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Review

Advanced airway interventions for paediatric cardiac arrest: A systematic review and meta-analysis

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Abbreviations: AAW, advanced airway; ALS, advanced life support; aOR, adjusted odds ratio; BMV, bag mask ventilation; CI, 95% confidence interval; CPR, cardiopulmonary resuscitation; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; IHCA, in hospital cardiac arrest; ILCOR, International Liaison Committee on Resuscitation; M-H, Cochran–Mantel–Haenszel; OHCA, out of hospital cardiac arrest; SGA, supraglottic airway; TI, tracheal intubation; RD, risk difference.

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https://doi.org/10.1016/j.resuscitation.2019.02.040
Received 8 January 2019; Received in revised form 19 February 2019; Accepted 26 February 2019

Abstract

Aim: To assess the use of advanced airway interventions (tracheal intubation (TI) or supraglottic airway (SGA) placement), compared with bag mask ventilation (BMV) alone, for resuscitation of children in cardiac arrest.

Methods: We searched Medline, EMBASE, and Cochrane Controlled Register of Trials (CENTRAL) for human trials and observational studies published before September 24, 2018 for clinical trials and observational studies with a comparison group. Two investigators reviewed studies for relevance, extracted data, and assessed risk of bias using the GRADE and CLARITY frameworks. Study authors were contacted when necessary to obtain additional data. Critically important outcomes included survival to hospital discharge and survival with good neurological outcome.

Results: We identified 14 studies, including 1 pseudorandomised clinical trial, 3 observational cohort studies using propensity matching, and 8 simple cohort studies suitable for meta-analysis. The overall certainty of evidence was low to very low. For the critically important outcomes of survival to hospital discharge with good neurologic outcome and survival to hospital discharge results suggested better outcomes achieved with BMV than either TI or SGA; limited data favored SGA over TI. The majority of studies involved out-of-hospital cardiac arrest, with few studies of in-hospital cardiac arrest.

Conclusions: TI or SGA are not superior to BMV for resuscitation of children in cardiac arrest, but the overall certainty of evidence is low to very low. Well designed randomised efficacy trials are needed to address this important question.

Introduction and background

Airway management is central in paediatric resuscitation. Placement of an advanced airway (AAW) device, such as a supraglottic airway device (SGA) or tracheal (a.k.a. endotracheal) tube (TI), may allow more effective resuscitation than the alternative of bag-mask ventilation (BMV). Current treatment recommendations from the International Liaison Committee on Resuscitation (ILCOR) recommend TI as the ideal, definitive way to manage the airway during resuscitation, with SGA as an acceptable alternative to BMV that may have advantages when BMV ventilation is difficult.[1] In contrast with adult resuscitation, there are no recent clinical trials to inform choices of airway management in children, but several large, sophisticated observational studies have been published since 2015.

This systematic review and meta-analysis was commissioned by the ILCOR Pediatric Life Support Task Force (PLS TF) in order to determine whether AAW interventions (TI and/or SGA placement) improve outcomes in resuscitation from cardiac arrest in children when compared to BMV or each other.

Methods

Scope

Children and infants in cardiac arrest from any cause, in any setting, excluding neonatal resuscitation.

Protocol registration

This systematic review was registered as PROSPERO 2018 CRD42018102430.

Eligibility criteria

Randomised controlled trials and non-randomised comparison studies of patients aged 2 days to 18 years in cardiac arrest were included. Case reports, unpublished studies, abstracts, protocols, studies involving resuscitation of newborn infants, and non-human studies were excluded. Case series in which all patients received the same attempted intervention (e.g. all cases in which TI was attempted) were excluded. Combined adult/paediatric studies were included if they contained identifiable paediatric results.

Information sources

A professional librarian (NT) searched the MEDLINE (Ovid SP), EMBASE (Ovid SP), and Cochrane Controlled Central Register of Controlled Trials (CENTRAL) databases using a peer-reviewed search strategy. In addition, the authors reviewed international clinical trials registries, the bibliographies of published systematic reviews and of included studies, and review group members provided a list of known relevant studies.

Search

The complete search strategy is provided in the Supplemental materials.

Study selection

Two authors (EJL, SO) independently reviewed the titles and abstracts of all articles identified in the search. Copies were obtained of articles identified by either author. Both authors then reviewed the full text and identified articles meeting inclusion criteria. Disagreements were resolved by discussion.

Data collection process

Two authors (EJL, SO) separately extracted data from each included article to a Microsoft Excel spreadsheet. Discrepancies were resolved by discussion with reference to the original article. When necessary, authors of included studies were contacted to clarify results.

Data items

From each study, the number of children receiving each intervention (TI, SGA, and BMV) and the number of patients achieving successful resuscitation outcomes from each intervention were extracted. Patients in whom an intervention was attempted were included regardless of whether the intervention was successful (e.g. we analyzed all children who received TI attempts, even if correct placement of the tube in the trachea did not occur). Propensity-matched data were used when available. Outcomes were compiled in the Summary of Findings table. When case-level data could not be obtained from the publication or author, the study was not included in the meta-analysis and instead author-calculated adjusted odds ratios (aORs) for each outcome were provided. Some studies presented pooled data for all patients with AAW attempts, combining outcomes achieved with TI and SGA. In these cases, we first attempted to contact the

author for separate data for patients receiving TI and SGA attempts. If separate data could not be obtained, we categorized the study based on whether the majority of the AAW interventions were TI or SGA.[2,3]

Selection of outcomes

The PLS TF identified two critically important outcomes, survival to hospital discharge with good neurologic outcome and survival to hospital discharge, and two important outcomes, survival to hospital admission and return of spontaneous circulation (ROSC). When different studies measured specific outcomes at different time points, these were combined for analysis (i.e. results for survival with good neurologic outcome measured at discharge or 1 month later were combined; survival to hospital discharge was combined with 1-month and 1-year survival; ROSC during the prehospital period, ROSC overall, and ROSC sustained 20 min were combined; good neurologic outcome defined as cerebral performance score 1–2 or paediatric cerebral performance score 1–2 were combined).

Results of analysis for the two critically important outcomes are presented in the manuscript, and results of all analyses are provided in the Supplemental materials.

