects, particularly mortality and aspiration risk. Although HFNO demonstrates a similar trend, definitive evidence is lacking. Taking available resources and patient characteristics into account, NIV may be considered the first-line option in clinical practice, while HFNO may be considered an alternative when NIV is not feasible.

GRADE evidence classification tables demonstrating the levels of evidence of the included studies are presented in Supplementary File 5.

Research gaps

Most studies are single-center. Blinding is particularly difficult to achieve for this research topic, and this limitation may influence outcomes. It is observed that outcome assessor blinding was either not ensured or not reported in the studies. The fact that the majority of studies were conducted in ICUs limits the generalizability of the results. There is a need for RCTs conducted in EDs in which outcome assessor blinding is ensured. In addition, studies targeting specific subgroups – such as hypoxic versus nonhypoxic patients, obese patients, and those with or without heart failure or respiratory failure – would be beneficial to allow more selective application of these interventions. Considering ease of application and the current paucity of evidence, there is a greater need for studies evaluating the effectiveness of HFNO.

Although both HFNO and NIV appear to be safe with respect to safety outcomes, it should not be overlooked that the lack of differences between groups in terms of aspiration risk may be related to insufficient sample sizes or methodological differences among studies. In this context, there is a need for further evaluation with higher-quality RCTs to reassess whether BVM and NIV increase the risk of aspiration.

Scenario-2

During RSI in the ED, is apneic oxygenation - used in addition to standard preoxygenation - an effective and safe treatment option in terms of the incidence of severe hypoxia (SpO2 <80%) and the lowest SpO_2 value [Table 3]?

Rationale and background

During the performance of RSI procedures in EDs, particularly in critically ill patients, hypoxemia is the most important complication that can lead to mortality.[17-20] To avoid this complication, preoxygenation has traditionally been applied using various methods before induction, with the aim of replenishing oxygen reserves for potentially prolonged apneic periods.[3,20] However, especially in critically ill patient populations – most notably those with predominant respiratory failure – preoxygenation alone may be insufficient and may contribute to morbidity and mortality.[3] For this reason, in recent years, studies have been published investigating the effectiveness of administering oxygen during the apneic period (the interval from induction until passage of the endotracheal tube through the vocal cords), in addition to preoxygenation, when performing RSI procedures in critically ill patients in ED and ICU settings. This method, defined as apneic oxygenation, has in fact been applied for many years through placement of a cannula in the nasopharyngeal region or through a nasal cannula placed in the nostrils. With the widespread availability of HFNO devices, this therapy has regained popularity. However, review of the literature reveals differing opinions and findings among studies addressing this topic.[21-27] In this guideline, the aim is to provide evidence-based recommendations regarding the use of apneic oxygenation in addition to preoxygenation during RSI procedures for emergency physicians encountering critically ill patients with an indication for intubation in the ED.

Study selection

Because the keywords of studies comparing preoxygenation methods and those comparing apneic oxygenation are very similar, and due to the lack of standardized concepts and definitions in the existing literature, a common literature search was conducted for both topics, and the articles were subsequently classified into two main categories through rapid abstract screening. Accordingly, a systematic literature search using the relevant keywords [Supplementary File 2] identified a total of 89 articles related to apneic oxygenation. Among these, a total of 79 studies were excluded because they had non-RCT study designs despite the availability of sufficient RCTs on the topic, were not related to the clinical question, or involved populations other than ED or critically ill patients. The remaining 10 RCTs were included in the final evaluation [Supplementary File 3].

In the risk of bias assessment performed using the Cochrane RoB 2 tool for studies with a randomized clinical trial design, five articles were identified as having a low-risk-of-bias, four as having a moderate-risk-of-bias, and one as having a high-risk-of-bias [Figure 4]. Summaries of the studies are presented in Supplementary File 4.

Overview of the studies and outcome measures

When the clinical settings of the studies are examined, three studies were conducted in critically ill patients with an indication for RSI in the ED,[21-23] while four studies were conducted in patients with an indication for RSI in the ICU.[24-27] The remaining three studies were conducted in patient populations with an indication for intubation due to emergency surgical indications.[28-30]

When the efficacy outcomes of studies conducted in ED and ICU patients are examined, all reported the lowest

Table 3: Scenario-2

Scenario-2	
Apneic oxygenation	
During rapid sequence intubation in the emergency department, is apneic oxygenation used in addition to standard preoxygenation practices an effective and safe treatment option in terms of the incidence of severe hypoxia (SpO_2<80%) and the lowest SpO_2 value as outcomes?	
Levels of recommendation and recommendations	**Level of evidence**
Moderate	
We do not recommend the routine use of apneic oxygenation in addition to preoxygenation during rapid sequence intubation in the emergency department	Moderate
Expert opinion: In patients at high risk of hypoxemia who receive high-flow nasal oxygen therapy during the preoxygenation phase, continuation of oxygenation with high-flow nasal oxygen during the apneic period may be considered	

SpO_2: Peripheral oxygen saturation

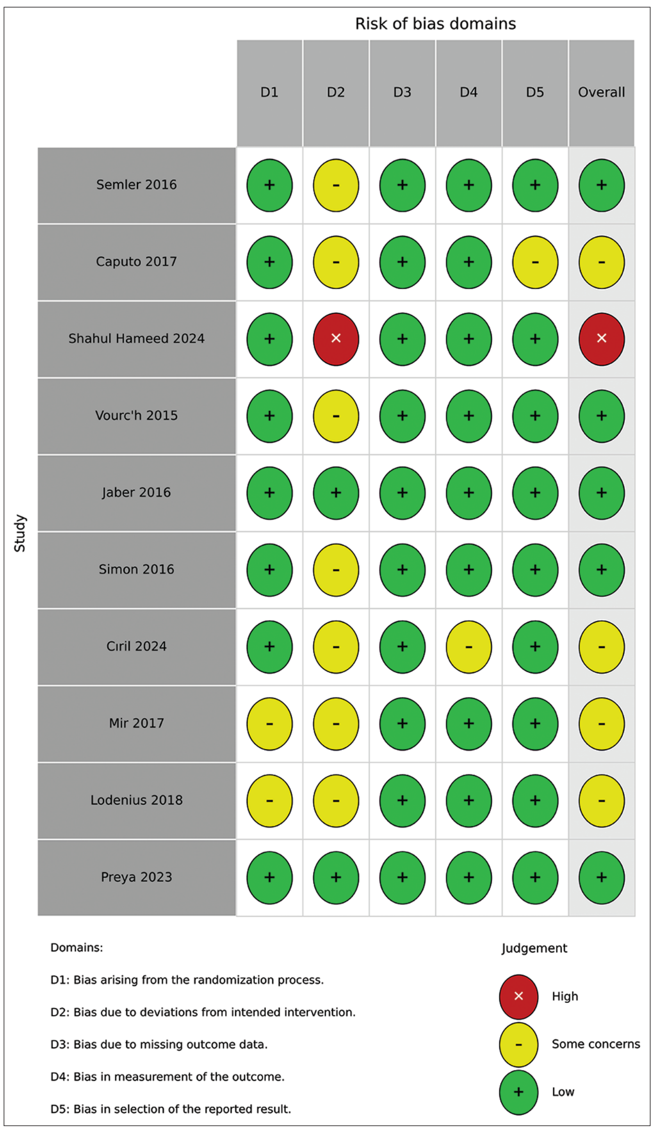

Figure 4: Traffic light plots of randomized clinical trials evaluating apneic oxygenation applied in addition to standard preoxygenation during rapid sequence intubation in the emergency department (RoB 2 risk of bias assessment)

SpO_2 values during intubation as the primary outcome, and in addition, except for the study by Shahul Hameed *et al*.,[24] the number of patients experiencing severe desaturation was also reported in the remaining six studies. Although the lowest SpO_2 value was recorded as the primary outcome in these studies, the panel preferred to base discussions and recommendations primarily on the outcome of "incidence of severe hypoxia," as it was considered to have greater clinical significance in this guideline. Effect sizes for both outcomes were pooled through meta-analysis in all but one of the studies.

