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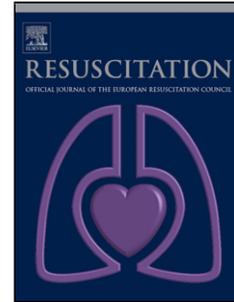
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Title

Ventilation rate in adults with a tracheal tube during cardiopulmonary resuscitation: a systematic review

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Abstract

AIM: The optimal ventilation rate during cardiopulmonary resuscitation (CPR) with a tracheal tube is unknown. We evaluated whether in adults with cardiac arrest and a secure airway (tracheal tube), a ventilation rate of 10 min⁻¹, compared to any other rate during CPR, improves outcomes.

METHODS: A systematic review up to 14 July 2016. We included both adult human and animal studies. A GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach was used to evaluate the quality of evidence for each outcome.

RESULTS: We identified one human observational study with 67 patients and ten animal studies (234 pigs and 30 dogs). All studies carried a high risk of bias. All studies evaluated for return of spontaneous circulation (ROSC). Studies showed no improvement in ROSC with a ventilation rate of 10 min⁻¹ compared to any other rate. The evidence for longer-term outcomes such as survival to discharge and survival with favourable neurological outcome was very limited.

CONCLUSION: A ventilation rate recommendation of 10 min⁻¹ during adult CPR with a tracheal tube and no pauses for chest compression is a very weak recommendation based on very low quality evidence.

KeyWords: Cardiac arrest; neurological outcome; outcome; resuscitation; ROSC; tracheal tube; ventilation rate

Introduction

Current guidelines recommend a ventilation rate of 10 min⁻¹ without pausing chest compressions during cardiopulmonary resuscitation (CPR) with a tracheal tube in place.^{1,2} Numerous observational studies show that ventilation rates greater than 10 min⁻¹ are common during actual CPR.³⁻¹¹ A reduced ventilation rate could be sufficient to maintain a normal ventilation to perfusion ratio during CPR as the cardiac output generated by chest compressions is only 10-15% of normal.¹² An increased ventilation rate during CPR can increase the mean intrathoracic pressure reducing venous return to the heart, increase lung volume and pulmonary vascular resistance, reduce cardiac output, and decrease coronary perfusion pressure and aortic blood pressure.^{5,6,13-16}

Positive pressure ventilation can also increase intracranial pressure and thus reduce cerebral perfusion.^{13,15,17} Conversely, the relative negative intrathoracic pressures generated during the decompression phase of chest compression can increase the return of venous blood to the heart and increase blood flow to the myocardium and the brain during chest compressions.^{15,17-19} Positive pressure ventilation could therefore negate these beneficial effects of chest wall recoil.^{15,20}

The optimal ventilation rate to ensure adequate gas exchange without reducing the perfusion of vital organs is uncertain.²¹ In a pig study, increasing the compression:ventilation (C:V) ratio from 15:2 to 15:1 improved coronary and cerebral perfusion pressure.¹⁷ In another pig study, there was improved coronary perfusion pressure with a ventilation rate of 10 min⁻¹ compared to 35 min⁻¹ but no difference in 1 hour and 24 hour survival.²² Other studies do not report similar improvements in organ perfusion.^{23,24} During the first five minutes of CPR, a ventilation rate of 2 min⁻¹ resulted in lower carotid blood flow and brain oxygen tension than a ventilation rate of 10 min⁻¹.²¹ In another study, a lack of ventilation during CPR was associated with atelectasis, arterial hypoxaemia and compromised haemodynamics.²⁵

This systematic review was conducted as part of the 2015 International Liaison Committee on Resuscitation (ILCOR) Consensus on Science and Treatment Recommendation (CoSTR) process.²⁶⁻²⁸ We evaluated whether in adults with cardiac arrest and a secure airway (tracheal tube), the current recommended ventilation rate of 10 min⁻¹, compared to any other rate during CPR, improves outcomes.

Methods

This systematic review followed the process described by ILCOR for its 2015 Consensus on Science and Treatment Recommendation (CoSTR) process.²⁶ Worksheet evaluation experts reviewed the search strategy and its findings. The

method was informed and validated against the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.²⁹ The PRISMA checklist is completed and attached as Supplementary Appendix 1. In addition, the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) working group (www.gradeworkinggroup.org) approach to evidence evaluation and to achieve evidence based recommendations was used. Our searches have been updated since the 2015 ILCOR CoSTR and our conclusions are distinct from the ILCOR recommendations.

