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Review

Advanced airway management during adult cardiac arrest: A systematic review

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Abstract

Aim: To systematically review the literature on advanced airway management during adult cardiac arrest in order to inform the International Liaison Committee of Resuscitation (ILCOR) consensus on science and treatment recommendations.

Methods: The review was performed according to PRISMA guidelines and registered on PROSPERO (CRD42018115556). We searched Medline, Embase, and Evidence-Based Medicine Reviews for controlled trials and observational studies published before October 30, 2018. The population included adult patients with cardiac arrest. Two investigators reviewed studies for relevance, extracted data, and assessed the risk of bias of individual studies.

Results: We included 78 observational studies and 11 controlled trials. Most of the observational studies and all of the controlled trials only included patients with out-of-hospital cardiac arrest. The risk of bias for individual observational studies was overall assessed as critical or serious, with confounding and selection bias being the primary sources of bias. Three of the controlled trials, all published in 2018, were powered for clinical outcomes with two comparing a supraglottic airway to tracheal intubation and one comparing bag-mask ventilation to tracheal intubation. All three trials had some concerns regarding risk of bias primarily due to lack of blinding and variable adherence to the protocol. Clinical and methodological heterogeneity across studies, for both the observational studies and the controlled trials, precluded any meaningful meta-analyses.

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Conclusions: We identified a large number of studies related to advanced airway management in adult cardiac arrest. Three recently published, large randomized trials in out-of-hospital cardiac arrest will help to inform future guidelines. Trials of advanced airway management during in-hospital cardiac arrest are lacking.

Keywords: Cardiac arrest, Airway, ILCOR, Supraglottic, Bag-mask, Intubation

Introduction

Airway management during cardiac arrest is considered an integral part of cardiac arrest management with potential impact on patient outcome. The traditional approach has usually been initial bag-mask ventilation followed by advanced airway management with either a supraglottic airway or tracheal intubation[1,2] although there is limited supporting evidence for any of these approaches.[3] Bag-mask ventilation has been considered to be a relatively simple technique and part of basic life support. However, bag-mask ventilation may be technically difficult with concerns that it might not provide adequate ventilation and oxygenation and there is a risk of aspiration using this approach. Tracheal intubation offers a secure airway and could therefore lower the risk of aspiration of gastric content. However, tracheal intubation might result in interruptions in chest compression and delays in other interventions. Furthermore, tracheal intubation is a skill that requires expertise and experience[4] and esophageal intubation (or subsequent dislodgment of the tube) could result in unsuccessful resuscitation. Supraglottic airways are airway devices that are inserted blindly and placed in the hypopharynx to facilitate ventilation.[2] These devices are relatively easy to insert and provide a middle-ground intervention between bag-mask ventilation and tracheal intubation. Given that all three approaches are currently being used in clinical practice and considering the theoretical pros and cons for each[5], there has been a need for randomized trials to guide clinical practice.

During 2018 a number of randomized clinical trials[6–8] were published addressing advanced airway management during adult cardiac arrest. These trials have included airway management strategies of bag-mask ventilation, supraglottic airway devices, and tracheal intubation. This systematic review will inform the International Liaison Committee on Resuscitation (ILCOR) consensus on science and treatment recommendations for advanced airway management during adult cardiac arrest.

Methods

Protocol and registration

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[9] The PRISMA checklist is provided in the Supplementary Contents. The protocol was prospectively submitted to the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42018115556). The protocol is provided in the Supplementary Contents. The review was commissioned by ILCOR.

Eligibility criteria and outcomes

The study question was framed using the PICO (Population, Intervention, Comparison, Outcome) format: In adults (generally $\geq$ 18 years) in any setting (in-hospital or out-of-hospital) with cardiac arrest from any aetiology (P), does a specific advanced airway management method (e.g. intubation or a supraglottic airway device) (I) as compared to a different advanced airway management method or no advanced airway management method (e.g. bag-mask ventilation) during cardiac arrest (C) improve outcomes (O).