Although all studies included in the meta-analysis primarily investigated the effect of apneic oxygenation administered in addition to preoxygenation, different preoxygenation techniques were also used in four studies.[24-27] Therefore, this represents a potential confounding factor affecting outcomes. For this reason, stratification was applied during meta-analysis, with three studies that used similar preoxygenation methods grouped into one subgroup[21-23] and four studies with different preoxygenation methods grouped into a separate subgroup. For preoxygenation, techniques such as BVM, nonrebreather face mask, and noninvasive ventilation were used in the included studies. For apneic oxygenation, HFNO was the most commonly used method, although nasopharyngeal oxygen and standard nasal cannula oxygen were also used.

In most studies conducted in patients with emergency surgical indications, the presence of respiratory distress or low baseline SpO_2 values was defined as an exclusion criterion. Therefore, these studies have the potential to provide only indirect evidence for the clinical question being addressed. In addition, in most of these studies, the outcome measure was defined as PaO_2 rather than SpO_2, and thus, they were not included in the meta-analysis. The results of these three articles were discussed separately.

Occurrence of severe hypoxia (SpO_2 <80%) during intubation

When the results of the meta-analysis pooling data from 693 patients across six studies reporting this outcome[21,22,24-27] were examined, it was found that apneic oxygenation used in addition to preoxygenation did not result in a significant reduction in the incidence of severe hypoxia compared with the control group (preoxygenation alone) (OR: 1.14, 95% CI: 0.70–1.86; P = 0.59). Subgroup analyses based on whether preoxygenation techniques were similar or not also demonstrated that apneic oxygenation applied in addition to preoxygenation did not provide a significant reduction in the incidence of severe hypoxia compared with preoxygenation alone [Figure 5].

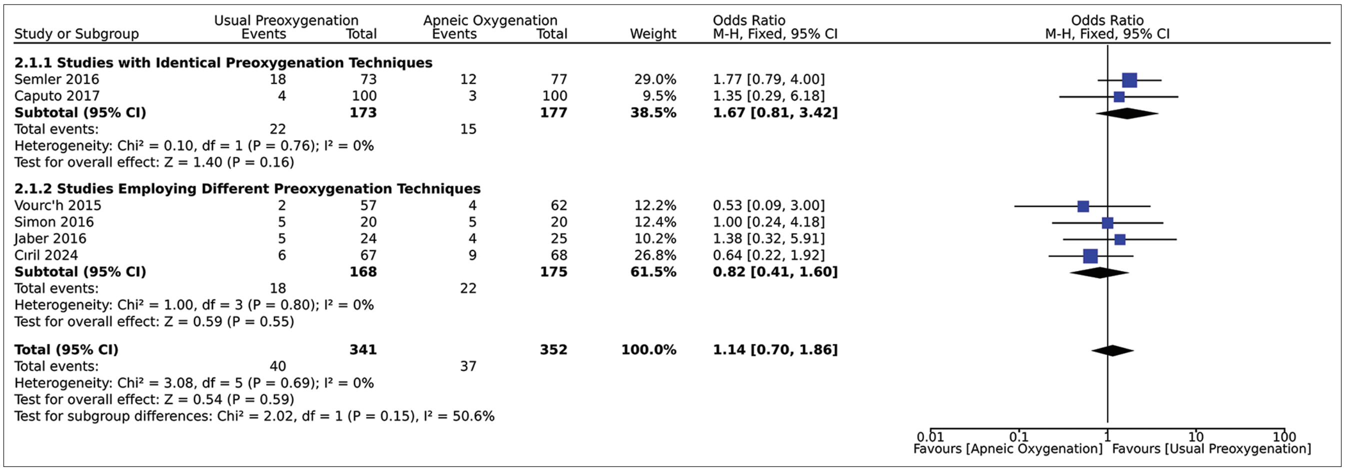

Figure 5: Forest plot showing the meta-analysis results of randomized clinical trials comparing apneic oxygenation applied in addition to standard preoxygenation with preoxygenation alone, in terms of the incidence of severe hypoxia (SpO_2 <80%) during rapid sequence intubation in the emergency department. ED: Emergency department; M-H: Mantel–Haenszel method, CI: Confidence interval

Although none of the studies conducted for emergency surgical indications reported severe hypoxia (SpO_2 <80%), in the study by Lodenius *et al*.,[29] five patients (12.5%) were reported to have desaturated to below 93% in the control group, whereas no desaturation was observed in the group receiving apneic oxygenation with HFNO.[29] Mir *et al*.[28] reported that no patients in either group experienced desaturation below 90%.[28]

Lowest SpO_2 recorded during intubation (lowest SpO_2)

When the results of the meta-analysis pooling data from 769 patients across seven studies reporting this outcome were examined, it was observed that apneic oxygenation used in addition to preoxygenation did not result in a significant difference in the lowest SpO_2 values recorded during intubation compared with preoxygenation alone (mean difference: 0.10, 95% CI: 1.02–1.22, P = 0.87). Subgroup analyses based on whether preoxygenation techniques were similar or not also showed that apneic oxygenation did not result in a significant difference in the lowest SpO_2 values observed during the RSI procedure compared with preoxygenation alone [Figure 6].

Among studies conducted in patients who underwent intubation due to emergency surgical indications, only the study by Lodenius *et al*.[29] reported the lowest SpO_2 values and demonstrated no significant difference between the treatment arms.[29] In the study by Preya *et al*.,[30] the lowest SpO_2 value was not reported; instead, the lowest arterial PaO_2 measured during the apneic period was reported, and arterial PaO_2 values were shown to be higher in the group receiving apneic oxygenation with HFNO compared with the group receiving preoxygenation alone.[30]

Mortality and other adverse outcome measures

When all studies are evaluated, it is observed that different studies reported different adverse event–safety outcomes. Therefore, pooling effect sizes for these outcomes was not preferred; instead, selected outcomes were discussed separately on a study-by-study basis. With respect to mortality outcomes, Caputo *et al*.[22] compared 24-h mortality between treatment arms, while four studies compared 20–30-day mortality; however, none demonstrated a statistically significant difference.[21,24,25,27] In four studies, first-pass intubation success was compared, and no significant difference was shown between the two treatment arms.[21,22,24,28] Cıril *et al*.[27] investigated intubation duration as a secondary outcome and reported no significant difference.[27]

In conclusion, across all secondary outcomes – including the safety outcomes reported by the studies themselves – apneic oxygenation applied in addition to preoxygenation was not found to differ from preoxygenation alone.

Conclusion

Considering the results of RCTs evaluating the effectiveness of apneic oxygenation applied in addition to preoxygenation during RSI procedures – particularly in critically ill patients in the ED – it is observed that apneic oxygenation does not result in a difference in terms of the incidence of severe hypoxia or the lowest measured SpO_2 values. Similarly, apneic oxygenation does not lead to additional deterioration in secondary outcomes such as mortality, first-pass intubation success, and intubation duration. When interpreting the results of the studies, it should be taken into account that four of the studies included in the meta-analysis also differed in their preoxygenation methods, representing a potential confounding factor. Considering that the remaining studies – those evaluating the pure effect of apneic oxygenation with identical preoxygenation methods – had limited total sample sizes, we believe that larger studies with uniform preoxygenation methods are needed. GRADE evidence classification tables

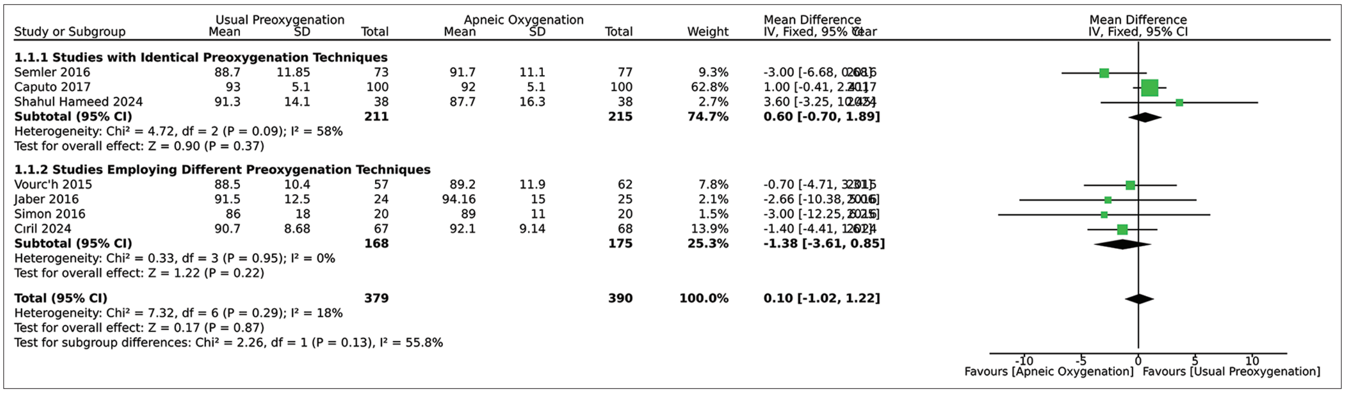

Figure 6: Forest plot presenting the meta-analysis results of randomized clinical trials comparing apneic oxygenation applied in addition to standard preoxygenation with preoxygenation alone, in terms of the lowest SpO_2 values recorded during the procedure during rapid sequence intubation in the emergency department. SD: Standard deviation, IV: Inverse variance, CI: Confidence interval

demonstrating the levels of evidence of the included studies are presented in Supplementary File 5.

