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EMS Treatment Guidelines in Major Traumatic Brain Injury With Positive Pressure Ventilation

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Invited Commentary

Supplemental content

IMPORTANCE The Excellence in Prehospital Injury Care (EPIC) study demonstrated improved survival in patients with severe traumatic brain injury (TBI) following implementation of the prehospital treatment guidelines. The impact of implementing these guidelines in the subgroup of patients who received positive pressure ventilation (PPV) is unknown.

OBJECTIVE To evaluate the association of implementation of prehospital TBI evidence-based guidelines with survival among patients with prehospital PPV.

DESIGN, SETTING, AND PARTICIPANTS The EPIC study was a multisystem, intention-to-treat study using a before/after controlled design. Evidence-based guidelines were implemented by emergency medical service agencies across Arizona. This subanalysis was planned a priori and included participants who received prehospital PPV. Outcomes were compared between the preimplementation and postimplementation cohorts using logistic regression, stratified by predetermined TBI severity categories (moderate, severe, or critical). Data were collected from January 2007 to June 2017, and data were analyzed from January to February 2023.

EXPOSURE Implementation of the evidence-based guidelines for the prehospital care of patient with TBI.

MAIN OUTCOMES AND MEASURES The primary outcome was survival to hospital discharge, and the secondary outcome was survival to admission.

RESULTS Among the 21 852 participants in the main study, 5022 received prehospital PPV (preimplementation, 3531 participants; postimplementation, 1491 participants). Of 5022 included participants, 3720 (74.1%) were male, and the median (IQR) age was 36 (22-54) years. Across all severities combined, survival to admission improved (adjusted odds ratio [aOR], 1.59; 95% CI, 1.28-1.97), while survival to discharge did not (aOR, 0.94; 95% CI, 0.78-1.13). Within the cohort with severe TBI but not in the moderate or critical subgroups, survival to hospital admission increased (aOR, 6.44; 95% CI, 2.39-22.00), as did survival to discharge (aOR, 3.52; 95% CI, 1.96-6.34).

CONCLUSIONS AND RELEVANCE Among patients with severe TBI who received active airway interventions in the field, guideline implementation was independently associated with improved survival to hospital admission and discharge. This was true whether they received basic airway interventions or advanced airways. These findings support the current guideline recommendations for aggressive prevention/correction of hypoxia and hyperventilation in patients with severe TBI, regardless of which airway type is used.

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The burden of traumatic brain injury (TBI) is enormous, affecting more than 2.8 million individuals in the US annually.[1,2] The hope that mitigating secondary brain injury may improve outcomes[3-17] has led to promulgation of evidence-based prehospital TBI treatment guidelines.[3-5,8] The recently reported results of the Excellence in Prehospital Injury Care (EPIC) study[18] and EPIC4Kids study[19] demonstrated that implementation of the emergency medical service (EMS) guidelines was associated with improved survival among patients with severe TBI. This implementation, a statewide initiative in Arizona,[3,4] emphasized prevention and treatment of hypoxia, hypotension, and hyperventilation.[4]

Airway management has been a controversial component of the guidelines, with various investigations reporting either positive[20-22] or negative[23-25] outcomes. Of those studies reporting detrimental outcomes, several factors have been suggested as the cause: hypoxia during airway management,[7,26-29] misplaced or nonfunctional advanced airways,[23,26,30] and hyperventilation after intubation.[4,7,28,31]

The objective of this study was to evaluate the association between guideline implementation and outcomes in patients with major TBI who received positive pressure ventilation (PPV) in the field via bag-valve-mask (BVM), supraglottic airway (SGA), or endotracheal intubation (ETI).

Key Points

Question Did implementation of the prehospital traumatic brain injury (TBI) evidence-based guidelines impact survival among patients with prehospital positive pressure ventilation (PPV)?

Findings In this subanalysis of the EPIC study, guideline implementation was associated with improved survival to hospital admission and discharge among patients with severe TBI who received prehospital PPV.

Meaning Prehospital TBI guideline implementation, focusing on avoiding hypoxia and hyperventilation, was independently associated with improved survival in patients who required PPV prior to arrival to the emergency department.