Relevant outcomes were prioritized by the ILCOR Advanced Life Support Task Force. For observational studies, we included short-term survival (various definitions of return of spontaneous circulation [ROSC] and survival to admission), mid-term survival (survival at discharge, 28 days, 30 days, or 1 month), mid-term favourable functional/neurological outcome (usually a cerebral performance category [CPC] score of 1 or 2 or a modified Rankins Scale (mRS) score of 1, 2 or 3 at discharge, 28 days, 30 days, or 1 month), and reported long-term outcomes (after 1 month) such as survival and favourable functional/neurological outcome. In addition to these outcomes, we also included the following outcomes for controlled trials: 72-h survival, poor functional/neurological outcome (i.e. a CPC score of 3 or 4 or a mRS score of 4 or 5) at discharge, 28 days, 30 days, or 1 month, success rates for advanced airways, ventilation success rates, regurgitation/aspiration, and cardiopulmonary resuscitation (CPR) quality.

Randomized trials, non-randomized controlled trials, and observational studies (cohort studies and case-control studies) comparing at least two airway strategies were included. Animal studies, ecological studies, case series, case reports, reviews, abstracts, editorials, comments, and letters to the editor were not included. Studies with $\leq$ 10 patients in either group and studies without quantitative results were excluded. There were no limitations on publication year or manuscript language. Studies assessing cost-effectiveness and the timing of advanced airway interventions were also considered.

Information sources and search strategy

We searched the following electronic databases on October 30, 2018: Medline, Embase, and Evidence-Based Medicine Reviews (which includes the Cochrane Library). We used a combination of various text and indexing search terms for cardiac arrest and airway management. The reference lists of included articles were reviewed for potential additional articles. To identify ongoing trials, we searched the International Clinical Trials Registry Platform (http://www.who.int/ictrp/en/) (which includes entries in ClinicalTrials.gov) on January 9, 2019. The search strategies for each database and the Clinical Trials Registry Platform are provided in the protocol and in the Supplementary Contents.

Study selection

Pairs of two reviewers, using pre-defined screening criteria, independently screened all titles and abstracts retrieved from the systematic search. The reviewers were blinded to authors and journal titles during the screening stage. Any disagreements regarding inclusion or exclusion were resolved via discussion between the reviewers and with a third reviewer as needed until consensus was reached. Two reviewers then reviewed the full text-reports of all potentially relevant publications passing the first level of screening. Any disagreement regarding eligibility was resolved via discussion until consensus was reached. The Kappa-value for inter-observer variance was calculated.

Data collection

Two reviewers, using a pre-defined standardized data extraction form, extracted data from individual studies. Any discrepancies in the extracted data were identified and resolved via discussion and consensus.

Risk of bias in individual studies

Two investigators independently assessed risk of bias for individual studies. Risk of bias was assessed using the revised Cochrane risk-of-bias tool[10] for controlled trials and the ROBINS-I tool[11] for observational studies. For controlled trials, the assessment tool for individually-randomized parallel-group trials or the supplement for cluster-randomized parallel-group trial were used as appropriate. Disagreements were resolved via discussion between the two investigators. The bias assessment was performed per outcome but is generally presented per comparison rather than per outcome, since there were no meaningful differences in bias across outcomes except as noted.

Data synthesis and confidence in cumulative evidence

Studies were assessed for clinical (i.e. participants, interventions, and outcomes), methodological (i.e. study design or risk of bias), and statistical heterogeneity if appropriate.[12] Meta-analyses were planned as described in the protocol.

The certainty of the overall evidence for a given comparison and outcome was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology ranging from very low certainty of evidence to high certainty of evidence.[13]

Results

Study selection

The search identified 6400 unique titles/abstracts of which 6172 were excluded based on initial review (Kappa = 0.60). Of the 228 full-text articles reviewed, 141 were excluded for various reasons (Kappa = 0.91, Fig. 1). As two additional articles were identified through review of reference lists, a total of 89 articles were included. No studies assessing cost-effectiveness were identified.

Observational studies

Seventy-eight observational studies were included. Nine studies addressed timing of advanced airway management while 71 studies included 121 comparisons of different airway management strategies. Studies related to timing were published between 2003 and 2018 and were from Asia (n = 6) and North-America (n = 3). Three included IHCA[14–16] while six included OHCA[17–22]. The 71 comparative studies were published between 1985 and 2018 and were primarily from North-America (n = 24), Asia (n = 23), and Europe (n = 20). Sixty-one studies included OHCA[17,22–81], nine included IHCA[82–90], and one combined OHCA and IHCA[91]. Additional details including results of the individual studies are provided in the Supplemental Content.