Risk of bias in individual studies

Risk of bias was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology for clinical trials and the CLARITY framework for cohort studies.[4,5]

Summary measures

All comparisons were described in terms of risk difference, with 95% confidence intervals (CIs) calculated using Cochran–Mantel–Haenszel statistics. Because of heterogeneity in study settings, patient populations, and outcomes definitions, a random effects model was used for combination of results. All summary effects were presented in the form of Risk Difference (RD) with CIs. Summary effects were not reported if heterogeneity between studies was very high (I^2 statistic >75%).[6–8]

Synthesis of results

Results were compiled into Summary of Findings tables using the GRADEpro Guideline Development tool.[9] Statistical calculations and Forest plot generation were performed using RevMan 5.3.[10] Summary effect measures were generated for each study type (clinical trial, propensity-matched cohort study, or simple cohort study), but studies of differing design were not further combined.

Risk of bias across studies

The risk of bias across studies was evaluated using the GRADE framework. Inconsistency was considered serious if the I^2 statistic was greater than 50%, and very serious if greater than 75%. Indirectness was considered serious if more than half the resuscitations in a study category were conducted prior to 2000 because of subsequent changes to standard resuscitation. Imprecision was considered serious if the CI for risk difference crossed two of the following points: +0.05 (clinically important benefit to the intervention, determined by the Task Force), 0.00 (equipoise), and −0.05 (appreciable harm), and very serious if all three points were crossed.

Additional analyses

The following subgroup analyses were prespecified: out-of-hospital cardiac arrest (OHCA), in-hospital cardiac arrest (IHCA), primary respiratory arrest, other causes of cardiac arrest including traumatic, patients presenting with shockable or non-shockable rhythms, infants (age 2 days to 1 year), young children (1–12 years), adolescents (13–18 years), and airway management by paramedics, physicians, and other health care professionals. In addition, the protocol planned to study the timing of AAW placement (immediate or only after ROSC), but this analysis was deemed synonymous with the main analysis because TI is a key component of post-resuscitation care. Post hoc, the study group added analyses of recently-conducted studies, excluding resuscitations conducted prior to the year 2000.

Results

Study selection

The initial search was conducted on April 5, 2018, and updated on September 24, 2018. Detailed results of each stage of the search are provided in the Supplemental materials. First-pass agreement was 94.0% on stage 1 and 85.7% on stage 2 of article screening. The search identified 2980 non-duplicate articles, of which 14 met inclusion criteria

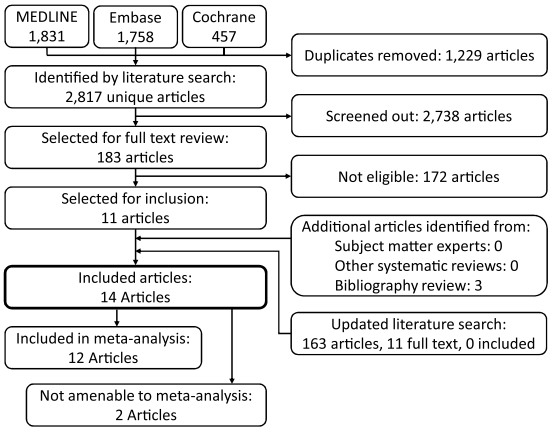

Fig. 1 – Article selection.

Table 1 – Characteristics of included studies.

Study	Years conducted	Setting	Location	Percent with trauma	Means of allocation	Advanced airway interventions studied	Outcomes assessed	Unsuccessful TI/ SGA attempts counted as	Notes
Clinical trials									
Gausche et al.[13]	1994–1997	OHCA	USA	Less than 23%	Even/odd day	TI	• SGNF • SHD	TI	
Cohort studies – propensity-matched									
Andersen et al.[12]	2000–2014	IHCA	USA	Less than 12%	Unclear	TI	• SGNF • SHD • ROSC (sustained 20 min)	BMV	Time-dependent propensity matching
Hansen et al.[14]	2013–2015	OHCA	USA	0%	Unclear	TI, SGA	• SGNF • SHD • SHA	BMV	
Ohashi-Fukuda et al.[15]	2011–2012	OHCA	Japan	Less than 56%	Unclear	TI, SGA	ROSC (sustained 20 min) • SGNF (assessed at 1 month) • SHD (1-month survival) • ROSC (prehospital ROSC)	BMV	Unpublished data provided by author. Excluded infants
Cohort studies – not propensity-matched									
Abe et al.[16]	2005–2008	OHCA	Japan	Unclear	Unclear	TI	• SHA SHD (1 month survival)	TI	Infants only; unpublished data provided by author
Aijian et al.[17]	1984–1987	OCHA	USA	0%	Unclear	TI	• SHD • SHA	TI	Groups 2 and 3 pooled for analysis
Deasy et al.[18]	1999–2007	OHCA	Australia	8%	Unclear	TI	• SHD	BMV	Table 1
del Castillo et al.[19]	2007–2009	IHCA	Argentina, Brazil, Columbia, Chile, Ecuador Honduras, Italy, Paraguay, Portugal, Spain,	16%	Unclear	TI	• SGNF (assessed at 1 year)	BMV	Table 3
Guay and Lortie[20]	1983–1987	IHCA	Canada	2%	Unclear	TI	• SHD (1 year survival)	TI	Author clarified that study compared TI attempts to non-attempts
Pitetti et al.[21]	1995–1999	OHCA	USA	27%	Unclear	TI	• SHD • SHA	All ALS patients assumed to have TI attempted (92% were successfully intubated)	ALS group patients also received epinephrine, atropine, and bicarbonate
Sirbaugh et al.[22]	1992–1995	OHCA	USA	29%	Unclear	TI	• SGNF • SHD • ROSC (prehospital ROSC)	BMV	Author clarified all patients not intubated had TI attempted

(continued on next page)

Table 1 (continued)

Study	Years conducted	Setting	Location	Percent with trauma	Means of allocation	Advanced airway interventions studied	Outcomes assessed	Unsuccessful TI/ SGA attempts counted as	Notes
Tham et al.[23]	2009–2012	OHCA	Japan, Korea, Malaysia, Singapore, Taiwan, Thailand, UAE	25%	Geographic; within ALS-capable areas, allocation unclear	TI and SGA combined (63% SGA and 23% "other advanced airway")	• SHD	BMV	Unpublished data and clarifications provided by author
Cohort studies: not propensity-matched, not amenable to meta-analysis									
Fink et al.[2]	2007–2012	OHCA	USA	0%	Unclear	TI and SGA combined (92% TI)	• SHD • SHA	AAW	Raw data not available
Tijssen et al.[3]	2005–2012	OHCA	Canada, USA	0%	Unclear	TI and SGA combined (93% TI)	• SHD	AAW	Raw data not available

