Predefibrillation end-tidal CO_2 and defibrillation success in out-of-hospital cardiac arrest: an observational cohort study

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ABSTRACT

Background Predefibrillation end-tidal CO_2 ($ETCO_2$) may predict defibrillation success and could guide defibrillation timing in ventricular fibrillation (VF) cardiac arrest. This relationship has only been studied using advanced airways. Our aim was to evaluate this relationship using both basic (bag–valve–mask (BVM)) and advanced airways (supraglottic airways and endotracheal tubes).

Methods Prehospital patient records and defibrillator files were abstracted for patients with out-of-hospital cardiac arrest in Ontario, Canada, with initial VF cardiac rhythms between 1 January 2018, and 31 December 2019. Analyses assessed the relationship between each predefibrillation $ETCO_2$ reading and defibrillation outcomes at the subsequent 2 min pulse check (ie, VF, asystole, pulseless electrical activity (PEA) or return of spontaneous circulation (ROSC)), accounting for airway types used during resuscitation. Multivariable logistic regression evaluated the association between the first documented predefibrillation $ETCO_2$ and postshock VF termination or ROSC.

Results Of 269 cases abstracted, 153 had predefibrillation $ETCO_2$ measurements and were included in the study. Among these cases, 904 shocks were delivered and 44.4% (n=401) had predefibrillation $ETCO_2$ measured. The first $ETCO_2$ reading was more often from BVM (n=134) than advanced airways (n=19). $ETCO_2$ readings were lower when measured through BVM versus advanced airways (30.5 mm Hg (4.06 kPa) (±14.4 mm Hg (1.92 kPa)) vs 42.1 mm Hg (5.61 kPa) (±22.5 mm Hg (3.00 kPa)), $_{adj}$ANOVA p<0.01). Of all shocks with $ETCO_2$ reading (n=401), no difference in preshock $ETCO_2$ was found for subsequent shocks that resulted in persistent VF (32.2 mm Hg (4.29 kPa) (±15.8 mm Hg (2.11 kPa))), PEA (32.8 mm Hg (4.37 kPa) (±17.1 mm Hg (2.30 kPa))), asystole (32.4 mm Hg (4.32 kPa) (±20.6 mm Hg (2.75 kPa))) or ROSC (32.5 mm Hg (4.33 kPa) (±15.3 mm Hg (2.04 kPa))), analysis of variance p=0.99. In the multivariate analysis using the initial predefibrillation $ETCO_2$, there was no association with VF termination on the subsequent shock (adjusted OR ($_{adj}$OR) 0.99, 95% CI 0.97 to 1.02, p=0.57) or ROSC ($_{adj}$OR 1.00, 95% CI 0.97 to 1.03, p=0.94) when evaluated as a continuous or categorical variable.

Conclusion Predefibrillation $ETCO_2$ measurement is not associated with VF termination or ROSC when basic and advanced airways are included in the analysis. The role of predefibrillation $ETCO_2$ requires careful consideration of the type of airway used during resuscitation.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Recent literature suggests that predefibrillation end-tidal CO2 ($ETCO_2$) measured using advanced airways may predict defibrillation success in ventricular fibrillation cardiac arrest. Although bag–valve–masks (BVMs) are frequently used in cardiac arrest, $ETCO_2$ measurements from BVMs have not been included in previous studies.

WHAT THIS STUDY ADDS

⇒ This study incorporates both basic airway and advanced airway management when evaluating the association between predefibrillation $ETCO_2$ and shock success. There was no difference in subsequent rhythms according to preshock $ETCO_2$. We found no statistically significant relationship between the first documented predefibrillation $ETCO_2$ reading and defibrillation success.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ $ETCO_2$-guided defibrillation should not be used in situations without advanced airways, and clinicians should interpret $ETCO_2$ obtained from BVMs cautiously.

INTRODUCTION

Ventricular fibrillation (VF) is the presenting cardiac rhythm in over 20% of all out-of-hospital cardiac arrests (OHCAs) and has up to a 12-fold increased likelihood of survival compared with other presenting rhythms.[1] There is conflicting evidence regarding the optimal timing of VF defibrillation delivery.[2 3] Some animal and human trials have shown evidence for delayed defibrillation in favour of an extended period of cardiopulmonary resuscitation (CPR) to improve myocardial perfusion before defibrillation.[4–7] Other trials, however, have shown no such benefit when compared with early defibrillation.[8 9] The 2020 American Heart Association guidelines recommend immediate initial defibrillation over extended CPR and delayed defibrillation.[10]

Predefibrillation end-tidal CO_2 ($ETCO_2$) has emerged as a potential tool to guide the optimal timing

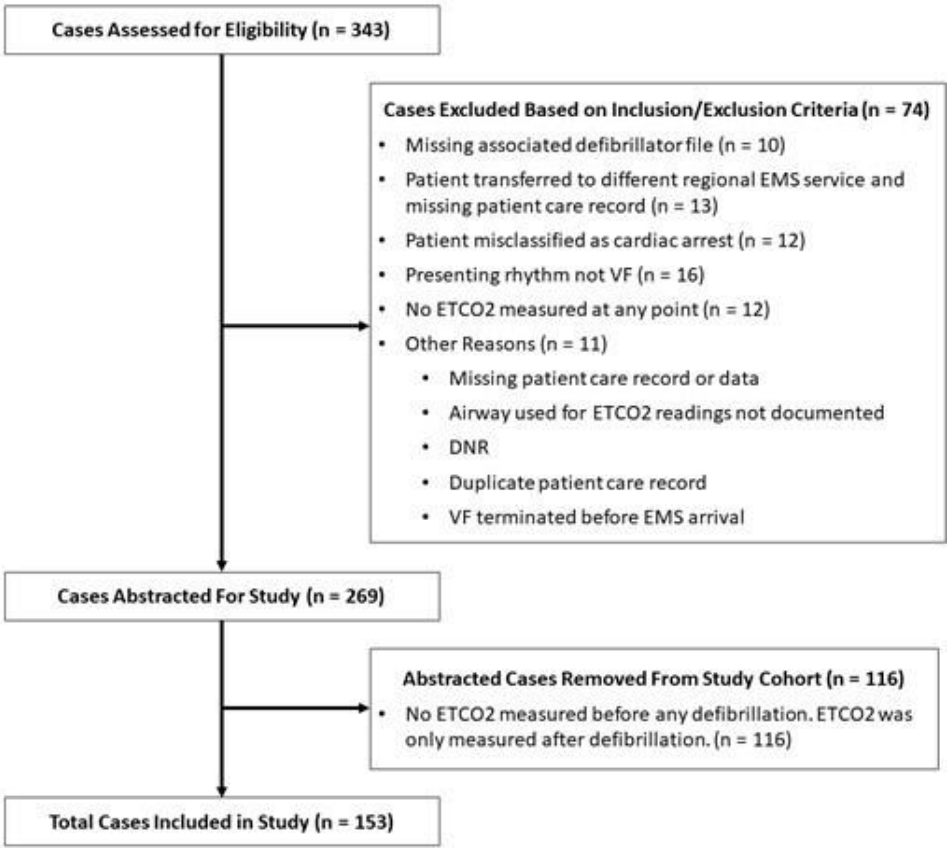

Figure 1 Flow diagram of included patients. DNR, do not resuscitate; $ETCO_2$, end-tidal CO_2.