The detailed bias assessment is provided in the Supplemental Content. For studies related to timing, all were judged as having a critical risk of bias primarily due to a risk of confounding and selection bias. For the comparative studies, 114 of the comparisons were judged to have a critical risk of bias while seven comparisons (six in OHCA and one in IHCA) were considered to have a serious risk of bias. The primary concerns were confounding and selection bias.

Due to the risk of bias, clinical and methodological heterogeneity between studies, and the availability of controlled trials, no meta-analyses were performed for observational studies.

Controlled trials

Eleven controlled trials, published between 1986 and 2018, were identified.[6–8,92–99] The trials included a total of 14 comparisons between airway management strategies and included between 76 and 9289 patients with only three trials including more than 500 patients. Four trials were conducted in North-America, one in Asia, and six in Europe. All trials only included patients with OHCA. A brief overview of the trials is provided in Table 1 while more detailed data, including additional results, are presented in the Supplemental Content.

An overview of the bias assessment of the individual trials is provided in Table 2 and a more detailed description, including signalling questions, is provided in the Supplemental Content. Overall, seven trials were judged to have a high risk of bias, whereas for the remaining four, some concerns relating to potential bias was noticed. Lack of blinding and low adherence to the assigned intervention were the two main concerns leading to risk of bias.

Given the clinical and methodological heterogeneity between studies, especially related to the intervention (i.e. different supraglottic airways or bag-mask ventilation), the comparison group (i.e. markedly different intubation success rates), and the providers, no meta-analyses were performed.

An overview of registered, but currently unpublished trials, is provided in the Supplemental Content.

Certainty of evidence across studies

An overview of the assessment of the overall certainty of evidence, using GRADE, is provided in Table 3 and additional details are provided in the Supplemental Content.

A comparison of intubation success rates across the three large randomized trials[6–8] revealed that two of the three trials had a substantially lower proportion of intubation success.[7,8] For this reason and in order to better guide future guidelines, the GRADE assessment was replicated considering three different settings namely OHCA with a high intubation success rate, OHCA with a low intubation success rate, and IHCA. When a specific trial was conducted in a different setting, the certainty in evidence was downgraded for indirectness. Using this approach, the certainty of evidence ranged from very low to moderate depending on the comparison and the setting.

Discussion

In this systematic review on airway management in adult cardiac arrest, which was commissioned by ILCOR to inform an update of international

