Comparing Effectiveness of Initial Airway Interventions for Out-of-Hospital Cardiac Arrest: A Systematic Review and Network Meta-analysis of Clinical Controlled Trials

Chih-Hung Wang, MD, PhD; An-Fu Lee, MD; Wei-Tien Chang, MD, PhD; Chien-Hua Huang, MD, PhD; Min-Shan Tsai, MD, PhD; Eric Chou, MD; Chien-Chang Lee, MD, ScD*; Shyr-Chyr Chen, MD; Wen-Jone Chen, MD, PhD

*Corresponding Author. E-mail: hit3transparency@gmail.com or cclee100@gmail.com.

Study objective: We compare effectiveness of different airway interventions during cardiopulmonary resuscitation for patients with out-of-hospital cardiac arrest.

Methods: We systematically searched the PubMed and EMBASE databases from their inception through August 2018 and selected randomized controlled trials or quasi randomized controlled trials comparing intubation, supraglottic airways, or bag-valve-mask ventilation for treating adult out-of-hospital cardiac arrest patients. We performed a network meta-analysis along with sensitivity analyses to investigate the influence of high intubation success rate on meta-analytic results.

Results: A total of 8 randomized controlled trials and 3 quasi randomized controlled trials were included in the network meta-analysis: 7,361 patients received intubation, 7,475 received supraglottic airway, and 1,201 received bag-valve-mask ventilation. The network meta-analysis indicated no differences among these interventions for survival or neurologic outcomes at hospital discharge. Rather, network meta-analysis suggested that supraglottic airway improved the rate of return of spontaneous circulation compared with intubation (odds ratio 1.11; 95% confidence interval 1.03 to 1.20) or bag-valve-mask ventilation (odds ratio 1.35; 95% confidence interval 1.11 to 1.63). Furthermore, intubation improved the rate of return of spontaneous circulation compared with bag-valve-mask ventilation (odds ratio 1.21; 95% confidence interval 1.01 to 1.44). The sensitivity analyses revealed that the meta-analytic results were sensitive to the intubation success rates across different out-of-hospital care systems.

Conclusion: Although there were no differences in long-term survival or neurologic outcome among these airway interventions, these system-based comparisons demonstrated that supraglottic airway was better than intubation or bag-valve-mask ventilation and intubation was better than bag-valve-mask ventilation in improving return of spontaneous circulation. The intubation success rate greatly influenced the meta-analytic results, and therefore these comparison results should be interpreted with these system differences in mind. [Ann Emerg Med. 2020;75:627-636.]

Please see page 628 for the Editor's Capsule Summary of this article.

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SEE EDITORIAL, P. 637.

INTRODUCTION

Background

Out-of-hospital cardiac arrest affects approximately 28 to 44 people per 100,000 population annually,[1] resulting in poor outcomes.[2] Intubation is often regarded as an integral part of the standard of care for resuscitating critically ill patients. Nonetheless, since 2010, the use of intubation for out-of-hospital cardiac arrest patients has been deemphasized[3] because it may interrupt chest compression during cardiopulmonary resuscitation (CPR).[4]

The 2015 guidelines[5,6] suggest that the intubation can be deferred until the return of spontaneous circulation, and the bag-valve-mask ventilation can be continued throughout the entire CPR process.[7,8] Nevertheless, the effective use of bag-valve-mask ventilation is challenging, even for skilled clinicians.[9] Alternatively, a supraglottic airway may be used to provide better oxygenation and ventilation than can be provided by bag-valve-mask ventilation.[5,6] When rescuers are proficient in using all 3 of

Editor's Capsule Summary

What is already known on this topic

Several randomized clinical trials and quasi randomized controlled trials make pairwise comparisons between intubation, supraglottic airways, and bag-valve-mask ventilation in out-of-hospital cardiac arrest.

What question this study addressed

How do these 3 techniques compare in regard to survival?

What this study adds to our knowledge

Systematic review and network meta-analysis of 11 studies involving 16,225 patients found that supraglottic airway was associated with higher rates of return of spontaneous circulation but not other outcomes, including survival and neurologic status. In a ranking probability analysis, supraglottic airway was the preferred airway intervention.

How this is relevant to clinical practice

Medical directors and policymakers may use these data to guide airway management strategies in out-of-hospital cardiac arrest. Intubation success is an important consideration.

these airway interventions, bag-valve-mask ventilation, supraglottic airway, and intubation can be used interchangeably during CPR; however, the evidence supporting this strategy is limited.[5,6]

Importance

Because of the importance of airway management during CPR, many studies have been performed to compare different airway intervention strategies. Previous meta-analyses of observational studies[10-12] suggested that bag-valve-mask ventilation was better than intubation or supraglottic airway, and intubation was better than supraglottic airway in regard to improving the outcomes of out-of-hospital cardiac arrest patients. Although most observational studies[10-12] have used advanced statistical methods to account for confounding factors, the effects of unmeasured factors could not be adjusted, leading to potential biases when the meta-analytic results were interpreted.[10-12] Moreover, those meta-analyses[10-12] conducted only pairwise comparisons, the results of which could not be easily applied in clinical practice because clinicians have 3 alternative airway interventions from which to choose when conducting CPR for out-of-hospital cardiac arrest patients.

