Circulation

ORIGINAL RESEARCH ARTICLE

Bag-Valve-Mask Ventilation and Survival From Out-of-Hospital Cardiac Arrest: A Multicenter Study

Ahamed H. Idris, MD; Elisabete Aramendi Ecenarro, PhD; Brian Leroux, PhD; Xabier Jaureguibeitia, MSc; Betty Y. Yang, MD, MS; Sarah Shaver, MD; Mary P. Chang, MD, MPH; Tom Rea, MD, MPH; Peter Kudenchuk, MD; Jim Christenson, MD; Christian Vaillancourt, MD, MSc; Clifton Callaway, MD, PhD; David Salcido, PhD; Jonas Carson; Jennifer Blackwood, MPH; Henry E. Wang, MD, MS, MPH

BACKGROUND: Few studies have measured ventilation during early cardiopulmonary resuscitation (CPR) before advanced airway placement. Resuscitation guidelines recommend pauses after every 30 chest compressions to deliver ventilations. The effectiveness of bag-valve-mask ventilation delivered during the pause in chest compressions is unknown. We sought to determine: (1) the incidence of lung inflation with bag-valve-mask ventilation during 30:2 CPR; and (2) the association of ventilation with outcomes after out-of-hospital cardiac arrest.

METHODS: We studied patients with out-of-hospital cardiac arrest from 6 sites of the Resuscitation Outcomes Consortium CCC study (Trial of Continuous Compressions versus Standard CPR in Patients with Out-of-Hospital Cardiac Arrest). We analyzed patients assigned to the 30:2 CPR arm with ≥2 minutes of thoracic bioimpedance signal recorded with a cardiac defibrillator/monitor. Detectable ventilation waveforms were defined as having a bioimpedance amplitude ≥0.5 Ω (corresponding to ≥250 mL V_T) and a duration ≥1 s. We defined a chest compression pause as a 3- to 15-s break in chest compressions. We compared the incidence of ventilation and outcomes in 2 groups: patients with ventilation waveforms in <50% of pauses (group 1) versus those with waveforms in ≥50% of pauses (group 2).

RESULTS: Among 1976 patients, the mean age was 65 years; 66% were male. From the start of chest compressions until advanced airway placement, mean±SD duration of 30:2 CPR was 9.8±4.9 minutes. During this period, we identified 26 861 pauses in chest compressions; 60% of patients had ventilation waveforms in <50% of pauses (group 1, n=1177), and 40% had waveforms in ≥50% of pauses (group 2, n=799). Group 1 had a median of 12 pauses and 2 ventilations per patient versus group 2, which had 12 pauses and 12 ventilations per patient. Group 2 had higher rates of prehospital return of spontaneous circulation (40.7% versus 25.2%; $P<0.0001$), survival to hospital discharge (13.5% versus 4.1%; $P<0.0001$), and survival with favorable neurological outcome (10.6% versus 2.4%; $P<0.0001$). These associations persisted after adjustment for confounders.

CONCLUSIONS: In this study, lung inflation occurred infrequently with bag-valve-mask ventilation during 30:2 CPR. Lung inflation in ≥50% of pauses was associated with improved return of spontaneous circulation, survival, and survival with favorable neurological outcome.

Key Words: cardiography, impedance ■ cardiopulmonary resuscitation ■ heart arrest ■ patient outcome assessment ■ ventilation

Editorial, see p 1857

Correspondence to: Ahamed H. Idris, MD, Department of Emergency Medicine, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390-8579. Email ahamed.idris@utsouthwestern.edu

This manuscript was sent to Michael Kurz, Guest Editor, for review by expert referees, editorial decision, and final disposition.
Supplemental Material, the podcast, and transcript are available with this article at https://www.ahajournals.org/doi/suppl/10.1161/CIRCULATIONAHA.123.065561.
For Sources of Funding and Disclosures, see page 1855.

Circulation is available at www.ahajournals.org/journal/circ

Clinical Perspective

What Is New?

- The 30:2 strategy of cardiopulmonary resuscitation pauses chest compressions to optimize bag-valve-mask ventilation. No previous studies have verified if ventilations are effectively delivered during such cardiopulmonary resuscitation pauses.
- In this analysis of data from the 30:2 arm of the ROC CCC trial (Trial of Continuous Compressions versus Standard CPR in Patients with Out-of-Hospital Cardiac Arrest), we applied novel signal-processing techniques to identify ventilations during chest compression pauses.
- In 60% of patients, lung inflation (ventilation) was detectable in <50% of pauses. Patients receiving detectable lung inflation in ≥50% of pauses had better clinical outcomes.

What Are the Clinical Implications?

- Bag-valve-mask ventilation is often ineffective during cardiopulmonary resuscitation.
- Improving ventilation may lead to improved clinical outcomes.

Nonstandard Abbreviations and Acronyms

BVM	bag-valve-mask
CCC	Trial of Continuous Compressions versus Standard CPR in Patients with Out-of-Hospital Cardiac Arrest
CPR	cardiopulmonary resuscitation
ED	emergency department
EMS	emergency medical services
NS	nonsignificant
OHCA	out-of-hospital cardiac arrest
ROC	Resuscitation Outcomes Consortium
ROSC	return of spontaneous circulation
RR	relative risk

More than 400 000 out-of-hospital cardiac arrests (OHCAs) occur annually in the United States.[1,2] Multiple, large-scale observational and experimental studies have informed cardiopulmonary resuscitation (CPR) guidelines on the best practices of delivering chest compressions, including rate, depth, and fraction (the proportion of time spent doing chest compressions).[3–7] The findings have improved OHCA patient care and clinical outcome.[1] In contrast to reporting chest compression metrics, ventilation metrics have not been investigated because there have been no readily available methods to routinely measure ventilation in the out-of-hospital setting, especially during the initial and most important stages of resuscitation. Thus, it is uncertain whether the quality of ventilations or specific ventilation metrics are factors affecting patient outcomes.

Chest compressions alone do not generate sufficient tidal volume for adequate gas exchange.[8–10] Therefore, professional responders usually give some form of rescue ventilation during CPR, often using a bag-valve-mask (BVM) device with the goal of delivering enough volume to achieve visible chest rise as an indication of successful lung inflation. The tidal volume associated with detectable chest wall movement is estimated to be between 300 and 500 mL.[11] Capnography can be used to determine whether ventilation is present; however, capnography is usually measured only after placement of an advanced airway, which typically occurs later in the advanced life support stage of CPR. There are no widely available technologies for detecting ventilations during BVM ventilation, the most crucial initial phase of resuscitation.