BMV: bag mask ventilation; IHCA: in-hospital cardiac arrest; OHCA: out-of-hospital cardiacarrest; ROSC: return of spontaneous circulation SGA: supraglottic airway; SGNF: survival with good neurologic function; SHA: survival to hospital admission; SHD: survival to hospital discharge; TI: tracheal intubation; USA: United States of America.

and 12 were amenable to combination by meta-analysis. For the remaining 2 studies, after unsuccessful attempts to obtain raw data from the authors, adjusted odds ratio (aOR) results were reported. We identified two analyses of the same data set, and included the version containing more comprehensive data (Fig. 1).[11,12]

Study characteristics

One pseudorandomised clinical trial,[13] three propensity score-matched observational studies[12,14,15], and 10 other observational studies[2,3,16–23] were identified. Characteristics of these studies are described in Table 1. Three studies of IHCA and 11 studies of OHCA were identified, involving 14,191 children from 23 countries. All studies compared TI with BMV, and 4 studies compared SGA with BMV and TI. One study excluded infants and one was of infants only; the remainder included wide paediatric age groups. Twelve of the 14 studies were amenable to combination by meta-analysis.

Risk of bias within studies

The risk of bias in each study is presented in the Supplemental materials. One pseudorandomised clinical trial was identified as having low risk of bias.[13] Adherence to the intended intervention was transparent and high, though some cross-over was reported.

Three retrospective cohort studies using propensity-matching methods were judged to have serious risk of bias.[12,14,15] These studies each utilized rigorously-collected registry data and applied propensity-matching methods to attempt to account for the likelihood that TI would be attempted, or not attempted, for a given patient. However, none of these studies were able to distinguish patients who did not have attempts at TI from those in whom TI was attempted unsuccessfully.

Ten retrospective cohort studies that did not use propensity matching were judged to have very serious risk of bias, primarily because it was impossible to determine why some patients were intubated and some were not. Eight of these studies contained results amenable to meta-analysis, either in the published manuscript or provided by the author.[16–23] Two studies were not amenable to combination by meta-analysis.[2,3] These studies provided only pooled results reporting the adjusted odds ratios (aORs) of survival to hospital discharge among patients managed with AAW (92% and 93% CI, 8% and 7% SGA) compared with BMV. The authors were successfully contacted but unable to provide separate data by intervention or raw outcome data. These results were presented in the Supplemental materials. In addition, two studies compared patients treated with a suite of ALS interventions to those with BLS resuscitation only.[21,23]

Risk of bias across studies

Despite major differences in study design and setting, there was little heterogeneity in study results. Small numbers of subjects in many studies and the low proportion of patients with good outcome contribute to imprecision in the estimate of treatment effect for most comparisons.

Synthesis of results

GRADE Summary of Findings Tables for the critical outcome comparisons are presented in Tables 2–4, and data for all comparisons are provided in the Supplemental materials. Forest plots for the critical outcome comparisons are presented in Figs. 2–4 and forest plots for all analyses are presented in the Supplemental materials.

Table 2 – Summary of findings: tracheal intubation vs. bag mask ventilation for the critical outcomes of survival with good neurologic function and survival to hospital discharge.

Certainty assessment							No. of patients		Effect[e]		Certainty	Importance
No. of studies	Study design	Risk of bias[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Other considerations	Tracheal intubation	Bag-mask ventilation alone	Relative (95% CI)	Absolute (95% CI)		
Survival with good neurologic function												
Clinical trials												
1	Randomised trials	Not serious	Not serious	Serious	Serious	None	10/290 (3.4%)	15/301 (5.0%)	RR 0.69 (0.32–1.52)	15 fewer per 1000 (from 17 more to 48 fewer)	⊕⊕◯◯ Low	Critical
Cohort studies — propensity matched												
3	Observational studies	Serious	Not serious	Not serious	Not serious	None	219/1745 (12.6%)	316/2110 (15.0%)	RR 0.59[f] (0.29–1.19)	49 fewer per 1000 (from 21 fewer to 77 fewer)	⊕◯◯◯ Very low	Critical
Cohort studies — not propensity matched												
3	Observational studies	Very serious	Very serious	Serious	Very serious	None	102/318 (32.1%)	72/870 (8.3%)	RR 2.76 (0.40–18.99)	63 more per 1000 (from 399 more to 274 fewer)	⊕◯◯◯ Very low	Critical
Survival to hospital discharge												
Clinical trials												
1	Randomised trials	Not serious	Not serious	Serious	Serious	None	24/290 (8.3%)	24/301 (8.0%)	RR 1.04 (0.60–1.79)	3 more per 1000 (from 47 more to 41 fewer)	⊕⊕◯◯ Low	Critical
Cohort studies — propensity matched												
3	Observational studies	Serious	Not serious	Not serious	Not serious	None	466/1893 (24.6%)	607/2262 (26.8%)	RR 0.75 (0.46–1.23)	53 fewer per 1000 (from 20 fewer to 87 fewer)	⊕◯◯◯ Very low	Critical
Cohort studies — not propensity matched												
7	Observational studies	Very serious	Very serious	Not serious	Serious	None	60/854 (7.0%)	344/3685 (9.3%)	RR 0.78[f] (0.45–1.35)	20 fewer per 1000 (from 46 more to 87 fewer)	⊕◯◯◯ Very low	Critical

CI: confidence interval; RR: risk ratio.

[a] See risk of bias table for individual studies (Supplemental materials).

[b] Assessed as serious inconsistency if the I^2 statistic was greater than 50%, and very serious if greater than 75%.

[c] Assessed as serious indirectness if more than half of the resuscitations in a study category were conducted prior to the year 2000, because standard resuscitation has changed markedly.

[d] Assessed as serious imprecision if the CI crossed two of the following cut-off point: absolute risk difference +0.05 (appreciable benefit to intervention), 0.00 (equipoise), and −0.05 (appreciable harm from intervention). Assessed as very serious imprecision if the CI crossed all three of these points.

[e] Calculations performed using RevMan 5.3.

[f] Confidence intervals for risk ratio may be affected by studies with 0 values in cells.

Table 3 – Summary of findings: supraglottic airway vs. bag mask ventilation for the critical outcomes of survival with good neurologic function and survival to hospital discharge.