PICO question

The ILCOR ALS Task Force prioritised this topic for review and agreed the PICO question for this systematic review: (P) in adults with cardiac arrest with a secure airway (tracheal tube) receiving chest compressions (in any setting – in and out-of-hospital), (I) does a ventilation rate of 10 min⁻¹, (C) compared to any other ventilation rate, (O) improve outcome? Outcomes were scored 1 to 9 from the perspective of the patient (Table 1). Critical outcomes are 7-9, important outcomes 4-6 and outcomes of limited importance 1-3.³⁰

Study eligibility

We included original articles fulfilling the following eligibility criteria: (1) the article was published in English, Dutch, French or German; (2) the study was a human or animal study (3) the study population involved adults aged 18 years or older; (4) the patients had a cardiac arrest (5) the patients had a secure airway; (6) the patient was receiving chest compressions in any setting – in and out-of-hospital; (7) clinical outcome was reported. The exclusion criteria were: (1) studies related to traumatic cardiac arrest (2) studies where the patients did not receive any form of ventilation at all; (3) studies that used a device that could influence the compression-decompression physiology (e.g. inspiratory impedance threshold device (ITD)); (4) systematic reviews and meta-analyses. A decision to include animal studies was made a

priori based on the ALS Task Force's prior knowledge of this topic and that existing recommendations were based primarily on evidence from animal studies. A secure airway was defined as the presence of a tracheal tube when the effect of ventilation rate was studied.

Data sources

The following bibliographic databases were searched up to 14 July 2016: PubMed and the Cochrane Library. The detailed search strategy is included in Supplementary Appendix 2. Searches were supplemented by hand searching the reference lists of the studies, and through discussion within ILCOR ALS Task Force members.

Study selection and data collection

Two reviewers (GV and KGM) independently applied the selection criteria and screened the citation titles and abstracts that were retrieved from the literature searches individually. A full text version was obtained of the articles that could neither be excluded by their citation titles nor by their abstracts. The two reviewers then reviewed the full text articles and selected studies for inclusion. A comparison of the selected studies was made. A third reviewer (JS) checked the final studies and adjudicated when there was disagreement between the primary reviewers. The full selection process is shown in Figure 1. Relevant data were extracted by one reviewer (GV), using a predesigned data extraction form, and verified by the co-authors.

GRADE approach

After extracting the data, a GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach was used to evaluate the overall quality of evidence with respect to five different domains of quality:³¹⁻³⁵ (1) limitation of study design and execution; (2) inconsistency; (3) indirectness; (4) imprecision; and (5) publication bias across all included studies. An evidence profile was created with one row dedicated to each outcome. Initial ratings were conducted by one author (GV),

and then checked by the co-authors. A four-point rating scale, ranging from 'very low quality' to 'high quality' was used to judge overall quality of evidence.³⁶

Results

Study selection

The search strategy identified 839 potentially relevant studies of which 680 were excluded after screening the titles and abstracts (Figure 1). Of the 159 remaining studies, 148 were excluded after reviewing the full text. Eleven studies of ventilation with a tracheal tube during CPR that assessed ventilation rate were included in the systematic review.

Study characteristics

One human observational study with 67 subjects³ and 10 animal studies including 234 pigs and 30 dogs met the inclusion criteria.^{5,6,16,22,23,37-41} The study characteristics are shown in Table 2. No human randomised controlled trials (RCTs) were identified. A large human RCT of 23,711 patients with out-of-hospital cardiac arrest was excluded because the patients did not have a secure airway during the ventilation intervention (continuous compressions with positive pressure ventilation versus compressions interrupted for ventilation at a ratio of 30 to two ventilations).⁴²

The only human study included retrospective observational data from CPR during in-hospital cardiac arrest.³ This observational study analysed the association of ROSC with differing ventilation rates during CPR. The lead author of the study was contacted to verify the presence of a tracheal tube at the time of ventilation assessment.