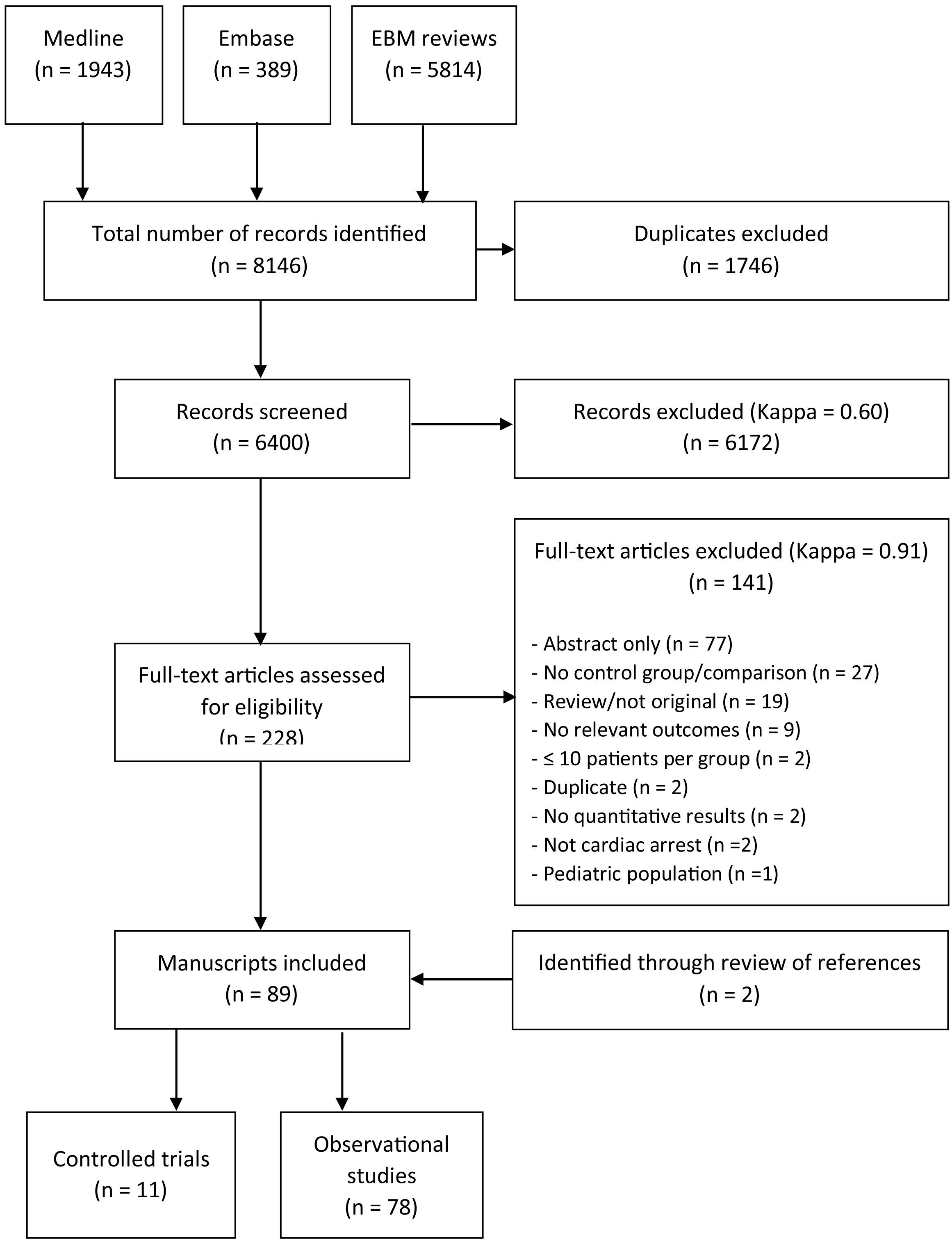

Fig. 1 – PRISMA diagram.
Diagram illustrating the flow of articles throughout the selection procedures.

guidelines, a large number of studies were identified. Despite the extensive literature on this topic, we only identified three large randomized clinical trials in OHCA[6–8] and due to heterogeneity between these trials, we were unable to perform any meta-analyses.

More than 70 observational studies have been published on advanced airway management in cardiac arrest. Unfortunately, these studies are all at a high risk of bias primarily due to confounding and selection bias. Confounding, which is inherent to many observational studies, occurs when certain characteristics are associated with both the exposure and the outcome and therefore leads to a spurious association between the exposure and the outcome. Many such characteristics, e.g. patient (including a difficult airway) and provider features as well as

Table 1 – Brief overview of controlled trials.

Study (first author, year)	Country	Intervention	Comparator	Survival to hospital discharge	
				Intervention	Comparator
Wang, 2018[7]	United States	Laryngeal tube	Tracheal intubation	163/1504 (10.8)	121/1495 (8.1)
Benger, 2018[8]	United Kingdom	i-gel	Tracheal intubation	392/4882 (8.0)	372/4407 (8.4)
Jabre, 2018[6]	Belgium and France	Bag-mask ventilation	Tracheal intubation	55/1018 (5.4)	54/1022 (5.2)
Fiala, 2017[99],[a]	Austria	LTS-D	Bag-mask ventilation	1/35 (3)	1/41 (2)
Benger, 2016[98]	United Kingdom	Supraglottic airway (multiple)	Usual care	14/174 (8)[b] 24/232 (10)[c]	19/209 (9)
Ono, 2015[97],[d]	Japan	Laryngeal tube	Laryngeal mask	9/148 (6)	7/165 (4)
Maignan, 2015[96]	France	LTS-D	Bag-mask ventilation	1/41 (2)	1/41 (2)
Rabitsch, 2003[95]	Austria	Oesophageal tracheal combitube	Tracheal intubation	5/89 (6)	2/83 (3)
Rumball, 1997[94]	Canada	Supraglottic airway (multiple)	Bag-mask ventilation	3/142 (2)[e] 10/147 (7)[f] 4/90 (4)[g]	3/91 (3)
Staudinger, 1994[93]	United States	Oesophageal tracheal combitube	Tracheal intubation	3/38 (8)	3/48 (6)
Goldenberg, 1986[92]	United States	Oesophageal gastric tube airway	Tracheal intubation	11/85 (13)	10/90 (11)