Methods

Study Design, Setting, and Oversight

The EPIC study evaluated the impact of prehospital TBI guideline implementation using a controlled, before/after, multisystem, intention-to-treat design.[18,32,33] This report is the preplanned subanalysis of the participants who received active airway interventions. The EPIC study methodology has been reported in detail.[18,19,34-40] This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

The University of Arizona Institutional Review Board and Arizona Department of Health Services Human Subjects Review Board approved the study.[34-37] Informed consent was waived, as this study was a public health initiative. While not a randomized trial, the EPIC study is registered at ClinicalTrials.gov.[41]

Data Collection

The Arizona State Trauma Registry contains extensive data on patients taken to level I trauma centers. From this dataset, participants meeting inclusion criteria between January 2007 and June 2015 were linked to EMS data by accessing paper or electronic patient care records from participating agencies. This yielded a comprehensive prehospital/trauma center database (the EPIC study database).[34]

Selection of Participants

For the parent EPIC study, participants with major TBI were defined as those with physical trauma who (1) were transported directly or transferred to a level I trauma center by participating agencies; (2) had a hospital diagnosis (or diagnoses) consistent with TBI (isolated or multisystem); and (3) had at least 1 of the following injury criteria: US Centers for Disease Control and Prevention Barell Injury Diagnosis Matrix Type 1 injury[42-44] or Abbreviated Injury Scale (AIS)-Head score of 3 or more. To prevent selection bias, all participants meeting injury criteria were included whether EMS data were obtained or not.[45,46] This subanalysis included patients who received PPV in the field. Patients were subdivided into 3 cohorts, identified a priori, by *International Classification of Diseases, Ninth Revision*–based regional severity score–head (RSS-H), which is an AIS score equivalent: moderate TBI (RSS-H score of 1 to 2), severe TBI (RSS-H score of 3 to 4), and critical TBI (RSS-H score of 5 to 6). Patients were assigned to airway management subgroups based on the technique used (BVM only, SGA, or ETI). Patients with attempts at both SGA and ETI were classified as ETI, whether the intubation was successful or not (these represented failed intubations, rather than primary use of SGA). Race and ethnicity were determined by responding EMS personnel.

Interventions

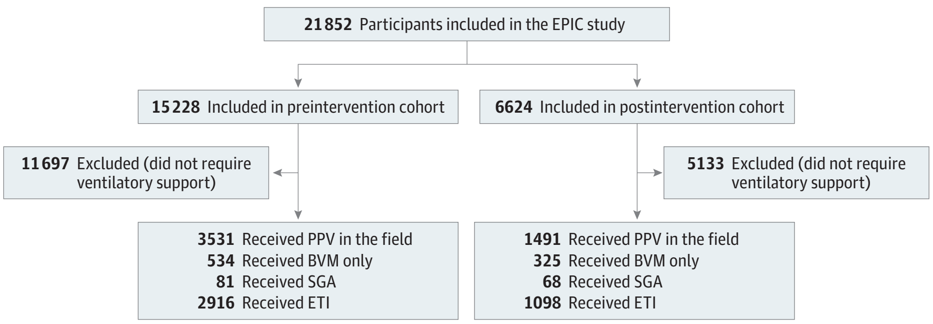
All Arizona EMS agencies were invited to participate. Participation required adoption of the guideline-based treatment protocols and provision of EMS. Training emphasized guideline use in patients with physical trauma, reported or apparent loss of consciousness, and injury sufficient to warrant transport to a hospital.[34]

Training focused on the avoidance and aggressive treatment of hypotension and 3 airway-related goals: (1) prevention or treatment of hypoxia through early, high-flow oxygen administration; (2) airway interventions to optimize oxygenation or ventilation when high-flow oxygen was insufficient; and (3) prevention of hyperventilation or hypocapnia by using ventilation adjuncts (ie, rate timers, flow-controlled ventilation bags, end-tidal carbon dioxide monitoring). The same training was provided to all levels of health care professionals, and a major training emphasis was to reserve ETI/SGA for instances where basic airway interventions were inadequate.