Two animal studies were from the same group and included the same trial data.^{5,6} In both these studies, three groups of seven pigs with cardiac arrest were used to study survival with a ventilation rate of 12 min⁻¹ (100% oxygen), 30 min⁻¹ (100% oxygen) or 30 min⁻¹ (95% oxygen and 5% CO₂). Five studies compared at least two different

ventilation rates during CPR^{5,22,37,38}, five compared at least two different compression to ventilation (C:V) ratios.^{16,23,39-41} Relevant data was extracted from studies. For example, in one animal study the group treated with continuous insufflation using a nasal cannula placed in the oropharynx to administer oxygen continuously at 10 L min⁻¹ was excluded.²² Data regarding the ITD from two studies comparing CPR with and without an ITD in addition to comparing different ventilation rates, was not included.^{16,41}

The quality of evidence for each outcome was rated according to the GRADE criteria.⁴³ In addition to the five main quality domains used to assess RCTs (risk of bias, inconsistency, indirectness, imprecision, publication bias), for the observational human study³ three additional quality domains were considered: (1) dose-response effect; (2) magnitude of effect; (3) confounding. We found that this study was unclear with regards to these additional domains. With respect to outcomes, all but one study reported ROSC, the other reporting 24-hour survival.⁴⁰ No studies included survival at discharge/30 days, 60 days, 180 days and/or 1 year, or survival with favourable neurological outcome at discharge/30 days, 60 days, 180 days and/or 1 year as an outcome. Although the only human study referred to survival to hospital discharge it did not report this data.³

Risk of bias

There was an overall high risk of bias for the studies included and our bias assessments are summarised in Table 3.^{34,35} The only human study was a non-RCT and therefore had a high risk of bias.³ For the animal studies, two were randomised with a computer-generated process^{16,41}, one used sealed envelopes³⁹, one randomised in blocks of four³⁸, and the others provided little or no detail of the randomisation process.

Allocation concealment did not apply to the observational human study.³ Patients and resuscitation team members were both blinded to the real time CPR data thus reducing the risk of performance bias. In all the animal studies, the lack of blinding led to a risk of performance bias. Two studies specifically stated that those doing the neurological evaluations were not blinded to the intervention leading to the possibility of detection bias.^{22,40}

In the human study, segments of CPR performance data were excluded due to artefacts leading to the possibility of attrition bias.³ Nine animal studies had no loss to follow-up and an intention to treat analysis reducing risk of bias^{5,6,16,22,23,37,38,40,41}, whilst in one study an animal was excluded after showing no signs of circulation during CPR.³⁹

There was an industry or commercial interest in five studies^{3,5,6,16,41}, and no mention of interests for two studies^{23,40} making these all prone to publication bias.

Inconsistency

Inconsistency could not be considered for the observational human study as it was the only study in this category.³ For the outcome of ROSC, there was serious inconsistency across the animal studies.³³ Four studies found no significant difference in ROSC at various ventilation rates^{22,23,38,39}, two studies that appear to report the same data observed decreased ROSC with a ventilation rate of 30 min⁻¹ compared with 12 min⁻¹^{5,6}, one study reported decreased ROSC with a C:V ratio of 15:2 compared with 30:2⁴¹ whilst another reported opposite findings.³⁷

Indirectness

The animal studies suffer from very serious indirectness because the evidence is being extrapolated from a study population (i.e. animals) that differs from that defined in the PICO (adult humans).³² There was further indirectness as all the animal studies

only studied untreated ventricular fibrillation, and most of these studies did not include a comparison with a ventilation rate of 10 min^{-1} .^{16,23,37,40,41} In addition those studies using a C:V ratio included a pause in compressions for ventilation as opposed to continuous chest compressions and continuous asynchronous ventilation.

Imprecision

All the studies were small with complete data reported for only 60 patients in the human study³, and 12 in the largest subgroup in the animal studies.²² This resulted in an overall assessment of serious imprecision.³¹

Outcomes

Applying the GRADE criteria categorised all evidence regarding ROSC as very low quality evidence.³⁶ Only three studies presented data (Table 4) to make a comparison possible for ROSC.^{16,22,39}

A summary of the results for each study is shown in Table 5. Five studies reported a C:V ratio instead of a ventilation rate as defined in the PICO.^{16,23,37,40,41} To estimate mean ventilation rate, the compression rate was divided by the C:V ratio. For example, resuscitation with compressions at a mean rate of 120 min^{-1} and a 30:2 C:V ratio, has an estimated mean ventilation rate of 8 min^{-1} . Unfortunately, this approach generated very serious indirectness.³² The only human study documented that the patients achieving ROSC had a mean ventilation rate of 20 min^{-1} (SD=7), compared to 22 min^{-1} (SD=9) in the patients who did not achieve ROSC ($P=0.17$).³ Gazmuri et al. only stated that there were no statistical associations between ROSC and the ventilation patterns in their study but did not provide further details.³⁸ Figure 2 shows the relationship between ventilation rate and ROSC.