Research gaps

The studies are single-center with small sample sizes, and preoxygenation methods are generally not standardized. Therefore, there is a need for large-sample studies in which preoxygenation methods are the same in both arms. In particular, there is a priority need for studies evaluating HFNO therapy in the apneic oxygenation arm, given its ease of applicability.

Scenario-3

During intubation in the ED, does the use of a GEB, compared with standard intubation (with or without a stylet), increase first-attempt intubation success and affect intubation duration [Table 4]?

Rationale and background

In airway management in the ED, first-pass success of endotracheal tube placement is a critical quality indicator, as multiple intubation attempts are independently associated with severe hypoxemia, aspiration, and cardiac arrest during intubation. Some clinicians do not use any facilitating instrument during endotracheal tube placement. However, although the use of a stylet is the default adjunct to facilitate tube passage in many centers, an increasing number of emergency physicians are using the GEB as a primary or rescue device. Owing to its small external diameter and preshaped distal angulation of 35°–40°, the GEB may facilitate tube passage in situations with limited laryngeal visualization. Nevertheless, within the unique context of the ED – characterized by variable operator experience, high illness severity, and frequent physiologic deterioration – whether these theoretical advantages translate into measurable improvements in first-pass success and procedure duration is decisive for widespread adoption of the device. This clinical policy guideline aims to evaluate, in an evidence-based manner, the effects of GEB use during RSI compared with standard intubation (with or without a stylet), particularly with respect to first-pass success and procedure duration.

Table 4: Scenario-3

Scenario-3	
Comparison of the gum elastic Bougie and standard intubation	
During intubation in the emergency department, does the use of a gum elastic bougie, compared with standard intubation (with or without a stylet), increase first-attempt intubation success and affect intubation duration?	
Levels of recommendation and recommendations	**Level of evidence**
Moderate	
In adult patients with a predicted difficult airway in the emergency department, the use of a gum elastic bougie is recommended instead of standard intubation (with or without a stylet)	Low
Weak	
Routine use of a gum elastic bougie may be considered during adult patient intubation in the emergency department	Low

Study selection

A systematic literature search using the relevant keywords [Supplementary File 2] identified 942 articles. Of the 186 articles related to the research question, 18 had an RCT design, while the remaining articles were observational studies. Given the sufficient number of RCTs, observational studies were not included [Supplementary File 3].

Of the 18 RCTs, manikin studies, animal and cadaver studies, studies using modified stylets/tracheal tubes, and studies involving mixed procedures conducted with additional adjunctive devices such as video laryngoscopy (VL) were excluded, and 11 RCTs were included for evaluation. In contrast, studies in which additional adjunctive methods not specified in the protocol were used at the clinician's discretion were not excluded.[12,31-42]

In the risk-of-bias assessment performed using the Cochrane RoB 2 tool for RCTs, 6 studies were identified as having a high-risk-of-bias, 1 study a moderate risk, and 4 studies a low-risk-of-bias [Figure 7]. Summaries of the included studies are presented in Supplementary File 4.

Overview of the studies and outcome measures

When the clinical settings of the studies were examined, it was notable that the patient population predominantly consisted of operating room patients. Less frequently, the remaining studies were conducted in the ED, ICU, and prehospital settings. In all studies, GEB was used in the intervention arm. In the comparator arm, the use of a stylet was reported in 6 studies, while in 5 studies, it was not explicitly stated whether a stylet was used. Instead, the comparator arm was described as the standard treatment/intubation arm. In the analyses, all of these studies were grouped into a single comparator arm and evaluated as the standard intubation arm (with or without a stylet).

Figure 7: Traffic light plots of randomized controlled trials comparing the use of a gum elastic bougie with standard intubation (with or without a stylet) during intubation in the emergency department (RoB 2 risk-of-bias assessment)

When focusing on studies with low and moderate-risk-of-bias, 3 studies were conducted under operating room conditions,[31,34,36] The 2018 study by Driver *et al*.[33] was conducted in the ED, while their 2021 study included both ED and ICU patients.[32,33] Of the studies with a high-risk-of-bias, 5 were conducted in the operating room,[35,38-41] whereas only the study by Heegaard *et al*.[37] was conducted in the prehospital setting.[37]

First-attempt intubation success

Among studies with low/moderate-risk-of-bias, of the 4 studies analyzing first-attempt intubation success, three reported no statistically significant difference, while only the 2021 study by Driver *et al*.[32] reported a statistically significant result in favor of GEB.[32] In the meta-analysis of these 4 studies, although the pooled effect appeared to favor GEB numerically, this effect was not statistically significant (OR: 1.36, 95% CI: 0.49–3.76). For the same outcome, among the 6 studies with high-risk-of-bias, 3 studies – by Gataure *et al*.,[35] Sut *et al*.,[41] and Khan *et al*.[38] – reported a statistically significant benefit in favor of GEB, while the remaining studies reported no significant difference; the pooled effect of the high-risk-of-bias studies demonstrated a marked benefit in favor of GEB (OR: 4.18, 95% CI: 2.39–7.29). When considering the overall pooled effect of all 10 RCTs (low-, moderate-, and high-risk-of-bias) addressing this outcome, GEB was associated with a statistically significantly higher first-attempt intubation success rate (OR: 2.34, 95% CI: 1.14–4.80) [Figure 8]. Although the overall pooled effect of the 10 RCTs favors GEB for first-attempt intubation success, it should be noted that this benefit is largely driven by studies with high-risk-of-bias, whereas the pooled effect of low-risk-of-bias studies did not demonstrate a statistically significant difference.

In the stratified meta-analysis performed according to the clinical settings in which the studies were conducted, the overall pooled effect across all strata again demonstrated higher first-attempt intubation success in favor of GEB (OR: 2.03, 95% CI: 1.10–3.74). However, when studies were stratified by clinical setting, it was notable that the benefit in favor of GEB was predominantly derived from prehospital and operating room studies, most of which had a high-risk-of-bias [Figure 9]. In contrast, studies with low and moderate-risk-of-bias conducted in the ED or ICU did not report a benefit in favor of GEB, and ED data in particular were conflicting. In the 2018 study