Outcomes

The primary outcome was survival to hospital discharge. The secondary outcome was survival to hospital admission, defined as surviving long enough to be admitted to operative/

Figure 1. Inclusion Tree of Patients in the Preimplementation and Postimplementation Phases



BVM indicates bag-valve-mask ventilation; EPIC, Excellence in Prehospital Injury Care; ETI, endotracheal intubation; PPV, positive pressure ventilation; SGA, supraglottic airway.

inpatient status or, very rarely, discharged from the emergency department.

Statistical Analysis

Descriptive statistics were used to analyze demographic characteristics and other patient characteristics. Continuous variables were summarized by medians and IQRs and were compared between groups (eg, survived vs died, airway subgroups) using the Wilcoxon rank sum test. Categorical variables were summarized by counts and frequencies and compared between groups by χ^2 test or Fisher exact test. Clopper-Pearson confidence intervals were provided for proportion estimates and score confidence intervals for estimates of proportion ratios.

The risk-adjusted associations between implementation and binary outcomes (survival to hospital discharge, survival to hospital admission) were examined by logistic regression. The regression models adjusted for predetermined important risk factors and potential confounders (age, sex, race and ethnicity, payment source, trauma type [blunt or penetrating], RSS-H, Injury Severity Score, multisystem TBI [TBI plus an injury in a region other than the head with a regional severity score of at least 3], prehospital cardiopulmonary resuscitation, and treating trauma center). Effects of age in the regression models were fitted nonparametrically using penalized thin-plate regression splines through the generalized additive model.[47] In all adjusted analyses, standard logistic regression was used when there were at least 200 patients with the outcome and 200 without. Otherwise, the Firth penalized-likelihood logistic regression was used.[48,49] To evaluate for potential clustering effects, random intercepts at the EMS agency level were added to the models in a sensitivity analysis to assess the impact of potential correlation on the outcomes of survival to admission and survival to discharge among patients treated by the same EMS agency.

The software environment R version 3.5.3 (The R Foundation) was used for the analysis, and the R packages mgcv version 1.8-28[47,50] and logistf were used for the regression models. All tests were 2-sided, and significance was set at $P < .05$.

Results

The parent study began for all agencies on January 1, 2007, and phase 1 (the preimplementation study phase) at each individual agency lasted until guideline training began at that agency. Phase 2 (the training/run-in phase) began and ended at different times for each agency (the first agency began training February 22, 2012; the last agency completed training on January 23, 2015). Phase 3 (the postimplementation phase) for each agency started on completion of training and ended for all agencies on June 30, 2015. Air and ground agencies participated, and care was provided by emergency medical technicians, advanced emergency medical technicians, paramedics, and critical care transport paramedics and nurses. Details of EPIC study enrollment were reported elsewhere.[18,19,34]

Study Participants

The parent study included 21 852 patients, of which 5022 received PPV in the field (preimplementation, 3531 patients; postimplementation, 1491 patients) (**Figure 1**). Patient characteristics and outcomes are shown in **Table 1**. Patients in the postimplementation phase were older than those in preimplementation phase (median [IQR] age, 38 [23-58] years vs 35 [21-53] years; $P < .001$). In addition, critical head injury (RSS-H score of 5 to 6) was more common in patients during the postimplementation phase than during the preimplementation phase (972 [65.2%] vs 2020 [57.2%]; $P < .001$). **Table 2** presents the patient characteristics and outcomes by prehospital airway technique (BVM, SGA, or ETI).

Treatment and Treatment-Related Physiological Changes

The goal of guideline implementation was to change patient care. In the overall EPIC study, implementation increased the likelihood of receiving guideline-based treatment.[18,19] In the current substudy, among patients who received active airway interventions, there was also an increase in provision of guideline care after implementation. For example, despite greater brain injury severity during the postimplementation phase (Table 1), the proportion of patients with BVM-only ventilation was much higher during the postimplementation phase (325 of 1491 [21.8%]; 95% CI, 19.7-24.0) than the preimplementation phase (534 of 3531 [15.1%]; 95% CI, 14.0-16.3; relative increase, 44.1%; 95% CI, 27.3-63.0; $P < .001$). Furthermore, ETI was less likely during the postimplementation phase (1098 of 1491 [73.6%]; 95% CI, 71.3-75.9) than the preimplementation phase (2916 of 3531 [82.6%]; 95% CI, 81.3-83.8; relative reduction, 10.8%; 95% CI, 7.8-13.9; $P < .001$).

