The effect of cricoid pressure on tracheal intubation in adult patients: a systematic review and meta-analysis

Effet de l'application d'une pression cricoïdienne sur l'intubation trachéale chez les patients adultes : revue systématique et méta-analyse

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Abstract

Purpose This meta-analysis aimed to assess the impact of cricoid pressure (CP) application on intubation outcomes.

Source Electronic databases (i.e., MEDLINE, PubMed, Embase, and Cochrane review) were searched from inception to 2 June 2020 for randomized-controlled trials that assessed the intubation outcomes in adult patients

using laryngoscopic approaches with and without the application of CP (i.e., CP vs non-CP group). The primary outcome was the successful first-attempt intubation rate (SFAIR), and the secondary outcomes were intubation time, incidences of poor laryngoscopic views (i.e., Cormack and Lehane grade 3-4), airway complications, and pulmonary aspiration.

Principal findings A total of five trials (published from 2005 to 2018) were included, and all tracheal intubations were performed by anesthesiologists or nurse anesthetists with a video ($n = 3$) or Macintosh laryngoscope ($n = 2$) in the operating room. We found no significant difference in

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SFAIR (risk ratio [RR], 0.98; $P = 0.37$), incidence of poor laryngoscopic views (RR, 1.49; $P = 0.21$), and risk of sore throat (RR, 1.17; $P = 0.73$) between the two groups. Nevertheless, the intubation time on the first successful attempt was slightly longer (weighted mean difference = 4.40 sec, $P = 0.002$) and risk of hoarseness was higher (RR, 1.70; $P = 0.03$) in the CP group compared with in the non-CP group. The secondary outcome “pulmonary aspiration” was not analyzed because only one trial was available.

Conclusion The application of CP did not have a negative impact on the SFAIR or laryngoscopic view. Nevertheless, this maneuver may slightly prolong intubation time and increase the risk of postoperative hoarseness.

Résumé

Objectif Cette méta-analyse a pour but d'évaluer l'impact de l'application d'une pression cricoïdienne (PC) sur les résultats de l'intubation.

Source Les bases de données électroniques (c.-à-d., MEDLINE, PubMed, Embase, et Cochrane review) ont été examinées de leur création jusqu'au 2 juin 2020 pour en tirer les études randomisées contrôlées évaluant les résultats d'intubation chez les patients adultes utilisant des approches laryngoscopiques avec ou sans application de PC (soit groupe PC et non-PC). Le critère d'évaluation principal était le taux d'intubations réussies à la première tentative, et les critères secondaires incluaient le temps d'intubation, l'incidence de mauvaises vues laryngoscopiques (grades 3-4 de Cormack et Lehane), les complications au niveau des voies aériennes et l'aspiration pulmonaire.

Constatations principales Cinq études au total (publiées entre 2005 et 2018) ont été incluses, et toutes les intubations trachéales ont été réalisées par des anesthésiologistes ou infirmiers anesthésistes à l'aide d'un vidéolaryngoscope ($n = 3$) ou d'une lame de Macintosh ($n = 2$) en salle d'opération. Nous n'avons trouvé aucune différence significative dans le taux d'intubations réussies à la première tentative (risque relatif [RR], 0,98; $P = 0,37$), dans l'incidence de mauvaises vues laryngoscopiques (RR, 1,49; $P = 0,21$) ou dans le risque de maux de gorge (RR, 1,17; $P = 0,73$) entre les deux groupes. En revanche, le temps d'intubation lors de la première tentative réussie était légèrement plus long (différence moyenne pondérée = 4,40 sec, $P = 0,002$) et le risque d'enrouement était plus élevé (RR, 1,70; $P = 0,03$) dans le groupe PC que dans le groupe non-PC. Le critère d'évaluation secondaire « aspiration pulmonaire » n'a pas été analysé parce qu'une seule étude le mesurait.

Conclusion L'application de PC n'a pas eu d'impact négatif sur le taux d'intubations réussies à la première tentative ou la vue laryngoscopique. Par contre, cette manœuvre pourrait légèrement prolonger le temps

d'intubation et augmenter le risque d'enrouement postopératoire.

