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## Clinical paper

# Association of small adult ventilation bags with return of spontaneous circulation in out of hospital cardiac arrest



Bonnie D. Snyder<sup>a,\*</sup>, Molly R. Van Dyke<sup>a</sup>, Robert G. Walker<sup>b</sup>, Andrew J. Latimer<sup>a</sup>, Bartholomew C. Grabman<sup>e</sup>, Charles Maynard<sup>d</sup>, Thomas D. Rea<sup>a</sup>, Nicholas J. Johnson<sup>a</sup>, Michael R. Sayre<sup>a,c</sup>, Catherine R. Counts<sup>a,c</sup>

### Abstract

**Introduction:** Little is known about the impact of tidal volumes delivered by emergency medical services (EMS) to adult patients with out-of-hospital cardiac arrest (OHCA). A large urban EMS system changed from standard adult ventilation bags to small adult bags. We hypothesized that the incidence of return of spontaneous circulation (ROSC) at the end of EMS care would increase after this change.

**Methods:** We performed a retrospective analysis evaluating adults treated with advanced airway placement for nontraumatic OHCA between January 1, 2015 and December 31, 2021. We compared rates of ROSC, ventilation rate, and mean end tidal carbon dioxide (ETCO<sub>2</sub>) by minute before and after the smaller ventilation bag implementation using linear and logistic regression.

**Results:** Of the 1,994 patients included, 1,331 (67%) were treated with a small adult bag. ROSC at the end of EMS care was lower in the small bag cohort than the large bag cohort, 33% vs 40% ( $p = 0.003$ ). After adjustment, small bag use was associated with lower odds of ROSC at the end of EMS care [OR 0.74, 95% CI 0.61 – 0.91]. Ventilation rates did not differ between cohorts. ETCO<sub>2</sub> values were lower in the large bag cohort ( $33.2 \pm 17.2$  mmHg vs.  $36.9 \pm 19.2$  mmHg,  $p < 0.01$ ).

**Conclusion:** Use of a small adult bag during OHCA was associated with lower odds of ROSC at the end of EMS care. The effects on acid base status, hemodynamics, and delivered minute ventilation remain unclear and warrant additional study.

**Keywords:** Out of hospital cardiac arrest, Ventilation, End tidal carbon dioxide, ETCO<sub>2</sub>

## Introduction

More than 350,000 Americans experience out-of-hospital cardiac arrest (OHCA) annually. With a mortality rate around 90%, identifying modifiable factors that could improve survival is a primary focus of many healthcare systems.<sup>1</sup> While there has been significant emphasis on optimizing compressions, little is known about how best to deliver supportive ventilation during cardiopulmonary resuscitation (CPR). Excess minute ventilation can adversely affect hemodynamics in OHCA by increasing intrathoracic pressure, decreasing venous return, and negatively impacting cardiac output.<sup>2–4</sup> Since carbon dioxide (CO<sub>2</sub>) is a major regulator of cerebral blood flow, hyperventilation causes cerebral vasoconstriction and can worsen secondary

brain injury.<sup>5–8</sup> Additionally, nearly half of all OHCA patients who survive to 48 hours develop acute respiratory distress syndrome (ARDS), which can be worsened by large tidal volumes.<sup>9</sup> Conversely, hypoventilation could produce atelectasis, worsen hypoxia, and worsen acidosis.

International guidelines recommend adults be ventilated with tidal volumes of 500–600 ml per breath during ongoing CPR, though these estimates are largely extrapolated from animal studies and healthy controls.<sup>10–12</sup> EMS systems commonly provide rescue breaths to adults with large adult ventilation bag devices (large bags).<sup>13</sup> Depending on manufacturer and model, large bags have maximum tidal volumes of 1500–1685 ml and deliver approximately 600–830 ml per one-handed squeeze.<sup>14–17</sup> Simulation-based studies

\* Corresponding author at: University of Cincinnati, College of Medicine, USA.

E-mail address: [snyderb9@ucmail.uc.edu](mailto:snyderb9@ucmail.uc.edu) (B.D. Snyder).

<https://doi.org/10.1016/j.resuscitation.2023.109991>

Received 11 August 2023; Received in Revised form 25 September 2023; Accepted 27 September 2023

indicate EMS providers often provide minute ventilation well above the recommended ranges to OHCA patients.<sup>18,19</sup>

To mitigate the perceived risk of hyperventilation, the Seattle Fire Department (SFD) replaced its large bags with small adult ventilation bag devices (small bags) in the summer of 2017. The small bag reduced the maximum volume from 1685 to 1000 ml and expected delivered tidal volume from 700 to 450 ml.<sup>17</sup> The delivered tidal volumes of the small bags more closely approximated tidal volumes used in patients receiving mechanical ventilation and known to be safe in patients with acute respiratory failure.<sup>20</sup> The primary aim of this study was to assess the relationship between small bag use and incidence of return of spontaneous circulation (ROSC) in OHCA. We hypothesized the incidence of ROSC at the end of EMS care would increase after this change due to the potentially favorable hemodynamic effects of lower minute ventilation.