Thoracic bioimpedance recordings have been shown and validated to measure ventilation frequency during CPR.[12–15] When a person inhales and exhales, the chest wall expands and contracts, and thoracic electrical resistance oscillates, which is detected by changes in thoracic bioimpedance. During CPR, thoracic bioimpedance is captured through the defibrillator pads placed on the chest and recorded by the defibrillator. During 30:2 CPR, chest compressions are paused, which prevents their concurrent confounding of the ventilation impedance signal. One recent single-site pilot study used thoracic bioimpedance to count ventilations during OHCA and emergency medical services (EMS) 30:2 CPR, and found that the number of ventilations was associated with outcome.[16]

The objectives of this multicenter study were to determine the incidence of bioimpedance-detected ventilation waveforms during BVM ventilation in 30:2 CPR and to assess the association of detectable ventilation (lung inflation) with outcomes from OHCAs.

METHODS

Design and Setting

We conducted a secondary analysis of clinical and continuous cardiac monitor data from 6 sites (Birmingham, AL; British Columbia, Canada; Dallas-Fort Worth, TX; King County, WA; Ottawa, ON, Canada; and Pittsburgh, PA) participating in the 30:2 arm of the Resuscitation Outcomes Consortium (ROC) CCC clinical trial (Trial of Continuous Compressions versus Standard CPR in Patients with Out-of-Hospital Cardiac Arrest).[17] Institutional review boards at participating sites approved the parent study under exception from informed consent. These institutional review boards later approved the present study.

Two ROC sites did not participate in the ROC CCC study, and 2 sites used only ZOLL defibrillators, which were excluded from our study because the defibrillator recordings do not include a useable bioimpedance signal.

To minimize the possibility of unintentionally sharing information that can be used to reidentify private information, a subset of the data generated for this study is available at National Institutes of Health BioLINCC and can be accessed at https://biolincc.nhlbi.nih.gov/studies/roc_ccc/.

Patient Population

The ROC CCC study used cluster-crossover randomization to assign EMS agencies to use either continuous chest compression CPR or 30:2 CPR (cycles of chest compressions interrupted by ventilation in a ratio of 30 chest compressions to 2 ventilations) before placement of an advanced airway. EMS crews (basic and advanced life support) used the assigned protocol for adults requiring CPR unless they had an obvious exclusion. EMS agencies were crossed over to the other arm twice per year. Details about cluster-crossover randomization are given in the parent trial publication and in the accompanying Supplemental Appendix.[17] We limited the analysis to patients with OHCAs assigned to the 30:2 arm of the study from June 2011 to May 2015 at the 6 ROC sites with files available from the LIFEPAK 12 [LP12] and LIFEPAK 15 [LP15] defibrillators [Physio-Control/Stryker], Redmond, WA) or the MRx defibrillator (Philips, Andover, MA). Patients were included if they had a nontraumatic cardiac arrest, were at least 18 years of age, and had defibrillator recordings with a minimum of 2 minutes of 30:2 CPR by EMS providers. Of the patients assigned to the 30:2 CPR arm from the 6 participating sites, we excluded patients who had a defibrillator other than LP12 or LP15 or the Philips MRx defibrillator applied during CPR. In addition, recordings sometimes could not be downloaded from the defibrillator or the file could not be identified in the site database (Figure 1). In addition, we excluded patients who received continuous chest compressions instead of the assigned 30:2 CPR or did not have obvious 30:2 CPR. We also excluded LP12, LP15, and MRx defibrillator files that lacked a usable recorded impedance signal or had <2 minutes of recorded 30:2 CPR. On occasion, an automated external defibrillator was applied before the arrival of a manual monitor/defibrillator. When an automated external defibrillator file was available, we included such data as chest compression metrics, initial cardiac rhythm, shocks or no shock advised, and start times. We combined the automated external defibrillator recording with the monitor/defibrillator recording for the same patient to create one continuous recording for analysis. It is unfortunate that automated external defibrillators were unable to record bioimpedance ventilation waveforms and that the first few minutes of ventilation data may be missing for some patients.

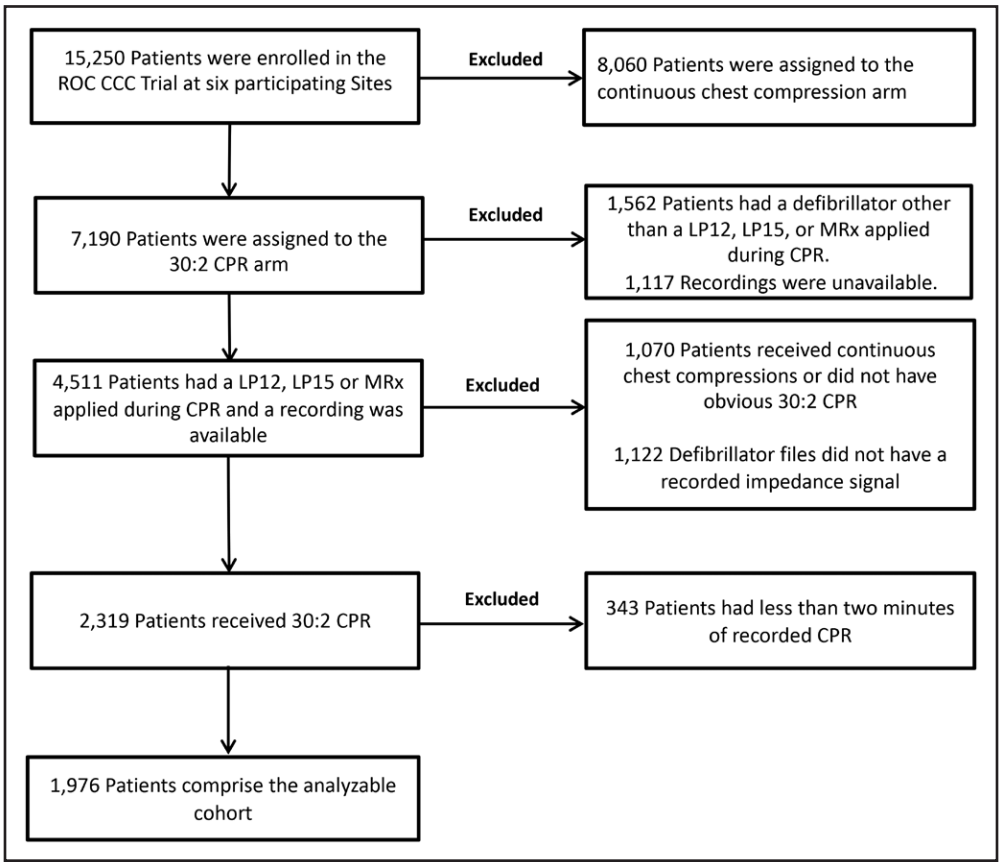

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) diagram: study cohort and exclusions.
30:2 refers to cycles of 30 chest compressions to 2 ventilations during CPR. CCC indicates Trial of Continuous Compressions versus Standard CPR in Patients with Out-of-Hospital Cardiac Arrest; CPR, cardiopulmonary resuscitation; LP, Physio-Control/Stryker LIFEPAK defibrillator (models LP12 and LP15); MRx, Philips MRx defibrillator; and ROC, Resuscitation Outcomes Consortium.