Discussion

The current ventilation rate recommendation of 10 min⁻¹ during CPR with a tracheal tube is a weak recommendation based on very low quality evidence. We did not identify any human studies that address the critical PICO outcomes (survival or survival with favourable neurologic/functional outcome at discharge/30 days, 60 days, 180 days, and/or 1 year).²⁸ For the important outcome of ROSC, we only identified very low quality evidence (downgraded for very serious risk of bias and indirectness, and serious inconsistency and imprecision) from 10 animal studies and one human observational study that did not enable us to estimate with confidence the effect of a ventilation rate of 10 min⁻¹ compared with any other rate.²⁸

The current ILCOR ventilation recommendation of 10 min⁻¹ was made in 2005 and stated that for a patient with an advanced airway in place, it is reasonable to ventilate the lungs at a rate of 8-10 ventilations min⁻¹ without pausing during chest compressions to deliver ventilations. This was based on evidence from a pig study of cardiac arrest that showed that a respiratory rate of 30 min⁻¹ as opposed to 12 min⁻¹ was associated with increased intrathoracic pressure, decreased coronary and cerebral perfusion, and decreased ROSC.^{5,6} The authors of the animal study also included a human case series in which they observed no survivors for out of hospital cardiac arrest patients with an advanced airway in place, the ventilation rate was greater than 10 min⁻¹ and the inspiration time more than 1 s.^{5,6} In addition, data was extrapolated from a pig study of severe shock that showed a ventilation rate of 6 min⁻¹ resulted in better oxygenation and an improved systolic blood pressure, coronary perfusion and cardiac output compared with ventilation rates above 12 min⁻¹.¹⁴ Subsequent ILCOR recommendations in 2010 and 2015 have not identified convincing new evidence to support or refute the 2005 recommendation. Indeed, the 2010 and 2015 recommendations are primarily because a rate of about 10 min⁻¹ is already in use

and there is insufficient evidence to suggest another ventilation rate. Our updated search since the 2015 ILCOR recommendation confirms the absence of significant new evidence.

Ventilation rate is just one component of ventilation, and our knowledge of other aspects of ventilation during CPR is also extremely limited. For example, our knowledge of the optimal tidal volume, inspired oxygen, airway pressure and interaction between chest compression and ventilation during CPR is very limited. This is likely to remain the case until our understanding of measurable physiological values (e.g. end-tidal carbon dioxide, cerebral oxygen saturation) improves so that rescuers can adjust interventions for individual patients during CPR according to a physiological target as opposed to a one size fits all recommendation. A further complication is the optimal choice of airway during CPR is also uncertain. Future studies will need to look at a combination of factors to help us understand the role of ventilation rate during CPR.

Our systematic review shows the major limitations of the evidence. Firstly, all but one study included was an experimental animal study of ventricular fibrillation cardiac arrest. Secondly, to study ventilation rates, we had to convert C:V ratios to estimate ventilation rates in five of the animal studies (Table 5), introducing further indirectness. These studies paused chest compression for ventilation, whilst current recommendations do not recommend a pause in compression for ventilations when a tracheal tube is in place. Our collated data based on this approach (Figure 2) did not show improved ROSC with a ventilation rate of 10 min^{-1} compared to any other rate. Thirdly, the results of studies did not show a consistent outcome with any particular ventilation rate. Fourthly, the only human data available was from an observational study where the assumption was that all the ventilation data was gathered whilst the

patient had a secure airway.³ Finally, we did not look specifically at studies looking at passive ventilation via the tracheal tube generated by chest compression with no actual positive pressure ventilation breaths. A human observational study during compression-only CPR in 17 patients found that the median tidal volume per compression was 41.5 ml (range 33.0–62.1 ml), which was less than the measured dead space in all patients.⁴⁴ This is an area that clearly requires further study.

Conclusion

A ventilation rate recommendation of 10 min⁻¹ during adult CPR with a tracheal tube and no pauses for chest compression is a very weak recommendation based on very low quality evidence. Ventilation rate is only one of many airway and breathing interventions. Future studies will need to look at a combination of factors to help us understand the role of ventilation rate during CPR with a tracheal tube.