of defibrillation.[11–14] Several groups have studied the association between the $ETCO_2$ value prior to defibrillation and the likelihood of termination of VF/pulseless ventricular tachycardia (pVT) and return of spontaneous circulation (ROSC) after defibrillation. One study found that in patients with $ETCO_2$ of <7 mm Hg (0.93 kPa), no shocks were successful at terminating VF, and in patients with $ETCO_2$ of >45 mm Hg (6.00 kPa), all shocks were successful.[11] All four studies concluded that higher predefibrillation $ETCO_2$ was associated with a significantly higher likelihood of achieving ROSC, with two of the studies showing a higher likelihood of achieving ROSC only after the first defibrillation.[11–14]

Many factors have been shown to augment $ETCO_2$ levels during cardiac arrest including chest compression quality metrics, such as depth and rate.[15 16] Murphy *et al* showed that a 10 mm increase in compression depth and 10 compression/min increase in rate increased $ETCO_2$ by 4.0% and 1.7%, respectively.[15] There are also distinct $ETCO_2$ trajectories over the course of resuscitation in patients who achieve ROSC compared with those who do not.[17] Porcine models have demonstrated that $ETCO_2$ may represent several haemodynamic factors during cardiac arrest, including myocardial perfusion pressure, which may be critical to early VF termination.[18 19] Therefore, given that $ETCO_2$ is known to be clinically modifiable in resuscitation, it represents a promising target for optimisation prior to defibrillation to increase the likelihood of VF termination and ROSC.

Although previous studies on this topic have measured predefibrillation $ETCO_2$ through an endotracheal tube (ETT) or supraglottic airway (SGA), none have included a bag–valve–mask (BVM). Given that current advanced cardiac life support (ACLS) guidelines recommend immediate cardiac rhythm analysis and defibrillation, the time to initial defibrillation may not be sufficient for ETT or SGA placement. The utility of predefibrillation $ETCO_2$ as a marker for VF defibrillation success may be limited if this relationship is not evaluated for $ETCO_2$ measurements through a BVM.

The primary objective of this study was to assess the relationship between the first documented predefibrillation $ETCO_2$ values (from BVM or advanced airways) and defibrillation outcomes. The secondary objective was to determine whether predefibrillation $ETCO_2$ measurements differ when measured through BVM versus advanced airways (ie, SGA or ETT).

METHODS

Study setting and data abstraction

This is a retrospective multicentre study with data abstracted from two regional paramedic services in Southern Ontario, Canada, Peel Regional Paramedic Service and Halton Region Paramedic Service. These regions have a mix of urban and rural areas with a combined population of two million. Peel Regional Paramedic Service and Halton Region Paramedic Service responds annually to approximately 120 000 and 50 000 calls, respectively.

We abstracted prehospital electronic patient care records (EPCRs) and associated defibrillator files for all patients who had OHCA with an initial VF cardiac rhythm between 1 January 2018 and 31 December 2019. The following cases were excluded from the study: <18 years of age, do not resuscitate order, traumatic cardiac arrest and absence of recorded $ETCO_2$. Standard demographic and Utstein variables were collected for each case. Sample size was pragmatic, based on the number of cases meeting the inclusion criteria.

Paramedics in these services are required to use quantitative $ETCO_2$ as a primary confirmation method of successful placement of an advanced airway. Measurement of $ETCO_2$, while taught as

Table 1 Utstein variables for all cases based on availability of predefibrillation $ETCO_2$ values

Patient characteristics	Total cases	Predefibrillation $ETCO_2$ measured	Predefibrillation $ETCO_2$ not measured	P value
Total cases	269	153	116	
Age (years), median (IQR)	63 (53–74)	64 (53–73)	63 (54–75)	0.88
Male, n (%)	211 (78.4)	121 (79.1)	90 (77.5)	0.88
ROSC at ED arrival, n (%)	129 (48.0)	61 (42.1) Missing=8	68 (64.2) Missing=10	< 0.01
Treatment characteristics				
Advanced airway used, n (%)Missing=2	187 (70.0)	111 (73.0)	75 (65.2)	0.17
ETT, n (% of advanced airways)	143 (76.5)	86 (77.5)	57 (76.0)	
SGA, n (% of advanced airways)	44 (23.5)	25 (22.5)	18 (24.0)	0.81
Epinephrine given, n (%)	223 (82.9)	139 (90.8)	84 (72.4)	< 0.01
Total amount of epinephrine (mg), median (IQR)	4.0 (2.0–5.0)	4.0 (3.0–6.0)	3.0 (2.0–4.0)	< 0.01
Amiodarone given, n (%)	136 (50.6)	103 (67.3)	33 (28.4)	< 0.01
Total amount of amiodarone (mg), median (IQR)	300 (300–450)	450 (300–450)	300 (300–450)	0.02
Sodium bicarbonate given, n (%)	30 (11.2)	25 (16.3)	5 (4.3)	< 0.01
Total amount of sodium bicarbonate (mEq), median (IQR)	50 (50–50)	50 (50–50)	50 (50–50)	0.13
Calcium gluconate given, n (%)	18 (6.7)	12 (7.8)	6 (5.2)	0.53
Total amount of calcium gluconate (mg), median (IQR)	1.0 (1.0–1.0)	1.0 (1.0–1.0)	1.0 (1.0–1.0)	0.35
Median time to EMS arrival (m:s) (IQR)	7:00 (5:00–9:00)	7:00 (6:00–9:00)	7:00 (5:25–9:00)	0.91
Median time to first $ETCO_2$ analysis from scene arrival (m:s) (IQR)	3:42 (2:41–5:00)	3:49 (2:46–5:07)	3:29 (2:35–5:00)	0.68
Median shocks per patient (IQR)	3.0 (2.0–4.0)	4.0 (3.0–6.0)	2.0 (1.0–3.0)	< 0.01
Total shocks (all cases)	904			
CPR quality metrics				
Chest compression rate (per min), median (IQR)	109.6 (106.1–114.8)	109.7 (106.1–114.2)	109.0 (106.1–115.6)	0.77
Chest compression depth (cm), median (IQR)	5.8 (5.1–6.4)	5.8 (5.3–6.4)	5.8 (5.1–6.1)	0.09
Chest compression fraction, median (IQR)	83.2 (77.6–86.9)	84.6 (78.5–86.9)	82.0 (76.5–6.6)	0.32
Preshock pause (s), median (IQR)	1.0 (1.0–3.0)	1.0 (1.0–3.3)	1.0 (1.0–3.0)	0.96
Postshock pause (s), median (IQR)	3.0 (2.0–4.0)	3.0 (2.0–4.0)	3.0 (2.0–4.0)	0.48

CPR, cardiopulmonary resuscitation; ED, emergency department; EMS, emergency medical services; $ETCO_2$, end-tidal CO_2; ETT, endotracheal tube; ROSC, return of spontaneous circulation; SGA, supraglottic airway.

good practice, is ultimately the discretion of the treating paramedics when using a BVM.