LTS-D: laryngeal tube suction-disposable.
[a] 28-day survival reported.
[b] Laryngeal mask.
[c] i-gel.
[d] 1-month survival reported.
[e] Pharyngeal tracheal lumen airway.
[f] Laryngeal mask.
[g] Oesophageal tracheal combitube.

Table 2 – Overview of risk of bias assessment for controlled trials.

Study (first author, year)	Domain[a]						
	Randomization	Recruitment[b]	Deviations from the intended intervention	Missing outcome	Measurement of the outcome	Selective reporting	Total
Wang, 2018[7]	Some concern	Low	Some concern	Low	Low[c]	Low	Some concern
Benger, 2018[8]	Low	Low	Some concern	Low	Low	Low	Some concern
Jabre, 2018[6]	Low	NA	Some concern	Low	Low	Low	Some concern
Fiala, 2017[99]	Low	NA	High	Low	Low	Some concern	High
Benger, 2016[98]	Low	Low	High	Low	Low	Low	High
Ono, 2015[97]	Low	Low	High	Low	Low[c]	Some concern	High
Maignan, 2015[96]	High	Low	Some concern	Low	Low	Some concern	High
Rabitsch, 2003[95]	High	NA	Some concern	Low	Low	Some concern	High
Rumball, 1997[94]	Low	NA	Some concern	Low	Low	Some concern	Some concern
Staudinger, 1994[93]	High	NA	Some concern	Low	Low	Some concern	High
Goldenberg, 1986[92]	Low	NA	High	Low	Low[c]	Some concern	High

[a]See Supplemental Content for additional details.
[b]Only applicable to cluster-randomized trials.
[c]Some concern for neurological outcomes.

Table 3 – Overview of the GRADE approach.[a]

Intervention	Comparator	Setting	Tracheal intubation success rate	Outcome	Risk difference (95% CI)	Risk difference based on	Certainty in evidence
Laryngeal tube	Tracheal intubation	OHCA	Low	Survival to hospital discharge	27 more per 1000 (from 6 more to 48 more)	Wang, 2018[7]	Low
Laryngeal tube	Tracheal intubation	OHCA	Low	Survival to hospital discharge with a favourable neurological outcome	21 more per 1000 (from 3 more to 38 more)	Wang, 2018[7]	Low
Laryngeal tube	Tracheal intubation	OHCA	High	Survival to hospital discharge	27 more per 1000 (from 6 more to 48 more)	Wang, 2018[7]	Very low
Laryngeal tube	Tracheal intubation	OHCA	High	Survival to hospital discharge with a favourable neurological outcome	21 more per 1000 (from 3 more to 38 more)	Wang, 2018[7]	Very low
Laryngeal tube	Tracheal intubation	IHCA	High	Survival to hospital discharge	27 more per 1000 (from 6 more to 48 more)	Wang, 2018[7]	Very low
Laryngeal tube	Tracheal intubation	IHCA	High	Survival to hospital discharge with a favourable neurological outcome	21 more per 1000 (from 3 more to 38 more)	Wang, 2018[7]	Very low
i-gel	Tracheal intubation	OHCA	Low	Survival to hospital discharge	4 fewer per 1000 (from 14 fewer to 8 more)	Benger, 2018[8]	Low
i-gel	Tracheal intubation	OHCA	Low	Survival to hospital discharge with a favourable neurological outcome	6 more per 1000 (from 16 fewer to 4 more)	Benger, 2018[8]	Low
i-gel	Tracheal intubation	OHCA	High	Survival to hospital discharge	4 fewer per 1000 (from 14 fewer to 8 more)	Benger, 2018[8]	Very low
i-gel	Tracheal intubation	OHCA	High	Survival to hospital discharge with a favourable neurological outcome	6 more per 1000 (from 16 fewer to 4 more)	Benger, 2018[8]	Very low
i-gel	Tracheal intubation	IHCA	High	Survival to hospital discharge	4 fewer per 1000 (from 14 fewer to 8 more)	Benger, 2018[8]	Very low
i-gel	Tracheal intubation	IHCA	High	Survival to hospital discharge with a favourable neurological outcome	6 more per 1000 (from 16 fewer to 4 more)	Benger, 2018[8]	Very low
Bag-mask ventilation	Tracheal intubation	OHCA	Low	28-day survival	1 more per 1000 (from 18 fewer to 21 more)	Jabre, 2018[6]	Low
Bag-mask ventilation	Tracheal intubation	OHCA	Low	28-day survival with a favourable neurological outcome	1 more per 1000 (from 13 fewer to 23 more)	Jabre, 2018[6]	Low
Bag-mask ventilation	Tracheal intubation	OHCA	High	28-day survival	1 more per 1000 (from 18 fewer to 21 more)	Jabre, 2018[6]	Moderate
Bag-mask ventilation	Tracheal intubation	OHCA	High	28-day survival with a favourable neurological outcome	1 more per 1000 (from 13 fewer to 23 more)	Jabre, 2018[6]	Moderate
Bag-mask ventilation	Tracheal intubation	IHCA	High	28-day survival	1 more per 1000 (from 18 fewer to 21 more)	Jabre, 2018[6]	Low
Bag-mask ventilation	Tracheal intubation	IHCA	High	28-day survival with a favourable neurological outcome	1 more per 1000 (from 13 fewer to 23) more)	Jabre, 2018[6]	Low