Keywords cricoid pressure · Sellick maneuver · intubation · rapid sequence intubation

Pulmonary aspiration (PA) from regurgitation of gastric contents, which is a rare complication during the perioperative period, may be associated with postoperative mortality or pulmonary morbidity. The incidence of aspiration pneumonia has been reported to range from one in 2,131 to one in 3,216 anesthetics^{1,2}; the mortality rate may be up to 5% when aspiration occurs during anesthesia.² Induction of anesthesia leads to a loss of protective upper airway reflexes, which may subsequently increase the risk of PA.¹ In support of this finding, a previous study on 83 surgical patients with perioperative PA showed that most incidents (47.1%) occurred during anesthesia induction.² Current strategies regarding the prevention of PA during the induction of anesthesia include adherence to the fasting guidelines, the use of pharmacotherapy (e.g., H_2 receptor antagonists), rapid sequence induction/intubation (RSI), and identification of predisposing factors such as pregnancy or morbid obesity.³ For patients with a high risk of PA, RSI is recommended to minimize the risk of aspiration with the application of cricoid pressure (CP) (known as the Sellick maneuver). The purpose of CP is to occlude the esophagus by compressing the cricoid cartilage against the fifth cervical vertebra, thereby preventing passive regurgitation of gastric content to the oropharynx.^{4,5} Another advantage of applying CP includes the prevention of gastric insufflation during mask ventilation.⁶

To date, there has been controversy regarding the effectiveness of CP in preventing gastric regurgitation.^{7,8} The application of CP has been reported to increase the risk of difficult intubation,^{9–11} and multiple tracheal intubation attempts may amplify the risk of PA or other complications (e.g., esophageal intubation).^{2,12,13} To add to the confusion, the American Heart Association Advanced Cardiac Life Support guidelines state that although CP may offer some airway protection against aspiration and gastric insufflation during bag ventilation, it may impede ventilation and interfere with the placement of advanced airways.¹⁴ Nevertheless, there are no current clinical guidelines on the application of CP in routine practice. To address this issue, we conducted a systematic review and meta-analysis to evaluate the association between CP and intubation outcomes. The primary outcome was to compare the successful first-attempt intubation rate (SFAIR) in adult patients with and without the application of CP. The

secondary outcomes were the time to successful intubation, rate of poor laryngoscopic views according to the Cormack and Lehane grade (CL grade), as well as the incidences of airway complications and PA.

Methods

The review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines.¹⁵ The predefined review protocol was registered at the PROSPERO international prospective register of systematic reviews (registration number CRD42020173682, registered on 24 March 2020).

Data sources, search strategy, and study selection

Two authors (K.C.H. and C.T.H.) independently searched MEDLINE, PubMed, EMBASE, and Cochrane Controlled Trials Register (CENTRAL) for randomized-controlled trials (RCTs) that compared SFAIRs with and without the application of CP during tracheal intubation. The last search was performed on 2 June 2020. To identify relevant articles, searches were performed using the keywords “tracheal intubation”, “rapid sequence induction”, “rapid sequence intubation”, “cricoid pressure”, “RSI”, and “Sellick maneuver” as medical subject headings components and text words. Results were combined using the Boolean operator “AND” with the search terms. We limited publications to those published in English, while the publication year was not limited. Two authors (K.C.H. and C.T.H.) independently examined the titles and abstracts, and another two authors (C.K.S. and M.H.C.) reviewed the retrieved articles to determine their suitability for inclusion according to the criteria described below. Any discrepancies in the study selection were resolved through discussion; or, if necessary, by consulting another author (Y.Y.P.) to make a final decision. The bibliographic lists of relevant articles and reviews were also searched for further trials that were potentially eligible.

Inclusion and exclusion criteria

The inclusion criteria for this meta-analysis were: 1) RCTs, 2) adult participants (≥ 18 yr) who received tracheal intubation with Macintosh laryngoscopes or video laryngoscopes, regardless of the induction technique (i.e., RSI or non-RSI), and 3) SFAIRs reported in a CP group and compared with those of the control group (non-CP group), in which a sham technique was used during tracheal intubation. Exclusion criteria were: 1) pediatric studies, and 2) patients with cervical spine disease or

injury. We also excluded mannequin studies, before-after studies, abstract publications, conference presentations, crossover trials, case reports, and reviews.