Disclaimer

This review includes information on resuscitation questions developed through the C2015 Consensus on Science and Treatment Recommendations (CoSTR) process, managed by the International Liaison Committee on Resuscitation (www.ilcor.org/seers). The questions were developed by ILCOR Task Forces, using strict conflict of interest guidelines. In general, each question was assigned to two experts to complete a detailed structured review of the literature, and complete a detailed evidence evaluation. Evidence evaluations were discussed at ILCOR meetings to reach consensus and were published in 2015 as the Consensus on Science and Treatment Recommendations (CoSTR).^{27,28}

Conflicts of Interest statement

GV has no conflicts of interest. JS is an editor of the journal Resuscitation and Chair of the ILCOR ALS Task Force. KGM is Honorary Secretary of ILCOR.

Author contributions

Study concept and design: Gino Vissers (GV), Koenraad G. Monsieurs (KGM)

Jasmeet Soar (JS). Performance of literature searches and selection of articles: GV,

KGM, JS. Analysis and interpretation of data: GV, KGM, JS. Creating figures, tables

and graphs: GV. Drafting of the manuscript: GV, JS. Critical revision of the manuscript:

KGM, JS. Study supervision: KGM, JS. All the authors approved the final manuscript.

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Figure Caption

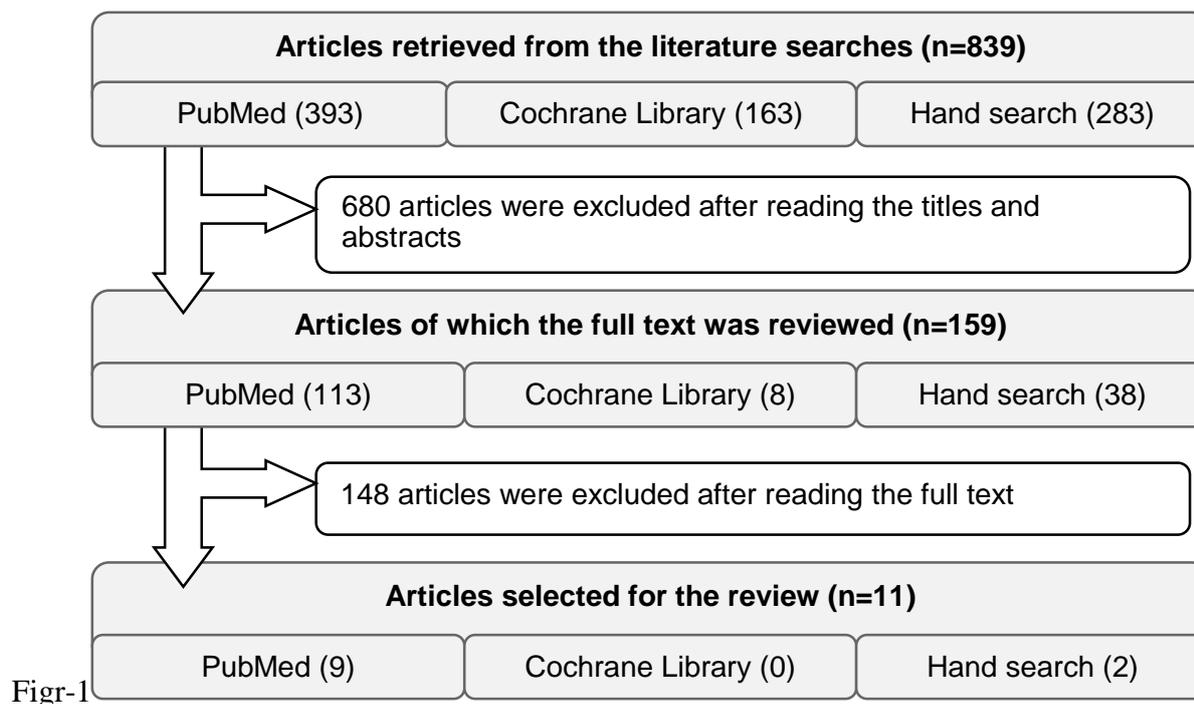


Figure 1. Flow chart of the study selection process.

The numbers of articles retrieved from the literature searches represent the original search results, i.e. with an overlap of identical studies found in different databases.