Goals of This Investigation

Given that the results of several large-scale randomized controlled trials have already been published, we performed a network meta-analysis of clinical trials to compare different initial airway interventions for out-of-hospital cardiac arrest patients in improving survival and neurologic outcomes.

MATERIALS AND METHODS

The current systematic review and network meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses Extension Statement for Reporting of Systematic Reviews Incorporating Network Meta-analyses of Health Care Interventions[13] and was registered in PROSPERO. Two investigators (C.-H.W. and A.-F.L.) independently searched the PubMed and EMBASE databases from inception through August 31, 2018. The search strings were as follows: PubMed, ((((airway management) OR Intubation) OR Supraglottic airway) OR Bag-valve-mask) OR Bag-mask AND (cardiac arrest) OR cardiopulmonary resuscitation; and EMBASE, "airway management" OR intubation OR "supraglottic airway" OR "bag-valve-mask" OR "bag-mask" AND "cardiac arrest" OR "cardiopulmonary resuscitation." No restrictions were set on publication year or language. To ensure completeness, we screened relevant review articles and meta-analyses for references not captured by our search strategy and screened relevant conference abstracts for pertinent data.

Two investigators (W.-T.C. and C.-H.H.) independently scanned the titles and abstracts of all retrieved articles and selected those pertinent to this review. The following prespecified inclusion criteria were used: being a randomized controlled trial or quasi randomized controlled trial; population included adult out-of-hospital cardiac arrest patients (≥18 years); comparisons were made between the use of intubation, supraglottic airway, or bag-valve-mask ventilation during CPR; and the results included a survival or neurologic outcome. After retrieving the full reports of potentially relevant trials, 2 reviewers (C.-H.W. and M.-S.T.) independently assessed each study's eligibility according to the inclusion criteria. Differences of opinion in regard to study eligibility were settled by consultation with a third investigator (W.-J.C.).

Data Collection and Processing

Two investigators (C.-H.W. and A.-F.L.) independently extracted qualitative and quantitative data, and a third investigator (S.-C.C.) adjudicated discordant assessments. Data were extracted for study design, patient characteristics (eg, age, sex, initial arrest rhythms), details of interventions (eg, main intervention performer, procedure success rate, definition of procedure success), and patient outcomes. Survival to hospital discharge was specified as the primary outcome; return of spontaneous circulation and a favorable neurologic outcome at hospital discharge (or 1 month after return of spontaneous circulation) were specified as secondary outcomes. The Cochrane Risk of Bias Tool was used to assess the risk of bias for each trial.[14] Each study was scored as high risk, low risk, or unclear with respect to random sequence generation, allocation concealment, blinding process, incomplete outcome data, and selective reporting.[14]

Primary Data Analysis

We performed a network meta-analysis within a frequentist framework by combining information from different studies that addressed the same resuscitation outcomes but used different initial airway interventions. When a specific comparison between 2 different airway interventions is performed, direct evidence can be obtained by combining studies that directly compare the 2 treatments (A versus B), whereas indirect evidence can be obtained by combining studies that have a common comparator (A versus C and B versus C). A network meta-analysis combines both direct and indirect evidence across a network of studies into a single effect size. A network geometry plot was created to confirm whether a multiple treatment comparison analysis could be performed. Inconsistency assumption, defined as the statistical disagreement between results obtained from direct and indirect comparison in a closed loop, was assessed locally with a loop-specific approach and globally with a model of design by treatment interaction.[15] Additionally, incoherence assumption (ie, the statistical disagreement between direct and indirect evidence in a closed loop) was also evaluated. A random-effects model assuming common heterogeneity was implemented across all comparisons, and odds ratios (ORs) with their associated 95% confidence intervals (CIs) were calculated. When possible, data for the response to treatment were analyzed on an intention-to-treat basis. The rank order of a comparator is presented as a surface under the cumulative ranking (SUCRA) probability.[16] The SUCRA is a numeric presentation of the overall ranking, which assigns a single number to each treatment. SUCRA values range from 0% to 100%, with higher values (closer to 100%) deemed as more likely to be effective and lower ones (closer to 0%) deemed as more likely to be ineffective. Publication bias was examined by visual inspection of a funnel plot.[17] Additionally, because of the concerns that high intubation success rate may influence the applicability of the meta-analytic results,[18] a sensitivity analysis was performed by removing studies with high intubation success rates ranked above the third quartile from meta-analysis. A 2-tailed $P<.05$ was considered statistically significant. All analyses were performed with the netmeta packages in Stata (version 14.1; StataCorp, College Station, TX). Ethics approval was not required for this study.

RESULTS

A total of 11 trials,[19-29] including 8 randomized controlled trials[19,21,23,25-29] and 3 quasi randomized controlled trials,[20,22,24] were included (Figure, Table 1). A total of 16,225 patients were included in the network meta-analysis: 7,361 patients who received intubation, 7,475 who received supraglottic airway, and 1,201 who received bag-valve-mask ventilation.