Reviewers identified 1976 files that met our inclusion criteria (Figure 1). We included ventilation data from the start of chest compressions until placement of an advanced airway. If an advanced airway was not placed (n=326), we analyzed the first 15 minutes of the recording from the start of chest compressions.

Ventilation Waveform Analysis

We previously developed and validated criteria specifying ventilation bioimpedance waveform characteristics associated with lung inflation from patients with OHCAs who received 30:2 CPR and attempted ventilation with a BVM device.[15] We then developed computer software that incorporated the criteria for bioimpedance ventilation waveforms that could automatically identify ventilation waveforms from defibrillator recordings. A detectable bioimpedance ventilation waveform has a bioimpedance amplitude of ≥0.5 Ω, with a duration ≥1 s. Our ventilation detection method has a sensitivity of >90% and a positive predictive value of >90% compared with capnography.[18–20]

Previous studies showed that >250 mL is a reasonable minimum tidal volume that can result in gas exchange.[21] The threshold of 250 mL approximates the minimum amount of tidal volume needed to overcome anatomical and physiological dead space and produce clinically meaningful gas exchange. We accordingly set the minimum bioimpedance waveform amplitude threshold to ≥0.5 Ω, which corresponds to ≥250 mL of tidal volume. We determined the bioimpedance amplitude/tidal volume relationship in a laboratory setting in human volunteers,[16] and it has also been validated in patients.[22] In addition, the threshold of 0.5 Ω is large enough to be distinguished reliably from artifact.[15]

We reviewed eligible defibrillator files manually to identify chest compression pauses with a duration of 3 to 15 s. We excluded pauses that were marked for special events, such as attempted defibrillation and rhythm and pulse checks.

Outcomes

We determined data elements about patient demographics, arrest circumstances, clinical care, and outcomes from dispatch, EMS, and hospital records using a standard data dictionary consistent with the Utstein template.

The primary outcome was survival to hospital discharge. Secondary outcomes were return of spontaneous circulation (ROSC) at any time, prehospital ROSC, ROSC on arrival at the emergency department (ED ROSC), survival to hospital admission, and survival with favorable neurological outcome (modified Rankin Scale score ≤3) at hospital discharge.

Statistical Analysis

We chose to perform a dichotomous analysis by prespecifying 2 groups a priori for comparison: patients with at least one lung inflation waveform in <50% of chest compression pauses (group 1) versus patients who had at least one lung inflation waveform in ≥50% of chest compression pauses (group 2).

We determined descriptive statistics for witnessed status, initial cardiac rhythm, chest compression rate and fraction over the first 6 minutes of CPR, ventilation quality metrics, prehospital ROSC, ED ROSC, ROSC at any time, survival at discharge, and survival with favorable neurological outcome. We present summary results as mean±SD or median with 25th percentile (Q1) and 75th percentile (Q3). For those with available data, we categorized the cases into 2 prespecified groups and compared them using unadjusted Poisson regression with a significance level of 0.05. We used a multiple Poisson regression model with robust standard errors to calculate unadjusted and adjusted relative risk (RR) and 95% CI of the association between those with ventilation waveforms in <50% of pauses versus those with ventilation waveforms in ≥50% of pauses for prehospital ROSC, ROSC at any time, ED ROSC, admission to hospital, survival to hospital discharge, and survival with favorable neurological outcome. The model contained potential confounding variables identified a priori, including age, sex, bystander-witnessed cardiac arrest, attempted bystander CPR, public location, first known EMS rhythm, and ROC site.

In addition, we determined dose-response relationships between the number of ventilations per pause and each of the outcomes (ROSC, hospital admission, survival at discharge, and survival with favorable neurological outcome [modified Rankin Scale score ≤3]) using natural cubic splines with a single knot point at ventilations per pause value of 1 using the library "splines" in the R statistical software package. All investigators, except the statistician (B.L.) and the database manager (J. Carson), were blinded to survival outcomes and other clinical data during the process of measuring ventilation. All statistical analyses were performed with commercially available statistical packages (SAS, version 9.1.3, Cary, NC; R, version 2.5.1, Vienna, Austria; Stata, version 11, College Station, TX).

RESULTS

Of the 7190 patients assigned to the 30:2 CPR arm from the 6 participating sites, we excluded 1562 patients who had a defibrillator applied other than the LP12 or LP15 or the Philips MRx defibrillator; 1117 patients were excluded if the recording could not be downloaded or could not be identified (Figure 1). In addition, 1070 patients were excluded because they received continuous chest compressions instead of the assigned 30:2 CPR or they did not have obvious 30:2 CPR. Another 1122 defibrillator files were excluded that lacked a usable recorded impedance signal and 343 cases had <2 minutes of recorded CPR. The analyzable cohort comprised 1976 patients.

The overall mean patient age was 65 years, with a 66% male predominance (Table 1). The mean±SD duration of 30:2 CPR was 9.8±4.9 minutes from the start of chest compressions until placement of an advanced airway. During this period, we identified a total of 26 861 pauses in compressions in the 1976 individual patient files. Most patients (n=1177; 60%) comprised the group with lung inflation waveforms in <50% of pauses (group 1), whereas 799 (40%) had waveforms in ≥50% of pauses (group 2; Table 1). There were differences between the 2 groups, in general, favoring group 2 regarding public location (18.0% versus 14.4%),

Table 1. Baseline Characteristics by Ventilation Group

Baseline characteristics	<50% of pauses with ventilation (n=1177)	≥50% of pauses with ventilation (n=799)
Age, mean±SD	65.8±16.1	64.9±17.7
Male, %	68.3	61.9
Obvious cause of arrest,* %	3.6	4.0
Public location, %	14.4	18.0
Bystander witnessed, %	38.9	44.8
Bystander cardiopulmonary resuscitation, %	49.1	52.2
Dispatch to first emergency medical services arrival in minutes, mean±SD	5.8±2.5	5.8±2.7
Dispatch to first emergency medical services arrival ≤4 min, %	21.1	22.6
Dispatch to first advanced life support arrival in minutes,† mean±SD	8.2±4.4	8.5±4.4
Treated by advanced life support, %	97.4	98.5
Initial cardiac rhythm, %		
Ventricular tachycardia/ventricular fibrillation	20.9	29.1
Pulseless electrical activity	15.9	19.1
Asystole	50.3	39.9
No shock advised	12.8	11.8
Site, %		
ARC	4.8	4.1
DAL	22.7	20.2
OTT	26.6	24.5
PGH	20.3	13.0
SKC	13.4	16.0
VAN	12.2	22.2

*Obvious causes include but are not limited to drug poisoning, foreign body obstruction, terminal illness, and respiratory.