Figr-2

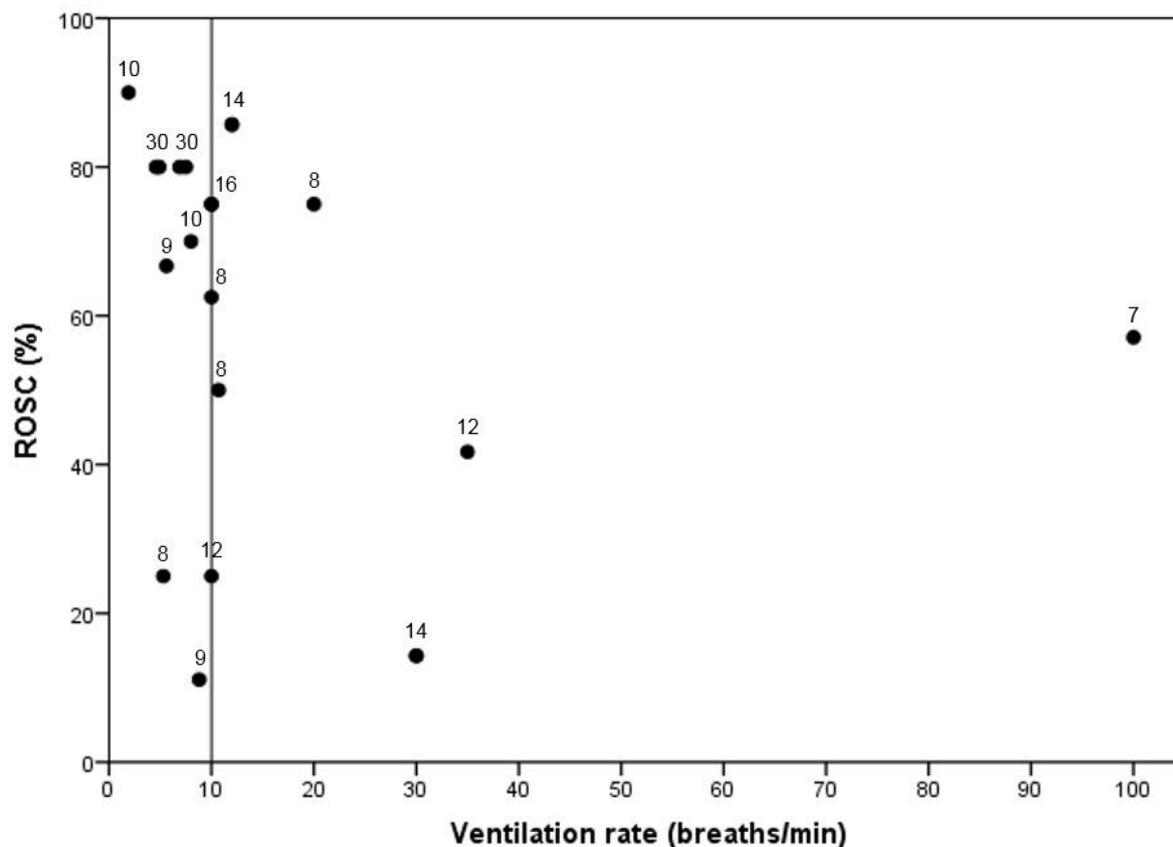


Figure 2. The association between ventilation rate and ROSC

ROSC: return of spontaneous circulation

Every dot represents a group of animals (in some cases from more than one study) who received one specific ventilation rate. The numbers represent the number of animals in each group.

Outcome	Score
ROSC	5
Survival at discharge	6
Survival at 30 days, 60 days, 180 days and/or 1 year	7
Survival with favourable neurological/functional outcome at discharge	8
Survival with favourable neurological/functional outcome at 30 days, 60 days, 180 days and/or 1 year	9