In 2 of the trials,[22,28] the airway interventions were performed by physicians in out-of-hospital settings, whereas in other trials, they were managed by emergency medical personnel.[19-21,23-27,29] The intubation success rates varied substantially across the included randomized controlled trials, ranging from 51% to 98%. The definitions of intubation success also varied in studies providing intubation success rates: some were defined on first attempt[23] or within 2 attemps[22,27]; the others were not explicitly defined.[19,20,28,29]

Except for one trial,[23] most trials reported the primary outcome of survival to hospital discharge[19-22,24-27,29] or 1 month after return of spontaneous circulation.[28] For the secondary outcomes, most trials[19,22-25,27-29] reported return of spontaneous circulation on hospital arrival or out-of-hospital return of spontaneous circulation.[26] There were 5 trials[19,20,27-29] reporting the neurologic outcomes of patients.

As shown in Table E1 (available online at http://www.annemergmed.com), 3 trials[20,22,24] used an alternate-date[20,22] or alternate-month[24] design and 4 trials[24,25,27,29] used cluster randomization to allocate patients. All of those trials[20-22,24,25,27,29] showed a high risk for bias in allocation concealment. Because of the nature of airway interventions, none of the trials could be performed in a blinded manner. All trials included an intention-to-treat analysis and the enrolled patients received completed follow-up. The numbers of allocated patients and outcome events based on the intention-to-treat analyses were extracted for use in our network meta-analysis.

For the primary outcome, the most common comparison was intubation versus supraglottic airway, with

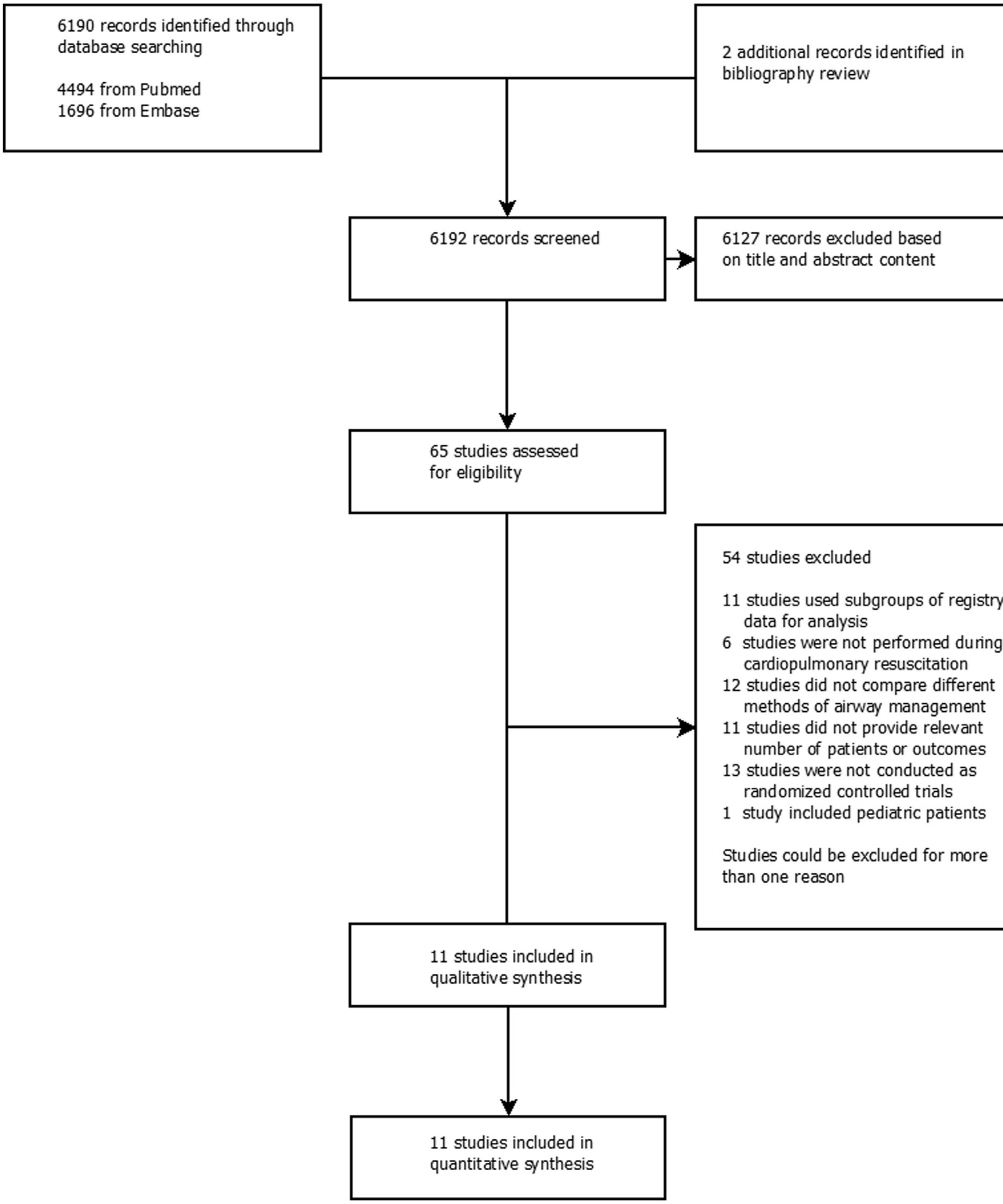

Figure. Literature search and study selection flow diagram.