CI: confidence intervals, OHCA: out-of-hospital cardiac arrest, IHCA: in-hospital cardiac arrest.
[a] See Supplemental Content for additional details.

concurrent treatments, exist for this specific question. Collecting detailed and valid data on such characteristics is difficult but should be the goal of future observational studies aiming at assessing the relationship between airway management and outcomes.

Another major concern with observational studies in cardiac arrest is "resuscitation time bias", a form of selection bias. A detailed explanation of "resuscitation time bias" has been provided elsewhere.[100,101] In brief, this bias primarily occurs when comparing advanced airway management to bag-mask ventilation. Since advanced airway management is generally more likely to occur with extended duration of the cardiac arrest and because longer cardiac arrest duration is strongly associated with poorer outcomes, results will be strongly biased to favour bag-mask ventilation.[100,101] Although there are methods to address such bias[100–102], these have rarely been used in the cardiac arrest literature.[82,103–105] Future observational studies should aim to collect detailed data on the timing of airway (and other) interventions to enable such methods to be applied. Some observational studies comparing different advanced airway strategies in OHCA did not have a critical risk of bias, but were not considered further given the availability of controlled trials.

We identified 11 controlled trials all including patients with OHCA. Of these, eight were smaller phase II/feasibility trials, while three trials, all published in 2018, were larger and powered for more relevant outcomes. Given the small sample sizes, the general high risk of bias, and the fact that some of these were published more than 15 years ago, the eight trials were not considered further for GRADE assessment. Jabre (n = 2043) compared bag-mask ventilation (with pre-defined potential rescue intubation) to tracheal intubation in a physician-based system. The primary outcome of favourable neurological function at 28 days was 4.3% in the bag-mask group and 4.2% in the tracheal intubation group.[6] Benger and Wang compared supraglottic airway devices to tracheal intubation in non-physician-based systems.[7,8] Specifically, Benger (n = 9296) compared the i-gel supraglottic airway to tracheal intubation and found that favourable functional outcome at hospital discharge or 30 days was 6.4% and 6.8%, respectively.[8] Wang et al. (n = 3004) compared the laryngeal tube with tracheal intubation and found that 72-h survival (the primary outcome) was 18.3% and 15.4%, respectively.[7] The difference in prehospital systems might have led to the substantial difference in tracheal intubation success rates which were 98% in the Jabre trial, 69% in the Benger trial, and 52% in the Wang trial. Although "success rates" were not defined identically in the three studies, this discrepancy leads to concerns aboutgeneralizability of the findings.[2] This concern led us to consider two different settings when evaluating the overall certainty of evidence (i.e. the GRADE approach) for out-of-hospital cardiac arrest, namely a setting with a low tracheal intubation success rate (as in the Wang and Benger trials) and a setting with a high tracheal intubation success rate (as in the Jabre trial). Although we cannot provide any specific threshold for high vs. low, we believe this provides the most transparent approach for evaluating the literature and informing guidelines.