Table 1. Patient Characteristics and Outcomes by Study Phase

Characteristic	No. (%)			P value[a]
	All patients (N = 5022)	Preimplementation phase (n = 3531)	Postimplementation phase (n = 1491)	
Age, median (IQR), y	36 (22-54)	35 (21-53)	38 (23-58)	<.001
Sex				
Female	1301 (25.9)	911 (25.8)	390 (26.2)	.82
Male	3720 (74.1)	2619 (74.2)	1101 (73.8)	
Unknown	1 (<0.1)	1 (<0.1)	0	
Race[b]				
American Indian or Alaska Native	358 (7.1)	251 (7.1)	107 (7.2)	.31
Asian	33 (0.7)	25 (0.7)	8 (0.5)	
Black	213 (4.2)	137 (3.9)	76 (5.1)	
Other race[c]	763 (15.2)	543 (15.4)	220 (14.8)	
White	3516 (70)	2494 (70.6)	1022 (68.5)	
Unknown	139 (2.8)	81 (2.3)	58 (3.9)	
Ethnicity[b]				
Hispanic	1241 (24.7)	898 (25.4)	343 (23)	.03
Non-Hispanic	3549 (70.7)	2447 (69.3)	1102 (73.9)	
Unknown	232 (4.6)	186 (5.3)	46 (3.1)	
Payer				
Private	1487 (29.6)	1022 (28.9)	465 (31.2)	<.001
AHCCCS/Medicaid	1458 (29)	1079 (30.6)	379 (25.4)	
Medicare	625 (12.4)	423 (12)	202 (13.5)	
Self-pay	1014 (20.2)	662 (18.7)	352 (23.6)	
Other	272 (5.4)	193 (5.5)	79 (5.3)	
Unknown	166 (3.3)	152 (4.3)	14 (0.9)	
Trauma type				
Blunt	4274 (85.1)	3008 (85.2)	1266 (84.9)	.92
Penetrating	746 (14.9)	523 (14.8)	223 (15)	
Unknown	2 (<0.1)	0	2 (0.1)	
Regional severity score-head				
1 to 3	932 (18.6)	712 (20.2)	220 (14.8)	<.001
4	1016 (20.2)	740 (21)	276 (18.5)	
5 to 6	2992 (59.6)	2020 (57.2)	972 (65.2)	
Unknown	82 (1.6)	59 (1.7)	23 (1.5)	
Injury Severity Scale score				
1 to 14	428 (8.5)	307 (8.7)	121 (8.1)	.44
16 to 24	822 (16.4)	590 (16.7)	232 (15.6)	
≥25	3770 (75.1)	2633 (74.6)	1137 (76.3)	
Unknown	2 (<0.1)	1 (<0.1)	1 (0.1)	
Body region				
Isolated TBI	2674 (53.2)	1870 (53)	804 (53.9)	.55
Multisystem TBI	2348 (46.8)	1661 (47)	687 (46.1)	
Transfer				
No	3984 (79.3)	2782 (78.8)	1202 (80.6)	.99
Yes	955 (19)	666 (18.9)	289 (19.4)	
Unknown	83 (1.7)	83 (2.4)	0	
CPR				
No	4178 (83.2)	2970 (84.1)	1208 (81)	.008
Yes	844 (16.8)	561 (15.9)	283 (19)	
Prehospital airway management				
BVM	859 (17.1)	534 (15.1)	325 (21.8)	<.001
SGA	149 (3)	81 (2.3)	68 (4.6)	
ETI	4014 (79.9)	2916 (82.6)	1098 (73.6)	

(continued)

Table 1. Patient Characteristics and Outcomes by Study Phase (continued)