Certainty assessment							No. of patients		Effect[e]		Certainty	Importance
No. of studies	Study design	Risk of bias[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Other considerations	Supraglottic airway	Bag-mask ventilation alone	Relative (95% CI)	Absolute (95% CI)		
Survival with good neurologic function												
Cohort studies — propensity matched												
2	Observational studies	Serious	Serious	Not serious	Not serious	None	25/530 (4.7%)	105/1127 (9.3%)	RR 0.62 (0.40–0.98)	29 fewer per 1000 (from 17 more to 75 fewer)	⊕◯◯◯ Very low	Critical
Cohort studies — not propensity matched												
1	Observational studies	Very serious	Not serious	Very serious	Not serious	None	3/109 (2.8%)	29/791 (3.7%)	RR 0.75 (0.23–2.42)	9 fewer per 1000 (from 24 more to 43 fewer)	⊕◯◯◯ Very low	Critical
Survival to hospital discharge												
Cohort studies — propensity matched												
2	Observational studies	Serious	Very serious	Not serious	Not serious	None	69/530 (13.0%)	147/1127 (13.0%)	RR 1.01 (0.53–1.92)	13 more per 1000 (from 81 more to 78 fewer)	⊕◯◯◯ Very low	Critical
Cohort studies — not propensity matched												
2	Observational studies	Very serious	Serious	Not serious	Serious	None	18/379 (4.7%)	311/3525 (8.8%)	RR 0.60 (0.23–1.54)	35 fewer per 1000 (from 18 more to 88 fewer)	⊕◯◯◯ Very low	Critical

CI: confidence interval; RR: risk ratio.

[a] See risk of bias table for individual studies (Supplemental Appendix).

[b] Assessed as serious inconsistency if the I^2 statistic was greater than 50%, and very serious if greater than 75%.

[c] Assessed as serious indirectness if more than half of the resuscitations in a study category were conducted prior to the year 2000, because standard resuscitation has changed markedly.

[d] Assessed as serious imprecision if the CI crossed two of the following cut-off point: absolute risk difference +0.05 (appreciable benefit to intervention), 0.00 (equipoise), and −0.05 (appreciable harm from intervention). Assessed as very serious imprecision if the CI crossed all three of these points.

[e] Calculations performed using RevMan 5.3.

Table 4 – Summary of findings: tracheal intubation vs. supraglottic airway for the critical outcomes of survival with good neurologic function and survival to hospital discharge.

Certainty assessment							No. of patients		Effect[e]		Certainty	Importance
No. of studies	Study design	Risk of bias[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Other considerations	Tracheal intubation	BBag-mask ventilation alone	Relative (95% CI)	Absolute (95% CI)		
Survival with good neurologic function												
Cohort studies — propensity matched												
2	Observational studies	Serious	Not serious	Not serious	Serious	None	34/758 (4.5%)	25/530 (4.7%)	RR 0.75[f] (0.41–1.37)	22 fewer per 1000 (from 6 more to 51 fewer)	⊕◯◯◯ Very low	Critical
Cohort studies — not propensity matched												
1	Observational studies	Very serious	Not serious	Not serious	Serious	None	3/18 (16.7%)	3/109 (2.8%)	RR 6.06 (1.32–27.70)	139 more per 1000 (from 314 more to 36 fewer)	⊕◯◯◯ Very low	Critical
Survival to hospital discharge												
Cohort studies — propensity matched												
2	Observational studies	Serious	Not serious	Not serious	Serious	None	55/758 (7.3%)	69/530 (13.0%)	RR 0.72 (0.47–1.10)	31 fewer per 1000 (from 11 more to 73 fewer)	⊕◯◯◯ Very low	Critical
Cohort studies — not propensity matched												
2	Observational studies	Very serious	Not serious	Not serious	Serious	None	15/203 (7.4%)	18/379 (4.7%)	RR 1.97 (0.99–3.93)	34 more per 1000 (from 74 more to 1 fewer)	⊕◯◯◯ Very low	Critical

CI: confidence interval; RR: risk ratio.

[a] See risk of bias table for individual studies (Supplemental materials).

[b] Assessed as serious inconsistency if the I^2 statistic was greater than 50%, and very serious if greater than 75%.

[c] Assessed as serious indirectness if more than half of the resuscitations in a study category were conducted prior to the year 2000, because standard resuscitation has changed markedly.

[d] Assessed as serious imprecision if the CI crossed two of the following cut-off point: absolute risk difference +0.05 (appreciable benefit to intervention), 0.00 (equipoise), and −0.05 (appreciable harm from intervention). Assessed as very serious imprecision if the CI crossed all three of these points.

[e] Calculations performed using RevMan 5.3.

[f] Confidence intervals for risk ratio may be affected by studies with 0 values in cells.