Defining predefibrillation $ETCO_2$ and outcomes

All $ETCO_2$ readings were recorded with the use of mainstream technology. Predefibrillation $ETCO_2$ readings were measured automatically by the defibrillator software (Zoll X series defibrillator; Zoll Medical, Chelmsford, Massachusetts, USA) by calculating the average reading over the preceding 30 s. We abstracted the $ETCO_2$ reading immediately preceding each defibrillation along with the type of airway used for the measurement. All cardiac rhythms and ROSC (defined as the presence of an organised rhythm on the defibrillator file accompanied by paramedic documentation of palpable pulse or blood pressure on the EPCR) were determined based on the attending paramedic's assessment and documentation in the patient care record. The outcome of each defibrillation attempt was defined using the paramedic's documented result (VF, pulseless electrical activity (PEA), asystole or ROSC) on the next pulse check, after shock delivery and 2 min of CPR according to current ACLS guidelines. Termination of VF was defined as conversion to any cardiac rhythm other than VF on the subsequent pulse check. A maximum of 10 shocks were recorded for each case. CPR quality metrics were measured using the impedance channel measures contained within the Zoll X Series defibrillators. Preshock and postshock pause data were abstracted from the defibrillator files by evaluating compression timing in relation to defibrillation.

Table 2 Preshock $ETCO_2$ readings based on subsequent shock results and airway used during measurement for cases included in the regression analyses.

Subsequent shock result	Preshock $ETCO_2$ reading	
Persistent VF (n=98)	32.0 mm Hg (kPa) (±16.6 mm Hg (kPa))	$_{adj}$ANOVA p=0.87
PEA (n=8)	24.5 mm Hg (kPa) (±17.0 mm Hg (kPa))	
Asystole (n=27)	32.0 mm Hg (kPa) (±13.6 mm Hg (kPa))	
ROSC (n=20)	27.5 mm Hg (kPa) (±12.6 mm Hg (kPa))	
Airway used	**Preshock $ETCO_2$ reading**	
Bag–valve–mask (n=134)	30.5 mm Hg (4.07 kPa) (±14.4 mm Hg (1.92 kPa))	$_{adj}$ANOVA p<0.01
Advance airway (n=19)	42.1 mm Hg (5.61 kPa) (±22.5 mm Hg (3.00 kPa))	

Analysis of variance adjusted for shock number.
$ETCO_2$, end-tidal CO_2; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; VF, ventricular fibrillation.

Data analysis

We used descriptive statistics to examine the study population and to make basic group-level univariate comparisons. Bivariate analyses were performed using Student's t-test, Welch t-test or analysis of variance (ANOVA) for continuous variables and χ^2 test for categorical variables. Predefibrillation $ETCO_2$ was compared based on defibrillation outcomes (ie, PEA, asystole, persistent VF or ROSC) in two ways using ANOVA: (1) including all 401 shocks and (2) including the first available shock with a preceding $ETCO_2$ reading for each case. Cases excluded from the study due to missing predefibrillation $ETCO_2$ measurements were compared with study cases based on Utstein variables.

The relationship between predefibrillation $ETCO_2$ and VF termination or ROSC was evaluated using multivariable logistic regression to examine the association between the first paramedic predefibrillation $ETCO_2$ reading for each case and the subsequent defibrillation outcome (ie, firefighter and public access defibrillation was not evaluated). Logistic regression analyses were performed incorporating predefibrillation $ETCO_2$ as a continuous variable as our primary analysis and divided into equally distributed tertials as a secondary analysis. $ETCO_2$ was assessed as a continuous variable as this provides the most informative analysis of the relationship between $ETCO_2$ and our outcomes of interest. Non-linearity of the relationship between $ETCO_2$ and outcomes was assessed

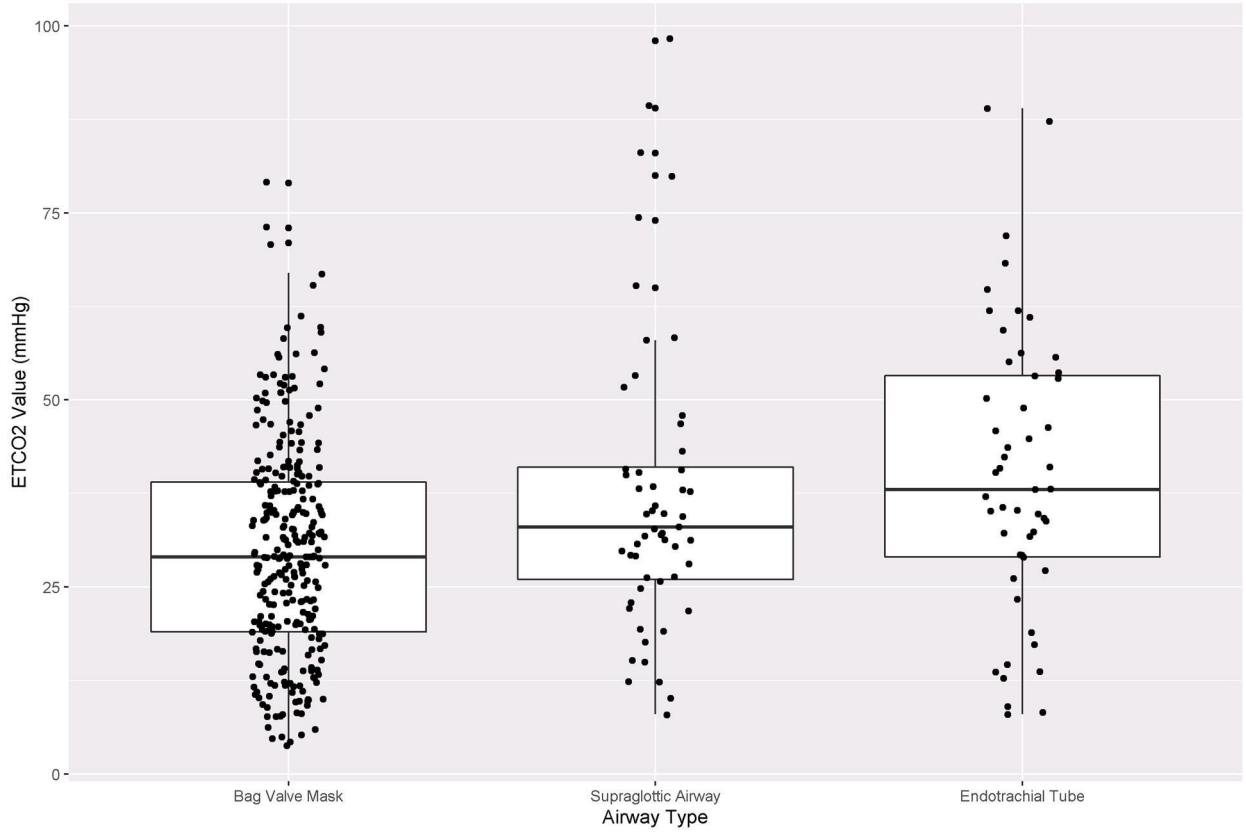

Figure 2 Predefibrillation $ETCO_2$ measurements according to airway type used for measurement. $ETCO_2$, end-tidal CO_2.

by examining $ETCO_2$ as a second-order variable. We included a predefined secondary analysis categorising $ETCO_2$ into equally distributed tertials according to convention from previously published studies. Only cases with complete data for all covariates were included in the multivariable regression analysis. Due to sample size constraints, we did not account for repeat measures within the same patient, and only the first measured predefibrillation $ETCO_2$ for each case was used in the multivariate regression. Regression models were developed starting with a set of a priori determined covariates and then proceeding with a backward stepwise regression approach (online supplemental appendix A). The type of airway used during $ETCO_2$ measurement was forced into all models as a covariate and was assessed for effect modification as an interaction term. Minimisation of model Akaike Information Criterion (AIC) was used to determine covariate elimination.