## Methods

### Study design and setting

This is a retrospective, observational cohort analysis of prospectively acquired OHCA and advanced airway management registries managed by our quality improvement staff. The Seattle Fire Department is the primary responding 911 EMS provider in Seattle, WA. The tiered response model used has been previously described.<sup>21</sup> This study was approved by the University of Washington Institutional Review Board and adhered to STROBE guidelines for reporting observational studies.<sup>22</sup>

Emergency medical technicians (EMTs) and advanced life support (ALS) intensive care paramedics are trained to deliver manual compressions at a rate of 100–120 per minute with an interposed breath after each 10th compression, yielding an expected rate of 10–12 breaths per minute. Ventilations are delivered manually with supplemental oxygen, without positive end expiratory pressure, and without an impedance threshold device. To maintain competency, providers complete simulation-based resuscitation training annually. Paramedics perform endotracheal intubation as the primary method of advanced airway management during OHCA. An iGel is the only supraglottic airway device available for use.

### Participants

We evaluated all patients treated with an advanced airway for non-traumatic OHCA from 2015 through 2021. We excluded patients with any of the following: age <18, received basic life support (BLS) only, termination of resuscitation due to advance directives, ALS interventions prior to EMS arrival, insufficient capnography data, cricothyrotomy, advanced airway placed while patient had spontaneous circulation, airway was managed with BVM only, or did not receive CPR while under EMS ALS care.

### Exposures and outcomes

The primary exposure was ventilation with a Mercury Medical CPR-2 small ventilation bag. Patients treated prior to July 1st, 2017 were considered to be in the large bag cohort, and patients treated after September 30th, 2017 were considered to be in the small bag cohort. Both large and small bags were used during a transition period of July - September, 2017, thus this period was excluded from analysis.

The primary outcome was ROSC at the end of EMS care which was defined as the time point when the EMS crew crossed the threshold into the receiving emergency department or terminated efforts in the field. Secondary outcomes were ventilation rate and mean end-tidal CO<sub>2</sub> (ETCO<sub>2</sub>) value during CPR.

### Data sources and measurement

Every OHCA is abstracted into a registry incorporating data from the 911 call, prehospital care record, cardiac monitor, and hospital records.<sup>23</sup> Cardiac monitors (LIFEPAK 15, Stryker Emergency Care, Redmond, WA) record real-time audio, peripheral oxygen saturation, continuous quantitative ETCO<sub>2</sub> waveform, ECG waveform, and transthoracic impedance. Written records are compared to cardiac monitor files and audio recordings to adjudicate differences before integrating into the registry stored in REDCap (Vanderbilt University, Nashville, TN).<sup>24</sup>

Advanced airway placement was defined as an endotracheal tube or iGel supraglottic airway placement confirmed by the treating paramedics and subsequent ETCO<sub>2</sub> reading. The time point of advanced airway placement was determined by review of monitor audio recordings and ETCO<sub>2</sub> readings. Ventilations following advanced airway placement were identified from the continuous ETCO<sub>2</sub> waveform and reported by CODESTAT Reviewer v.12.0 software (Stryker Emergency Care, Redmond, WA). The proprietary Stryker breath detection algorithm uses a combination of several signal processing techniques to analyze the raw ETCO<sub>2</sub> waveform, and achieves approximately 95% sensitivity and 95% positive predictive value compared to manually annotated breaths. The data was then exported using the Research Exporter function of CODESTAT. Using Stata (Version 16, StataCorp, College Station, TX), the data stream was divided into 30 second intervals beginning with the time of advanced airway placement. Intervals when ETCO<sub>2</sub> values were missing for 20 seconds or more in a 30 second interval or when the maximum ETCO<sub>2</sub> value was below the ventilation detection threshold were excluded. The maximum value following each ventilation serves as the ETCO<sub>2</sub> value for that ventilation. We then calculated mean values for ventilation rate and ETCO<sub>2</sub> across all included 30 second intervals after advanced airway placement.

### Statistical analysis

Stata and Tableau (Version 2023.1, Tableau Software, LLC., Seattle, WA) were used to conduct statistical analyses. Differences between the cohorts were compared with the Chi-square statistic for categorical variables and the Student's t-test for continuous variables. Standard deviations and 95% confidence intervals (CI) were calculated. Logistic regression was used to examine the association between bag size and ROSC at the end of EMS care. Linear regression was used to assess the association of ventilation rate and average ETCO<sub>2</sub> with bag size as measured for each interval of resuscitation. Standard errors of the regression coefficients were adjusted for potential correlated error due to multiple observations per patient with the Huber White Sandwich Estimator. Multivariable models adjusted for Utstein covariates, including age, sex, witnessed arrest, bystander CPR, and initial rhythm. In a post-hoc analysis, we added additional covariates to the multivariable models including public arrest location, medical etiology, 9-1-1 call to initiation of CPR by EMS, 9-1-1 call to final airway placement, and total epinephrine dose.