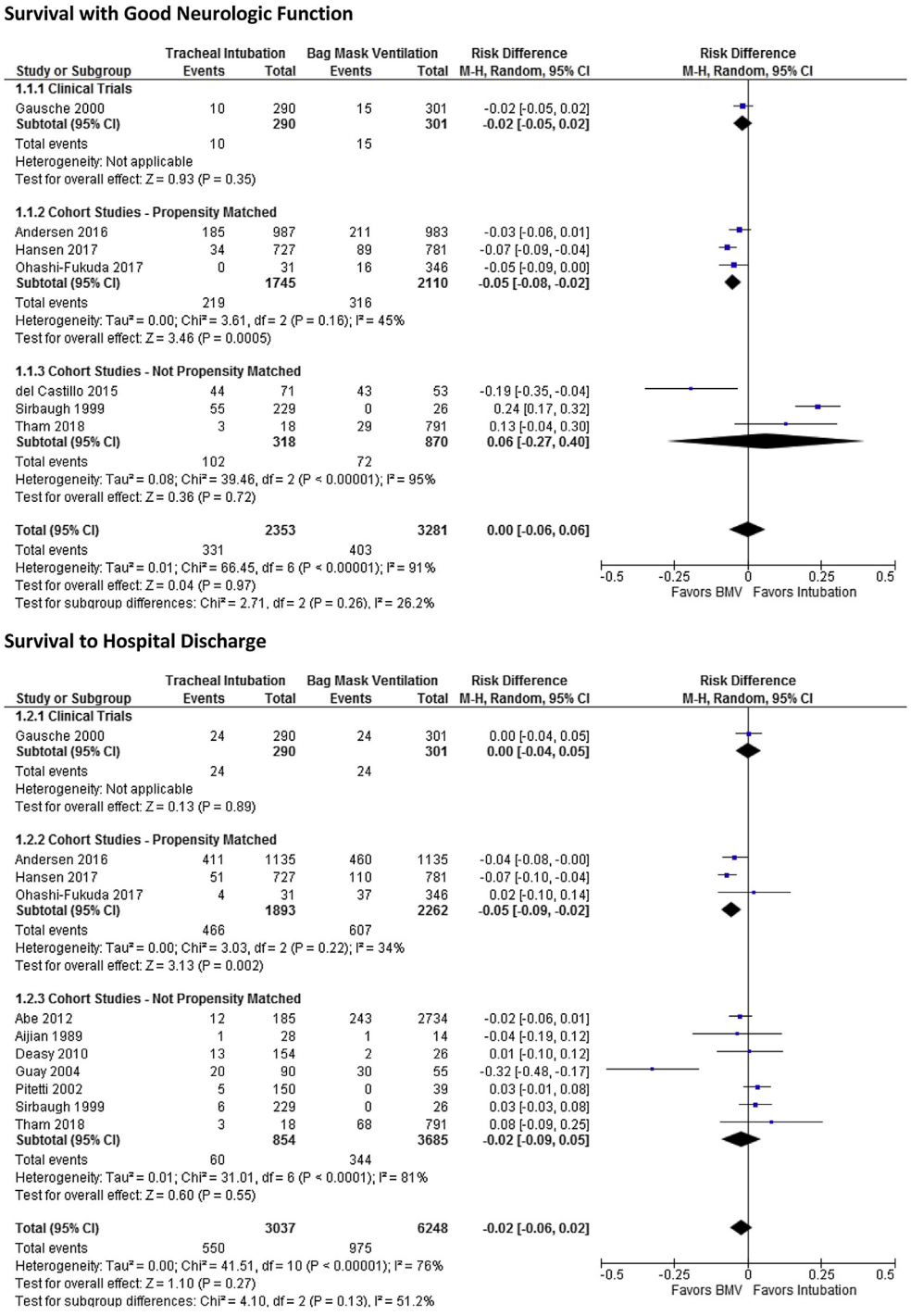

Fig. 2 – Forest plots comparing tracheal intubation to bag mask ventilation for the critical outcomes of survival with good neurologic function and survival to hospital discharge. BMV: bag mask ventilation. M–H = Cochran-Mantel-Haenszel. 95% CI: 95 percent confidence interval.

Tracheal intubation (TI) compared to bag mask ventilation (BMV)

Survival with good neurologic outcome

Low certainty evidence comes from one pseudorandomised trial involving 591 children with out-of-hospital cardiac arrest (OHCA).[13] This methodologically excellent trial was downgraded due to indirectness because of changes in standard resuscitation since the trial was conducted (1994–1996). Analysis was based on intention-to-treat. No statistical difference was found (15 fewer children surviving with good neurologic outcome per 1000 randomised to TI; CI: 48 fewer to 17 more).

Additional, very low certainty evidence comes from three propensity-adjusted cohort studies, downgraded because none