Patient and public involvement

Patients and the public were not directly involved in the design, conduct, reporting or dissemination plans of this study.

RESULTS

Of the 343 cases identified for review, 269 cases remained after exclusion criteria were applied. Of the 269 cases abstracted, 116 cases were removed for only measuring $ETCO_2$ after all shocks were administered. The final case count was 153 (figure 1). The median age of the cohort was 63 (IQR 53–74) years and 78.9% of cases were male (table 1). ROSC on ED arrival was achieved in 48% of the cases. The total number of shocks recorded was 904 with a median of 3.0 (IQR 2.0–4.0) shocks per patient.

Table 1 shows the comparison of Utstein variables between cases with predefibrillation $ETCO_2$ measurements (n=153) and the cases excluded for not having any predefibrillation $ETCO_2$ measurements (n=116). Cases with no predefibrillation $ETCO_2$ were significantly more likely to have ROSC at ED arrival (68% vs 61%, p<0.01) than cases with a predefibrillation $ETCO_2$ measurement. They were also less likely to have epinephrine (72.4% vs 90.9%, p<0.01), amiodarone (28.4% vs 67.9%, p<0.01) or sodium bicarbonate (3.4% vs 16.9%, p<0.01) administered and had fewer median shocks per case (2.0 vs 4.0, p<0.01).

Predefibrillation $ETCO_2$ measurements were recorded for 44.4% (401/904) of all shocks. Predefibrillation $ETCO_2$ was measured more frequently through a BVM (73.3%, 294/401) than through either an SGA (13.7%, 55/401) or ETT (13.0%, 52/401). Of all predefibrillation $ETCO_2$ measurements recorded, 76.1% (305/401) occurred after the second shock (online supplemental appendix C). Advanced airways were inserted before hospital arrival in 187/269 (69.5%) patients.

When considering only the first predefibrillation $ETCO_2$ reading for each patient, values were significantly lower when measured through a BVM than an advanced airway (mean $ETCO_{2BVM}$ –30.5 mm Hg (4.07 kPa) (±14.4 mm Hg (1.92 kPa)) (n=134) vs mean $ETCO_{2SGA/ETT}$ –42.1 mm Hg (5.61 kPa) (±22.5 mm Hg (3.00 kPa)) (n=19), $_{adj}$ANOVA p<0.01 adjusted for shock number; between-group difference $ETCO_{2SGA/ETT–BVM}$ –11.6 mm Hg (1.55 kPa) (±7.54 mm Hg (1.01 kPa))) (table 2). Advanced airway use and $ETCO_2$ measurement were more likely to occur after the second shock (online supplemental appendix C). Of all $ETCO_2$ measurements recorded with an advanced airway, 86.9% (93/107) occurred after the second shock (ie, before the third shock).

Including all predefibrillation measurements, results showed that mean $ETCO_2$ by airway type were BVM –30.1 mm Hg (4.01 kPa) (±14.3 mm Hg (1.91 kPa)), SGA –37.0 mm Hg (4.93 kPa) (±19.6 mm Hg (2.61 kPa)), ETT –40.3 mm Hg (5.37 kPa) (±19.0 mm Hg (2.53 kPa)) (figure 2). There was no difference

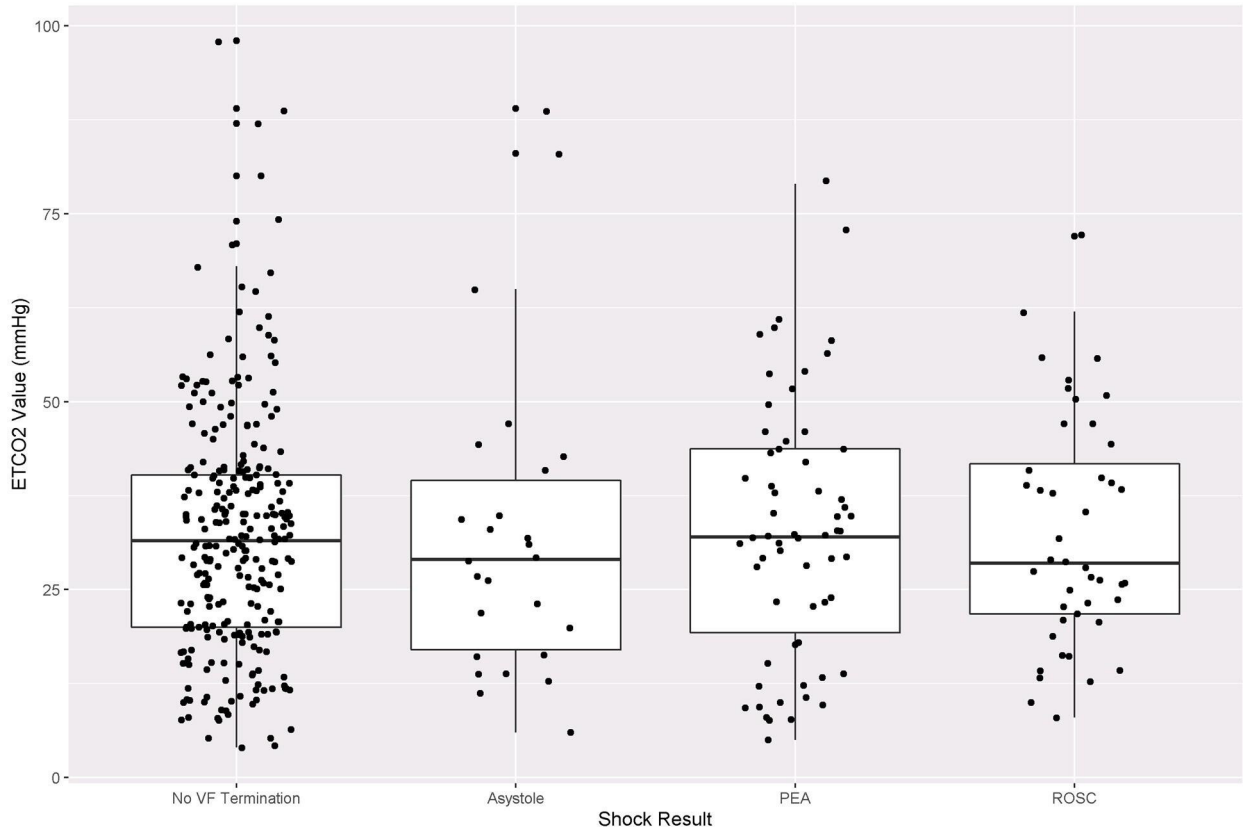

Figure 3 Predefibrillation $ETCO_2$ measurements according to defibrillation result. $ETCO_2$ measurements recorded through all airway types are included. $ETCO_2$, end-tidal CO_2.