†For those cases with advanced life support on scene.

ARC indicates Alabama Resuscitation Center; DAL, Dallas-Fort Worth; OTT, Ottawa; PGH, Pittsburgh; SKC, Seattle/King County; and VAN, Vancouver/British Columbia.

witnessed status (44.8% versus 38.9%), bystander CPR (52.2% versus 49.1%), and initial shockable cardiac rhythm (29.1% versus 20.9%; Table 1).

For group 1 and group 2, respectively, the median (Q1, Q3) number of pauses per minute was 1.3 (0.8, 1.8) versus 1.4 (0.9, 1.9 (nonsignificant [NS]), the median number of pauses over the time period assessed by the study was 12 (7, 19) versus 12 (7, 17; NS), whereas the median number of ventilations was 2 (1, 5) versus 12 (6, 21; $P<0.0001$; Table 2). Furthermore, for group 1 versus group 2, respectively, the median duration of pauses was 5.8 s (5.0, 6.7) versus 5.8 s (5.1, 6.8; NS). For group 1 versus group 2, respectively, the interval from the first recorded chest compression to the first recorded ventilation waveform was 170 s versus 56 s, median chest compression fraction was 0.78 (0.71, 0.84) versus 0.78 (0.70, 0.83; NS), and median chest compression rate was 108 (102, 115) versus 109 (103, 117) compressions per minute (NS). Advanced airway placement success for group 1 versus group 2, respectively, was 73.1% versus 79.5%.

The 2 prespecified groups were compared using unadjusted Poisson regression. Those with ventilation waveforms in ≥50% of pauses had associated improved ROSC on ED arrival (30.7% versus 18.7%; $P<0.0001$), admission to hospital (32.0% versus 20.6%; $P=0.0005$), survival to hospital discharge (13.5% versus 4.1%; $P<0.0001$), and survival with favorable neurological outcome (10.6% versus 2.4%; $P<0.0001$; Table 3).

Patient survival outcomes were also analyzed using unadjusted and adjusted multiple Poisson regression models with robust standard errors. Compared with patients with at least one lung inflation in <50% of pauses, patients who had at least one lung inflation in ≥50% of pauses had improved ROSC at ED arrival (unadjusted RR 1.6 [95% CI, 1.4–1.9]), survival to hospital admission (unadjusted RR, 1.6 [95% CI, 1.3–1.8]), survival to hospital discharge (unadjusted RR, 3.3 [95% CI, 2.4–4.6]), and survival with favorable neurological outcome (modified Rankin Scale score ≤3; unadjusted RR, 4.4 [95% CI, 2.9–6.7]; Table 3). After adjustment, RR for ROSC at ED was 1.4 (95% CI, 1.2–1.6), RR for survival to hospital admission was 1.6 (95% CI, 1.1–1.5), RR for survival to hospital discharge was 2.2 (95% CI, 1.6–3.0), and RR for survival with favorable neurological outcome was 2.8 (95% CI, 1.8–4.3; Table 3).

Table 2. Treatment Characteristics by Ventilation Group

Treatment characteristics	<50% of pauses with ventilation (n=1177)	≥50% of pauses with ventilation (n=799)
Time interval from machine on to first compression (s), median (Q1, Q3)	47 (26, 77)	50 (25, 78)
Time interval from machine on to first ventilation (s), median (Q1, Q3)	244 (136, 398)	119 (71, 188)
Time interval from first compression to first ventilation (s), median (Q1, Q3)	170 (75, 324)	56 (19, 107)
Advanced airway successful, n/N (%)	857/1173 (73.1)	621/781 (79.5)
Chest compression fraction, median (Q1, Q3)	0.78 (0.71, 0.84)	0.78 (0.70, 0.83)
Chest compression rate, median (Q1, Q3)	108 (102, 115)	109 (103, 117)
Number of defined pauses, median (Q1, Q3)	12 (7, 19)	12 (7, 17)
Duration of defined pauses (s), median (Q1, Q3)	5.8 (5.0, 6.7)	5.8 (5.1, 6.8)
Number of ventilations, median (Q1, Q3)	2 (1, 5)	12 (6, 21)

Q1 indicates 25th percentile; and Q3, 75th percentile.

Table 3. Outcomes by Ventilation Group

Outcomes	<50% of pauses with ventilation (n=1177), n/N (%)	≥50% of pauses with ventilation (n=799), n/N (%)	Difference (95% CI), %	Unadjusted risk ratio (95% CI)*	Adjusted risk ratio (95% CI)†	*P* value
Prehospital return of spontaneous circulation	297/1177 (25.2)	325/799 (40.7)	15.5	1.6 (1.4–1.8)	1.3 (1.2–1.5)	<0.0001
Return of spontaneous circulation at emergency department arrival	220/1176 (18.7)	244/794 (30.7)	12.0	1.6 (1.4–1.9)	1.4 (1.2–1.6)	<0.0001
Any return of spontaneous circulation	345/1177 (29.3)	359/799 (44.9)	15.6	1.5 (1.4–1.7)	1.3 (1.2–1.5)	<0.0001
Admitted to hospital	243/1177 (20.6)	256/799 (32.0)	11.4	1.6 (1.3–1.8)	1.3 (1.1–1.5)	0.0005
Survival to hospital discharge	48/1175 (4.1)	107/793 (13.5)	9.4	3.3 (2.4–4.6)	2.2 (1.6–3.0)	<0.0001
Survival with mRS score ≤3‡	28/1175 (2.4)	84/793 (10.6)	8.2	4.4 (2.9–6.7)	2.8 (1.8–4.3)	<0.0001

*All *P* values are <0.0001.

†Adjusted for age, sex, bystander-witnessed cardiac arrest, attempted bystander cardiopulmonary resuscitation, public location, first known emergency medical services rhythm, and Resuscitation Outcomes Consortium site.

‡mRS (modified Rankin Scale; favorable neurological outcome).

Unadjusted and adjusted dose-response relationships using natural cubic spline models demonstrate a positive dose-response relationship whereby an increasing number of ventilations per pause (0–2) is associated with a greater likelihood of favorable outcomes (Figure 2).

DISCUSSION

Ventilation during OHCA resuscitation has been difficult to study during early phases of CPR because a method for measurement had been lacking. This investigation is the first multicenter study that measured bioimpedance ventilation waveforms during 30:2 CPR for OHCA and its association with survival outcomes. In this novel investigation, we showed that detectable ventilation occurred in only 40% of pauses overall. In patients who had measurable ventilation in at least half of the pauses in 30:2 CPR, there was an associated improvement in ROSC, survival to hospital discharge, and survival with favorable neurological outcome.