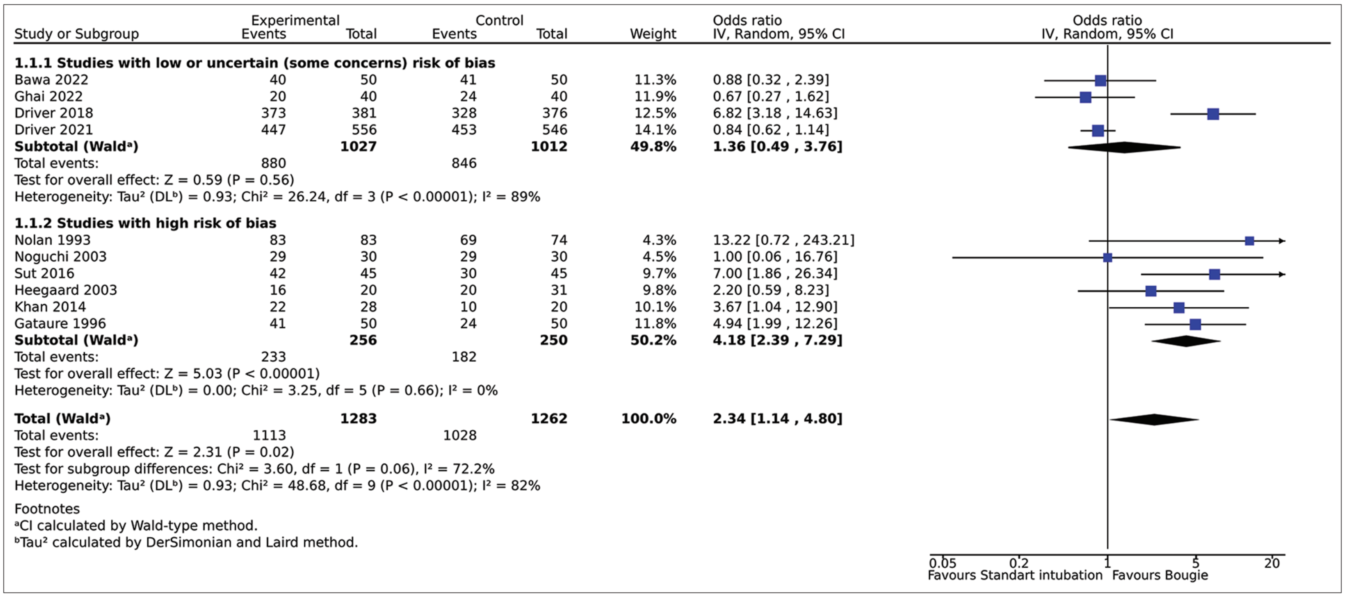

Figure 8: Forest plot showing the meta-analysis results of first-attempt intubation success in randomized clinical trials comparing the use of a gum elastic bougie with standard intubation (with or without stylet) during emergency department intubation, stratified according to the risk of bias of the studies. IV: Inverse variance, CI: Confidence interval

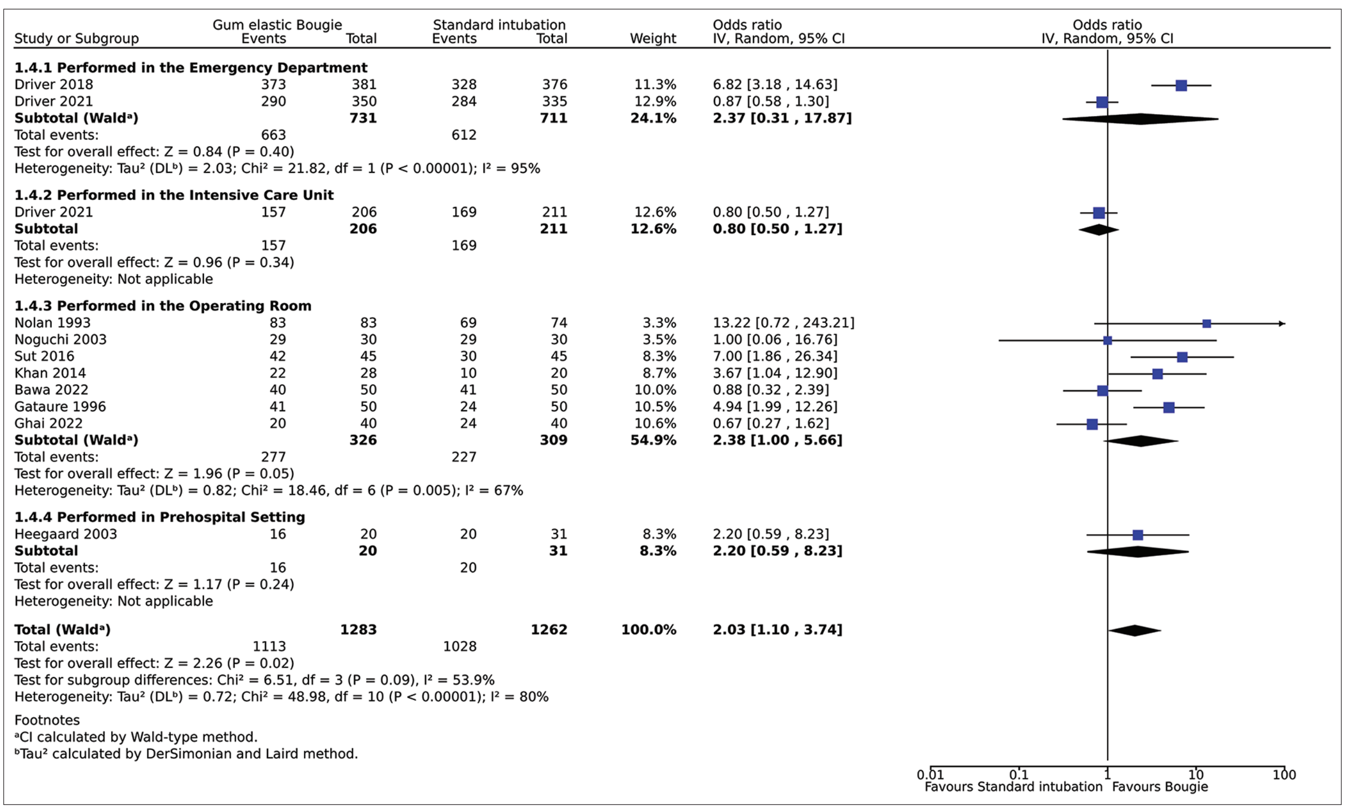

Figure 9: Forest plot showing the results of a stratified meta-analysis of randomized clinical trials comparing the use of a gum elastic bougie with standard intubation (with or without a stylet) during intubation in the ED, stratified by clinical setting, for first-attempt intubation success rates

by Driver *et al*.,[33] a statistically significant advantage was observed with GEB (98% vs. 87%).[33] However, in the 2021 study by the same authors, there was no significant difference between treatment arms (80% vs. 83%), and the intubation time was on average 12 s longer in the GEB group.[32] Although the meta-analysis overall suggests a trend in favor of GEB, the CIs are wide, and heterogeneity is substantial. In this context, while a potential benefit of GEB for first-attempt intubation success appears plausible, it should be emphasized that results from RCTs with good methodological quality and low-risk-of-bias do not support this finding. In addition, methodological differences and certain limitations across studies may have influenced the results. In both the 2018 and 2021 studies by Driver *et al*.,[33] the use of VL was not standardized and was left to the clinician discretion. In the 2018 study, VL was used significantly less frequently in the GEB arm compared with the control group, which was considered an important methodological limitation. Unequal distribution of a confounder, such as VL use between treatment arms, may have influenced the results. Notably, despite less frequent VL use, outcomes favored GEB, suggesting that the true beneficial effect of GEB may be greater than the reported effect.

When focusing exclusively on studies conducted in patients with a difficult airway, the statistically significant and pronounced benefit of GEB is noteworthy. Across studies with low/moderate as well as high-risk-of-bias, both stratified analyses and the overall pooled effect demonstrate that GEB significantly increases first-attempt intubation success (OR: 2.11, 95% CI: 1.47–3.01) [Figure 10].

In conclusion, although GEB may be associated with a statistically significant improvement in first-attempt intubation success across all patients, large studies with low-risk-of-bias do not confirm this finding. Therefore, while a potential benefit of GEB in this scenario appears plausible, it remains debatable. However, when focusing on patients with a difficult airway, the approximately twofold increase in the odds of first-attempt intubation success with GEB is noteworthy, and the benefit of GEB in this subgroup can be stated with greater confidence.

Overall intubation failure

Most studies reported first-attempt intubation success or the total number of attempts as outcomes. The limited number of studies reporting overall intubation failure generally defined overall failure as the absence of successful intubation after two attempts and/or failure to achieve successful intubation within >60 s, and we likewise defined overall intubation failure accordingly. Among the studies reporting overall failure rates, the study by Ghai *et al*.[36] was assessed as having a moderate-risk-of-bias, while the other three studies were assessed as having a high-risk-of-bias.[31-34] In the meta-analysis, no difference was observed between treatment arms in the Ghai *et al*.'s[36] study with low or moderate-risk-of-bias (OR: 2.11, 95% CI: 0.36–12.24), whereas the pooled results of the three studies with high-risk-of-bias demonstrated a statistically significantly lower overall intubation failure rate in the GEB group (OR: 0.21, 95% CI: 0.06–0.68). When the overall pooled effect of all studies was considered, although a numerical benefit in favor of GEB was observed, this benefit was not statistically significant (OR: 0.39, 95% CI: 0.09–1.62) [Figure 11].