## Results

### Participants/descriptive data

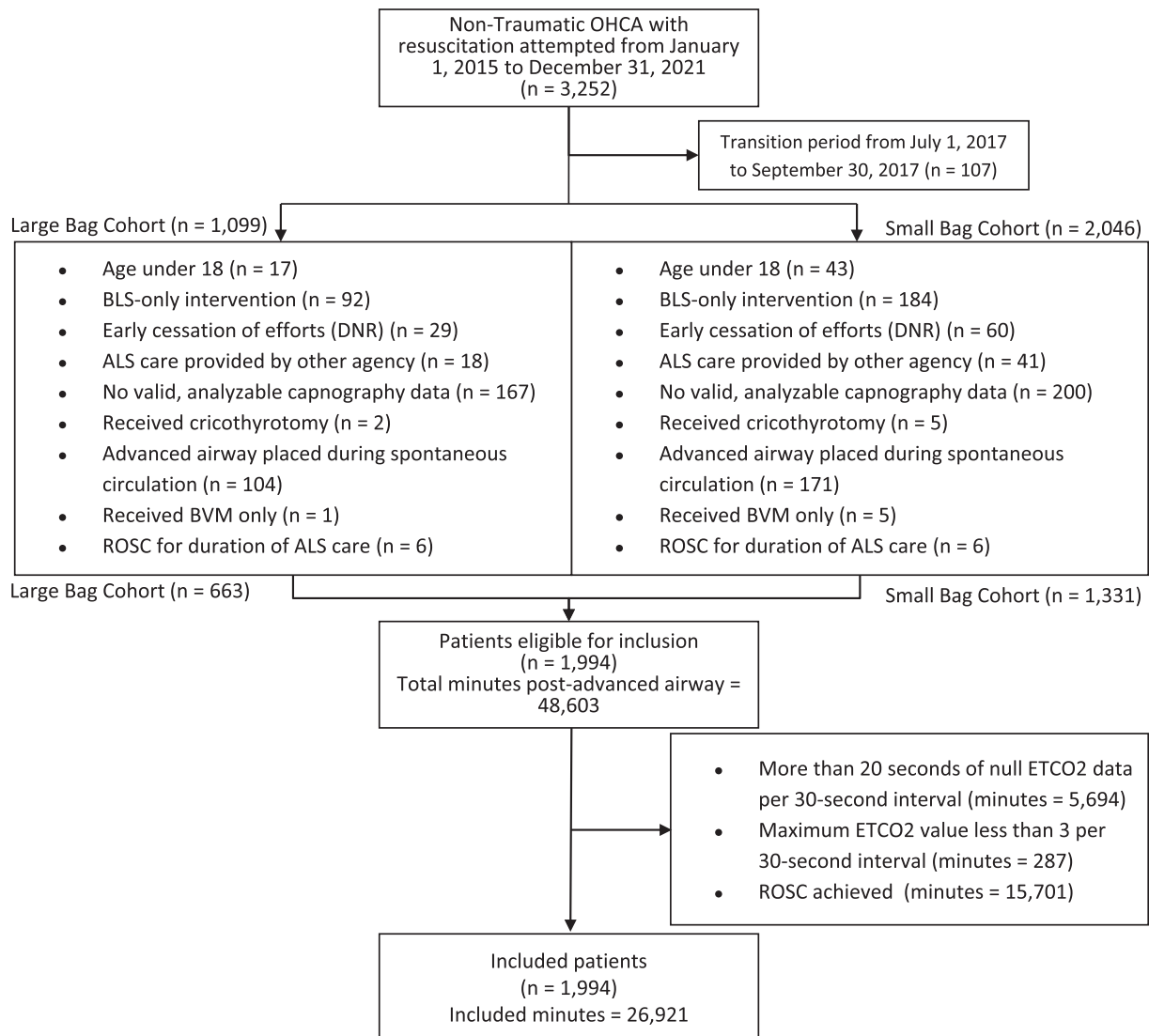
From January 1, 2015 to December 31, 2021, 1,994 of 3,252 patients treated by SFD for non-traumatic OHCA met inclusion criteria (Fig. 1). The included cases totaled 48,603 minutes of resuscitation; but 15,701 (32.3%) were recorded while the patient had spontaneous circulation and were excluded from this analysis. Following exclusions, 280,107 unique ventilations were analyzed within 9,135 and 17,786 minutes of data for the large bag and small bag cohorts, respectively.

Across both cohorts, mean  $\pm$  SD age was  $61.7 \pm 17.7$  years old, 35% of patients were female, and the duration of resuscitation was  $34 \pm 12$  minutes (Table 1). Medical etiology of the arrest was present in 87% of cases, and 21% initially presented with a shockable rhythm. These characteristics were similar between cohorts. More patients in the small bag cohort received bystander CPR (64% versus 59%), fewer patients in the small bag cohort arrested in public

(22% vs 27%), and the intervals from 9-1-1 call to start of SFD CPR and advanced airway placement were longer in the small bag cohort (10 vs. 9 minutes and 20 vs. 18 minutes, respectively). The cohorts had a similar chest compression fraction (93% vs. 94%) and similar pH on hospital arrival (7.09 vs 7.06).

### Primary outcome

The incidence of ROSC on hospital arrival was significantly lower in the small bag cohort when compared with the large bag cohort, 33% vs 40% (unadjusted odds ratio [OR] 0.74, 95% CI = 0.61–0.90,  $p < 0.003$ ) (Table 2). After adjusting for age, sex, witnessed arrest, bystander CPR, and initial rhythm, the odds of ROSC on hospital arrival for the small bag cohort did not change (adjusted odds ratio [aOR] 0.74, 95% CI = 0.61–0.91) (Fig. 2). A post hoc power calculation found that using the Chi-square test there was 85% likelihood of achieving the observed difference of ROSC at the end of resuscitation assuming a 2-sided test at  $\alpha = 0.05$ .