Bioimpedance as a Surrogate for Lung Inflation

Various aspects of ventilation in patients with OHCAs have been studied, such as the compression to ventilation ratio, ventilation frequency, and methods of ventilation.[23] Most OHCA studies have not attempted to measure lung inflation. The tidal volume associated with visually detectable chest wall movement is between 300 and 500 mL.[11] However, studies show that >250 mL is a reasonable minimum tidal volume that can result in gas exchange.[18] Because bioimpedance can likely detect chest wall movement at lower volumes than visualization alone, we set a minimum bioimpedance waveform amplitude threshold to 0.5 Ω to detect lung inflation of ≥250 mL of tidal volume.[16] We also found that reviewers could reliably distinguish this bioimpedance waveform amplitude from artifact.[15]

Although some have used capnography to detect ventilation, this measurement typically becomes available only after advanced airway placement. In our study, the mean time interval for advanced airway placement was 9.8 minutes after the start of CPR. Thus, capnography measurement usually does not include this vital interval during the initial phases of professional rescuer CPR. Most EMS protocols call for early placement of a defibrillator during CPR to detect the presence of a shockable rhythm. Hence, the advantage of bioimpedance for ventilation measurement is that it is recorded as soon as the defibrillator chest pads are applied.

Adequate Ventilation by BVM

Our study showed a difference in the number of ventilations between group 1 and group 2 patients (2 versus 12 ventilations) during >9 minutes of 30:2 CPR, but the number of defined pauses between group 1 and group 2 patients (12 versus 12 pauses) did not differ. This contrast between number of ventilations and pauses suggests that the rescuers in both groups attempted ventilation approximately the same number of times per patient, but these attempts frequently did not result in lung inflation. Thus, lung inflation cannot be assumed to have occurred during CPR with a BVM device, but it must be measured to understand fully the effect of ventilation on outcomes.

In this study, only 40% of patients received lung inflation in more than half of the pauses in chest compressions, demonstrating that most pauses do not have detectable ventilation. This suggests overall poor oxygenation and ventilation during initial OHCA resuscitation using a BVM device. Adequate ventilation through BVM remains a difficult skill to perform properly and must be practiced to maintain proficiency.[24–26] To maintain an open airway, the person performing ventilation must extend the neck and perform a jaw thrust maneuver or place an oral airway. In addition, a tight mask seal

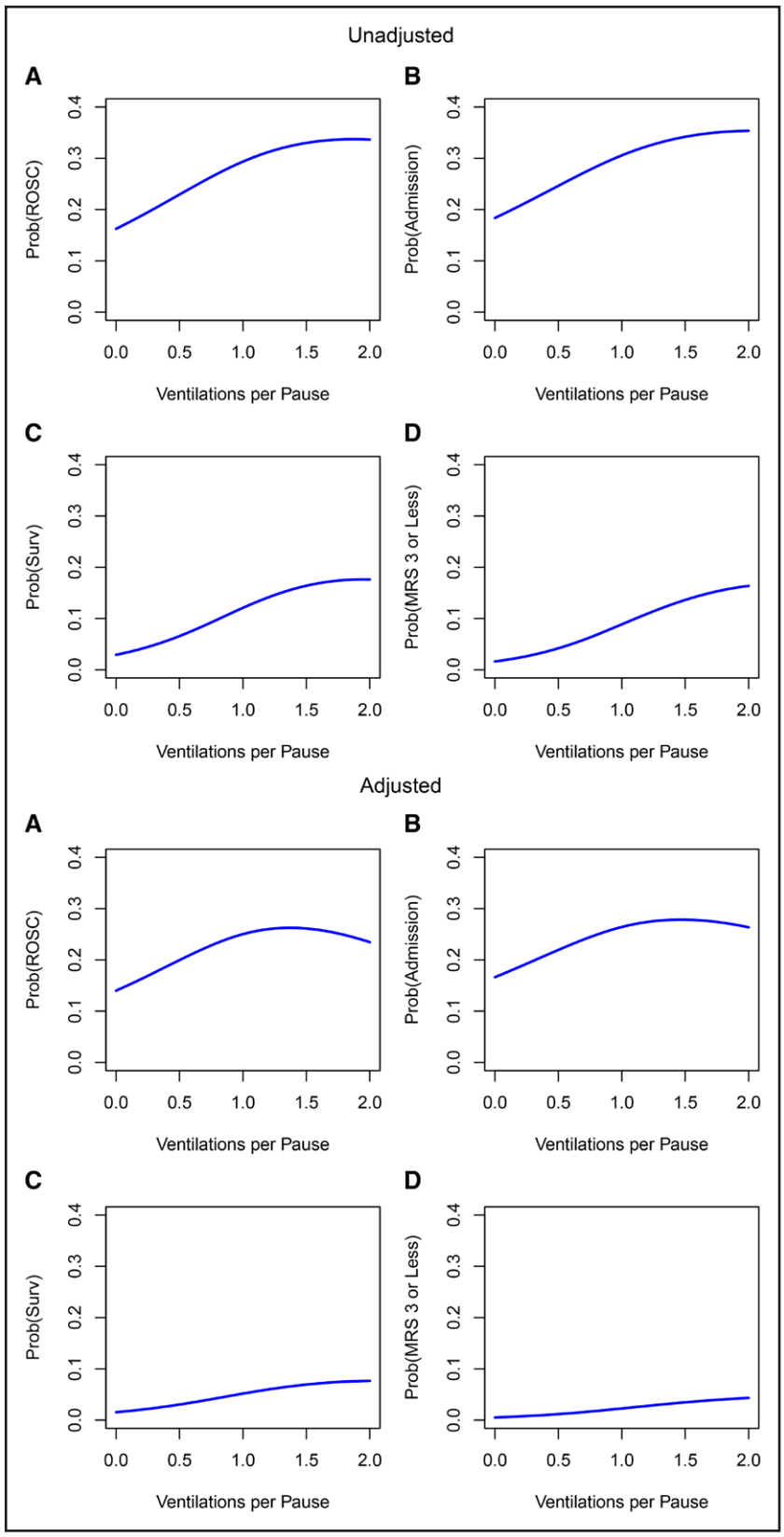

Figure 2. Ventilations per pause and outcomes.
Association of the number of ventilations per pause vs outcomes using natural cubic spline models (unadjusted and adjusted): **A**, Probability (prob) of return of spontaneous circulation (ROSC) on arrival at the emergency department (ED) vs ventilations per pause (**B**) probability of hospital admission (admission) vs ventilations per pause (**C**) probability of survival to hospital discharge vs ventilations per pause (**D**) probability of mRS (modified Rankin Score) of 3 or less (favorable neurological outcome) vs ventilations per pause. Adjusted cubic spline models were adjusted for age, sex, bystander-witnessed cardiac arrest, attempted bystander cardiopulmonary resuscitation, public location, first known emergency medical services rhythm, and Resuscitation Outcomes Consortium site.

on the face must be maintained to prevent air from leaking around the mask, and the rescuer must then simultaneously squeeze the self-inflating bag for 1 to 1.5 s for each breath. In a simulation study, highly trained prehospital providers delivered breaths and ventilation that did not meet guidelines for rate or tidal volumes for the

majority of patients, providing lower respiratory rates and lower volumes.[27] BVM ventilation performance could be improved by having 1 rescuer maintain a tight facemask seal continuously while another rescuer squeezes the self-inflating bag.[28] With 30:2 CPR, the chest compressor could squeeze the self-inflating bag during interruptions in chest compression. However, this is not possible during continuous chest compression CPR, and 3 rescuers may be required.