6 trials involved (Figure E1, available online at http://www.annemergmed.com). The results of tests for inconsistency at the global and local levels showed that an assumption of consistency could be accepted (χ^2_1)=0.05; P=.82) (Figure E2, available online at http://www.annemergmed.com). The network meta-analysis indicated no significant differences among intubation, supraglottic airway, or bag-valve-mask ventilation in regard to patient survival to hospital discharge (Table 2).

For the secondary outcomes, supraglottic airway improved the rate of return of spontaneous circulation compared with intubation (OR 1.11; 95% CI 1.03 to

Table 1. Characteristics of the studies included in the network meta-analysis.

Study*	Region/Care Provider	Study Year	Patient No.	Procedure Success Rate, %	SGA Type	Return of Spontaneous Circulation†			Survival at Hospital Discharge†			Favorable Neurologic Outcome†		
						ETI	SGA	BMV	ETI	SGA	BMV	ETI	SGA	BMV
Goldenberg,[19] 1986	US/paramedic	NA	175	ETI: 90 SGA: 92	EGTA	58/90 (64.4)	46/85 (54.1)	NA	10/90 (11.1)	11/85 (12.9)	NA	5/90 (5.6)	7/85 (8.2)	NA
Staudinger,[20] 1994	US/paramedic	1988–1990	86	ETI: 71 SGA:71	ETC	NA	NA	NA	3/48 (6.3)	3/38 (7.9)	NA	3/48 (6.3)	3/38 (7.9)	NA
Rumball,[21] 1997	Canada/ paramedic	1991–1995	470	SGA: 80	PTL/LM/ETC	NA	NA	NA	NA	17/379 (4.5)	3/91 (3.3)	NA	NA	NA
Rabitsch,[22] 2003	Austria/physician	NA	172	ETI: 94 SGA: 98	ETC	34/83 (41.0)	34/89 (38.2)	NA	2/83 (2.4)	5/89 (5.6)	NA	NA	NA	NA
Mulder,[23] 2013	Netherlands/ paramedic	2011–2012	188	ETI: 56 SGA: 79	LMAS	36/101 (35.6)	40/87 (46.0)	NA	NA	NA	NA	NA	NA	NA
Maignan,[24] 2015	France/nurse	2011–2012	82	SGA: 77	LT	NA	7/41 (17.1)	9/41 (22.0)	NA	1/41 (2.4)	1/41 (2.4)	NA	NA	NA
Benger,[25] 2016	England/ paramedic	2012–2013	615	ETI: NA SGA: 96	LMAS/i-Gel	67/209 (32.1)	123/406 (30.3)	NA	19/209 (9.1)	38/406 (9.4)	NA	NA	NA	NA
Fiala,[26] 2017	Austria/EMT	2012–2014	97	SGA: 74	LTS-D	NA	9/46 (19.6)	7/51 (13.7)	NA	1/46 (2.2)	1/51 (2.0)	NA	NA	NA
Benger,[27] 2018	England/ paramedic	2015–2017	9,296	ETI: 69 SGA: 85	i-Gel	1,249/4,410 (28.3)	1,495/ 4,886 (30.6)	NA	372/4,410 (8.4)	392/4,886 (8.0)	NA	300/ 4,410 (6.8)	311/4,886 (6.4)	NA
Jabre,[28] 2018	Belgium and France/ physician	2015–2017	2,040	ETI: 98	NA	397/1,022 (38.8)	NA	348/1,018 (34.2)	54/1,022 (5.3)	NA	55/1,018 (5.4)	43/1,022 (4.2)	NA	44/1,018 (4.3)
Wang,[29] 2018	US/EMT and paramedic	2015–2017	3,004	ETI: 51 SGA: 90	LT	365/1,499 (24.3)	420/1,505 (27.9)	NA	121/1,499 (8.1)	163/1,505 (10.8)	NA	75/1,499 (5.0)	107/1,505 (7.1)	NA

SGA, Supraglottic airway; *ETI*, intubation; *BMV*, bag-valve-mask ventilation; *NA*, not available; *EGTA*, esophageal gastric tube airway; *ETC*, esophageal-tracheal Combitube; *PTL*, pharyngeal tracheal lumen airway; *LM*, laryngeal mask; *LMAS*, laryngeal mask airway supreme; *EMT*, emergency medical technician; *LTS-D*, laryngeal tube suction-disposable; *LT*, laryngeal tube.
*The studies are arranged by publication year and alphabetic order of the name of the first author.
†Outcomes are expressed as events/total numbers of patients. Proportions are shown in parentheses.

Table 2. League table presenting network meta-analytic estimates of comparisons between airway interventions for primary and secondary outcomes.