Data collection

Data were extracted from each study separately by two researchers (K.C.H. and C.T.H.), and discrepancies were discussed until an agreement was attained. If data were not reported in the retrieved studies, we asked the authors to provide the missing data. If a response was not given, the article was excluded. The extracted data included the name of the first author, year of publication, number of participants, patient characteristics and clinical information, anesthesia-related data (e.g., airway devices), study design, and outcomes. For categorical outcomes, the number of patients and events in both arms were extracted. For continuous outcomes, the numbers of patients in both CP and non-CP groups as well as the mean and standard deviation of the data included in the eligible studies were extracted.

Risk of bias assessment

Two authors (C.K.S. and M.H.C.) independently assessed the risk of bias of the included studies, and any disputes were resolved by consensus. The Cochrane Risk of Bias tool (RoB 2.0) was used for assessing the risk of bias.¹⁶ The Cochrane tool assesses five domains, including bias arising from the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. For each domain, bias was classified as either low, uncertain, or high. The overall risk of bias judgement was then determined by the worst judgement of any single domain. A risk of bias graph was constructed to present the results.

Primary and secondary outcomes

The primary outcome was the SFAIR. Secondary outcomes were intubation time on the first successful attempt as well as the incidences of poor laryngoscopic views (i.e., CL grades 3 or 4), laryngo-pharyngeal complications (i.e., sore throat and hoarseness), and PA.

Statistical analysis

Data from individual clinical studies adopting an intention-to-treat design were used for this meta-analysis. We used the Cochrane Review Manager (RevMan 5.3; Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) for data synthesis and analysis. A random effects

model that used the DerSimonian and Laird method was applied when pooling individual estimates. For dichotomous outcomes (e.g., SFAIR), the selected effect size was the risk ratio (RR) with the 95% confidence interval (CI) calculated from the 2×2 cross-table. For continuous outcome (i.e., intubation time), the selected effect size was the weighted mean difference (WMD). We did not select the standardized mean difference because the units of continuous outcome were identical in the included studies.

The I^2 statistics was utilized for heterogeneity assessment, where a value greater than 0.5 suggests substantial heterogeneity among studies.¹⁷ Sources of heterogeneity among studies were explored by prespecified subgroup analyses on the intubation devices selected (i.e., direct vs indirect laryngoscopy). We performed sensitivity analyses to explore the potential impact of a single trial on the overall results by omitting the trials from the meta-analysis one at a time. To assess the potential for publication bias, a funnel plot was visually checked for symmetry and Egger's test was performed using Comprehensive Meta-Analysis software v3 (CMA v3, Biostat, Inc., USA). The significance level was set at 0.05 for all analyses.

Results

Literature search

Figure 1 is the PRISMA flow diagram that summarizes the reasons for the exclusion of records. Of a total of 1,518 potentially eligible reports retrieved from the database

search, 624 records were removed as they were duplicates. We then excluded 878 records after the initial review of the title and abstract. Overall, 16 studies were considered relevant and the full text was read. Another 11 articles were excluded because of a crossover design ($n = 2$), tracheal intubation without the use of laryngoscopic approach ($n = 6$), non-RCT ($n = 1$), mere description of a study protocol ($n = 1$), and lack of data on the SFAIR ($n = 1$). Finally, a total of five full-text randomized trials (published between 2005 and 2018)^{11,18–21} were included in the current meta-analysis (Fig. 1).

Characteristics of trials and patients

The Table presents the characteristics of the five included studies. All studies were conducted in the operating room. Four studies^{11,18–20} included patients without risks for aspiration and difficult airway scheduled for elective surgery without RSI during anesthetic induction. A trial that investigated 3,471 patients with risk for aspiration undergoing elective or emergent surgery with RSI reported intermediate risk for difficult intubation in up to approximately one third of patients.²¹ Two studies^{11,21} specifically applied the bimanual technique (i.e., the assistant's hand was placed behind the neck) during airway management and two studies^{18,19} adopted the one-hand technique, while one study did not specify the technique.²⁰ Intubations were performed via the oral route in operating theaters with the use of neuromuscular blocking agents. In terms of intubators, while tracheal intubations were exclusively performed by anesthesiologists in four studies,^{11,18–20} nurse anesthetists were responsible for 66% of the intubations, with the rest