Characteristic	No. (%) All patients (N = 5022)	Preimplementation phase (n = 3531)	Postimplementation phase (n = 1491)	*P* value[a]
Survival to discharge				
No	2521 (50.2)	1707 (48.3)	814 (54.6)	<.001
Yes	2501 (49.8)	1824 (51.7)	677 (45.4)	
Survival to hospital admission				
No	993 (19.8)	707 (20)	286 (19.2)	.52
Yes	4029 (80.2)	2824 (80)	1205 (80.8)	

Abbreviations: AHCCCS, Arizona Health Care Cost Containment System; BVM, bag-valve-mask ventilation; CPR, cardiopulmonary resuscitation; ETI, endotracheal intubation; SGA, supraglottic airway; TBI, traumatic brain injury.

[a] Fisher exact test or χ^2 test, as appropriate, were used for categorical variables and Wilcoxon rank sum test for numerical variables; the unknown category, if present, is excluded from the testing procedure.

[b] Race and ethnicity were determined by responding EMS personnel.

[c] The other race category included Native Hawaiian or Other Pacific Islander, multiracial, not identified, or other race.

Training was also associated with an increase in the likelihood of intubated patients having at least 1 EMS oxygen saturation value of 100% (postimplementation: 482 of 885 [54.5%]; 95% CI, 51.1-57.8; preimplementation: 985 of 2226 [44.2%]; 95% CI, 42.2-46.3; relative increase, 23.1%; 95% CI, 13.9-32.7; *P* < .001). As would be expected from the emphasis on reducing hyperventilation, among intubated patients, the rate of hypocapnia (any EMS end-tidal carbon dioxide less than 35 mmHg) decreased significantly after implementation (postimplementation: 419 of 688 [60.9%]; 95% CI, 57.1-64.6; preimplementation: 947 of 1492 [66.3%]; 95% CI, 63.8-68.7; relative decrease, 8.1%; 95% CI, 1.6-14.5; *P* = .02).

Main Results

The overall (all severity) analysis (**Figure 2**) revealed that survival to hospital admission increased during the postimplementation phase (aOR, 1.59; 95% CI, 1.28-1.97), while there was no evidence of change in survival to hospital discharge (aOR, 0.94; 95% CI, 0.78-1.13). In addition, in the all-severity analysis, there was no evidence of change in survival to discharge in any of the airway subgroups (Figure 2).

As in the parent study, in the severe TBI cohort (RSS-H score of 3 to 4), there was a dramatic improvement in outcomes. Among those with severe TBI and PPV, guideline implementation was associated with a 6-fold improvement in adjusted odds of survival to hospital admission (aOR, 6.44; 95% CI, 2.39-22.00) and more than a 3-fold improvement in survival to hospital discharge (aOR, 3.52; 95% CI, 1.96-6.34). Furthermore, in the severe TBI cohort, the improvement in adjusted odds of survival to discharge was present in each of the airway subgroups (**Figure 3**). Among patients with moderate TBI (RSS-H score of 1 to 2), there was no statistically significant change in survival to hospital admission or discharge. Among patients with critical TBI (RSS-H score of 5 to 6), there was an improvement in survival to hospital admission (aOR, 1.40; 95% CI, 1.12-1.75) and a decreased survival to hospital discharge (aOR, 0.71; 95% CI, 0.58-0.88). The sensitivity analysis to evaluate for potential EMS agency clustering effects demonstrated no significant change in the results.

Discussion

In patients with TBI, prehospital airway management (and especially ETI) has been controversial for decades.[5,8,21,23-25,32,51-53] However, in studies finding an association of prehospital intubation with negative outcomes,[23,24,32,53,54] it is unclear whether the primary issue was the procedure itself or the high proportion of patients receiving inadvertent hyperventilation after ETI.[9,31,51,55-57]

To our knowledge, the EPIC substudy is the first large EMS investigation to assess the impact of implementing the prehospital guidelines in patients with active airway management. Implementation was associated with improved survival among patients with severe TBI with actively managed ventilation, regardless of whether basic or advanced airway techniques were used. The survival improvement was remarkable, with a more than 6-fold increase in the adjusted odds of survival to hospital admission and 3-fold increase in the adjusted odds of survival to discharge.