Primary outcome: survival to hospital discharge		
SGA (SUCRA, 80%)		
1.14 (0.69–1.87)	BMV (SUCRA, 40%)	
1.14 (0.89–1.44)	1.00 (0.63–1.58)	ETI (SUCRA, 30%)
Secondary outcome: return of spontaneous circulation		
SGA (SUCRA, 100%)		
1.11 (1.03–1.20)*	ETI (SUCRA, 50%)	
1.35 (1.11–1.63)*	1.21 (1.01–1.44)*	BMV (SUCRA, 0%)
Secondary outcome: favorable neurologic outcome at hospital discharge		
SGA (SUCRA, 70%)		
1.14 (0.54–2.39)	BMV (SUCRA, 50%)	
1.17 (0.81–1.69)	1.03 (0.54–1.96)	ETI (SUCRA, 30%)

The unlabeled data are ORs and 95% CIs. An OR greater than 1 suggests that the upper left intervention is associated with higher odds for each outcome compared with the corresponding lower right intervention. The order of intervention from upper left to lower right is ranked by SUCRA curve.
*Statistically significant difference.

1.20) or bag-valve-mask ventilation (OR 1.35; 95% CI 1.11 to 1.63), and intubation improved the rate of return of spontaneous circulation compared with bag-valve-mask ventilation (OR 1.21; 95% CI 1.01 to 1.44) (Table 2, Figure E3 [available online at http://www.annemergmed.com]). However, there were no differences among these airway interventions in regard to neurologic outcome (Table 2, Figure E4 [available online at http://www.annemergmed.com]). In the SUCRA analysis (Table 2), supraglottic airway was ranked as the most favorable initial method of airway intervention of all 3 outcomes. There was no visually remarkable asymmetry of the funnel plot, indicating the absence of significant publication bias (Figure E5, available online at http://www.annemergmed.com).

Table 3. Sensitivity analyses demonstrating the influence of removing 2 studies with high intubation success rates.

Primary outcome: survival to hospital discharge		
SGA (SUCRA, 70%)		
1.11 (0.87–1.43)	ETI (SUCRA, 40%)	
1.27 (0.43–3.77)	1.14 (0.38–3.48)	BMV (SUCRA, 40%)
Secondary outcome: return of spontaneous circulation		
SGA (SUCRA, 80%)		
1.06 (0.49–2.30)	BMV (SUCRA, 50%)	
1.12 (1.04–1.21)*	1.05 (0.49–2.28)	ETI (SUCRA, 20%)

The unlabeled data in the boxes are ORs and 95% CIs. An OR > 1 suggests that the upper left intervention is associated with higher odds of return of spontaneous circulation than the corresponding lower right intervention. The order of intervention from upper left to lower right is ranked by SUCRA curve.
*Statistically significant difference.

The third quartile of the intubation success rate was 92%. Therefore, in the sensitivity analysis, the trials by Rabitsch et al[22] (success rate 94%) and Jabre et al[28] (success rate 98%) were excluded from meta-analysis. The median intubation success rate was 69% for the remaining studies included in the sensitivity analysis. As shown in the network geometry (Figure E6, available online at http://www.annemergmed.com), when these 2 trials[22,28] were excluded, for neurologic outcome, only the studies comparing intubation and supraglottic airway remained in the network, and accordingly network meta-analysis was not performed. As shown in Table 3 and Figure E7 (available online at http://www.annemergmed.com), supraglottic airway improved the rate of return of spontaneous circulation compared with intubation (OR 1.12; 95% CI 1.04 to 1.21). There were no differences in survival to hospital discharge among these airway interventions. For the outcomes of survival to hospital discharge and return of spontaneous circulation, the SUCRA rankings in sensitivity analysis were different from those of the primary analysis when the 2 trials[22,28] were removed from the quantitative synthesis (Tables 2 and 3).

LIMITATIONS

First, because of the number of included trials, we could not perform subgroup analyses according to different types of supraglottic airway; therefore, we are unable to recommend a specific type of supraglottic airway. Second, according to consensus of the International Liaison Committee on Resuscitation,[18] we selected only intubation success rate as a reference to separate studies into different groups in sensitivity analyses. Intubation success rate might be a practical reference for formulating policies in regard to which advanced airway intervention should be adopted. Third, as outlined in the sensitivity analyses, the study by Jabre et al[28] greatly influenced the meta-analytic results because of the high intubation success rate and its unique position in the network geometry, providing the only direct comparison between intubation and bag-valve-mask ventilation. It may be preferable, theoretically, to synthesize randomized controlled trials with homogenous features such as similar intubation success rates. Nevertheless, it may be unrealistic to wait for a randomized controlled trial comparing intubation and bag-valve-mask ventilation in an out-of-hospital care system with low or moderate intubation success rates because it would be ethically and logistically challenging to perform such a trial. Therefore, the current network meta-analysis may still provide the best available evidence despite these limitations.