Fig. 1 Meta-analysis flowchart for selecting eligible studies

Table Characteristics of the five randomized trials included in the meta-analysis

Author and year	Sample size	ASA	Male (%)	AR	RDA	RSI	Head position*	Muscle relaxants	Setting	CP	CP technique	CP training†	Airway devices
Birenbaum 2019 ²¹	3,471	NA	51	MH	Moderate	Yes	Sniff	Succinylcholine	OR	30 N	Bimanual	Yes	Macintosh laryngoscope
Komasawa 2016 ¹¹	60	I–III	28.3	Low	Low	No	Neutral	Rocuronium	OR	30 N	Bimanual‡	Yes	Pentax AWS TM
Komasawa 2017 ²⁰	60	NA	58.3	Low	Low	No	Sniff	Rocuronium	OR	30 N	NA	NA	McGrath TM
Kumar 2011 ¹⁹	50	I–II	24	Low	Low	No	Neutral	Vecuronium	OR	40 N	Single-hand	Yes	Truview Evo2 TM blade
Turgeon 2005 ¹⁸	700	I–III	49.7	Low	Low	No	Sniff	Rocuronium**	OR	30 N	Single-hand	Yes	Macintosh laryngoscope

American Society of Anesthesiologists (ASA) physical status; AR = aspiration risk; CP = cricoid pressure; NA = not available; OR = operating room; RDA = risk of difficult airway; RSI = rapid sequence induction. *Head position during airway manipulation; †Assistants were trained to perform cricoid pressure before the study; ‡cricoid pressure with support of the neck; **Rocuronium or rocuronium combined with succinylcholine; N = Newtons

being undertaken by anesthesiologists in one large trial.²¹ The SFAIR and intubation time were reported in all studies. CL grades 3/4, laryngo-pharyngeal complications, and aspiration pneumonia were reported in four, two, and one of the studies, respectively. The secondary outcome “aspiration pneumonia” was not analyzed because only one study²¹ was available.

Risk of bias

The risks of bias of individual studies and the overall risk of bias are summarized in Fig. 2 and Fig. 3, respectively. All included studies were found to give sufficient details

about randomization and assigned a low risk of allocation bias. Besides, because all studies adopted methods to keep both the intubators and the investigators unaware of the patient’s CP or non-CP status, the risk of performance bias was considered low. Other risks of bias including attrition bias, measurement bias, reporting bias, and overall bias were also considered to be low. Additional details regarding the risks of bias are provided in the Electronic Supplementary Material (ESM) eTable 1.

Outcomes

Successful first-attempt intubation rate

Five studies with a total of 4,341 patients including 2,164 in the CP group and 2,177 in the non-CP group were available for analysis.^{11,18–21} A forest plot is presented in Fig. 4. Pooled analysis showed that the SFAIR was not significantly different between the CP and non-CP groups (RR, 0.98; 95% CI, 0.94 to 1.02; $P = 0.37$). The heterogeneity among studies was substantial ($I^2 = 59\%$). Subgroup analysis showed a lower SFAIR in the CP group than that in the non-CP group when indirect laryngoscopy was used, although the difference was of borderline significance ($P = 0.05$) (Fig. 4). Sensitivity analysis showed that this outcome was not significantly impacted by omitting certain trials (ESM eTable 2). The funnel plot showed apparent asymmetry with the Egger’s test, showing borderline significance ($P = 0.055$; ESM eFigure A), suggesting the possibility of publication bias.

Fig. 2 Risks of bias of individual studies

Fig. 3 Overall risks of bias of the five included studies **Fig. 4** Forest plot for the successful first-attempt intubation rate between cricoid pressure (CP) groups and non-CP groups. CI = confidence interval; M-H = Mantel-Haenszel; RR = risk ratios

Time to successful intubation

Five studies with a total of 4,341 patients including 2,164 in the CP group and 2,177 in the non-CP group analyzed the intubation time.^{11,18–21} The definition of “intubation time” varied among the included studies. Two studies measured intubation time from oral laryngoscope insertion to inflation of the tracheal tube cuff,^{18,21} while two studies defined intubation time as the time between the handling of intubation devices and the first capnographic confirmation following intubation.^{11,20} One study reported intubation time as the period from picking up of the tracheal tube to removal of the intubation device from the mouth.¹⁹ A forest plot is presented in Fig. 5, which shows a slightly but

significantly longer intubation time on the first successful attempt in the CP group than that in the non-CP group (WMD, 4.40 sec; 95% CI, 1.59 to 7.21; $P = 0.002$). Pooled data synthesis for this outcome showed marked heterogeneity ($I^2 = 92\%$).