EPIC training emphasized reserving advanced airways for patients with a markedly depressed level of consciousness and in whom basic interventions were inadequate for oxygenation and protecting the airway.[3-5,8] Given this emphasis, it is not surprising that the proportion of BVM-only ventilation increased and the proportion of ETI decreased in the postintervention phase. Another primary goal of guideline training was the prevention of hypoxia.[18] This likely accounts for the 23% relative increase in the likelihood of intubated patients having at least 1 oxygen saturation value of 100%. These findings provide strong evidence that the goal-directed interventions were followed and that the implementation of these interventions was the most plausible cause of improvements in outcome.

It is notable that the 3-fold improvement in adjusted survival among patients with severe TBI receiving PPV was observed despite a relatively modest improvement in more proximate process outcomes (eg, 23% increase in the number of intubated patients with at least 1 oxygen saturation value of 100%). One possible explanation for this is that the bundling

Table 2. Patient Characteristics and Outcomes by Prehospital Airway Management

Characteristic	Prehospital airway management, No. (%)			P value[a]
	BVM (n = 859)	SGA (n = 149)	ETI (n = 4014)	
Phase				
Preimplementation	534 (62.2)	81 (54.4)	2916 (72.6)	<.001
Postimplementation	325 (37.8)	68 (45.6)	1098 (27.4)	
Age, median (IQR), y	38 (23-54)	37 (23-53)	35 (22-54)	
Sex				
Female	230 (26.8)	38 (25.5)	1033 (25.7)	.80
Male	628 (73.1)	111 (74.5)	2981 (74.3)	
Unknown	1 (0.1)	0	0	
Race[b]				
American Indian or Alaska Native	48 (5.6)	6 (4)	304 (7.6)	<.001
Asian	4 (0.5)	1 (0.7)	28 (0.7)	
Black	46 (5.4)	18 (12.1)	149 (3.7)	
Other race[c]	127 (14.8)	21 (14.1)	615 (15.3)	
White	613 (71.4)	102 (68.5)	2801 (69.8)	
Unknown	21 (2.4)	1 (0.7)	117 (2.9)	
Ethnicity[b]				
Hispanic	228 (26.5)	25 (16.8)	988 (24.6)	.04
Non-Hispanic	606 (70.5)	119 (79.9)	2824 (70.4)	
Unknown	25 (2.9)	5 (3.4)	202 (5)	
Payer				
Private	255 (29.7)	49 (32.9)	1183 (29.5)	.07
AHCCCS/Medicaid	280 (32.6)	40 (26.8)	1138 (28.4)	
Medicare	109 (12.7)	13 (8.7)	503 (12.5)	
Self-pay	156 (18.2)	38 (25.5)	820 (20.4)	
Other	39 (4.5)	4 (2.7)	229 (5.7)	
Unknown	20 (2.3)	5 (3.4)	141 (3.5)	
Trauma type				
Blunt	751 (87.4)	118 (79.2)	3405 (84.8)	.02
Penetrating	108 (12.6)	31 (20.8)	607 (15.1)	
Unknown	0	0	2 (<0.1)	
Regional severity score-head				
1 to 3	186 (21.7)	12 (8.1)	734 (18.3)	<.001
4	183 (21.3)	23 (15.4)	810 (20.2)	
5 to 6	479 (55.8)	111 (74.5)	2402 (59.8)	
Unknown	11 (1.3)	3 (2)	68 (1.7)	
Injury Severity Scale score				
1 to 14	80 (9.3)	6 (4)	342 (8.5)	<.001
16 to 24	163 (19)	12 (8.1)	647 (16.1)	
≥25	615 (71.6)	131 (87.9)	3024 (75.3)	
Unknown	1 (0.1)	0	1 (<0.1)	
Body region				
Isolated TBI	453 (52.7)	60 (40.3)	2161 (53.8)	.005
Multisystem TBI	406 (47.3)	89 (59.7)	1853 (46.2)	
Transfer				
No	816 (95)	148 (99.3)	3020 (75.2)	<.001
Yes	30 (3.5)	1 (0.7)	924 (23)	
Unknown	13 (1.5)	0	70 (1.7)	
CPR				
No	794 (92.4)	106 (71.1)	3278 (81.7)	<.001
Yes	65 (7.6)	43 (28.9)	736 (18.3)	