**Fig. 1 – Inclusion Criteria. Application of inclusion and exclusion criteria by cohort. OHCA out-of-hospital cardiac arrest, BLS basic life support, DNR do not resuscitate, ALS advanced life support, BVM bag valve mask, ROSC return of spontaneous circulation.**

**Table 1 – Baseline characteristics.**

	Large Bag Cohort (n = 663)	Small Bag Cohort (n = 1331)	p-value
Age (years), mean (SD)	61.9 (17.7)	61.7 (17.8)	0.79
Female	220 (33%)	469 (35%)	0.38
<b>Witness of Arrest</b>			0.10
Layperson	210 (32%)	418 (31%)	
EMS Personnel	66 (10%)	176 (13%)	
Unwitnessed Arrest	387 (58%)	737 (55%)	
Received Bystander CPR*	352/597 (59%)	744/1155 (64%)	0.025
<b>Location of Arrest</b>			0.019
Home/Other Residence	387 (58%)	855 (64%)	
Public (Indoor or Outdoor)	179 (27%)	288 (22%)	
Healthcare Facility (outpatient clinic or nursing home)	70 (10%)	108 (8%)	
Other	97 (15%)	188 (14%)	
<b>Etiology of Arrest by Utstein Classification</b>			0.07
Medical	588 (88%)	1151 (86%)	
Drug Overdose	56 (8%)	124 (9%)	
Drowning	3 (1%)	12 (1%)	
Electrocution	0 (0%)	1 (0%)	
Asphyxial	10 (1%)	38 (3%)	
Other	6 (1%)	5 (0%)	
<b>Initial rhythm</b>			0.25
VF/VT	147 (22%)	264 (20%)	
Asystole	305 (46%)	632 (48%)	
PEA	195 (29%)	384 (29%)	
Other	16 (3%)	51 (4%)	
Received iGel	11 (2%)	100 (8%)	<0.0001
Received Paralytics During CPR	68 (10%)	147 (11%)	0.59
Advanced Airway Ventilation Duration (minutes), mean (SD)**	24.7 (13.2)	23.8 (11.4)	0.13
Resuscitation Duration (minutes), mean (SD)***	34.0 (13.4)	34.0 (11.8)	0.89
CPR Fraction mean (SD)	93% (4%)	94% (5%)	<0.0001

SD standard deviation, CPR cardiopulmonary resuscitation, EMS emergency medical services, VF/VT ventricular fibrillation or pulseless ventricular tachycardia, PEA pulseless electrical activity.

\*Excludes patients whose arrest was witnessed by EMS personnel.

\*\*Advanced airway ventilation duration was calculated as the interval from insertion of an iGel or endotracheal tube to the end of EMS care.

\*\*\*Resuscitation duration was calculated as the minutes from the start of CPR to the end of the case (declared dead vs. transfer of care at the hospital), this could include periods of ROSC.