Multiple different types of supraglottic airway exist[106] and many have been used in the setting of cardiac arrest. In the Wang trial[7], the laryngeal tube was used while the i-gel was used in the trial by Benger et al.[8] As these airways are very different in design and function, no combination of the two studies was considered reasonable. Although the Wang trial found a survival benefit with the laryngeal tube, it is difficult to make any comparisons of the two different supraglottic airways given the differences between the two trials in both the tracheal intubation success rate and trial design. This also limited our ability to perform network meta-analyses.[107] Whether one type of supraglottic airway is superior to another in the setting of cardiac arrest therefore remains unknown.

As is the case for cardiac arrest trials in general[108], studies in OHCA far outnumbered studies in IHCA. We identified no controlled trials in the IHCA setting and only 9 observational studies exclusively included IHCA patients. When considering the overall certainty of evidence (i.e. the GRADE approach), we therefore extrapolated from the OHCA setting. Given the differences between OHCA and IHCA, including the difference in providers and timing of interventions, additional studies of airway management in IHCA are needed.

Airway management during cardiac arrest is a complex procedure and may include a number of sequential steps. For example, airway management might begin with simple airway manoeuvres such as a chin lift or jaw thrust and mouth-to-mouth or bag-mask ventilation (i.e. basic airway management), and then progress to advanced airway methods (i.e. tracheal intubation or a supraglottic airway) if needed. The choice of techniques will also depend on the skills of the provider. This sequential approach raises the question of what is the most appropriate timing for advanced airway management if advanced airway management is to be performed. We identified nine studies specifically addressing timing of advanced airway management. However, as these were all considered to be of critical risk of bias, we could draw no conclusions about the optimal timing. It is possible, although speculative, that the optimal airway approach and timing might depend on the patient and the specific circumstances of the cardiac arrest. For example, in a patient where the cardiac arrest is caused by hypoxia and there is obvious aspiration, a secure airway (i.e. tracheal intubation) might be preferable early in the course of the cardiac arrest. The most appropriate airway might likewise be dependent on the success of previous airway manoeuvres. For example, if bag-mask ventilation is adequate, advanced airway management can be postponed until ROSC is established and other important tasks (e.g. chest compression and defibrillation) can be prioritized. In contrast if bag-mask ventilation is inadequate despite optimal positioning of the patient, it might be appropriate to proceed to advanced airway management. This sequential and titrated approach complicates any study of airway management. As such, future trials might consider comparing differently defined strategies of airway management that allows for progression of care, as oppose to fixed treatments.

Limitations

The overall Kappa for the review of titles/abstracts was relatively low (Kappa = 0.60) which likely reflects difficulties in correctly identifying observational studies of airway management. However, based on subsequent review of reference lists and contact with content experts, we did not identify any additional articles that were missed during the review process and therefore do not believe this is a major limitation. Many of the decisions made in the process of this review are inherently subjective (e.g. assessment of bias and heterogeneity). Although we used validated tools and aimed to be explicit in our decisions, others might have come up with different assessments.

Conclusion

We identified a large number of studies related to advanced airway management in adult cardiac arrest. However, the majority were at a high risk of bias and heterogeneity across studies precluded any meaningful meta-analyses. Three recently published, large randomized trials on OHCA have improved the certainty of evidence and will help inform future guidelines. Trials addressing advanced airway management during IHCA are lacking.

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Conflicts of interest

Some of the authors (LWA, AG, MD, JS) and collaborators (JN) have published manuscripts related to advanced airway management. However, none of the authors have any financial conflicts of interests and none of the authors have academic conflicts related to ongoing or planned trials. Authors with identified conflicts of interest as per the guidance of the ILCOR Conflict of Interest Committee were not involved in the decision to include/exclude those articles and did not perform the initial data extraction or bias assessment.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2019.04.003.

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