(continued)

Table 2. Patient Characteristics and Outcomes by Prehospital Airway Management (continued)

Characteristic	Prehospital airway management, No. (%) BVM (n = 859)	SGA (n = 149)	ETI (n = 4014)	*P* value[a]
Survival to discharge				
No	357 (41.6)	99 (66.4)	2065 (51.4)	<.001
Yes	502 (58.4)	50 (33.6)	1949 (48.6)	
Survival to hospital admission				
No	99 (11.5)	47 (31.5)	847 (21.1)	<.001
Yes	760 (88.5)	102 (68.5)	3167 (78.9)	

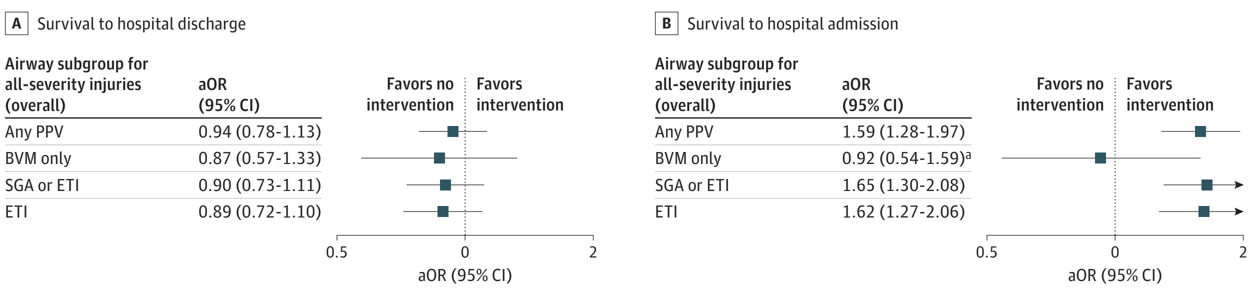
Abbreviations: AHCCCS, Arizona Health Care Cost Containment System; BVM, bag-valve-mask ventilation; CPR, cardiopulmonary resuscitation; ETI, endotracheal intubation; SGA, supraglottic airway; TBI, traumatic brain injury.

[a] Fisher exact test or χ^2 test, as appropriate, were used for categorical variables and Wilcoxon rank sum test for numerical variables; the unknown category, if present, is excluded from the testing procedure.

[b] Race and ethnicity were determined by responding EMS personnel.

[c] The other race category included Native Hawaiian or Other Pacific Islander, multiracial, not identified, or other race.

Figure 2. Adjusted Odds of Survival to Hospital Admission and Discharge Among the Airway Subgroups (All-Severity Analysis)



The values for adjusted odds ratios (aORs) are plotted on a log scale. BVM indicates bag-valve-mask ventilation; ETI, endotracheal intubation; PPV, positive pressure ventilation; SGA, supraglottic airway.

[a] Firth logistic regression was used due to fewer than 200 deaths before discharge.

effect of implementing the guidelines (addressing multiple physiological abnormalities) was additive or synergistic in its impact on outcome. Indeed, our prior work suggests that the combined harm of hypotension and hypoxia is at least additive.[37] Furthermore, there is now growing evidence that near hypotension may be very detrimental to TBI outcomes.[35,38] Since the health care professionals were trained to prevent hypotension rather than waiting until the patient was already hypotensive, it is possible that treatment of patients who were near hypotensive might have had a significant, unanticipated effect on outcomes.