DISCUSSION

Main Results

The current meta-analysis included 8 randomized controlled trials[19,21,23,25-29] and 3 quasi randomized controlled trials[20,22,24] (16,225 patients) that compared the effectiveness of intubation, supraglottic airway, or bag-valve-mask ventilation as an initial airway intervention in adult out-of-hospital cardiac arrest patients. The majority of comparisons were made between intubation and supraglottic airway (6 trials). The network meta-analysis indicated there were no differences between these interventions in regard to survival or neurologic outcome at hospital discharge. Nevertheless, network meta-analysis demonstrated that supraglottic airway improved the rate of return of spontaneous circulation compared with intubation or bag-valve-mask ventilation, and intubation improved the rate of return of spontaneous circulation compared with bag-valve-mask ventilation. A probability analysis ranked supraglottic airway as the most effective method for improving the rate of return of spontaneous circulation, followed by intubation as the second-best method. Our sensitivity analyses did, however, demonstrate that the pooled results may differ according to the intubation success rates of out-of-hospital care systems.

Contrary to the rank order suggested by our network meta-analysis, previous meta-analyses of observational studies[10-12] suggested that for out-of-hospital cardiac arrest patients, bag-valve-mask ventilation was the most effective method of airway management, followed by intubation and then supraglottic airway. Moreover, even though a propensity-score-matching analysis was used to obtain less biased effect estimates, the rank order indicated by several large observational studies[30-33] was still consistent with the previous meta-analyses[10-12] as opposed to the current network meta-analysis.

There are a few plausible explanations for this difference. For example, in these meta-analyses[10-12] and propensity-score-matching studies,[30-33] patients included in a bag-valve-mask ventilation group may be those who had a short CPR duration and were therefore more likely to have a favorable outcome. In contrast, patients who receive advanced airway interventions (supraglottic airway or intubation) tend to have longer CPR durations and therefore have worse outcomes. This problem of confounding by indication, or resuscitation time bias,[30] may have been an important limitation of many observational studies. Furthermore, previous observational studies[10-12,30-33] categorized patients according to their final airway intervention. In contrast, all the randomized controlled trials[19,22-29] included in our network meta-analysis adopted an intention-to-treat analysis and grouped patients according to their initial airway intervention. Therefore, it is plausible that supraglottic airway was ranked as the least effective airway intervention in previous studies[10-12,30-33] because it was used as a final effort for patients who either could not be ventilated by bag-valve-mask ventilation or could not be intubated. In other words, the effect estimates of supraglottic airway in those studies may have been biased by confounding by indication.

Indeed, in a recently published population-based study, Izawa et al[34] used a time-dependent propensity score sequential matching analysis to account for resuscitation time bias to demonstrate that advanced airway interventions were associated with better survival rates at hospital discharge among out-of-hospital cardiac arrest patients with nonshockable rhythms, supporting the current network meta-analysis.

To avoid confounding by indications inherent in observational studies, the current network meta-analysis included only randomized controlled trials or quasi randomized controlled trials. Nonetheless, among these included studies, there were substantial differences present in the out-of-hospital care systems. For example, in the 2 studies[22,28] with intubation success rates higher than the third quartile, physicians were responsible for the out-of-hospital cardiac arrest resuscitation. In contrast, some trials[27,29] allocated their patients by cluster randomization in an attempt to be pragmatic and achieve maximum external validity. Because of the pragmatic study design, the paramedics who performed the intubation did not receive a specialized airway management lecture beyond their usual training courses. Therefore, the intubation success rates varied substantially across the included randomized controlled trials, raising concerns about conducting the network meta-analysis.[18]

We acknowledge that substantial heterogeneity existed among the included trials, such as the included supraglottic airway types and intubation success rates. In principle, quantitative meta-analysis should be considered when a group of studies is sufficiently homogeneous in terms of participants, interventions, and outcomes, However, we tend to agree with the viewpoint that it is often appropriate to take a broader perspective in a meta-analysis than in a single randomized controlled trial.[35] It has been said that meta-analyses bring together apples and oranges, yielding a meaningless result. Although this argument is fair if apples and oranges are of intrinsic interest on their own, it may be less sound if they are used to answer a question about fruit.

Therefore, the comparisons between different airway interventions per se may not be of interest; rather, the system-based comparisons between these airway interventions should be the main focus because the effects of these airway interventions cannot be independent of the out-of-hospital care providers who use them.

It can therefore be posited that the intubation success rate may be viewed as an inherent feature of a given out-of-hospital care system. In the SUCRA analysis, supraglottic airway was ranked as the optimal initial airway intervention, suggesting that for most out-of-hospital care systems, it may be a better initial strategy for out-of-hospital cardiac arrest patients. Because of the difficulties in performing out-of-hospital intubations,[36,37] many out-of-hospital care systems may not yield intubation success rates as high as those of supraglottic airway. Accordingly, despite the possibilities that intubation may outperform supraglottic airway in efficacy, the latter may be superior to intubation in regard to effectiveness. By combining different randomized controlled trials, it may be easier for readers to interpret the trade-offs between efficacy and effectiveness and evaluate the performance of different airway interventions across different systems.