In addition to the meta-analysis, when study-specific results are examined, noteworthy findings emerge. For example, in the study by Gataure *et al*.,[35] all patients in the standard treatment arm who could not be intubated after two attempts were successfully intubated using a GEB as a rescue intervention.[35] Similarly, in the 2018 study by Driver *et al*.,[33] among a total of 56 patients in whom first-attempt intubation failed in both arms (48 patients in the standard intubation arm and 8 patients in the GEB arm), 49 were successfully intubated using a GEB as a rescue intervention.[33] In both studies, the preferential use of a GEB as a rescue intervention after failed attempts, and the fact that the majority of these interventions resulted in successful intubation, is noteworthy.

Endotracheal intubation time

Although first-attempt intubation success is the most critical outcome in RSI protocols in the ED, the duration

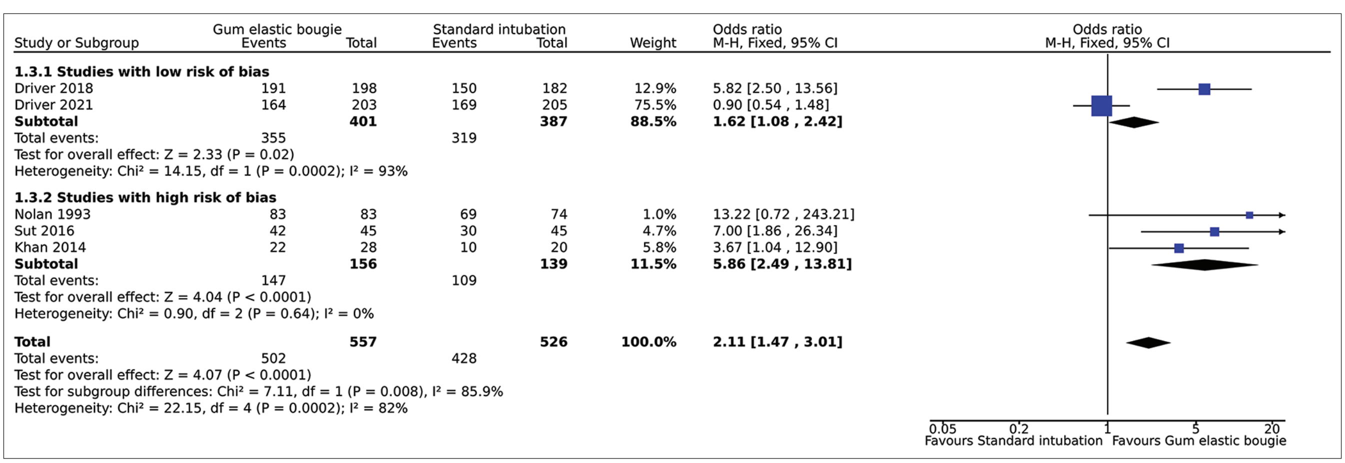

Figure 10: Forest plot showing the results of a meta-analysis of randomized clinical trials comparing the use of a gum elastic bougie with standard intubation (with or without a stylet) for first-attempt intubation success in difficult airway cases in the emergency department. M-H: Mantel–Haenszel method, CI: Confidence interval

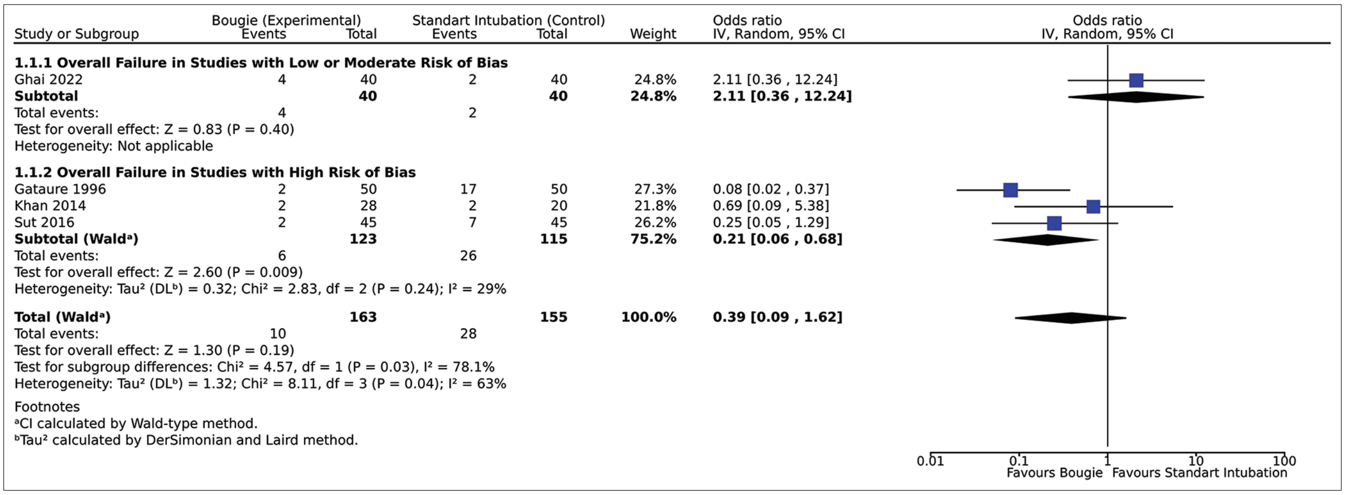

Figure 11: Forest plot showing the results of a meta-analysis of randomized clinical trials comparing the use of a gum elastic bougie with standard intubation (with or without a stylet) for overall intubation failure rates during intubation in the emergency department. IV: Inverse variance, CI: Confidence interval

of the intubation procedure is another important quality indicator. Increased intubation duration has been shown to be associated with hypoxemia and periresuscitative arrest.

Among the RCTs included in the analysis, 8 reported intubation times for GEB and standard intubation. In 6 of these studies, intubation times were reported as mean and standard deviation, whereas in the two studies by Driver *et al*.,[32,33] times were reported as median and IQR. Although attempts were made to contact the authors by e-mail to request the data as mean and standard deviation, no response was obtained. Therefore, intubation times in these two studies were recalculated as mean and standard deviation using the formula proposed by Luo *et al*.,[12] and these values were included in the meta-analysis.[12]

Marked differences in reported intubation times across studies are notable and are thought to be related to the lack of standardization in the definition of intubation time. In most studies, detailed information on how this duration was measured was not clearly described. Of the 8 studies, 5 had low/moderate-risk-of-bias, and when the pooled effect of these studies was examined, the standard intubation arm was found to have a statistically significantly shorter intubation time. Although the pooled effect of the 3 studies with high-risk-of-bias did not demonstrate a significant difference between groups, inclusion of these studies resulted in an overall pooled effect across all 8 studies indicating a statistically significantly shorter intubation time in favor of standard intubation (mean difference: 3.7 s, 95% CI: 1.02–6.38). However, considering the 95% CI, this disadvantage – ranging between 1 and 6 seconds – has debatable clinical implications and may be regarded as a limited negative effect for GEB. While this time difference may be relevant in hypoxemic patients, it is likely to be clinically tolerable for the general patient population [Figure 12].

Complications

A wide range of outcomes were evaluated as complications across the studies, and some studies did not report any complication data. Because no outcomes were suitable for meta-analysis, this section was discussed on a study-by-study basis.