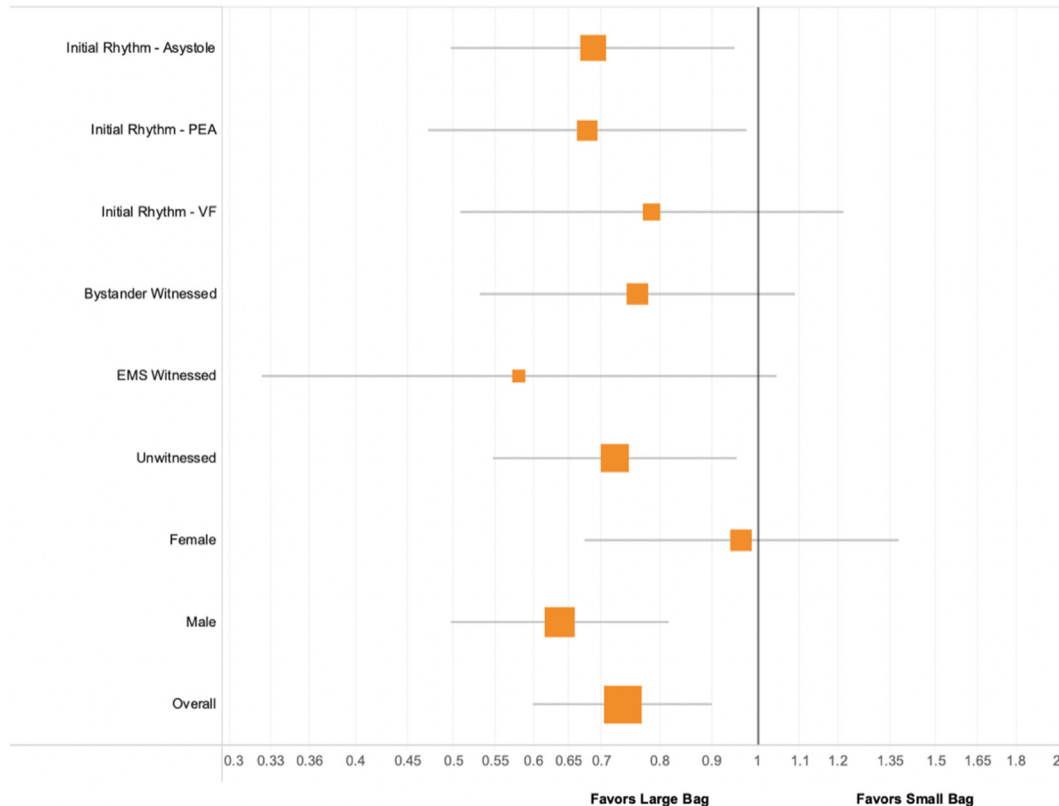
**Table 2 – Outcomes.**

	Large Bag Cohort (n = 663)	Small Bag Cohort (n = 1331)	Unadjusted Odds Ratio (CI)	Adjusted Odds Ratio* (CI)	p-value
Achieved ROSC at Any Time	341 (51%)	625 (47%)	0.84 (0.69–1.01)	0.85 (0.70–1.03)	0.06
ROSC at End of EMS Care, All Rhythms	265 (40%)	441 (33%)	0.74 (0.61–0.90)	0.74 (0.61–0.91)	0.003
<b>ROSC at End of EMS Care by Initial Rhythm</b>					
VF/VT	78/147 (53%)	128/264 (48%)	0.83 (0.56–1.25)	0.82 (0.54–1.24)	0.37
Asystole	85/305 (28%)	140/632 (22%)	0.74 (0.54–1.01)	0.71 (0.52–0.98)	0.06
PEA	93/195 (48%)	161/384 (42%)	0.79 (0.56–1.12)	0.74 (0.52–1.05)	0.19
Survival to Admission	276 (42%)	460 (35%)	0.74 (0.61–0.90)	0.73 (0.60–0.90)	0.002
Survival to Discharge	80 (12%)	125 (9%)	0.76 (0.56–1.02)	0.79 (0.57–1.09)	0.16
<b>Neurological Function</b>					0.052
CPC 1/2	49 (7%)	63 (5%)	0.62 (0.42–0.92)**	0.65 (0.43–0.99)**	
CPC 3/4	31 (5%)	62 (5%)			
Deceased	583 (88%)	1206 (91%)			

ROSC return of spontaneous circulation, EMS emergency medical services, VF/VT ventricular fibrillation or pulseless ventricular tachycardia, PEA pulseless electrical activity, CPC cerebral performance category.

\*Adjusted for age, sex, witness status, bystander CPR, and initial rhythm.

\*\*Outcome defined as 0-CPC 3/4 or deceased, 1-CPC ½.



**Fig. 2 – Odds of ROSC at the End of EMS Care.** Shown are the odds ratios and 95% confidence intervals for the primary outcome (ROSC at the end of EMS care) in the small bag cohort as compared with the large bag cohort by arrest characteristic. Odds ratios were adjusted for age, sex, witnessed arrest, bystander CPR, and initial rhythm when applicable. Weight of square demonstrative of number of patients evaluated. Odds ratios less than 1 indicate a lower likelihood of achieving ROSC at the end of EMS care. ROSC return of spontaneous circulation, PEA pulseless electrical activity, VF/VT ventricular fibrillation or pulseless ventricular tachycardia, EMS emergency medical services.

### Secondary outcomes

Ventilation rates were similar in the large and small bag cohorts,  $11.9 \pm 5.3$  vs.  $12.0 \pm 4.8$  ( $p = 0.60$ ) breaths/min respectively (Fig. 3). Measured ventilations rates ranged from 6-18 breaths/min for 82.7% and 86.1% of periods in the large and small bag cohorts, respectively (Supplement Fig. S1). Adherence to guideline recommended ventilation rates of about 10 breaths/min (9 to 11) was more common in the small bag cohort (28.4% vs 31.2% of periods).<sup>8</sup> Rates > 18 breaths/min were reported for 10.6% and 9.7% of evaluated periods in the large and small bag cohorts, respectively.

ETCO<sub>2</sub> values were lower in the large bag cohort,  $33.2 \pm 17.2$  mmHg vs.  $36.9 \pm 19.2$  mmHg ( $p < 0.01$ ) (Table 3). ETCO<sub>2</sub> less than 15 mmHg was measured more frequently in the large bag cohort, 17.6% vs. 12.6%. Periods of ETCO<sub>2</sub> > 45 mmHg were more common in the small bag cohort, 19.9% vs 27.3%. For patients with ROSC and a pH recorded on ED arrival, the mean ETCO<sub>2</sub> at the end of EMS care was  $38.9 \pm 16.8$  in the large bag cohort and  $43.2 \pm 19.3$  in the small bag cohort.

### Subgroups

Mean ventilation rates were similar between cohorts when stratified by presenting rhythm but were higher in patients presenting with a shockable rhythm compared with asystole and PEA (Table 3). ETCO<sub>2</sub> values were lower in the large bag cohort when compared