in mean $ETCO_2$ for shocks that resulted in VF (mean 32.2 mm Hg (4.29 kPa) (±15.8 mm Hg (2.11 kPa)) (n=268)), PEA (mean 32.8 mm Hg (4.37 kPa) (±17.1 mm Hg (2.28 kPa)) (n=27)), asystole (mean 32.4 mm Hg (4.32 kPa) (±20.6 mm Hg (2.75 kPa)) (n=62)) or ROSC (mean 32.5 mm Hg (4.33 kPa) (±15.3 mm Hg (2.04 kPa)) (n=44)), ANOVA p=0.99 (figure 3).

Of the 153 cases included in the regression analyses, 134 cases had predefibrillation $ETCO_2$ measured using a BVM, and 19 were measured using an advanced airway. Sensitivity analyses found these two groups were comparable except that cases with $ETCO_2$ measured through BVM had significantly lower time to initial $ETCO_2$ measurement (7:42 vs 12:08, p<0.01) (online supplemental appendix B). Predefibrillation $ETCO_2$ assessed as a continuous variable was not associated with VF termination ($_{adj}$OR 0.99, 95% CI 0.97 to 1.02, p=0.57) or ROSC ($_{adj}$OR 1.00, 95% CI 0.97 to 1.03, p=0.94) (table 3). Three equally distributed tertials were created to evaluate $ETCO_2$ as a categorical variable (T_1: <26 mm Hg (3.47 kPA), T_2: 26–36 mm Hg (3.47–4.80 kPA), T_3: >36 mm Hg (4.80 kPa)). When predefibrillation $ETCO_2$ was assessed as a categorical variable, we again found no association with VF termination ($T_{2\ adj}$OR: 1.33, 95% CI 0.55 to 3.20, p=0.53; $T_{3\ adj}$OR 1.13, 95% CI 0.46 to 2.76, p=0.80–T_1 reference; $ETCO_2$ group significance p=0.82) or ROSC ($T_{2\ adj}$OR 1.05, 95% CI 0.33 to 3.37, p=0.94; $T_{3\ adj}$OR 1.07, 95% CI 0.31 to 3.66, p=0.91–T_1 reference; $ETCO_2$ group significance p=0.99) (table 3). Airway type was not a significant effect modifier in any models (ANOVA, $ETCO_2$ evaluated as a continuous variable: VF termination model p=0.52, ROSC model p=0.81; $ETCO_2$ evaluated as a categorical variable: VF termination model p=0.98, ROSC model p=0.39). Amiodarone use was the only significant covariate identified when predefibrillation $ETCO_2$ was assessed as a continuous variable ($_{adj}$OR 0.34, 95% CI 0.15 to 0.77, p=0.01).

DISCUSSION

We did not find an association between the first documented predefibrillation $ETCO_2$ values and VF termination or ROSC measured as either a continuous or categorical variable. We also did not find a difference in predefibrillation $ETCO_2$ and shocks resulting in PEA, asystole, persistent VF, or ROSC. This was consistent when analyses included all available $ETCO_2$ readings, as well as when only the first available measurement was used. This is in contrast to previous studies using only advanced airways which have shown that predefibrillation $ETCO_2$ for all shocks can predict defibrillation success resulting in VF termination or ROSC.[11–14] Our ability to measure predefibrillation $ETCO_2$ readings through BVM and SGAs, in addition to ETT, is an important distinguishing factor and strength of our study that may explain the difference in results.

The body of literature examining the use of $ETCO_2$ during cardiac arrest has typically focused on advanced airways.[20] Early defibrillation success, however, is the most important in determining a good patient outcome, and including early defibrillation attempts is essential for determining the utility of $ETCO_2$ in predicting defibrillation success in clinical practice.[10 21] Failure to include BVM ventilations in previous analyses may limit the clinical applicability of these studies. Exclusive measurement of $ETCO_2$ through advanced airways could also suggest that they were inserted before the first defibrillation. Delays in defibrillation due to advanced airway placement before the first defibrillation may have resulted in higher $ETCO_2$ values which may skew the results of this analysis but ultimately are known to result in worse neurological outcomes.[22] The distinct differences

Table 3 Unadjusted univariate analyses and adjusted logistic regression evaluating predefibrillation $ETCO_2$ as a continuous variable (top panel) and as categorical variables (tertials) (bottom panel)

Variable	OR_{unadj} (95% CI)	P value	OR_{adj} (95% CI)	P value
Association between $ETCO_2$ (continuous variable) and VF termination				
$ETCO_2$ value (per 5 mm Hg (0.67 kPa))	0.99 (0.90 to 1.10)	0.92	0.97 (0.87 to 1.08)	0.58
Advanced Airway (SGA or ETT) (reference: BVM)	1.24 (0.46 to 3.30)	0.67	0.78 (0.27 to 2.21)	0.64
Amiodarone used	0.49 (0.24 to 0.99)*	0.05	0.34 (0.15 to 0.77)*	0.01
Epinephrine used	1.57 (0.47 to 5.29)	0.46	3.50 (0.89 to 13.82)	0.07
Association between $ETCO_2$ (continuous variable) and ROSC				
$ETCO_2$ value (per 5 mm Hg (0.67 kPa))	1.00 (1.00 to 1.00)	0.38	0.99 (0.84 to 1.17)	0.91
Advanced airway (SGA or ETT) (reference: BVM)	0.71 (0.15 to 3.35)	0.67	1.37 (0.26 to 7.37)	0.71
EMS unwitnessed arrest (reference: EMS witnessed arrest)	0.30 (0.05 to 1.73)	0.18	0.19 (0.03 to 1.32)	0.09
Time to $ETCO_2$ first measurement (/min)	1.00 (1.00 to 1.00)	0.29	1.00 (1.00 to 1.00)	0.10
Shock number	1.11 (0.75 to 1.64)	0.61	1.53 (0.87 to 2.71)	0.14
Variable	**OR_{unadj} (95% CI)**	**P value**	**OR_{adj} (95% CI)**	**P value**
Association between $ETCO_2$ tertials and VF termination				
$ETCO_2$ low (≤25 mm Hg (3.33 kPa))	Ref			
$ETCO_2$ mid (25 mm Hg (3.33 kPa) <$ETCO_2$ <37 mm Hg (4.93 kPa))	1.14 (0.50 to 2.60)	0.64	1.33 (0.55 to 3.20)	0.53
$ETCO_2$ high (≥37 mm Hg (4.93 kPa))	1.09 (0.48 to 2.51)	0.83	1.13 (0.46 to 2.76)	0.80
$ETCO_2$ level group significance			X^2=0.40 (df=2, p=0.82)	
Advanced airway (SGA or ETT) (reference: BVM)	As above		1.07 (0.37 to 3.07)	0.91
Sex (reference: male)	1.73 (0.76 to 3.93)		1.93 (0.81 to 4.62)	0.14
Amiodarone used	As above		0.33 (0.14 to 0.74)*	0.01
Epinephrine used	As above		3.04 (0.76 to 12.17)	0.12
Association between $ETCO_2$ tertials and ROSC				
$ETCO_2$ low (≤ 25 mm Hg (3.33 kPa))	Ref			
$ETCO_2$ medium (25 mm Hg (3.33 kPa) <$ETCO_2$ <37 mm Hg (4.93 kPa))	0.96 (0.31 to 2.96)	0.93	1.05 (0.33 to 3.37)	0.94
$ETCO_2$ high (≥37 mm Hg (4.93 kPa))	0.84 (0.26 to 2.70)	0.77	1.07 (0.31 to 3.66)	0.91
$ETCO_2$ level group significance			X^2=0.01 (df=2, p=0.99)	
Advanced airway (SGA or ETT) (reference: BVM)	As above		1.34 (0.25 to 7.16)	0.73
EMS unwitnessed arrest (reference: EMS witnessed arrest)	As above		0.18 (0.03 to 1.24)	0.08
Time to $ETCO_2$ first measurement (/min)	As above		1.00 (1.00 to 1.00)	0.09
Shock number	As above		1.55 (0.87 to 2.74)	0.14