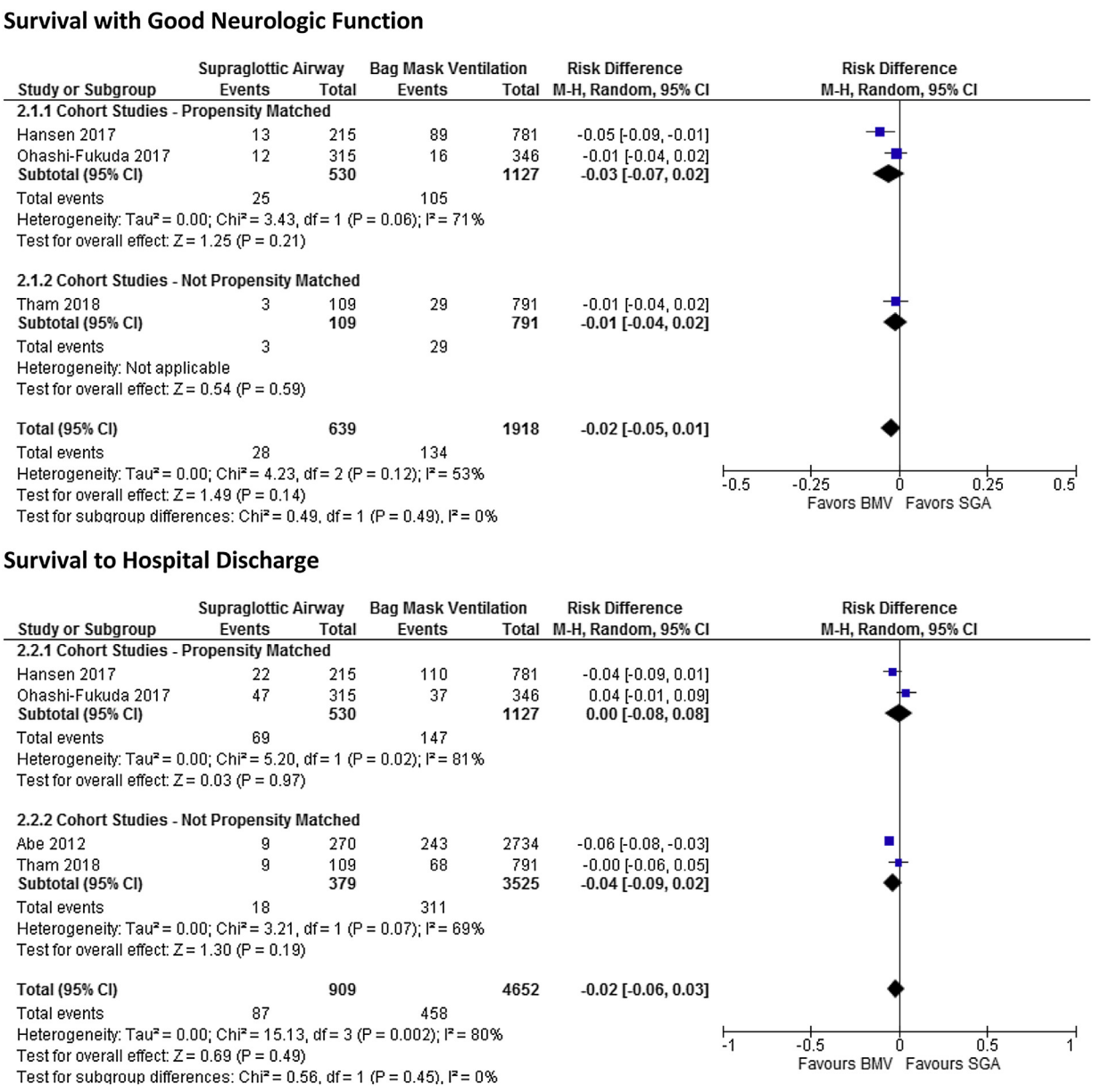

Fig. 3 – Forest plots comparing supraglottic airway placement to bag mask ventilation for the critical outcomes of survival with good neurologic function and survival to hospital discharge. BMV: bag mask ventilation. M–H = Cochran-Mantel-Haenszel. SGA: supraglottic airway. 95% CI: 95 percent confidence interval.

could differentiate children with failed attempts at TI from those in whom TI was not attempted.[12,14,15] These studies included 3855 children with in-hospital cardiac arrest (IHCA) or OHCA and reported reduced survival with good neurologic outcome associated with TI (49 fewer survivors per 1000 resuscitations; CI: 77 fewer to 21 fewer). The three simple cohort studies found discordant results (I^2: 95%).[19,22,23]

Survival to hospital discharge

The best evidence for survival to hospital discharge is of low certainty, coming from the pseudo-randomised trial, which did not demonstrate superiority of TI when compared with BMV-only resuscitation (3 more patients surviving to discharge per 1000 assigned to TI; CI: 41 fewer to 47 more).[13]

Very low certainty evidence is provided by three propensity-adjusted cohort studies including 4155 children.[12,14,15] Taken together, these studies support harm with TI when compared to BMV (53 fewer survivors per 1000 patients; CI: 86 fewer to 20 fewer). Seven simple observational studies provide discordant results (I^2: 81%).[16–18,20–23] Finally, very low certainty evidence is available from 2 simple observational studies involving 3992 children. These studies, which were not amenable to meta-analysis, reported no significant difference in outcomes between TI and BMV (aOR for survival to discharge in patients treated with TI: aOR 0.64 (CI 0.37–1.13) and aOR 0.69 (CI: 0.43–1.10).[2,3]

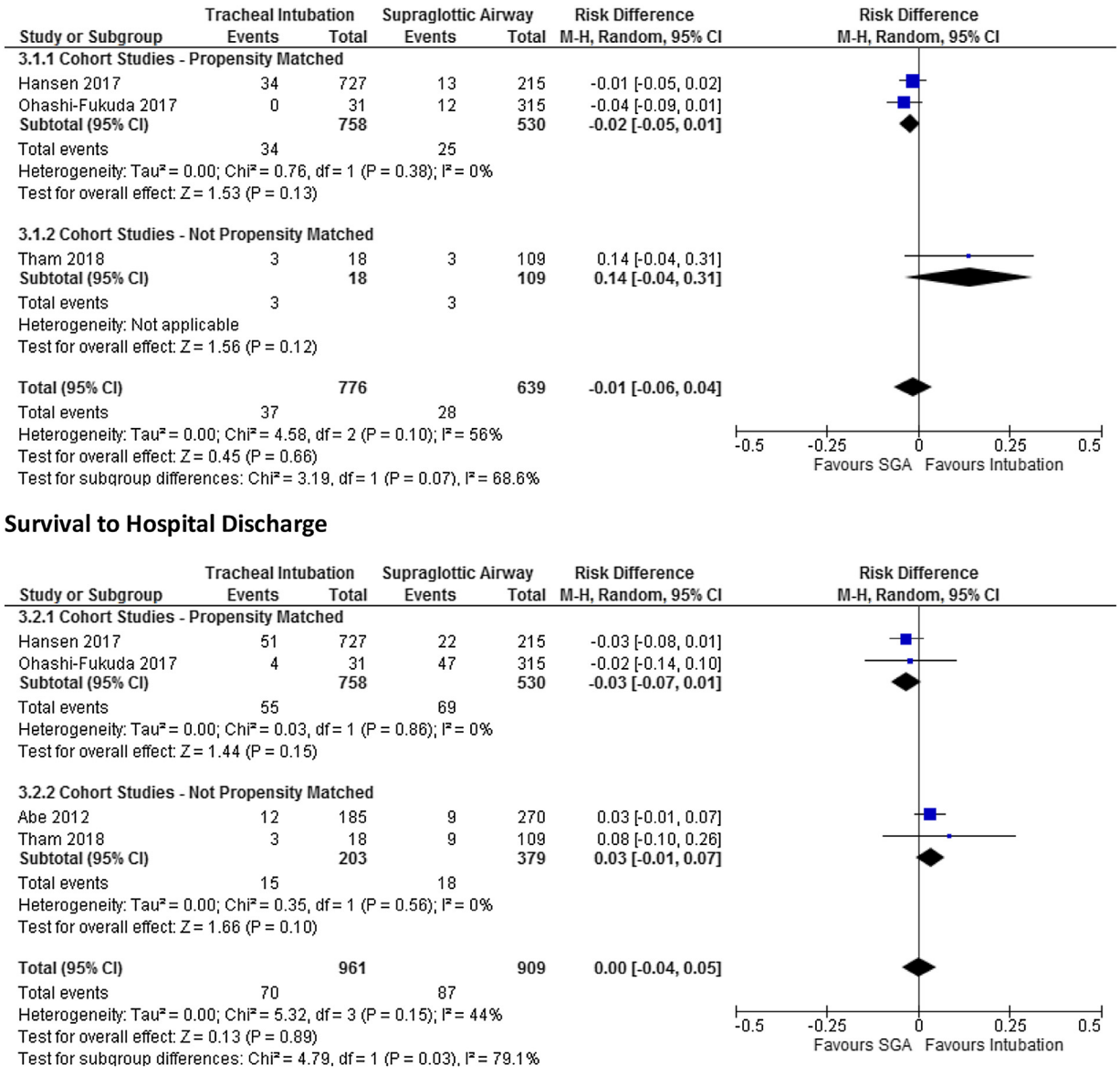

Fig. 4 – Forest plots comparing tracheal intubation to supraglottic airway placement for the critical outcomes of survival with good neurologic function and survival to hospital discharge. BMV: bag mask ventilation. M–H = Cochran-Mantel-Haenszel. 95% CI: 95 percent confidence interval.