In four studies, treatment arms were compared with respect to the complication of esophageal intubation, and all reported similar rates between groups.[31,36-38]

In the 2021 study by Driver *et al*.,[32] the rate of cardiovascular collapse within 1 h was reported to be statistically significantly higher in the standard intubation arm (91 [16.7%] vs. 68 [12.2%]; absolute difference: 4.4, 95% CI: 0.1–8.8).[32]

Because complication-related outcomes were defined differently across studies, very few studies reported overlapping complication data. When studies were examined individually, treatment groups were reported to be similar with respect to laryngospasm, stridor, airway obstruction, airway mucosal trauma, SpO_2 <80%, witnessed aspiration, newly developed pneumothorax, sore throat, hoarseness, lip laceration, dental trauma, and hypoxemia-related complications.[31,34,36-39]

Conclusion

The available evidence indicates that, compared with standard intubation, GEB is associated with a statistically significant benefit in first-attempt intubation success, particularly in patients with a difficult airway, although it is also associated with a modest prolongation of intubation time. When interpreting these results, it should be noted that the studies are heterogeneous, especially with respect to

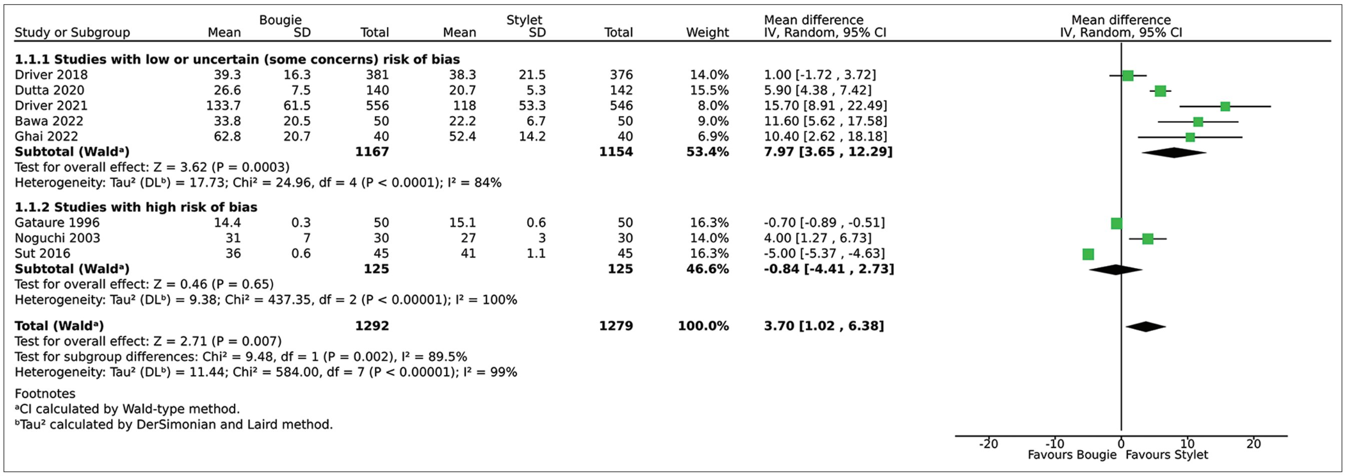

Figure 12: Forest plot showing the results of a meta-analysis of randomized clinical trials comparing the use of a gum elastic bougie with standard intubation (with or without a stylet) for endotracheal intubation time during intubation in the emergency department. SD: Standard deviation, IV: Inverse variance, CI: Confidence interval

first-attempt intubation success, and that the meta-analyses are therefore sensitive to this heterogeneity; the potential benefit appears to be driven largely by prehospital and operating room studies. GRADE evidence classification tables summarizing the certainty of evidence for the included studies are presented in Supplementary File 5.

In patients with a difficult airway (defined as Cormack–Lehane Grade III view or the presence of vomitus, bleeding, deformity, etc., around the airway), GEB provides a clear and meaningful benefit, and the use of GEB during RSI should be preferred over standard intubation (with or without a stylet) in these patients. In patients in whom standard intubation is selected as the initial approach and the first attempt is unsuccessful, GEB may be considered as a rescue intervention.

Although a benefit in first-attempt intubation success rates in favor of GEB can be suggested, there is insufficient strong evidence to support the routine use of GEB in all patients. However, considering that patients in the ED – unlike those in operating room or ICU settings where most studies were conducted – often present with much more rapidly evolving clinical scenarios, virtually every ED patient may be regarded as a potential difficult airway case. Taking this into account, together with the favorable safety profile of GEB in terms of complications, we recommend preferring GEB over standard intubation (with or without a stylet) across the entire patient population. Nevertheless, for GEB to be used routinely during RSI in all patients, it is essential that personnel in the relevant clinical settings have received adequate training in the use of GEB.

Research gaps

There is a need for ED-focused, multicenter RCTs to investigate differences in first-attempt tube passage success. In existing studies, the lack of a standardized definition for "tube placement time" is notable; this concept should be standardized, and the comparison between GEB and standard intubation should be repeated accordingly. In addition, RCTs specifically focusing on obese patients, trauma patients, and physiologically critically ill patients are needed to enable subgroup analyses in these populations.

Scenario-4

In adult patients in the ED who are hypotensive or at high risk of hypotension, does the administration of push-dose vasopressors (VPs) (phenylephrine, epinephrine, etc.) during or immediately before RSI, in addition to standard treatments, improve the incidence of peri-intubation hypotension and clinical outcomes [Table 5]?

Rationale and background

RSI performed in critically ill patients in the ED may be associated with a risk of hemodynamic instability. The sedative and paralytic agents used during this process can lead to abrupt decreases in blood pressure and impaired organ perfusion. This risk may increase morbidity and mortality, particularly in patients who are at high risk of hypotension.[42,43]

In clinical practice, some clinicians may prefer the use of push-dose VPs during or immediately before RSI to mitigate this risk. Agents such as phenylephrine and epinephrine are commonly favored because of their rapid onset of action and feasibility for peripheral administration.[44,45] However, data in the literature regarding the efficacy and safety of this approach are limited. In recent years, a meta-analysis including 24 RCTs demonstrated that prophylactic administration of push-dose VP before orotracheal intubation was

Table 5: Scenario-4

Scenario-4
Push-dose vasopressor administration during rapid sequence intubation
In adult patients in the emergency department who are hypotensive or at high risk of hypotension, does administration of a push-dose vasopressor (phenylephrine, epinephrine, etc.) during or immediately before rapid sequence intubation, in addition to standard treatments, reduce the incidence of peri-intubation hypotension and improve clinical outcomes?
Recommendation
Because the available evidence in the literature is indirect and of low quality and is insufficient to adequately answer this question, the panel makes no recommendation for or against this intervention Expert Opinion: Although the panel chose not to make a recommendation on this issue, it is known that push-dose vasopressor therapy is used in certain clinician-specific practices. Based on this, the panel believes that each institution should determine, through its own local clinical policy, whether push-dose vasopressors should be administered during rapid sequence intubation in critically ill adult patients who are hypotensive or at risk of hypotension

associated with higher postintubation mean arterial pressures and systolic arterial pressures (mean difference: 7.6 mmHg, 95% CI: 4.3–10.8).[46] Nevertheless, this study focused entirely on elective intubations performed in the operating room in American Society of Anesthesiologists physical status I–II patients and therefore provides only very limited indirect evidence for the use of this approach during RSI in critically ill patients who are already hypotensive.

This guideline aims to provide evidence-based recommendations regarding the use of push-dose VPs during RSI for emergency physicians managing critically ill patients in the ED who are hypotensive or at risk of hypotension and have an indication for RSI.

Study selection

As a result of the systematic literature search conducted using the relevant keywords, a total of 98 studies were identified [Supplementary File 2]. Of these, 7 studies evaluating the use of push-dose VP during the peri-intubation period in critically ill patients who were hypotensive or at risk of hypotension were included for assessment. In these studies, phenylephrine was most commonly used as the VP; however, because this agent is not available in our country, three additional observational studies evaluating the efficacy of push-dose VP in clinical scenarios other than the peri-intubation period, and assessing epinephrine – which is more readily available locally – in addition to phenylephrine, were also included. These studies were considered in the recommendation development process because they provided comparative data on the efficacy and safety profiles of sympathomimetic agents such as phenylephrine and epinephrine [Supplementary File 3].

All included studies were observational in design, and no separate tool was used for risk-of-bias assessment; instead, because most were single-arm observational studies, all were considered to have a high-risk-of-bias. Summaries of the studies are presented in Supplementary File 4.

Overview of the studies and outcome measures

There are no RCTs that directly compare the use of push-dose VP during RSI in critically ill patients at risk of hypotension. Instead, the majority of the studies included for evaluation consist of observational studies or secondary analyses of previously conducted RCTs.

Studies evaluating the effectiveness of push-dose vasopressors during the peri-intubation period

Of the seven studies evaluating the effectiveness of push-dose VP during the RSI procedure, five were single-arm observational studies with limited sample sizes.[47-51] In all of these studies, changes in vital signs – primarily blood pressure – before and after push-dose VP administration were assessed. When the results were evaluated, it was generally observed that clinically meaningful increases in blood pressure (approximately 10–20 mmHg) were achieved after administration compared with baseline. However, adverse events such as arrhythmias and rebound hypertension were also reported at varying frequencies within these patient series. Because these studies lacked comparator arms, it is not possible to determine with certainty whether these adverse event rates – and similarly the observed effectiveness – were attributable specifically to push-dose VP administration.