Analyses restricted to the first shock for each case (see online supplemental appendix A for the full list of covariates* used during model selection)
*Covariates included in the initial regression model (online supplemental appendix A) predefibrillation $ETCO_2$, advanced airway use (with interaction term), number of EMS response vehicles, bystander CPR, bystander witnessed arrest, bystander automated external defibrillator (AED) use, EMS witnessed arrest, age, patient sex, amiodarone use, epinephrine (epinephrine) use, calcium gluconate use, EMS response time, time to initial $ETCO_2$ measurement, shock number and EMS.
.BVM, bag–valve–mask; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; $ETCO_2$, end-tidal CO_2; ETT, endotracheal tube; ROSC, return of spontaneous circulation; SGA, supraglottic airway; VF, ventricular fibrillation.

in $ETCO_2$ measurements when using advanced airways compared with BVM has important implications on the utility of $ETCO_2$ in VF cardiac arrest. By including these measurements, we also included early shocks, which may not have been included in previous studies. Because of the frequent use of BVM early in resuscitation, our study offers an important and realistic representation of the $ETCO_2$ and shock success relationship in current clinical practice.

$ETCO_2$ measurements from BVM were significantly lower across almost all shocks when compared with measurements recorded through an advanced airway (figure 3). This trend was also seen consistently as resuscitation progressed and demonstrated an overall early increase (until approximately the third shock) and subsequent decline. We considered two possible reasons for this observation. First, poor BVM mask seal may lead to air leakage and falsely decreased $ETCO_2$ readings. A simulated study of paramedics found significantly lower $ETCO_2$ readings from BVM compared with various supraglottic devices and air leakage due to a poor BVM mask seal, suggesting inaccurate readings.[23] Although the effectiveness of different prehospital airway devices continue to be debated,[24] advanced airways likely provide more consistent and accurate readings of $ETCO_2$. Second, lower BVM $ETCO_2$ measurements may be attributed to BVM use earlier during resuscitation. Einav *et al* measured the $ETCO_2$ tracing during the resuscitation of patients in VF/pVT and found that patients with ROSC were more likely to have an increasing $ETCO_2$over time.[17] Early $ETCO_2$ measurements through a BVM may preferentially collect lower values compared with advanced airways. Use of ACLS medications and prolonged CPR may also increase $ETCO_2$ as resuscitation proceeds.[25] However, when our regression analyses included airway type as a covariate or interaction term, they were not statistically significant. This may suggest that the relationship between $ETCO_2$ and VF termination or ROSC may be complex, influenced by many factors beyond just the airway type used to measure $ETCO_2$.

In our study, the median time to first $ETCO_2$ measurement was 3.7 min (IQR 2.6–5.0). Of the 269 cases, only 56.9% (153/269) had any predefibrillation $ETCO_2$ measured, mostly due to ROSC or arrival at ED before any $ETCO_2$ was measured. Our comparison of cases with and without predefibrillation $ETCO_2$ measurements found that cases without predefibrillation $ETCO_2$ were likely shorter, with fewer shocks and ACLS medications delivered, and were more likely to have ROSC at ED arrival. We suspect that paramedics focused on high-quality CPR and early defibrillation and that $ETCO_2$ measurement and advanced airway placement were frequently left until after the second shock or later. Current evidence suggests that these are the highest yield interventions for patients in OHCA.[10] If predefibrillation $ETCO_2$ is proposed as a marker for the optimal timing of VF defibrillation,[11–14] a measure of CPR quality and patient prognostication, a more easily accessible and reliable measure is likely required. Only then will we be able to gradually move away from the current algorithmic approach to ACLS management. Given the equivalent outcomes between the

i-gel SGA and intubation,[26] as well as its speed of insertion,[27] the i-gel may be a suitable candidate for $ETCO_2$ measurement.

Another unique feature is that we study this relationship in a population composed exclusively of patients presenting in VF. Given the increasing emphasis of $ETCO_2$ in resuscitation, this study would suggest that advanced airways will play more of a critical role instead of less, as some have recently suggested.[28]

There are some important limitations with our study. This study was not adequately powered to perform repeated measures analyses, which limited our regression analyses to only include the first defibrillation. Future studies should use larger sample sizes to allow for repeated measures. Another limitation is that we were unable to identify the specific timing of ACLS medication administration in relation to the shocks used in the regression analyses. Medications were likely administered after the shock used in our regression because we used the first shock during the resuscitation with a predefibrillation $ETCO_2$ measurement. All medications recorded for use in regression analyses were administered before the study outcomes (ie, VF termination or ROSC). A more thorough analysis into $ETCO_2$ waveform during resuscitation could evaluate the quality of BVM mask seal and its subsequent influence on the relationship between $ETCO_2$ and VF shock success. We also had a significant number of missing values of predefibrillation $ETCO_2$, and these were frequently associated with short transport times with BVM use. While an important limitation, this may also reflect the reality of cardiac arrest management where the focus is on early defibrillation and not ventilation. Lastly, our analyses had low numbers of $ETCO_2$ measurements from advanced airways. Therefore, our analyses predominantly examine the BVM-$ETCO_2$ and shock success relationship, which may be different from previous studies that only used ETT–$ETCO_2$ readings.

CONCLUSION

The initial predefibrillation $ETCO_2$ measurement is not associated with VF termination or ROSC on the subsequent shock when basic and advanced airways are included in analysis. $ETCO_2$ measurements from BVM were significantly lower than advanced airways. The role of predefibrillation $ETCO_2$ requires careful consideration of the type of airway used during resuscitation.