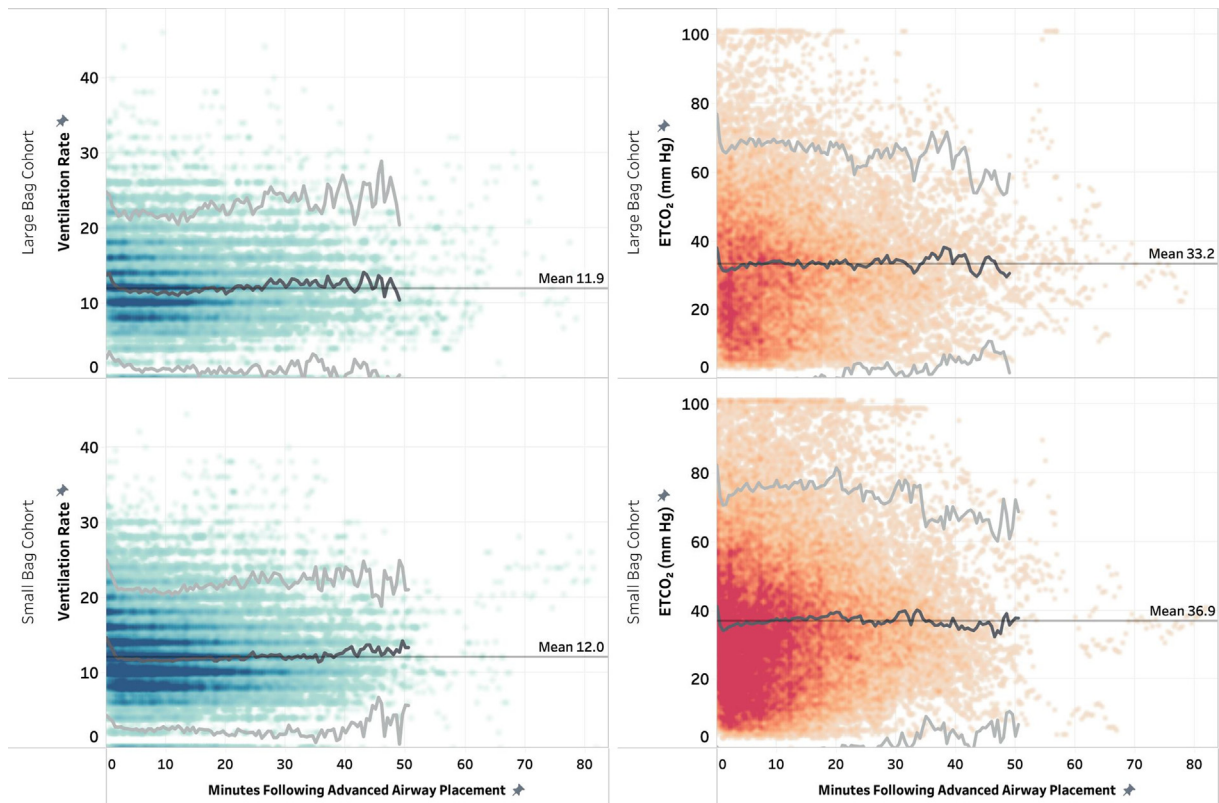
with the small bag cohort in all presenting rhythm groups. The incidence of ROSC did not differ by initial rhythm (Table 2).

### Sensitivity and exploratory analyses

Once we reviewed the results of the prespecified analyses, we performed a series of sensitivity and exploratory analyses (Supplement Table S3). First, events occurring after COVID-19 was recognized in our county were censored from the analysis. When the OHCA occurred prior to February 27, 2020, the small bag cohort had a similarly lower odds of ROSC on hospital arrival (OR 0.75, 95% CI = 0.60–0.93,  $p = 0.008$ ). After adjusting for initial rhythm, age, sex, witnessed arrest, and bystander CPR, the odds of ROSC on hospital arrival in the small bag cohort continued to be lower (aOR 0.76, 95% CI = 0.61–0.95,  $p = 0.018$ ).

Next, we added variables to the logistic regression to assess for potential confounding. After adjusting for medical etiology, public arrest location, time interval from 9-1-1 call to initiation of CPR by EMS, total epinephrine dose received, and time interval from 9-1-1 call to advanced airway placement, in addition to the aforementioned variables, the association between small bag size and lower odds of ROSC on hospital arrival remained (OR 0.79, 95% CI = 0.62–0.99).

Finally, we assessed secular trends over time by visualizing the incidence of ROSC on hospital arrival by month for the seven year period (Supplement Fig. 2). We did not detect a significant change



**Fig. 3 – Ventilation Rate and ETCO<sub>2</sub> Values in Cardiopulmonary Resuscitation. Density plot of ventilation rates and ETCO<sub>2</sub> values during cardiopulmonary resuscitation following advanced airway placement. Ventilation dots represent ventilation rate for each evaluated 30 second period. ETCO<sub>2</sub> dots represent unique ETCO<sub>2</sub> values from each measured ventilation. Mean value across each minute with 95% confidence interval lines are displayed. ETCO<sub>2</sub> end tidal carbon dioxide.**

in slope before and after the implementation of the small bag using z transformation ( $p = 0.06$ ).

## Discussion

Among patients with non-traumatic OHCA who received an intra-arrest advanced airway, small bag use was associated with lower odds of ROSC at the end of EMS care. This result was unexpected since we implemented the smaller adult size ventilation bag to reduce delivery of excessive tidal volume and avoid complications related to hyperventilation. EMS providers in our study delivered a mean ventilation rate of 12 breaths/min and delivered ventilations between 9 and 11 breaths/min, close to the guideline recommended rate of 10 breaths/min, in 24% of the evaluated time periods.<sup>10</sup> Ventilation rates above 18 breaths per minute were uncommon, present in about 10% of all time periods measured.