Ventilation and Clinical Outcomes

Our study reported detailed information regarding ventilation during 30:2 CPR for OHCA and associations with clinical outcomes. We showed that ventilation in more than half of the pauses in chest compressions during 30:2 CPR for OHCA was associated with better outcomes for ROSC, survival to hospital discharge, and survival with favorable neurological outcome. Further analysis demonstrated a dose-response relationship between the number of ventilations per pause and outcomes.

Oxygenation is important to sustaining vital organs, and, in resuscitation, the goal is to artificially provide such support until restoration of function. Although ventilation may be omitted during the first few minutes of CPR because there is sufficient oxygen stored on hemoglobin to last ≈4 minutes, as blood flow during CPR is only 20% to 25% of baseline, at best; ventilation should probably be delivered soon after EMS arrival.[29] Most patients have not received oxygen for 10 to 20 minutes by the time EMS arrives (time intervals for rescuer to recognize an emergency and to call 911 plus EMS response time interval, plus time interval to assemble the airway equipment and to give a breath). Moreover, multiple previous studies have shown that passive ventilation associated with chest compressions is likely insufficient for gas exchange or oxygenation because chest compressions alone provide negligible tidal volume compared with dead space.[8–10]

In addition, multiple studies have indicated that early advanced airway management is associated with improved outcomes.[30–32] This may be another reason group 2 patients had improved outcomes in our study, as they received more effective early BVM ventilation compared with group 1 patients. Decreasing time to restore specific physiological functions to the normal steady state is key to mitigate the effects of post-cardiac arrest syndrome.[33]

Protocol Compliance

In the parent clinical trial, of those assigned to receive 30:2 CPR, only 48% had CPR that was compliant with the 30:2 CPR protocol as indicated by having at least 1.5 pauses/min in chest compressions.[34] In the parent trial, the 30:2 CPR group had a mean of 1.3±0.7 pauses/min. In our study, median pauses in chest compressions per minute for group 1 versus group 2, respectively, were 1.3 (0.8, 1.8) versus 1.4 (0.9, 1.9; NS). Although some patients in our study received CPR that was not compliant (had fewer pauses than expected) with the 30:2 CPR protocol, there was no difference in compliance between the 2 groups.

We did a sensitivity analysis of those patients who had chest compressions with ≥1.5 pauses/min during 30:2 CPR (ie, received CPR that was compliant with the 30:2 CPR protocol; data not shown). The analysis showed an association of improvement for all outcomes with ventilation waveforms in ≥50% of pauses in chest compression and is comparable to the findings in group 2 of the main cohort.

Future Work

Our study reported detailed information regarding ventilation during 30:2 CPR for OHCAs, including ventilation incidence and frequency and the number and duration of pauses. Future studies are needed to evaluate these metrics when continuous chest compression CPR is used and the effect of ventilation metrics on patient survival outcomes during an OHCA. This is especially important because EMS frequently uses continuous chest compression CPR before and after advanced airway placement according to guideline recommendations. Clinical trials are urgently needed comparing ventilation strategies during early CPR and their effects on survival.

A portable spirometer has recently been developed that can be used in the EMS out-of-hospital setting, and a manufacturer has developed a spirometer that can be coupled with its defibrillator. These devices make it possible to obtain more detailed measurement of ventilation metrics than was previously possible during early CPR.

Limitations

The defibrillator files were from 2 device manufacturers. Several brands of defibrillator either did not record bioimpedance or the recording was of insufficient quality. We excluded patients who were randomly assigned to the 30:2 CPR group if they received continuous chest compression CPR, the defibrillator could not record thoracic bioimpedance or the recording could not be located, and some patients had <2 minutes of recorded 30:2 CPR. Some patients received CPR that was not compliant with the 30:2 CPR protocol.

In addition, this study is a secondary observational analysis of data from a clinical trial that addresses a question that was not the purpose of the original trial. Associations between ventilation and outcomes may not represent causal effects. Given the retrospective and observational study design, we cannot account for

residual confounding whereby undetected ventilation may be a marker for some other causal patient or care characteristics responsible for outcome differences. A high body mass index may affect bioimpedance amplitude inversely and could affect detection of ventilation waveforms. Such patients may be more difficult to ventilate, and the observation of poor initial ventilation and outcome may reflect such factors.

These limitations should be balanced against the strengths of the study, in having drawn data from a high-quality multicenter clinical trial, and the outcomes of which were adjusted for EMS response interval, quality of CPR, bystander CPR rates, initial cardiac rhythm, and other confounders. In addition, we used an automated program to annotate ventilation waveforms. This increased consistency and reproducibility of the review and reduced potential bias. Finally, all investigators, except the statistician (B.L.) and database manager (J. Carson), were blinded to survival outcomes and other clinical data during the course of measuring ventilation metrics.

Conclusions

This novel multicenter study demonstrates that lung inflation occurs infrequently with BVM ventilation during 30:2 CPR for OHCAs. Ventilation with measurable lung inflation in ≥50% of pauses was associated with significantly increased rates of ROSC, survival, and increased likelihood of favorable neurological outcome.

ARTICLE INFORMATION

Received May 11, 2023; accepted August 28, 2023.

Affiliations

Department of Emergency Medicine, University of Texas Southwestern Medical Center, Dallas (A.H.I, B.Y.Y., S.S., M.P.C.). Department of Communications Engineering, University of the Basque Country, Bilbao, Spain (E.A.E., X.J.). Department of Biostatistics (B.L., J.C.), Department of Medicine (Emergency Medicine) (T.R.), Department of Medicine (Cardiology) (P.K.), University of Washington, Seattle. Department of Emergency Medicine, University of British Columbia, Vancouver, Canada (J.C.). Department of Emergency Medicine, University of Ottawa, Ontario, Canada (C.V.). Department of Emergency Medicine, University of Pittsburgh, PA (C.C., D.S.). Public Health-Seattle & King County, Emergency Medical Services Division, Seattle, WA (J.B.). Department of Emergency Medicine, The Ohio State University, Columbus (H.E.W.).