We undertook subgroup analysis by assessing the type of intubation device used (i.e., direct vs indirect laryngoscopy) (Fig. 5). Subgroup analysis showed that the impact of CP on intubation time was influenced by the intubation device selected. When direct laryngoscopy was used, there was no significant difference in intubation time between CP and non-CP groups (WMD, 2.31 sec; 95% CI, -0.33 to 4.96; $P = 0.09$) despite the high heterogeneity ($I^2 = 95\%$ for direct laryngoscopy and $I^2 = 85\%$ for indirect

Fig. 5 Forest plot for the time to successful intubation between CP groups and non-CP groups. CI = confidence interval; CP = cricoid pressure; IV = inverse variance; WMD = weighted mean difference

Fig. 6 Forest plot for the incidence of poor laryngoscopic views between CP groups and non-CP groups. CI = confidence interval; CP = cricoid pressure; M-H = Mantel–Haenszel; RR = risk ratios

Fig. 7 Forest plot for the incidence of postoperative hoarseness between CP and non-CP groups. CI = confidence interval; CP = cricoid pressure; M-H = Mantel–Haenszel; RR = risk ratios

laryngoscopy). Sensitivity analysis, by omitting certain studies, showed that the pooled effect became non-significant when a large trial²¹ was removed (WMD, 5.19 sec; 95% CI, -0.07 to 10.46) (ESM eTable 2). The funnel plot showed apparent asymmetry with a significant Egger's test ($P = 0.015$; ESM eFigure B).

Poor laryngoscopic view

Data regarding the incidence of poor laryngoscopic views were available in four trials.^{11,18,20,21} Although poor laryngoscopic views (i.e., CL grade 3–4) was not reported in two small-scale studies using video laryngoscopes, the authors reported significant differences

Fig. 8 Forest plot for the incidence of sore throat between CP groups and non-CP groups. CI = confidence interval; CP = cricoid pressure; M-H = Mantel-Haenszel; RR = risk ratios

in difficulty on transglottic passage of a tracheal tube with the application of CP.^{11,20} Of the two studies in which Macintosh laryngoscopes were selected, one large-scale study reported an increased incidence of poor laryngoscopic views after application of CP.²¹ Although the other study did not show an increased occurrence of poor laryngoscopic views, it showed an elevated incidence of lateral laryngeal shift with the application of CP.¹⁸

Pooled analysis of the incidence of poor laryngoscopic views in two studies^{18,21} including 4,280 patients revealed no significant difference between the CP and non-CP groups (RR, 1.49; 95% CI, 0.79 to 2.82; $P = 0.21$) (Fig. 6). The heterogeneity was substantial ($I^2 = 61\%$). Although a single large trial²¹ reported a higher incidence of poor laryngoscopic views in the CP group compared with in the non-CP group, a pooled analysis of the two studies^{18,21} in the present meta-analysis did not show significant differences between the two groups.

Laryngo-pharyngeal complications

Two studies with a total of 120 patients^{11,20} were included in the analysis on the incidence of sore throat or hoarseness. Pooled analysis showed a significantly higher incidence of hoarseness in the CP group than that in the non-CP group (RR, 1.70; 95% CI, 1.06 to 2.75; $P = 0.03$) (Fig. 7) with a low heterogeneity ($I^2 = 0\%$). On the other hand, the incidence of postoperative sore throat did not significantly differ between the CP and non-CP groups (RR, 1.17; 95% CI, 0.48 to 2.84; $P = 0.73$) (Fig. 8) with low to moderate heterogeneity ($I^2 = 44\%$).