The most important message conveyed by the current network meta-analysis may not be the final meta-analytic results themselves, but rather the mechanism by which procedure proficiency may influence the meta-analytic results. As presented in the primary and sensitivity analyses, by synthesizing different randomized controlled trials with different intubation success rates, the dynamic changes in the effect estimates and ranking caused by procedure proficiency are presented in a clearer and more transparent way. Despite that the ranking by SUCRA varied according to the included randomized controlled trials, supraglottic airway remained the optimal initial airway intervention across a wide range of out-of-hospital care systems. Therefore, if policymakers would like to develop strategies of advanced airway interventions for out-of-hospital cardiac arrest in their out-of-hospital care system, they may choose supraglottic airway as the preferred advanced airway intervention even though they do not have the previous intubation success rate for reference. For systems in which the intubation success rate is already known to be close to those pooled in the sensitivity analysis (median intubation success rate 69%), policymakers may still choose supraglottic airway as a preferred initial airway intervention accordingly. Alternatively, in systems in which the intubation success rate is known to be as high as that in the study by Jabre et al,[28] these agencies might be justified in continuing to use intubation as the initial strategy, given that chest compressions are not interrupted. Providers and medical directors may want to consider the procedural competence of the local health care providers before making policy changes,[18] which may be done more easily with visualized meta-analytic data as a reference.

Although there were no differences in survival to hospital discharge or neurologic outcome among these airway interventions, these system-based comparisons demonstrated that supraglottic airway was better than intubation or bag-valve-mask ventilation and intubation was better than bag-valve-mask ventilation in improving return of spontaneous circulation. The intubation success rate greatly influenced the meta-analytic results, and therefore these comparison results should be interpreted with these system differences in mind.

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Author affiliations: From the Department of Emergency Medicine, National Taiwan University Hospital, Taipei, Taiwan (Wang, A-F Lee, Chang, Huang, Tsai, C-C Lee, S-C Chen, W-J Chen); the Department of Emergency Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan (Wang, Chang, Huang, Tsai, C-C Lee, S-C Chen, W-J Chen); the Department of Emergency Medicine, Baylor Scott & White All Saints Medical Center–Fort Worth, Fort Worth, TX (Chou); and the Division of Cardiology, Department of Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan (W-J Chen).