Acknowledgments

The authors are indebted to the firefighters and paramedics participating in the Resuscitation Outcomes Consortium for their hard work and dedication. The authors also thank the data coordinators at each Resuscitation Outcomes Consortium site for their extraordinary diligence and focus in abstracting the data for this study.

Sources of Funding

This study was funded by National Institutes of Health/National Heart, Lung, and Blood Institute grant 1 R21 HL156196-02 (Dr Idris) and multiple cooperative agreements (5U01 HL077863, University of Washington Data Coordinating Center; HL077867, University of Washington; HL077871, University of Pittsburgh; HL077881, University of Alabama at Birmingham; HL077885, Ottawa Hospital Research Institute; HL077887, University of Texas Southwestern Medical Center; HL077885 and FAS 06-2603, University of British Columbia), and PID2021-122727OB-I00 grant funded by MCIN/AEI/10.13039/501100011033 and European Regional Development Fund, a way of making Europe (Dr Ecenarro and X. Jaureguibeitia), and by Basque Government grant IT-1717-22 (Dr Ecenarro and X. Jaureguibeitia).

Disclosures

Dr Idris receives grant support from the US National Institutes of Health (NIH) and the Centers for Disease Control and Prevention. He serves as an unpaid volunteer on the American Heart Association national emergency cardiovascular care committee and the Stryker, Inc. (Belfast) clinical advisory board. Dr Kudenchuk receives grant support from NIH as institutional principal investigator for the SIREN Network. Dr Wang received research funds from NIH and the US Department of Defense, site research funds from Marinus, Vasomune, and Quidel, travel funds from Fisher-Paykel, Inc., and consulting fees from the American College of Emergency Physicians as the editor in chief of *JACEP Open*.

Supplemental Material

Appendix

REFERENCES

1. Tsao CW, Aday AW, Almarzooq ZI, Anderson CAM, Arora P, Avery CL, Baker-Smith CM, Beaton AZ, Boehme AK, Buxton AE, et al; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics–2023 update: a report from the American Heart Association [published correction appears in *Circulation*. 2023;147:e622]. *Circulation*. 2023;147:e93–e621. doi: 10.1161/CIR.0000000000001123
2. Taniguchi D, Baernstein A, Nichol G. Cardiac arrest: a public health perspective. *Emerg Med Clin North Am*. 2012;30:1–12. doi: 10.1016/j.emc.2011.09.003
3. Idris AH, Guffey D, Pepe PE, Brown SP, Brooks SC, Callaway CW, Christenson J, Davis DP, Daya MR, Gray R, et al; Resuscitation Outcomes Consortium Investigators. Chest compression rates and survival following out-of-hospital cardiac arrest. *Crit Care Med*. 2015;43:840–848. doi: 10.1097/CCM.0000000000000824
4. Christenson J, Andrusiek D, Everson-Stewart S, Kudenchuk P, Hostler D, Powell J, Callaway CW, Bishop D, Vaillancourt C, Davis D, et al; Resuscitation Outcomes Consortium Investigators. Chest compression fraction determines survival in patients with out-of-hospital ventricular fibrillation. *Circulation*. 2009;120:1241–1247. doi: 10.1161/CIRCULATIONAHA.109.852202
5. Stiell IG, Brown SP, Nichol G, Cheskes S, Vaillancourt C, Callaway CW, Morrison LJ, Christenson J, Aufderheide TP, Davis DP, et al; Resuscitation Outcomes Consortium Investigators. What is the optimal chest compression depth during out-of-hospital cardiac arrest resuscitation of adult patients? *Circulation*. 2014;130:1962–1970. doi: 10.1161/CIRCULATIONAHA.114.008671
6. Vaillancourt C, Petersen A, Meier EN, Christenson J, Menegazzi JJ, Aufderheide TP, Nichol G, Berg R, Callaway CW, Idris AH, et al; Resuscitation Outcomes Consortium Investigators. The impact of increased chest compression fraction on survival for out-of-hospital cardiac arrest patients with a non-shockable initial rhythm. *Resuscitation*. 2020;154:93–100. doi: 10.1016/j.resuscitation.2020.06.016
7. Berg RA, Hemphill R, Abella BS, Aufderheide TP, Cave DM, Hazinski MF, Lerner EB, Rea TD, Sayre MR, Swor RA. Part 5: adult basic life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care [published correction appears in *Circulation*. 2011;124:e402]. *Circulation*. 2010;122(18 Suppl 3):S685–S705. doi: 10.1161/CIRCULATIONAHA.110.970939
8. Idris AH, Banner MJ, Wenzel V, Fuerst RS, Becker LB, Melker RJ. Ventilation caused by external chest compression is unable to sustain effective gas exchange during {CPR}: a comparison with mechanical ventilation. *Resuscitation*. 1994;28:143–150. doi: 10.1016/0300-9572(94)90087-6
9. Deakin CD, O'Neill JF, Tabor T. Does compression-only cardiopulmonary resuscitation generate adequate passive ventilation during cardiac arrest? *Resuscitation*. 2007;75:53–59. doi: 10.1016/j.resuscitation.2007.04.002
10. McDannold R, Bobrow BJ, Chikani V, Silver A, Spaite DW, Vadeboncoeur T. Quantification of ventilation volumes produced by compressions during emergency department cardiopulmonary resuscitation. *Am J Emerg Med*. 2018;36:1640–1644. doi: 10.1016/j.ajem.2018.06.057
11. Baskett P, Nolan J, Parr M. Tidal volumes which are perceived to be adequate for resuscitation. *Resuscitation*. 1996;31:231–234. doi: 10.1016/0300-9572(96)00994-x
12. Risdal M, Aase SO, Stavland M, Eftestøl T. Impedance-based ventilation detection during cardiopulmonary resuscitation. *IEEE Trans Biomed Eng*. 2007;54:2237–2245. doi: 10.1109/tbme.2007.908328