Discussion

Tracheal intubation represents a complex interaction with regard to the clinical setting, patient factors, intubation devices used, and the skill of the individual performing the procedure. To evaluate the impact of CP on intubation outcomes, we assessed the SFAIR as the primary outcome. To the best of our knowledge, this is the first meta-analysis showing that application of CP did not affect the SFAIR,

the incidence of poor laryngoscopic views, or the risk of sore throat. Nevertheless, application of CP did slightly increase the intubation time and led to an increased risk of postoperative hoarseness. These results suggest that the use of CP may not impede tracheal intubation in experienced hands (i.e., anesthesiologists and nurse anesthetists) in a controlled anesthetic environment.

The rationale for our choosing the SFAIR as our primary outcome was that multiple intubation attempts in a non-operating room setting have been reported to increase airway complications (e.g., hypoxemia), risk of aspiration of gastric contents, and cardiac arrest.^{22–24} In addition, multiple tracheal intubations may potentiate bleeding, tissue trauma, and mucosal edema, which may lead to the scenario of “cannot ventilate, cannot intubate”.²⁵ In our study, there was no significant difference in the SFAIR between the CP and non-CP groups. Besides, there was no marked heterogeneity in the SFAIR among the included trials. Our findings, therefore, support the use of CP in the operating room setting when there are indications of an increased risk of aspiration. Nevertheless, the results should be treated with caution. First, our study only examined trials in the operating room setting and therefore may not be applicable to patients intubated in the intensive care unit (ICU) where different factors have to be taken into consideration (e.g., worse intubation conditions).²⁶ Indeed, the application of CP during tracheal intubation in the ICU setting has been reported to be as low as 36%,²⁷ suggesting that intensivists still have their concerns regarding the use of this maneuver in tracheal intubation. Second, subgroup analysis showed a lower SFAIR in the CP group than that in the non-CP group when indirect laryngoscopy was used, although the difference was of borderline significance ($P = 0.05$). Further large-scale studies are required to identify potential negative impacts of CP on the success rate with the use of a video laryngoscope.

Our study showed that the application of CP significantly increased the intubation time (WMD, 4.40 sec; 95% CI, 1.59 to 7.21; $P = 0.002$) (Fig. 5). This finding may be attributed to an association of CP with worse CL grades on performing direct laryngoscopy²¹ or increased

difficulty encountered during transglottic passage of tracheal tube using videolaryngoscopy.^{11,20} The increase in intubation time in our study was 4.40 sec, which might not be clinically significant in the operating room setting. Nevertheless, as respiratory failure and cardiopulmonary resuscitation are common indications for tracheal intubation among critically ill patients in the ICU,^{27,28} prolonged intubation time may be a concern in these patients who cannot tolerate even slightly prolonged apnea.

Our results regarding the intubation time should be interpreted with caution because of the high heterogeneity ($I^2 = 92\%$) among the included trials. The intubation devices used for tracheal intubation may partially contribute to this high heterogeneity. For example, Komasaawa *et al.* used a video laryngoscope for tracheal intubation and reported a longer intubation time compared with that in other trials.^{11,20} Previous studies have shown that tracheal intubation may fail because of impingement of the tube tip on the arytenoid cartilages during intubation with a video laryngoscope (i.e., Pentax-AWS) despite a clear view of the glottis.^{29,30} Komasaawa *et al.* also reported significant difficulty in transglottic tube passage,^{11,20} which may have contributed to the long intubation time in their studies. Nevertheless, we still found high heterogeneity in subgroup analysis irrespective of the intubation devices selected (Fig. 5). In addition to the difference in selected intubation devices, the high heterogeneity in intubation time may be multifactorial including discrepancies in the definitions of study parameters (e.g., intubation time), patient population (e.g., sex,³¹ risk of difficult airway), and experience of operators (e.g., anesthesiologists or nurse anesthetists). Therefore, the marked heterogeneity among the studies precluded the drawing of definite conclusions.

Although our study showed no evidence that the application of CP is related to poorer laryngoscopic views, this finding should be interpreted with caution. First, CP applied during Macintosh direct laryngoscopy has been reported to cause poorer laryngeal views in one of our included studies²¹ and other previous investigations.^{32,33} Although another included study with similar methodology did not report a positive association of CP with poor laryngoscopic views, an increased incidence of lateral laryngeal shift was noted by the intubators.¹⁸ On the other hand, although the laryngoscopic views may not be compromised when a video laryngoscope was used,^{11,20} CP-induced lateral shift of the larynx¹⁸ may cause difficulty in transglottic tube passage during indirect laryngoscopy.^{11,20} Large-scale studies are warranted to clarify the different impacts of CP application on airway management with direct or indirect laryngoscopy.