Given the unexpected result, we conducted a series of exploratory, post hoc analyses to examine any potential sources of confounding within these cohorts. For example, the negative association with use of the small bag remained largely unaffected when additional OHCA characteristics were added to the regression and when the analysis was restricted to the pre-COVID time period. The cohorts had similar proportions of patients with drug overdoses. Patients presenting with a shockable rhythm, however, varied markedly between years, ranging from 17% to 24% annually. Both the

time from 911 call to initiation of CPR and placement of an advanced airway lengthened over time (Supplement Table S1). However, adding these time period variables in our logistic regression did not significantly change the result.

In animal studies, excess minute ventilation leads to high intrathoracic pressure, lower coronary perfusion pressure, and lower cardiac output.<sup>2,25–27</sup> A seminal study demonstrated lower survival when pigs were hyperventilated during cardiac arrest.<sup>2</sup> Recent clinical studies have found no clear association between ventilation rate and ROSC.<sup>28–31</sup> While we were not able to measure delivered tidal volume, we found that 82.5% of measured ventilations were between 6–18 breaths per minute, differing from prior studies documenting very high<sup>2,32</sup> or very low<sup>28</sup> ventilation rates during OHCA in some EMS systems. Notably, EMS providers did not compensate for lower tidal volumes delivered by the small bag by delivering higher ventilation rates. Hyperventilation may have been mitigated by training providers to squeeze the ventilation bag with only one hand, use of a metronome to guide chest compression and ventilation rates (implemented June of 2015), and completion of annual high performance resuscitation training.<sup>33</sup> However, it is possible that ventilations delivered within the recommended rate range were inadequate in the setting of lower tidal volumes delivered by smaller bags.

Little is known about the effects of prehospital tidal volume in OHCA. Ventilation with low tidal volumes has become a cornerstone of critical care management of patients with, or at-risk for, lung injury or ARDS. One study demonstrated an association between tidal

**Table 3 – Ventilation Rate and ETCO<sub>2</sub> During Cardiac Arrest.**

	Large Bag Cohort	Small Bag Cohort	p-value
<b>All rhythms</b>			
Ventilation rate, mean (SD) (n = 30 second periods)	11.9 (5.3) (n = 18,270)	12.0 (4.8) (n = 35,572)	0.60*
ETCO <sub>2</sub> , mean (SD) (n = unique observations)	33.2 (17.2) (n = 96,926)	36.9 (19.2) (n = 183,181)	<0.0001*
Periods with ventilation rate between 9–11 (% of all periods)	4,147 (22.7%)	8,850 (24.9%)	<0.0001**
Periods with ventilation rate < 6 (% of all periods)	1,232 (6.7%)	1,467 (4.1%)	<0.0001**
Periods with ventilation rate 6–18 (% of all periods)	15,103 (82.7%)	30,639 (86.1%)	0.002**
Periods with ventilation rate > 18 (% of all periods)	1,935 (10.6%)	3,466 (9.7%)	0.39**
Periods with ETCO <sub>2</sub> < 15 mmHg (% of all periods)	3,213 (17.6%)	4,471 (12.6%)	0.001**
Periods with ETCO <sub>2</sub> > 45 mmHg (% of all periods)	3,637 (19.9%)	9,698 (27.3%)	<0.0001**
Ventilation rate when ETCO <sub>2</sub> > 45 (n = ETCO <sub>2</sub> observations)	12.4 (4.6) (n = 3,637)	12.3 (4.4) (n = 9,698)	0.80*
Ventilation rate when ETCO <sub>2</sub> ≤ 45 (n = ETCO <sub>2</sub> observations)	11.8 (5.5) (n = 14,633)	12.0 (5.0) (n = 25,874)	0.58*
<b>Initial rhythm VF/VT</b>			
Ventilation rate, mean (SD)	13.5 (5.3) (n = 4,838)	13.3 (5.3) (n = 7,891)	0.65*
ETCO <sub>2</sub> , mean (SD)	32.5 (13.0) (n = 29,081)	37.5 (15.4) (n = 45,236)	<0.0001*
<b>Initial rhythm asystole</b>			
Ventilation rate, mean (SD)	11.3 (5.2) (n = 7,732)	11.7 (4.6) (n = 15,743)	0.18*
ETCO <sub>2</sub> , mean (SD)	33.8 (18.7) (n = 38,845)	36.7 (20.6) (n = 78,225)	0.031*
<b>Initial rhythm PEA</b>			
Ventilation rate, mean (SD)	11.4 (5.2) (n = 5,411)	11.6 (4.6) (n = 10,485)	0.59*
ETCO <sub>2</sub> , mean (SD)	33.6 (18.7) (n = 27,459)	37.2 (20.3) (n = 52,249)	0.042*

SD standard deviation, ETCO<sub>2</sub> end tidal carbon dioxide, VF/VT ventricular fibrillation or pulseless ventricular tachycardia, PEA pulseless electrical activity.

\*by linear regression with correction of p-value for multiple observations per patient.

\*\*by 2 sample t-test.

volumes ≤ 8 ml/kg of predicted body weight and improved neurologic outcome in hospitalized patients who achieved ROSC after OHCA.<sup>34</sup> International CPR guidelines recommend that, for adults receiving ventilation during OHCA, tidal volumes should be about 500–600 ml and that “it may be reasonable for the healthcare provider to give rescue breaths at a rate of . . . about 10 breaths per minute”.<sup>10</sup> These weak recommendations have limited supporting data and are based on low-quality evidence, largely derived from studies from healthy patients undergoing general anesthesia. A pilot study in a nearby system demonstrated that, in nearly 90% of measured breaths, tidal volumes were delivered within a lung protective range of 4–10 ml/kg of predicted body weight, though more variation was seen among patients receiving CPR.<sup>35</sup> Interestingly, in that study, bag size did not seem to affect delivered tidal volume or peak pressure.