Table 1: Prioritisation of the outcomes

ROSC: return of spontaneous circulation

Study; Country	Design	Subjects	Protected airway	Interventions	Comparisons	Outcomes
Abella et al, 2005³; US	Observational human study	67 patients with in-hospital cardiac arrest	Unclear			ROSC
Aufderheide et al, 2004⁵; US	Randomised controlled animal study	21 pigs*	Endotracheal tube	Ventilation rate of 30 min ⁻¹	Ventilation rate of 12 min ⁻¹	ROSC
Aufderheide et al, 2004⁶; US (b)	Randomised controlled animal study	21 pigs*	Endotracheal tube	Ventilation rate of 30 min ⁻¹	Ventilation rate of 12 min ⁻¹	ROSC
Cavus et al, 2008³⁷; Germany	Randomised controlled animal study	24 pigs**	Endotracheal tube	CPR with a C:V ratio of 15:2	CPR with a C:V ratio of 30:2	ROSC
Gazmuri et al, 2012³⁸; US	Randomised controlled animal study	16 pigs	Endotracheal tube	Ventilation rate of 10 min ⁻¹ , tv of 18ml/kg. Ventilation rate of 33 min ⁻¹ , tv of 6ml/kg. Ventilation rate of 33 min ⁻¹ , tv of 18ml/kg	Ventilation rate of 10 min ⁻¹ , tv of 6ml/kg	ROSC
Hayes et al, 2007²²; US	Randomised controlled animal study	36 pigs***	Endotracheal tube	Ventilation rate of 35 min ⁻¹ , tv of 20 ml/kg	Ventilation rate of 10 min ⁻¹ , tv of 10ml/kg	ROSC
Hwang et al, 2008²³; Korea	Randomised controlled animal study	30 dogs	Endotracheal tube	CPR with a C:V ratio of 15:1 CPR with a C:V ratio of 15:2	CPR with a C:V ratio of 30:2	ROSC
Kill et al, 2014³⁹; Germany	Randomised controlled animal study	24 pigs	Endotracheal tube	Ventilation rate of 10 min ⁻¹ (bilevel) Ventilation rate of 100 min ⁻¹ (CCSV)	Ventilation rate of 10 min ⁻¹ (IPPV)	ROSC
Sanders et al, 2002⁴⁰; US	Controlled animal study	40 pigs****	Endotracheal tube	CPR with a C:V ratio of 50:5 CPR with a C:V ratio of 100:2	CPR with a C:V ratio of 15:2	24-hour survival
Yannopoulos et al, 2004¹⁶; US	Randomised controlled animal study	32 pigs**	Endotracheal tube	CPR with a C:V ratio of 5:1	CPR with a C:V ratio of 10:1	ROSC
Yannopoulos et al, 2006⁴¹; US	Randomised controlled animal study	20 pigs	Endotracheal tube	CPR with a C:V ratio of 15:2	CPR with a C:V ratio of 30:2	ROSC

Table 2: Characteristics of included studies

C:V ratio: compression: ventilation ratio, CPR: cardiopulmonary resuscitation, ROSC: return of spontaneous circulation, US: United States, tv: tidal volume, bilevel: pressure-controlled ventilation, CCSV: chest compression synchronised ventilation, IPPV: intermittent positive-pressure ventilation.

* 14 pigs were used in this review

** 16 pigs were used in this review

*** 24 pigs were used in this review

**** 30 pigs were used in this review

(b) Aufderheide et al. published two articles regarding the same trial.

Study	Randomisation	Allocation concealment	Blinding	Loss to follow up, Intention to treat analysis	Other	Overall risk for bias
Abella et al, 2005 ³	High	N/a	Low	High	High	High
Aufderheide et al, 2004 ⁵	Low	Unclear	High	Low	High	High
Aufderheide et al, 2004 ⁶ (b)	Low	Unclear	High	Low	High	High
Cavus et al, 2008 ³⁷	Low	Unclear	High	Low	High	High
Gazmuri et al, 2012 ³⁸	High	Unclear	High	Low	High	High
Hayes et al, 2007 ²²	Low	Unclear	High	Low	Low	High
Hwang et al, 2008 ²³	Low	Unclear	High	Low	High	High
Kill et al, 2014 ³⁹	Low	Unclear	High	High	High	High
Sanders et al, 2002 ³³	Unclear	Unclear	High	Low	High	High
Yannopoulos et al, 2004 ¹⁶	Low	Unclear	High	Low	High	High
Yannopoulos et al, 2006 ⁴¹	Low	Unclear	High	Low	High	High

Table 3: Risk of bias within the identified studies

N/a: not applicable.

Individual trials that have a crucial limitation in one or more criteria, sufficient to substantially lower the confidence in the estimate of effect, are considered at “high” risk of bias.

(b) Aufderheide et al. published two articles regarding the same trial.