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REFERENCES

1 Holmberg M, Holmberg S, Herlitz J. Incidence, duration and survival of ventricular fibrillation in out-of-hospital cardiac arrest patients in Sweden. *Resuscitation* 2000;44:7–17.
2 Simpson PM, Goodger MS, Bendall JC. Delayed versus immediate defibrillation for out-of-hospital cardiac arrest due to ventricular fibrillation: a systematic review and meta-analysis of randomised controlled trials. *Resuscitation* 2010;81:925–31.
3 Huang Y, He Q, Yang LJ, *et al*. Cardiopulmonary resuscitation (CPR) plus delayed defibrillation versus immediate defibrillation for out-of-hospital cardiac arrest. *Cochrane Database Syst Rev* 2014;2014:CD009803.
4 Niemann JT, Cruz B, Garner D, *et al*. Immediate countershock versus cardiopulmonary resuscitation before countershock in a 5-minute swine model of ventricular fibrillation arrest. *Ann Emerg Med* 2000;36:543–6.
5 Bradley SM, Gabriel EE, Aufderheide TP, *et al*. Survival increases with CPR by emergency medical services before defibrillation of out-of-hospital ventricular fibrillation or ventricular tachycardia: observations from the resuscitation outcomes Consortium. *Resuscitation* 2010;81:155–62.
6 Cobb LA, Fahrenbruch CE, Walsh TR, *et al*. Influence of cardiopulmonary resuscitation prior to defibrillation in patients with out-of-hospital ventricular fibrillation. *JAMA* 1999;281:1182.
7 Wik L, Hansen TB, Fylling F, *et al*. Delaying defibrillation to give basic cardiopulmonary resuscitation to patients with out-of-hospital ventricular fibrillation: a randomized trial. *JAMA* 2003;289:1389.
8 Baker PW, Conway J, Cotton C, *et al*. Defibrillation or cardiopulmonary resuscitation first for patients with out-of-hospital cardiac arrests found by paramedics to be in ventricular fibrillation? a randomised control trial. *Resuscitation* 2008;79:424–31.
9 Stiell IG, Nichol G, Leroux BG, *et al*. Early versus later rhythm analysis in patients with out-of-hospital cardiac arrest. *N Engl J Med* 2011;365:787–97.
10 Panchal AR, Bartos JA, Cabañas JG, *et al*. Part 3: adult basic and advanced life support: 2020 American heart association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2020;142:S366–468.
11 Savastano S, Baldi E, Raimondi M, *et al*. End-Tidal carbon dioxide and defibrillation success in out-of-hospital cardiac arrest. *Resuscitation* 2017;121:71–5.
12 Chicote B, Aramendi E, Irusta U, *et al*. Value of capnography to predict defibrillation success in out-of-hospital cardiac arrest. *Resuscitation* 2019;138:74–81.
13 Hubble MW, Van Vleet L, Taylor S, *et al*. Predictive utility of end-tidal carbon dioxide on defibrillation success in out-of-hospital cardiac arrest. *Prehosp Emerg Care* 2021;25:697–705.
14 Frigerio L, Baldi E, Aramendi E, *et al*. End-tidal carbon dioxide ($ETCO_2$) and ventricular fibrillation amplitude spectral area (AMSA) for shock outcome prediction in out-of-hospital cardiac arrest. Are they two sides of the same coin? *Resuscitation* 2021;160:142–9.
15 Murphy RA, Bobrow BJ, Spaite DW, *et al*. Association between prehospital CPR quality and end-tidal carbon dioxide levels in out-of-hospital cardiac arrest. *Prehosp Emerg Care* 2016;20:369–77.
16 Sheak KR, Wiebe DJ, Leary M, *et al*. Quantitative relationship between end-tidal carbon dioxide and CPR quality during both in-hospital and out-of-hospital cardiac arrest. *Resuscitation* 2015;89:149–54.
17 Einav S, Bromiker R, Weiniger CF, *et al*. Mathematical modeling for prediction of survival from resuscitation based on computerized continuous capnography: proof of concept. *Acad Emerg Med* 2011;18:468–75.
18 Segal N, Metzger AK, Moore JC, *et al*. Correlation of end tidal carbon dioxide, amplitude spectrum area, and coronary perfusion pressure in a porcine model of cardiac arrest. *Physiol Rep* 2017;5:e13401–8.
19 Weisfeldt ML, Becker LB. Resuscitation after cardiac arrest: a 3-phase time-sensitive model. *JAMA* 2002;288:3035.
20 Cereceda-Sánchez FJ, Molina-Mula J. Systematic review of Capnography with mask ventilation during cardiopulmonary resuscitation maneuvers. *J Clin Med* 2019;8:358.
21 Hasegawa M, Abe T, Nagata T, *et al*. The number of prehospital defibrillation shocks and 1-month survival in patients with out-of-hospital cardiac arrest. *Scand J Trauma Resusc Emerg Med* 2015;23:1–12.
22 Lee SGW, Park JH, Ro YS, *et al*. Time to first defibrillation and survival outcomes of out-of-hospital cardiac arrest with refractory ventricular fibrillation. *Am J Emerg Med* 2021;40:96–102.
23 Dörges V, Wenzel V, Knacke P, *et al*. Comparison of different airway management strategies to ventilate apneic, nonpreoxygenated patients. *Crit Care Med* 2003;31:800–4.

24 Wang C-H, Lee A-F, Chang W-T, *et al*. Comparing effectiveness of initial airway interventions for out-of-hospital cardiac arrest: a systematic review and network meta-analysis of clinical controlled trials. *Ann Emerg Med* 2020;75:627–36.
25 Sandroni C, De Santis P, D'Arrigo S. Capnography during cardiac arrest. *Resuscitation* 2018;132:73–7.
26 Benger JR, Lazaroo MJ, Clout M, *et al*. Randomized trial of the i-gel supraglottic airway device versus tracheal intubation during out of hospital cardiac arrest (AIRWAYS-2): patient outcomes at three and six months. *Resuscitation* 2020;157:74–82.
27 Gatward JJ, Thomas MJC, Nolan JP, *et al*. Effect of chest compressions on the time taken to insert airway devices in a manikin. *Br J Anaesth* 2008;100:351–6.
28 Lupton JR, Schmicker RH, Stephens S, *et al*. Outcomes with the use of Bag-Valve-Mask ventilation during out-of-hospital cardiac arrest in the pragmatic airway resuscitation trial. *Acad Emerg Med* 2020;27:366–74.