We observed a higher ETCO<sub>2</sub> in the smaller bag cohort, suggesting lower tidal volumes were delivered since ventilation rates were similar. Delivery of smaller tidal volumes may lead to physiologic changes that are potentially harmful. These include hypoventilation, increased dead space fraction, and alveolar derecruitment, which could cause atelectasis and shunt physiology. However, studies comparing arterial CO<sub>2</sub> (PaCO<sub>2</sub>) with ETCO<sub>2</sub> after OHCA have demonstrated poor correlation, as ETCO<sub>2</sub> is affected by a number of parameters, including cardiac output, cellular respiration, and pul-

monary circulation.<sup>36,37</sup> We are planning a randomized trial in OHCA patients comparing first responder ventilation with a face mask to iGel.<sup>38</sup> In that trial, we will measure delivered tidal volume in a subset of study subjects with smaller and larger ventilation bags.

Additionally, the effect of ventilation rate on PaCO<sub>2</sub> during cardiac arrest is complex. Ruiz de Gauna et al. showed that ETCO<sub>2</sub> decreases exponentially with increasing ventilation rate, but a small clinical trial comparing ventilation rates of 10 and 20 breaths/min did not discern any influence of ventilation rate on hypercapnia and acid-base status.<sup>39,31</sup> We found a slightly lower pH in the small bag cohort on hospital arrival (7.06 vs 7.09), but the clinical impact of a 0.03 change in pH is likely minimal. Because emergency department PaCO<sub>2</sub> values were not collected, we are unable to determine if the observed pH values are related to prehospital ventilation.

### Limitations

Our study has a number of limitations. We were unable to measure the delivered tidal volume per breath and thus could not calculate minute ventilation. We did not have a contemporaneous control group. The retrospective nature of our analysis introduces potential selection bias and limits our ability to establish causality. Prior to initiating the study, we elected ROSC at the end of EMS care as our primary endpoint to limit the impact of variability introduced by hospital care. Yet assessing the association between bag size and

ROSC at the end of the resuscitation is challenging, because it is not possible to completely delineate the independent effects of bag size and possible unmeasured confounding factors impacting survival. Our measured ventilation rate may occasionally not match the actual rate of ventilations delivered to the patients due to a leak in the endotracheal tube cuff, breath stacking, and disconnection of ETCO<sub>2</sub> measurement. ETCO<sub>2</sub> measurement was limited to the period of time after placement of an advanced airway during ongoing cardiac arrest. This study was performed within a single EMS system with significant focus on OHCA resuscitation, so results may not generalize to all systems. Finally, case review and data extraction is done by a heterogeneous team. Some variation likely exists over time in identification and categorization of coded variables.

These limitations should be considered in light of the strengths of our study. We comprehensively evaluated the ventilation patterns in almost 2,000 cardiac arrest cases using precise time points determined by review of capnography and audio recordings and utilized a ventilation identification algorithm available to many EMS systems.

## Conclusion

In conclusion, the use of small adult ventilation bags was associated with a lower likelihood of ROSC at the end of EMS care in non-traumatic, adult OHCA. Future studies should measure the relationship between tidal volume delivered and patient outcomes, as well as impact on downstream lung injury.

## CRedit authorship contribution statement

**Bonnie D. Snyder:** . **Molly R. Van Dyke:** Writing – review & editing, Software, Formal analysis, Data curation. **Robert G. Walker:** Writing – review & editing, Software, Resources. **Andrew J. Latimer:** Writing – review & editing, Conceptualization. **Bartholomew C. Grabman:** Writing – review & editing, Conceptualization. **Charles Maynard:** Writing – review & editing, Validation, Methodology, Formal analysis. **Thomas D. Rea:** Writing – review & editing, Validation. **Nicholas J. Johnson:** Writing – review & editing, Validation, Methodology, Conceptualization. **Michael R. Sayre:** Writing – review & editing, Visualization, Supervision, Methodology, Formal analysis, Conceptualization. **Catherine R. Counts:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Data curation, Conceptualization.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: This research did not receive any external funding. Robert Walker is a biomedical engineer employed by Stryker Emergency Care. Nicholas Johnson receives research funding from National Institutes of Health, Centers for Disease Control and Prevention, and University of Washington Royalty Research Fund for unrelated work and serves on a Scientific Advisory Board for Neuroptics, Inc. Thomas Rea has received support from Philips. Michael Sayre has received consulting fees from Stryker Emergency Care. The remaining authors have no conflicts of interest to report.

## Acknowledgements

Thanks to the paramedics, EMTs, dispatchers, and staff of the Seattle Fire Department for their commitment to and delivery of excellent patient care.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.resuscitation.2023.109991>.

## Author details

<sup>a</sup>University of Washington, School of Medicine, USA <sup>b</sup>Stryker Emergency Care, USA <sup>c</sup>Seattle Fire Department, USA <sup>d</sup>University of Washington, School of Public Health, USA <sup>e</sup>University of New Mexico, School of Medicine, USA

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