Ventilation rate and outcome in CPR: a systematic review

No of studies	Study Design	Risk of Bias* †	Inconsistency*	Indirectness*	Imprecision*	Study	ROC rate (VR 10min ⁻¹)	ROC rate (other)	Relative Risk (95% CI)	Absolute Risk Reduction (95%CI)	Quality of evidence***	Importance
Survival with favourable neurological/functional outcome at discharge, 30 days, 60 days, 180 days AND/OR 1 year												
0	-	-	-	-	-	-	-	-	-	-	-	Critical
Survival only at discharge, 30 days, 60 days, 180 days AND/OR 1 year												
0	-	-	-	-	-	-	-	-	-	-	-	Critical
ROC												
10	RCT animal studies	Very serious	Serious	Very serious	Serious	Aufderheide et al, 2004	0	7/14	-	-	⊕○○○ Very low	Important
						Aufderheide et al, 2004 (b)	0	7/14	-	-		
						Cavus et al, 2008	0	6/16	-	-		
						Gazmuri et al, 2012	unclear	unclear	-	-		
						Hayes et al, 2007	3/12	5/12	0.60 (0.18 to 1.97)	- 16.67% (-47.58 to 19.33)		
						Hwang et al, 2008	0	24/30	-	-		
						Kill et al, 2014	11/16	4/7	1.20 (0.58 to 2.48)	11.61% (-24.77 to 47.97)		
						Sanders et al, 2002	0	24/30	-	-		
						Yannopoulos et al, 2014	6/8	6/8	1.00 (0.57 to 1.76)	0.00% (-38.47 to 38.47)		
						Yannopoulos et al, 2006	unclear	unclear	-	-		
ROC												

1	Human observational study	Very serious	Not serious	Serious	Serious	Abella et al, 2005	27 cases, 33 controls	⊕○○○	Important Very low
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Table 4: Evidence profile table

CI: confidence interval, RCT: randomised controlled trial, ROSC: return of spontaneous circulation, VR: ventilation rate

* Classification across all studies for each outcome for: risk of bias/inconsistency/indirectness/imprecision. No serious limitations: most information is from studies at low risk of bias. Do not downgrade. Serious limitations: most information is from studies at moderate risk of bias. Rate down one level. Very serious limitation: most information is from studies at high risk of bias. Rate down two levels.

** Classification across all studies for each outcome for other: undetected or strongly suspected.

Conflicts of interest and industry sponsoring are already incorporated in table 3.

*** Quality of evidence across included studies for outcome: high, moderate, low, very low.

† More info about the risks of bias is reported in table 3.

(b) Aufderheide et al. published two articles regarding the same trial.

Ventilation rate and outcome in CPR: a systematic review

Study	C:V ratio	Mean compression rate (min ⁻¹)	Ventilation rate (min ⁻¹)	ROSC (%)
Abella et al, 2005 ³			-	-
Aufderheide et al, 2004 ⁵			12	85.7
			30	14.3
Aufderheide et al, 2004 ⁶ (b)			12	85.7
			30	14.3
Cavus et al, 2008 ³⁷	30:2	80	5.3*	25
	15:2	80	10.7*	50
Gazmuri et al, 2012 ^{38, **}			10 (6ml/kg)	
			10 (18ml/kg)	
			33 (6ml/kg)	
			33 (18ml/kg)	
Hayes et al, 2007 ²²			10 (10ml/kg)	25
			35 (20ml/kg)	41.7
Hwang et al, 2008 ²³	30:2	69.0	4.6*	80
	15:1	73.1	4.9*	80
	15:2	56.3	7.5*	80
Kill et al, 2014 ³⁹			10 (bilevel)	75
			10 (IPPV)	62.5
			100 (CCSV)	57.1
Sanders et al, 2002 ⁴⁰	100:2	93	1.9*	90
	50:5	69	6.9*	80
	15:2	60	8*	70
Yannopoulos et al, 2004 ¹⁶	10:1	100	10*	75
	5:1	100	20*	75

Yannopoulos et al, 2006 ⁴¹	30:2	84	5.6*	66.7
	15:2	66	8.8*	11.1

Table 5: Summary of results.

Bilevel: pressure-controlled ventilation, CCSV: chest compression synchronised ventilation, IPPV: intermittent positive-pressure ventilation.

* If ventilation rate was not mentioned in the study directly, it was calculated by C:V ratio and mean compression rate.

** Gazmuri et al. only made general statements regarding ROSC. They did not mention individual component outcomes.

(b) Aufderheide et al. published two articles regarding the same trial.