13. Alonso E, Ruiz J, Aramendi E, González-Otero D, Ruiz de Gauna S, Ayala U, Russell JK, Daya M. Reliability and accuracy of the thoracic impedance signal for measuring cardiopulmonary resuscitation quality metrics. *Resuscitation*. 2015;88:28–34. doi: 10.1016/j.resuscitation.2014.11.027
14. Losert H, Risdal M, Sterz F, Nysaether J, Köhler K, Eftestøl T, Wandaller C, Myklebust H, Uray T, Aase SO, et al. Thoracic impedance changes measured via defibrillator pads can monitor ventilation in critically ill patients and during cardiopulmonary resuscitation. *Crit Care Med*. 2006;34:2399–2405. doi: 10.1097/01.CCM.0000235666.40378.60
15. Aramendi E, Lu Y, Chang MP, Elola A, Irusta U, Owens P, Idris AH. A novel technique to assess the quality of ventilation during pre-hospital cardiopulmonary resuscitation. *Resuscitation*. 2018;132:41–46. doi: 10.1016/j.resuscitation.2018.08.016
16. Chang MP, Lu Y, Leroux B, Aramendi Ecenarro E, Owens P, Wang HE, Idris AH. Association of ventilation with outcomes from out-of-hospital cardiac arrest. *Resuscitation*. 2019;141:174–181. doi: 10.1016/j.resuscitation.2019.05.006
17. Nichol G, Leroux B, Wang H, Callaway CW, Sopko G, Weisfeldt M, Stiell I, Morrison LJ, Aufderheide TP, Cheskes S, et al; ROC Investigators. Trial of continuous or interrupted chest compressions during CPR. *N Engl J Med*. 2015;373:2203–2214. doi: 10.1056/NEJMoa1509139
18. Nassal MMJ, Jaureguibeitia X, Aramendi E, Irusta U, Panchal AR, Wang HE, Idris A. Novel application of thoracic impedance to characterize ventilations during cardiopulmonary resuscitation in the pragmatic airway resuscitation trial. *Resuscitation*. 2021;168:58–64. doi: 10.1016/j.resuscitation.2021.08.045
19. Jaureguibeitia X, Aramendi E, Wang HE, Idris AH. Impedance-based ventilation detection and signal quality control during out-of-hospital cardiopulmonary resuscitation. *IEEE J Biomed Health Inform*. 2023;27:3026–3036. doi: 10.1109/JBHI.2023.3253780
20. Jaureguibeitia X, Irusta U, Aramendi E, Owens PC, Wang HE, Idris AH. Automatic detection of ventilations during mechanical cardiopulmonary resuscitation. *IEEE J Biomed Health Inform*. 2020;24:2580–2588. doi: 10.1109/JBHI.2020.2967643
21. Serpa Neto A, Cardoso SO, Manetta JA, Pereira VG, Espósito DC, Pasqualucci MdeOP, Damasceno MC, Schultz MJ. Association between use of lung-protective ventilation with lower tidal volumes and clinical outcomes among patients without acute respiratory distress syndrome: a meta-analysis. *JAMA*. 2012;308:1651–1659. doi: 10.1001/jama.2012.13730
22. Berve PO, Irusta U, Kramer-Johansen J, Skålhegg T, Aramendi E, Wik L. Tidal volume measurements via transthoracic impedance waveform characteristics: the effect of age, body mass index and gender. A single centre interventional study. *Resuscitation*. 2021;167:218–224. doi: 10.1016/j.resuscitation.2021.08.041
23. Chang MP, Idris AH. The past, present, and future of ventilation during cardiopulmonary resuscitation. *Curr Opin Crit Care*. 2017;23:188–192. doi: 10.1097/MCC.0000000000000415
24. Bucher J, Vashisht R, Ladd M, Cooper J. *Bag Mask Ventilation*. StatPearls. Published online 2022. Accessed March 5, 2023. https://pubmed-ncbi-nlm-nih-gov.foyer.swmed.edu/28722953/
25. Lyng JW, Guyette FX, Levy M, Bosson N. Prehospital manual ventilation: an NAEMSP position statement and resource document. *Prehosp Emerg Care*. 2022;26:23–31. doi: 10.1080/10903127.2021.1981506
26. Jabre P, Penaloza A, Pinero D, Duchateau FX, Borron SW, Javaudin F, Richard O, de Longueville D, Bouilleau G, Devaud ML, et al. Effect of bag-mask ventilation vs endotracheal intubation during cardiopulmonary resuscitation on neurological outcome after out-of-hospital cardiorespiratory arrest: a randomized clinical trial. *JAMA*. 2018;319:779–787. doi: 10.1001/jama.2018.0156
27. Neth MR, Benoit JL, Stolz U, McMullan J. Ventilation in simulated out-of-hospital cardiac arrest resuscitation rarely meets guidelines. *Prehosp Emerg Care*. 2021;25:712–720. doi: 10.1080/10903127.2020.1822481
28. Gerber L, Botha M, Laher AE. Modified two-rescuer CPR with a two-handed mask-face seal technique is superior to conventional two-rescuer CPR with a one-handed mask-face seal technique. *J Emerg Med*. 2021;61:252–258. doi: 10.1016/j.jemermed.2021.03.005
29. Turner I, Turner S, Armstrong V. Does the compression to ventilation ratio affect the quality of CPR: a simulation study. *Resuscitation*. 2002;52:55–62. doi: 10.1016/s0300-9572(01)00435-x
30. Wang HE, Jaureguibeitia X, Aramendi E, Nichol G, Aufderheide T, Daya MR, Hansen M, Nassal M, Panchal AR, Nikolla DA, et al. Airway strategy and ventilation rates in the pragmatic airway resuscitation trial. *Resuscitation*. 2022;176:80–87. doi: 10.1016/j.resuscitation.2022.05.008
31. Benoit JL, McMullan JT, Wang HE, Xie C, Xu P, Hart KW, Stolz U, Lindsell CJ. Timing of advanced airway placement after witnessed out-of-hospital cardiac arrest. *Prehosp Emerg Care*. 2019;23:838–846. doi: 10.1080/10903127.2019.1595236
32. Fukuda T, Ohashi-Fukuda N, Inokuchi R, Kondo Y, Sekiguchi H, Taira T, Kukita I. Association between time to advanced airway management and neurologically favourable survival during out-of-hospital cardiac arrest. *Anaesth Crit Care Pain Med*. 2021;40:100906. doi: 10.1016/j.accpm.2021.100906
33. Neumar RW, Nolan JP, Adrie C, Aibiki M, Berg RA, Böttiger BW, Callaway C, Clark RSB, Geocadin RG, Jauch EC, et al. Post–cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication: A Consensus Statement from the International Liaison Committee on Resuscitation [American Heart Association, Australian and New Zealand Council on Resuscitation, European Resuscitation Council, Heart and Stroke Foundation of Cananda, InterAmerican Heart Foundation, Resuscitation Council of Asia, and the Resuscitation Council of Southern Africa); the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Clinical Cardiology; and the Stroke Council. *Circulation*. 2008;118:2452–2483. doi: 10.1161/CIRCULATIONAHA.108.190652
34. Schmicker RH, Nichol G, Kudenchuk P, Christenson J, Vaillancourt C, Wang HE, Aufderheide TP, Idris AH, Daya MR. CPR compression strategy 30:2 is difficult to adhere to, but has better survival than continuous chest compressions when done correctly. *Resuscitation*. 2021;165:31–37. doi: 10.1016/j.resuscitation.2021.05.027