Overall summary of findings

Overall, these results suggest with low to very low certainty that TI-based resuscitation is not superior to BMV-based resuscitation for cardiac arrest in children for the critically important outcomes of survival to hospital discharge and survival to hospital discharge with good neurologic outcomes.

Supraglottic airway (SGA) compared to bag mask ventilation (BMV)

No clinical trial studied SGA placement. The best available evidence for all outcomes is of very low certainty.

Survival with good neurologic outcome

Two propensity-adjusted cohort studies involving 1657 patients did found no association between SGA placement and survival with good neurological outcome (29 fewer survivors with good neurologic outcome per 1000 patients managed with SGA; CI: 75 fewer to 17 more).[14,15] Similar findings were obtained from a simple observational study of 900 children (9 fewer; CI: 43 fewer to 24 more).[23]

Survival to hospital discharge

Two propensity-matched cohort studies involving 1657 children found divergent associations between SGA placement and BMV for the outcome of survival to hospital discharge (I^2:

81%).[14,15] Two observational studies of 3904 children did not identify a statistical association between assignment to SGA (35 fewer survivors per 1000 treated with SGA; CI: 88 fewer to 18 more).[16,23]

Overall summary of findings

Although conflicting study results make any conclusion very uncertain, the overall data are most consistent with no treatment effect associated with SGA ventilation when compared with BMV for these critically important resuscitation outcomes in cardiac arrest in children.

Tracheal intubation (TI) compared to supraglottic airway (SGA)

No clinical trial studied the impact of SGA placement on resuscitation outcomes; the best available evidence is observational and of very low certainty.

Survival to hospital discharge with good neurologic outcome

Combined data from 2 propensity-adjusted cohort studies of 1288 children showed no statistical association between TI and SGA-based resuscitations in the likelihood of survival with good neurologic outcome (22 fewer neurologically intact survivors per 1000 patients managed with TI rather than SGA; CI: 51 fewer to 6 more).[14,15] In addition, a simple cohort study of 127 patients reported no significant difference in this outcome (139 more survivors with TI; CI: 36 fewer to 314 more).[23]

Survival to hospital discharge

Data from the same two propensity-adjusted cohort studies of 1288 children found no significant association between the choice of AAW technique and survival to hospital discharge (31 fewer children surviving per 1000 resuscitations using TI compared with SGA; CI: 73 fewer to 11 more).[14,15] The combined results of 2 simple cohort studies involving 582 children also show no statistical association between AAW modality and survival (34 more survivors per 1000 children managed with TI; CI: 6 fewer to 75 more).[16,23]

Overall summary of findings

Based on small and contradictory evidence base of very low certainty, it appears that critically important outcomes for children in cardiac arrest are not significantly different with TI resuscitation compared to SGA resuscitation.

Subgroup analyses

Results for all subgroup analyses, including Forest plots with calculations of absolute risk difference for each comparison and outcome, are included in the Supplemental materials.

Out-of-hospital and in-hospital cardiac arrest

Subgroup analyses were conducted for patients with OHCA and IHCA. Because the clinical trial was conducted in the OHCA setting, the best available evidence was low certainty for OHCA and very low certainty for IHCA. Only three observational studies examined outcomes in the setting of IHCA. Otherwise, no important differences were noted between these subgroups and each other, or the main analysis.

Initially shockable- and non-shockable rhythms

No study reported data on children who had an initially shockable rhythm. However, an earlier published version of an included study reported data on children with IHCA who had non-shockable rhythms.[11] Very low certainty evidence showed no association between survival and TI (10 more patients surviving to hospital discharge per 1000 resuscitations with TI; CI: 40 fewer to 50 more).

Analyses by age group

One retrospective cohort study of 455 infants (age less than one year) provides very low certainty evidence about survival to hospital discharge following OHCA.[16] This study reported no significant difference in survival to hospital discharge for children in cardiac arrest managed with TI compared with BMV (24 fewer survivors per 1000; CI: 61 fewer to 13 more), a significant survival disadvantage in patients managed with SGA compared with BMV (56 fewer survivors per 1000 managed with SGA; CI: 80 fewer to 32 fewer), and no significant difference in survival to hospital discharge when TI resuscitation was compared with SGA resuscitation (32 more survivors per 1000 resuscitations with TI compared with SGA; CI: 10 fewer to 73 more).

In an adjusted post hoc analysis providing very low certainty evidence, one retrospective study compared the odds of survival to hospital discharge associated with SGA-based airway management with BMV only.[23] The odds of survival to discharge were better when SGA was attempted in the resuscitation of younger children (aged 0–12 years) (aOR: 3.35; CI: 1.23–9.13), but not in adolescents (aOR: 0.4; CI: 0.13–1.26).

Traumatic vs. medical causes of cardiac arrest

Six studies either excluded patients with traumatic causes of cardiac arrest or included fewer than 10% of such patients in the study cohort.[2,3,14,17,18,20] Analyses of these studies of medical arrest found only very low certainty evidence, with similar results to the overall results described above. No studies were found of children in cardiac arrest due to trauma.

Recent studies

A post hoc analysis was performed limited to studies involving resuscitations conducted in the year 2000 or after.[12,14–16,18,19,23] The remaining evidence is of very low certainty, and does not differ significantly from the main analysis.

Subgroup analyses not conducted

No data could be found to support the preplanned subgroup analyses on the effect of AAW subdivided by type of arrest (primary respiratory arrest vs primary cardiac arrest), different SGA devices, or training of the person performing the AAW intervention. With the exception of three esophageal intubations reported in the clinical trial,[13] no study rigorously reported data about safety outcomes apart from the overall results of resuscitation, and the review committee judged that the main outcomes of resuscitation are the outcomes of interest.

Discussion

The management of the airway is central in paediatric resuscitation, especially since respiratory failure is a frequent cause of paediatric cardiac arrest. Placement of an AAW, whether TI or SGA, may allow more effective resuscitation than the alternative of BMV (with or without an oropharyngeal or nasopharyngeal airway). To effectively maintain an open airway and deliver sustained good ventilations using BMV can be difficult even in skilled hands. There are uncertainties, however, about the risks:benefits of using AAW interventions and the difficulties that may be incurred as compared with the relatively simpler system of BMV.