One of the remaining two studies was a secondary analysis reported by Fuchita *et al.*,[52] based on cohorts from two previously conducted RCTs.[52] In this study, two groups – those who did and did not receive push-dose VP – were created using propensity score matching to evaluate the effectiveness of push-dose VP. The authors reported that hypotension occurred more frequently in the group in which a VP infusion was initiated after push-dose VP compared with the group that did not receive any VP (53% vs. 41%, $P = 0.02$). However, as also noted by the authors, this finding may primarily reflect substantial selection bias. In both underlying RCTs, no standardized protocol for VP use was defined; instead, the decision to initiate VP therapy was left to the clinician discretion. Therefore, despite the use of propensity score matching to mitigate this bias, it is possible that patients who received VP were inherently more severely ill, which may have driven this result.

The final study evaluating the effectiveness of push-dose VP during RSI was the retrospective study by Schmitt *et al.*,[53] which was based on a secondary analysis of

2 years of intubation registry data.[53] In this study, bolus, infusion, and combined (bolus + infusion) VP administration groups created using propensity score matching were compared. The rate of poor outcomes was reported to be lower in the bolus VP group compared with the other two groups (80% vs. 88%; $P < 0.01$).

In most of the evaluated studies, phenylephrine was used. When dosing and frequency were assessed, phenylephrine was generally prepared by adding 1000 μg of phenylephrine to a 10-mL syringe to obtain a concentration of 100 μg/mL. The most commonly described approach in the literature involves administering a 100–200 μg phenylephrine bolus (1–2 mL of the prepared solution), followed by repeat dosing after 1–2 min if needed. However, this agent is not widely available in Türkiye. Therefore, the effectiveness of push-dose epinephrine, which can be used as an alternative to phenylephrine in Türkiye, was discussed by additionally including the studies summarized below.

Studies evaluating the use of push-dose epinephrine and phenylephrine in non–peri-intubation scenarios

In two separate studies evaluating data from ICU and ED patients who were hypotensive and critically ill and received push-dose phenylephrine or epinephrine for the management of hypotension, both agents were reported to produce significant increases in blood pressure; however, in both studies, the magnitude of this effect was greater with epinephrine than with phenylephrine.[54,55] However, in the study by Singer *et al.*,[54] epinephrine was reported to be associated with a higher incidence of adverse effects such as hypertensive episodes and tachycardia. In the study by Nam *et al.*,[55] dosing errors were reported to occur more frequently with epinephrine than with phenylephrine. Finally, in the study by Nawrocki *et al.*,[56] epinephrine administered as bolus therapy in critically ill hypotensive patients was reported to increase blood pressure to a clinically acceptable extent, while a lower rate of adverse events (approximately 2%) was reported compared with other studies.[56]

When the doses used were evaluated, all studies reported the administration of 10–20 μg (1:100,000) bolus epinephrine every 2 min.

Conclusion

The current literature provides insufficient evidence regarding the efficacy and safety of push-dose VP use. Although the panel has chosen not to issue a recommendation on this topic, it is a reality that push-dose VP therapy is used in some clinician-dependent practices. Based on this, the panel considers that, in critically ill patients who are hypotensive or at risk of hypotension, the decision of whether to administer push-dose VPs during the RSI procedure should be determined by each institution according to its own local clinical policy. If a local clinical policy decision is made to administer push-dose VP, the route of administration and dosing recommendations should be clearly specified in that policy. The recommended dosing varies depending on the selected agent (phenylephrine or epinephrine); however, in the available studies, dose ranges of 100–200 μg for phenylephrine and 10–20 μg for epinephrine have been used. Because phenylephrine is not widely available in Türkiye, low-dose epinephrine, which can provide similar hemodynamic responses, may be used as an alternative. If implemented, the panel recommends administering epinephrine at a dose of 10 μg, intravenously, as a push-dose over 1 min.

Scenario-5

In the ED management of adult patients at risk of increased intracranial pressure, is the use of ketamine during RSI a safe option [Table 6]?

Rationale and background

Severe acute brain injury (ABI) is frequently encountered in the ED in conditions such as traumatic brain injury, subarachnoid hemorrhage, intracerebral hemorrhage, acute ischemic stroke, and hypoxic brain injury, and due to the potential for increased intracranial pressure (ICP), the risk of secondary cerebral injury and poor prognosis is always present in this patient population.[57] In the ED management of patients with severe ABI, RSI is often required both to protect the airway and to prevent secondary brain injury. Among the induction agents commonly used during RSI in the ED is ketamine, an N-methyl-D-aspartate receptor antagonist. However, based on the findings of a few historically limited studies, the concern that ketamine may increase ICP remains widespread among clinicians.[58,59] Although several more recent studies have reported findings contrary to

Table 6: Scenario-5

Scenario-5 Ketamine use in patients at risk of increased intracranial pressure	
In the emergency department management of adult patients at risk of increased intracranial pressure, is ketamine use during rapid sequence intubation a safe option?	
Levels of recommendation and recommendations	**Level of evidence**
Moderate against	
Concerns that ketamine use during rapid sequence intubation causes an increase in intracranial pressure in patients with acute brain injury who are at risk of elevated intracranial pressure are anecdotal, and the current literature does not support this concern. Therefore, we do not support avoiding ketamine solely due to concerns about increased intracranial pressure	Very low

this concern, differing opinions persist regarding the use of ketamine during RSI, particularly in patients with severe ABI.[60,61] This guideline aims to provide evidence-based recommendations regarding the use of ketamine as an induction agent during RSI for emergency physicians managing patients with acute ABI in the ED. This guideline does not compare effectiveness across different clinical conditions.

Study selection

A systematic literature search conducted using the relevant keywords [Supplementary File 2] identified 85 articles. Of these, a total of 18 articles relevant to the research question were included for final evaluation; 7 had an RCT design, while the remaining 11 were observational studies [Supplementary File 3, at the end of the document].

Although all observational studies were considered to have a high-risk-of-bias, the risk-of-bias assessment performed using the Cochrane RoB 2 tool for the RCTs demonstrated that all 7 RCTs also had a high-risk-of-bias [Figure 13]. In answering the relevant clinical question, RCTs were taken as the primary evidence base; however, due to issues of indirectness related to population and outcomes in these studies, the main findings of the observational studies were also taken into consideration. Summaries of the included studies are presented in Supplementary File 4.

Figure 13: Traffic light plots of randomized clinical trials evaluating the use of ketamine during rapid sequence intubation in patients with acute brain injury at risk of increased intracranial pressure (RoB 2 risk-of-bias assessment)

Overview of the studies and outcome measures

None of the RCTs or observational studies fully address our research question. In none of the available RCTs were patients who were at risk of increased ICP and underwent RSI directly defined as the study population. Instead, in five RCTs, the effects of ketamine administered as a continuous infusion for sedation on ICP were evaluated in intubated patients with ICP elevation due to ABI.[61-65] In four of these five studies, ketamine administered as a continuous infusion for sedation was compared with opioids (fentanyl or sufentanil) also administered as continuous infusions [Figure 14a]. Similarly, in four studies, continuous ICP monitoring through intraventricular catheters was performed and reported in all patients. As common outcomes suitable for meta-analysis, ICP and CPP values measured at the end of the 1st day of infusion were accepted. Based on the meta-analysis results, ketamine infusion administered for sedation did not have an adverse effect on ICP or CPP compared with opioid infusion (for ICP: mean difference: 0.78 mmHg, 95% CI: 1.87-0.31; for CPP: mean difference: 1.07 mmHg, 95% CI: 7.95–5.80) [Figure 14b].

In the RCT conducted by Burman *et al*.,[65] intubated patients with severe ABI (GCS < 8) who were sedated with fentanyl and midazolam were randomized to receive additional sedation with a ketamine infusion or placebo.[65] In both treatment arms, continuous monitoring of ICP and CPP was performed through an intraventricular catheter throughout the 36-h infusion period. The authors reported that ICP values in the ketamine group generally tended to be lower than those in the placebo group, with this difference reaching statistical significance at the 4–6-h time points. Similarly, CPP values were generally higher in the ketamine group, and this difference was also statistically significant during the 4–6-h interval. Because the study did not report overall mean ICP and CPP values, its data could not be included in the meta-analysis.