Our study showed that the application of CP significantly increased the risk of postoperative hoarseness (RR, 1.70; 95% CI, 1.06 to 2.75; $P = 0.03$),

but not the incidence of sore throat. The occurrence of postoperative hoarseness may be associated with a prolonged intubation time partially attributable to the difficulty in transglottic tube passage after application of CP in the studies by Komasaawa *et al.*^{11,20} Inconsistent with our results, one previous study reported a reduction in the risk of postoperative hoarseness associated with CP application.³⁴ The inclusion of only two trials assessing laryngo-pharyngeal complications following tracheal intubation in the present study may have biased our results.

Large randomized-controlled trials with a patient population more than 1,000 have traditionally been considered to be the “gold standard” for evaluating the reliability of clinical interventions.³⁵ Nevertheless, even discrepancies may exist among large trials³⁶ and nearly a quarter of meta-analyses showed disagreement with large trials.³⁵ A previous study also suggested that, instead of attempting to fit a common estimate among different studies, one important role of meta-analyses is to address potential sources of heterogeneity.³⁵ For instance, although the results of a large trial ($n = 3,471$)²¹ showed a significant difference in the incidence of poor laryngoscopic views between the CP and non-CP groups, the results became insignificant after merging the results of that trial with those of another smaller trial ($n = 700$) with similar methodology¹⁸ (Fig. 6). While most tracheal intubations were performed by nurse anesthetists in the former trial,²¹ only anesthesiologists were involved in tracheal intubation in the latter study.¹⁸ Therefore, this finding highlights the potential impact of operator skill on intubation outcomes with the application of CP. Furthermore, because the two large RCTs used direct laryngoscopy to arrive at their conclusions, data from other intubation approaches (e.g., videolaryngoscopy) cannot be elucidated. After incorporating the results from smaller trials, subgroup analysis showed a lower SFAIR in the CP group than in the non-CP group when indirect laryngoscopy was used, although the difference was of borderline significance ($P = 0.05$). Our results further underscore the ability of a meta-analysis to elucidate the complex interactions between CP application and intubation outcomes, which may not be discernible based on the evidence of a single large trial.²¹

Some limitations in this meta-analysis warrant further consideration. First, although we did not exclude the critical and emergency settings, all tracheal intubations in the included studies were performed in the operating room and most RCTs did not include patients with anticipated difficult airway or obesity (i.e., a risk factor for difficult airway management).³⁷ Therefore, the results may not be extrapolated to other clinical scenarios. Second, the existence of publication bias in the association between CP application and intubation time in the current study may

be attributed to the small number of included studies because some small studies with negative results may not have been submitted or accepted for publication. Third, our analysis could neither assess the individual impacts of operator experience and choice of intubation device nor differentiate their influences on intubation time. A previous meta-analysis on novice intubators showed a shorter intubation time with a video laryngoscope compared with that when they handled a Macintosh laryngoscope.³⁸ Fourth, the marked heterogeneity from pooled and subgroup analyses precluded a strong conclusion on the association between CP application and prolonged intubation time. Fifth, assessing the laryngeal views with CL grading may not be a sensitive measure as different glottic areas may fall within the same grade.³⁹ Using the scale on percentage of glottic opening may be a more useful research tool for quantifying laryngeal exposure.⁴⁰ Lastly, although CP was designed to prevent the aspiration of gastric contents, we did not analyze its effect on PA as only one trial was available in our study.

Conclusion

In summary, this meta-analysis shows that the application of CP in the operating room did not have a negative impact on the SFAIR or glottic visualization in the hands of anesthesiologists and nurse anesthetists. Nevertheless, taking into account that the application of CP carried the risk of a slightly prolonged intubation time (i.e., 4.40 sec), further studies are warranted to clarify the impact of this maneuver on intubation outcomes and risk of aspiration pneumonia in the non-operating room settings.

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