Potential benefits of AAW placement include more effective ventilation, reduced aspiration of gastric contents (by preventing gastric distension and/or by mechanical protection of the upper airway), uninterrupted chest compressions, and more effective monitoring of CPR effectiveness/ROSC detection via monitoring of end-tidal carbon dioxide. Potential harms include incorrect tube placement or tube displacement leading to lack of lung ventilation or oxygenation, reduction in CPR quality due to prolonged interruption of CPR, hyperventilation leading to respiratory alkalosis, reduced cerebral perfusion, and barotrauma including pneumothorax. Thus, the utilization of AAW devices may improve or reduce a patient's likelihood of surviving and realizing neurologic recovery. Because of differences in the pathophysiology of arrest, timing of resuscitation interventions, and training and experience of resuscitation providers, the effect of AAW interventions may differ between the OHCA and IHCA settings. Similar statements can be made about resuscitation involving children of different ages and with different etiologies of cardiac arrest.

Despite decades of research creating a moderate-sized evidence base, the overall certainty of the available evidence about AAW interventions in paediatric cardiac arrest is low to very low. The one clinical trial, though rigorous in design and execution, was conducted more than 20 years ago, when standard resuscitation practice was quite different from current practice. In particular, the evidence base surrounding IHCA and SGA-based resuscitation involves only a few, observational studies and is therefore of very low certainty.

Effective BMV is a difficult skill that requires good initial training, practice, and quality control. Paediatric AAW programs require a moderate investment in equipment and a significant investment in training, skills maintenance, and quality control programs to be successful. However, TI is supported in essentially all hospital settings in the developed world, and as long as AAW support remains a standard component of care for respiratory arrest and in post-ROSC care, advanced life (ALS) support-capable emergency medical services agencies and IHCA teams will need to maintain this capability as well. The benefit or harm associated with AAW-based resuscitation is likely to differ between settings. The available data do not inform the questions of whether better outcomes might be achieved with AAW in long distance transportation/prolonged resuscitation situations, with highly experienced airway operators, when video laryngoscopy is utilized, when AAW placement is only attempted when BMV is difficult, etc.

Acknowledging this uncertainty, the current available data suggest, with low to very low certainty, that the critical outcomes of survival with good neurologic outcome and survival to hospital discharge are not significantly better when resuscitation is performed with TI or SGA, compared with BMV alone.

Limitations

Limitations to meta-analyses are well described. Mathematical combination of studies with differing designs, patient populations, and endpoint definitions are always problematic, and small differences in analytic technique may change the reported answers. Relative risk and risk difference calculations sometimes produce divergent results when cell totals are small, as happened frequently in this review. Several of the studies contain flaws that some would consider fatal. These include the inability to correctly classify patients with failed AAW attempts[12,14,15] and exposure to AAW versus BMV-based resuscitation based on the availability of ALS-level resuscitation.[19,23] Combining the outcome of survival with good neurologic function assessed at discharge or 1 month later may have added heterogeneity to the estimate of this critical outcome. Similar concerns affect the critical outcome of survival to hospital discharge, which various studies assessed at 0 days, 1 month, or 1 year after discharge. While differences in the timing of ROSC assessment in OHCA studies (ROSC during the prehospital period, ROSC overall, and ROSC sustained 20 min) may also have affected results, this outcome was not critical. Because the two studies in which we were unable to obtain separate data for TI and SGA recipients were also not amenable to meta-analysis, the overall effect of this pooling of interventions on study conclusions is negligible.[2,3]

Unmeasured factors, such as the training or experience level of the person performing airway management and ventilation, may be more important than the choice of technique or device. In addition, the benefit or harm associated with AAW-based resuscitation is likely to differ between settings. The available data do not inform the questions of whether better outcomes might be achieved by AAW-based strategies in long distance transportation/prolonged resuscitation situations, with highly experienced airway operators, when video laryngoscopy is utilized, if AAW placement is only attempted when BMV is difficult, etc. The analyzed data are only relevant to AAW interventions during CPR, and do not pertain to airway management in other critical situations.

Research priorities

There is a paucity of randomised controlled trials and high quality evidence to evaluate this important question in resuscitation, for a number of reasons. Cardiac arrests in children are rare. Using AAWs in cardiac arrest are established practices and randomization requires community equipoise and health care provider endorsement which may be challenging to achieve across multiple sites. Implementing a protocol in children that requires exemption from informed consent is demanding. Because cardiac arrests in children are rare, a trial needs to be multicenter and requires high quality research infrastructure and a data management centre which are expensive. There is very little funding for resuscitation research trials compared to other disease and injury states.[24,25]

Children are a precious resource and deserving of evidence-based care. An enormous investment is currently being made in equipment, initial and ongoing training, and quality control systems for AAW interventions that the best available data suggest may be ineffective or even harmful.

We believe that it is both ethical and critically important to conduct a clinical trial of AAW vs BMV ventilation for paediatric resuscitation in the OHCA and IHCA settings. Such studies could be similar in design to the trial conducted by Gausche and colleagues, with patients assigned to receive TI, SGA, or no AAW placement attempts prior to ROSC. An ideally designed study would be adequately powered to support planned subgroup analyses based on age and etiology of arrest (trauma vs non-trauma).

Conclusions

Based on low to very low certainty evidence, the use of TI or SGA in resuscitation does not appear to improve the critically important resuscitation outcomes of survival to hospital discharge and survival to hospital discharge with good neurologic outcomes in children in cardiac arrest.

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Funding

This Systematic Review was funded by the American Heart Association, on behalf of the International Liaison Committee on Resuscitation (ILCOR). The following authors and contributors received payment from this funding source to complete this systematic review: Eric Lavonas as Expert Systematic Reviewer; Nazi Torabi and Glyneva Bradley-Ridout as Information Services, St Michael's Hospital; Brooke Baker for literature assistance.

Disclosures of potential conflicts of interest

Dr. Morrison is the Robert and Dorothy Pitts Chair in Acute Care and Emergency Medicine and holds CIHR and HSFC grants in cardiac arrest and life threatening trauma. No author has conflict to disclose.

Acknowledgements

The following non-task force members are also acknowledged for their contribution: Matt Buchanan (organizational support), Eddy Lang (logistical guidance), and William Montgomery (organizational).

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.2019.02.040.

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