Although their study populations do not directly represent patients with established intracranial hypertension, the results of two RCTs were also considered in this guideline, because both studies involved direct measurement of ICP and reported early postketamine ICP data in a manner analogous to the early phase of an RSI procedure.[66,67] In the study by Ben Yehuda *et al*.,[67] published in 2006, a total of 39 pediatric patients undergoing lumbar puncture (LP) for suspected meningitis were randomized to receive

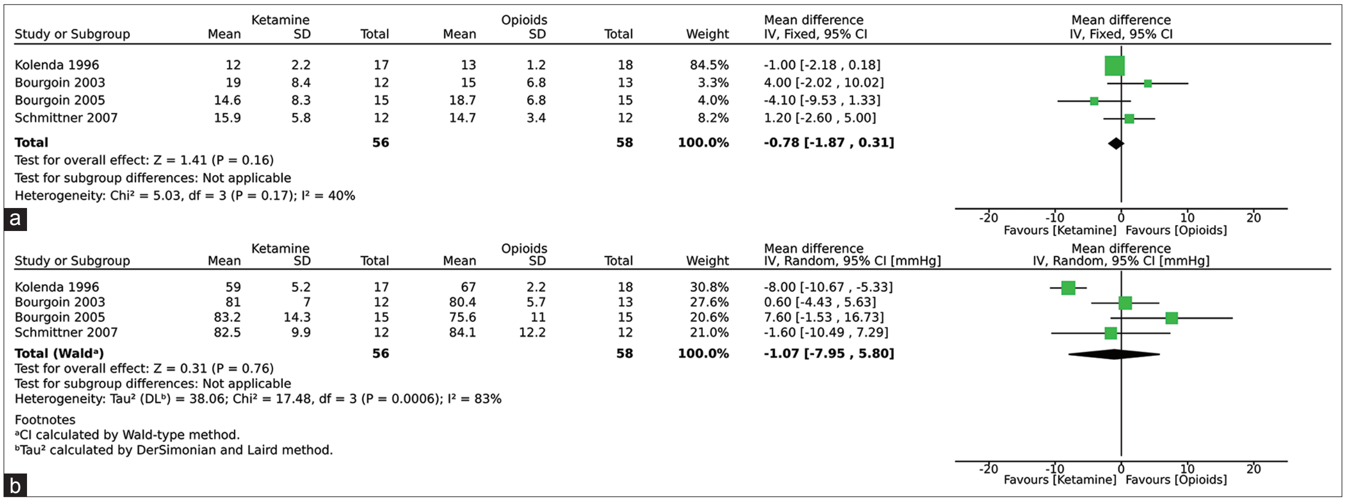

Figure 14: Forest plots showing the meta-analysis results of randomized clinical trials comparing the effects of ketamine infusion versus opioid infusion used for sedation on intracranial pressure (a) and cerebral perfusion pressure (b) in intubated patients with acute brain injury and elevated intracranial pressure. SD: Standard deviation, IV: Inverse variance, CI: Confidence interval

either ketamine + midazolam or midazolam alone for procedural sedoanalgesia.[67] The primary outcome was the post-LP opening pressure. The ketamine + midazolam group demonstrated a higher opening pressure compared with the midazolam-only group (24.4 ± 8.87 mmHg vs. 20 ± 3.74 mmHg). Similarly, in the RCT conducted by Michalczyk *et al*.,[66] sedation regimens were compared in 25 pediatric oncology patients undergoing a total of 84 LP procedures as part of their diagnostic follow-up.[66] Patients were assigned to one of three sedation strategies: ketamine + midazolam, propofol + fentanyl, or ketamine alone. The primary outcome was again post-LP opening pressure. In this study, the group receiving ketamine alone had significantly higher opening pressure values compared with the other two groups.

Eleven observational studies evaluating the effects of ketamine in ABI patients with suspected increased ICP were also assessed in this guideline. In seven of these studies, the study population consisted of patients with ABI who underwent RSI, and ketamine was compared with other agents as an induction agent. Although ICP or cerebral perfusion pressure were not defined as outcome measures in any of these studies, ketamine was reported to have no more adverse effects compared with other agents in the reported outcomes, including mortality, neurological outcomes, first-pass intubation success, and hemodynamic parameters.[68-73] Only in the study by Fouche *et al*.[74] was a higher incidence of postintubation hypotension reported in the ketamine group.[74] In the remaining four observational studies, patients undergoing RSI were not specifically defined as the study population; instead, the effects of ketamine used for sedation in intubated ABI patients were evaluated by monitoring ICP changes with continuous ICP monitoring. When the main results of these studies were examined, either no significant change in ICP and cerebral perfusion pressure values was observed, or ketamine was reported to have a favorable effect, particularly on cerebral perfusion pressure values.[75-78] [Supplementary File 4].

Conclusion

As discussed in detail above, although the available studies are at high-risk-of-bias and most were not conducted in an RSI scenario, there is no evidence to suggest that intravenous ketamine causes a greater increase in ICP compared with other agents or worsens neurological or other clinical outcomes in patients with ABI and suspected elevated ICP. Only two studies conducted in a pediatric population without ABI reported higher LP opening pressures. Therefore, we believe that there is no need to specifically avoid the use of ketamine as an induction agent during RSI in this patient group. However, clinicians should take into account that the available evidence is highly indirect and that there are no low-risk-of-bias RCTs conducted in patients at risk of increased ICP undergoing RSI. GRADE evidence certainty tables for the included studies are presented in Supplementary File 5.

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Author contributions statement

Authorship provides credit for a researcher's contributions to a study and carries accountability. All authors listed in this manuscript fulfil the authorship criteria recommended by the International Committee of Medical Journal Editors (ICMJE). Each author has made substantial contributions to the conception and/or design of the work; or the acquisition, analysis, and/or interpretation of data; or the creation of new software used in the work; or has drafted the work or substantively revised it for important intellectual content.

All authors have approved the submitted version (and any substantially modified version that involves the author's contribution to the study) and agreed to be personally accountable for their own contributions. In addition, all authors ensure that questions related to the accuracy or integrity of any part of the work, even those in which the author was not personally involved, are appropriately investigated, resolved, and documented in the literature.

CRediT roles: ŞKÇ: Conceptualization (equal); data curation (lead); investigation (lead); methodology (equal); project administration (equal); software (equal); supervision (equal); validation (lead); visualization (equal); writing – original draft (equal); writing – review and editing (lead). GA: Conceptualization (equal); data curation (supporting); formal analysis (lead); investigation (equal); methodology (lead); project administration (equal); resources (lead); software (lead); supervision (equal); validation (supporting); visualization (lead); writing – original draft (equal); writing – review and editing (lead). BB: Conceptualization (supporting); methodology (supporting); supervision (supporting); writing – review and editing (supporting). EA: Formal analysis (supporting); resources (supporting); visualization (supporting); writing – review and editing (supporting). FD: Conceptualization (supporting); data curation (supporting); investigation (supporting); resources (supporting); software (supporting); visualization (supporting); writing – original draft (supporting); writing – review and editing (lead). FSD: Formal analysis (supporting); investigation (supporting); supervision (supporting). EÜ: Resources (supporting); visualization (supporting). MMİ: Data curation (supporting); software (supporting); supervision (supporting). EK: Formal analysis (supporting); investigation (supporting); software (supporting). AŞ: Formal analysis (supporting); investigation (supporting); methodology (supporting); validation (supporting); writing – original draft (supporting). MK: Validation (supporting). GBB: Formal analysis (supporting). FNK: Data curation (supporting); resources (supporting); validation (supporting); visualization (supporting); writing – original draft (supporting). MOS: Data curation (supporting); resources (supporting); visualization (supporting). VA: Resources (supporting). HA: Conceptualization (supporting); investigation (supporting); methodology (supporting). Bİ: Validation (supporting). MEÇ: Resources (supporting). DD: Resources (supporting). RÇ: Data curation (supporting); resources (supporting); writing – original draft (supporting). İS: Validation (supporting). ENA: Data curation (supporting). ACT: Formal analysis (supporting). YHT: Resources (supporting). Funding acquisition: None.

Conflicts of interest

None Declared.

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