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REFERENCES

1. Berdowski J, Berg RA, Tijssen JG, et al. Global incidences of out-of-hospital cardiac arrest and survival rates: systematic review of 67 prospective studies. *Resuscitation*. 2010;81:1479-1487.
2. Ong ME, Shin SD, De Souza NN, et al. Outcomes for out-of-hospital cardiac arrests across 7 countries in Asia: the Pan Asian Resuscitation Outcomes Study (PAROS). *Resuscitation*. 2015;96:100-108.
3. Hazinski MF, Nolan JP, Billi JE, et al. Part 1: executive summary: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation*. 2010;122:S250-S275.
4. Kleinman ME, Brennan EE, Goldberger ZD, et al. Part 5: adult basic life support and cardiopulmonary resuscitation quality: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132:S414-S435.
5. Soar J, Nolan JP, Bottiger BW, et al. European Resuscitation Council guidelines for resuscitation 2015: section 3. Adult advanced life support. *Resuscitation*. 2015;95:100-147.
6. Link MS, Berkow LC, Kudenchuk PJ, et al. Part 7: adult advanced cardiovascular life support: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132:S444-S464.
7. Bobrow BJ, Clark LL, Ewy GA, et al. Minimally interrupted cardiac resuscitation by emergency medical services for out-of-hospital cardiac arrest. *JAMA*. 2008;299:1158-1165.
8. Bobrow BJ, Ewy GA, Clark L, et al. Passive oxygen insufflation is superior to bag-valve-mask ventilation for witnessed ventricular fibrillation out-of-hospital cardiac arrest. *Ann Emerg Med*. 2009;54:656-662.e1.
9. Plaisance P, Soleil C, Lurie KG, et al. Use of an inspiratory impedance threshold device on a facemask and endotracheal tube to reduce intrathoracic pressures during the decompression phase of active compression-decompression cardiopulmonary resuscitation. *Crit Care Med*. 2005;33:990-994.
10. White L, Melhuish T, Holyoak R, et al. Advanced airway management in out of hospital cardiac arrest: a systematic review and meta-analysis. *Am J Emerg Med*. 2018;36:2298-2306.
11. Jeong S, Ahn KO, Shin SD. The role of prehospital advanced airway management on outcomes for out-of-hospital cardiac arrest patients: a meta-analysis. *Am J Emerg Med*. 2016;34:2101-2106.
12. Benoit JL, Gerecht RB, Steuerwald MT, et al. Endotracheal intubation versus supraglottic airway placement in out-of-hospital cardiac arrest: a meta-analysis. *Resuscitation*. 2015;93:20-26.
13. Hutton B, Salanti G, Caldwell DM, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. *Ann Intern Med*. 2015;162:777-784.
14. Higgins JPT, Altman DG, Sterne JAC. Assessing risk of bias in included studies. In: Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (Updated March 2011)*. London, UK: Cochrane Collaboration; 2011. Available at: http://handbook-5-1.cochrane.org/. Accessed January 5, 2020.
15. Higgins JP, Jackson D, Barrett JK, et al. Consistency and inconsistency in network meta-analysis: concepts and models for multi-arm studies. *Res Synth Methods*. 2012;3:98-110.
16. Salanti G, Ades AE, Ioannidis JP. Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial. *J Clin Epidemiol*. 2011;64:163-171.
17. Chaimani A, Higgins JP, Mavridis D, et al. Graphical tools for network meta-analysis in STATA. *PloS One*. 2013;8:e76654.
18. Granfeldt A, Avis SR, Nicholson TC, et al. Advanced airway management during adult cardiac arrest: a systematic review. *Resuscitation*. 2019;139:133-143.
19. Goldenberg IF, Campion BC, Siebold CM, et al. Esophageal gastric tube airway vs endotracheal tube in prehospital cardiopulmonary arrest. *Chest*. 1986;90:90-96.
20. Staudinger T, Brugger S, Roggla M, et al. [Comparison of the Combitube with the endotracheal tube in cardiopulmonary resuscitation in the prehospital phase]. *Wien Klin Wochenschr*. 1994;106:412-415.
21. Rumball CJ, MacDonald D. The PTL, Combitube, laryngeal mask, and oral airway: a randomized prehospital comparative study of ventilatory device effectiveness and cost-effectiveness in 470 cases of cardiorespiratory arrest. *Prehosp Emerg Care*. 1997;1:1-10.
22. Rabitsch W, Schellongowski P, Staudinger T, et al. Comparison of a conventional tracheal airway with the Combitube in an urban emergency medical services system run by physicians. *Resuscitation*. 2003;57:27-32.
23. Mulder PJ, Oetomo SB, Vloet L, et al. Comparison in effectiveness and safety between a supraglottic airway device and endotracheal intubation in out-of-hospital cardiac arrest in the Netherlands. *Resuscitation*. 2013;84:S17.
24. Maignan M, Koch FX, Kraemer M, et al. Impact of laryngeal tube use on chest compression fraction during out-of-hospital cardiac arrest. A prospective alternate month study. *Resuscitation*. 2015;93:113-117.
25. Benger J, Coates D, Davies S, et al. Randomised comparison of the effectiveness of the laryngeal mask airway supreme, i-gel and current practice in the initial airway management of out of hospital cardiac arrest: a feasibility study. *Br J Anaesth*. 2016;116:262-268.
26. Fiala A, Lederer W, Neumayr A, et al. EMT-led laryngeal tube vs face-mask ventilation during cardiopulmonary resuscitation: a multicenter prospective randomized trial. *Scand J Trauma Resusc Emerg Med*. 2017;25:104.
27. Benger JR, Kirby K, Black S, et al. Effect of a strategy of a supraglottic airway device vs tracheal intubation during out-of-hospital cardiac arrest on functional outcome: the AIRWAYS-2 randomized clinical trial. *JAMA*. 2018;320:779-791.
28. Jabre P, Penaloza A, Pinero D, et al. Effect of bag-mask ventilation vs endotracheal intubation during cardiopulmonary resuscitation on neurological outcome after out-of-hospital cardiorespiratory arrest: a randomized clinical trial. *JAMA*. 2018;319:779-787.
29. Wang HE, Schmicker RH, Daya MR, et al. Effect of a strategy of initial laryngeal tube insertion vs endotracheal intubation on 72-hour survival in adults with out-of-hospital cardiac arrest: a randomized clinical trial. *JAMA*. 2018;320:769-778.
30. Sulzgruber P, Datler P, Sterz F, et al. The impact of airway strategy on the patient outcome after out-of-hospital cardiac arrest: a propensity score matched analysis. *Eur Heart J Acute Cardiovasc Care*. 2018;7:423-431.
31. McMullan J, Gerecht R, Bonomo J, et al. Airway management and out-of-hospital cardiac arrest outcome in the CARES registry. *Resuscitation*. 2014;85:617-622.
32. Hasegawa K, Hiraide A, Chang Y, et al. Association of prehospital advanced airway management with neurologic outcome and survival in patients with out-of-hospital cardiac arrest. *JAMA*. 2013;309:257-266.

33. Shin SD, Ahn KO, Song KJ, et al. Out-of-hospital airway management and cardiac arrest outcomes: a propensity score matched analysis. *Resuscitation*. 2012;83:313-319.
34. Izawa J, Komukai S, Gibo K, et al. Pre-hospital advanced airway management for adults with out-of-hospital cardiac arrest: nationwide cohort study. *BMJ*. 2019;364:l430.
35. Deeks JJ, Higgins JPT, Altman DG. Analysing data and undertaking meta-analyses. In: Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0*. London, UK: Cochrane Collaboration; 2011. Available at: http://handbook-5-1.cochrane.org/. Accessed January 5, 2020.
36. Wang HE, Yealy DM. How many attempts are required to accomplish out-of-hospital endotracheal intubation? *Acad Emerg Med*. 2006;13:372-377.
37. Wang HE, Kupas DF, Paris PM, et al. Preliminary experience with a prospective, multi-centered evaluation of out-of-hospital endotracheal intubation. *Resuscitation*. 2003;58:49-58.