APPENDIX A – List of Covariates Included in Regression Models

Model Covariate	Description
1. Pre-defibrillation ETCO2 (Continuous)	*Primary covariate. Forced into models.* Measurement of pre-defibrillation ETCO2 in increments of 5mmHg.
2. Pre-defibrillation ETCO2 (Categorical - Tertials)	*Primary covariate. Forced into models.* Measurement of pre-defibrillation ETCO2 split into three equally weighted groups.
3. Advanced Airway Use	*Forced into models as a confounder a priori.* Categorical variable designating either BVM or SGA use to measure pre-defibrillation ETCO2.
4. Advanced Airway Interaction Term	*Interaction term*. Interaction between advanced airway use and pre-defibrillation ETCO2.
5. Number of EMS response vehicles	Numerical variable specifying the number of EMS response vehicles that responded to the call.
6. Bystander CPR	Categorical variable specifying if bystander CPR was performed prior to EMS arrival.
7. Bystander Witnessed Arrest	Categorical variable specifying if the cardiac arrest was witnessed by a bystander.
8. Bystander AED Use	Categorical variable specifying if an AED was used by a bystander prior to EMS arrival.
9. EMS Witnessed Arrest	Categorical variable specifying if the cardiac arrest was witnessed by EMS.
10. Age	Numerical variable of patient age in years.
11. Patient Sex	Categorical variable of patient sex.
12. Amiodarone Administration	Categorical variable specifying if Amiodarone was administered in the cardiac arrest by EMS.
13. Epinephrine Administration	Categorical variable specifying if Epinephrine was administered in the cardiac arrest by EMS.
14. Calcium Gluconate Administration	Categorical variable specifying if Calcium Gluconate was administered in the cardiac arrest by EMS.
15. Response Time to Scene by EMS	Numerical variable of time from call received to EMS arrival at scene.
16. Time to First ETCO2 Measurement	Numerical variable of time from EMS arrival to the scene to the first ETCO2 measurement.
17. Shock Number	Numerical variable specifying the shock number since EMS arrival.
18. EMS Service	Categorical variable specifying the EMS service providing care.

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APPENDIX B – Table Comparing Cases Based on Airway Used to Measure ETCO2

Table A1. Utstein variables for cases included in regression analyses based on airway used to measure pre-defibrillation ETCO2. Chi-square tests and Welch two-sample t-tests were used for tests of significance. Yates' continuity correction and Fischer exact tests were used for samples with small cell sizes.

Patient Characteristics	**Bag-Valve Mask**	**Advanced Airway**	**p-value**
Total Cases	134	19	
Age (years), median (IQR)	64 (54, 74)	65 (54, 72)	0.64
Male, n (%)	109 (81.3)	12 (63.2)	0.13
ROSC at ED arrival, n (%)	53 (41.7) Missing = 7	8 (44.4) Missing = 1	0.98
Treatment Characteristics			
Adrenaline given, n (%)	120 (90.0)	19 (100.0)	0.22
Total amount of Adrenaline (mg), median (IQR)	4.0 (3.0, 6.0)	5.0 (3.0, 6.0)	0.59
Amiodarone given, n (%)	89 (66.4)	14 (73.7)	0.71
Total amount of Amiodarone (mg), median (IQR)	450 (300, 450)	300 (300, 450)	0.28
Sodium Bicarbonate given, n (%)	19 (14.2)	6 (31.6)	0.11
Total amount of Sodium Bicarbonate (meq), median (IQR)	50 (50, 50)	50 (50, 88)	0.28
Calcium Gluconate given, n (%)	11 (8.2)	1 (5.2)	0.09
Total amount of Calcium Gluconate (mg), median (IQR)	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	1.00
Median time to EMS arrival (m:s) (IQR)	7:00 (6:00, 8:55)	8:00 (6:26, 10:00)	0.12
Median time to first ETCO2 analysis from scene arrival (m:s) (IQR)	7:42 (6:03, 10:32)	12:08 (10:01, 21:01)	< 0.01
Median shocks per patient (IQR)	4.0 (3.0, 6.0)	3.0 (3.0, 4.0)	0.39
CPR quality metrics			
Chest compression rate (per minute), median (IQR)	109.7 (106.0, 114.2)	109.7 (107.9, 113.9)	0.56
Chest compression depth (cm), median (IQR)	5.8 (5.3, 6.4)	5.8 (5.3, 6.6)	0.78

Chest compression fraction, median (IQR)	84.4 (78.5, 86.8)	84.9 (74.0, 86.9)	0.74
Pre-shock pause (sec), median (IQR)	1.0 (1.0, 2.5)	1.0 (1.0, 1.5)	0.14
Post-shock pause (sec), median (IQR)	3.0 (2.0, 4.0)	3.0 (2.0, 3.0)	0.92

APPENDIX C – Figure comparing the pre-defibrillation ETCO2 according to shock number, stratified by airway type.

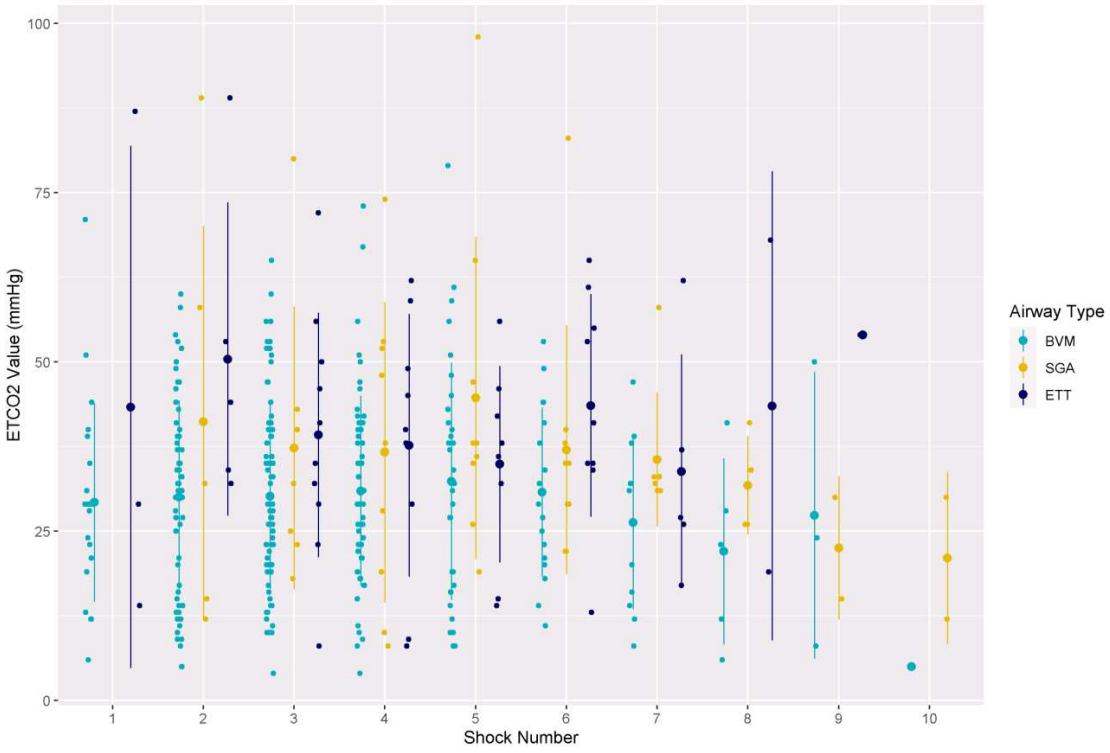

Figure A1. Pre-defibrillation ETCO2 measurements according to shock number. Values are stratified according to airway type used for measurement.