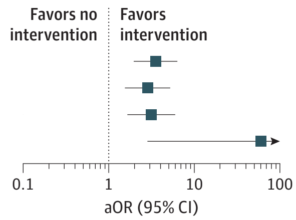
It is important to prevent a misinterpretation that could be made from our findings. While there was a significant move toward performing basic airway interventions and away from intubation after training, the associated survival improvement was not due to these shifts in airway technique. We did not compare outcomes among different airway interventions. This study was neither designed nor powered for that purpose. Rather, each airway type (BVM, SGA, and ETI) was compared with itself before and after implementation. Because of this, the most plausible explanation for the significant outcome improvement in patients with PPV was the other aspects of guideline implementation (ie, prevention of hyperventilation and hypoxia) rather than having anything to do with the airway interventions themselves.

These findings reveal the importance of proper emphasis on carefully managing end-tidal carbon dioxide and preventing hyperventilation and overventilation regardless of airway procedure. Since so much of the literature has focused on the airway interventions themselves (particularly ETI), it appears that the necessity of providing proper postprocedure ventilation has been underappreciated.[31]

Another major implication of our results is that they bring the findings of previous comparative airway studies into question. This is particularly true of those attempting to compare prehospital use of BVM with ETI in patients with TBI. To truly compare airway interventions, study design must account for differences in ventilation. Otherwise, the studies are at least partially studying unidentified differences in ventilation rather than the airway interventions themselves. A dramatic example of this was the San Diego Rapid Sequence Intubation Trial, which was ended early due to harm in the ETI arm.[23] The conclusion was that prehospital ETI caused the poor outcomes. However, one of the most telling aspects of this study came with the subsequent analysis by Davis et al[56] of the partial pressure of carbon dioxide (pCO_2) measurements. Remarkably, the proportion of intubated patients arriving at the trauma center with severe hypocapnia (pCO_2 of 20 to 29 mm Hg) was twice that of those managed with BVM. In contrast, the likelihood of patients in the basic airway arm arriving in the nor-

Figure 3. Comparison of Adjusted Odds of Survival During the Postimplementation vs Preimplementation Phases Among the Airway Subgroups

Airway subgroup in the severe TBI cohort (RSS-H score of 3-4)	aOR (95% CI)
Any PPV	3.52 (1.96 to 6.34)
SGA or ETI	2.84 (1.54 to 5.23)
ETI	3.14 (1.65 to 5.98)
BVM only	59.8 (2.83 to >100)[a]



The values for adjusted odds ratios (aORs) are plotted on log scale. BVM indicates bag-valve-mask ventilation; ETI, endotracheal intubation; PPV, positive pressure ventilation; RSS-H, regional severity score–head; SGA, supraglottic airway; TBI, traumatic brain injury.

[a] Firth logistic regression was used due to fewer than 200 deaths before discharge.

mal pCO_2 range (35 to 44 mm Hg) was more than double of that of the ETI cohort.[56] Thus, while the purpose of the trial was to randomize the airway intervention, the study inadvertently also randomized patients to receive good ventilation (in the BVM cohort) and poor ventilation or hypocapnia (in the ETI cohort).

These issues have implications for all airway investigations. To our knowledge, no previous prehospital TBI airway study has controlled for postprocedure ventilation. And thus, since ETI is associated with a much higher likelihood of hyperventilation or overventilation,[31] the negative outcomes (that come from hypocapnia) have been attributed to the intubation procedure itself. Unfortunately, this brings essentially the entire prehospital basic vs advanced airway literature into question.

This discussion brings the findings of the current study into perspective. What we did was compare standard (ie, typically poor) ventilation to better-managed, guideline-based ventilation across all airway cohorts. Thus, we did not evaluate different airway techniques but rather the outcomes of emphasizing good ventilation regardless of airway procedure. In this study, every airway group experienced dramatic improvement in outcome.

As with the overall EPIC study, outcomes in this airway subanalysis improved in the severe TBI group but not in those with moderate or critical TBI.[19,34] This finding suggests the existence of an interventional sweet spot in the TBI severity spectrum. That is, guideline treatment (prevention of hypoxia and hyperventilation) is most likely to have an impact in those with TBI severity between moderate and critical because patients with moderate TBI are likely to survive regardless of prehospital treatment, while those with critical TBI are likely to die due to their devastating primary brain injury.[18,19]

Among those patients with moderate TBI (RSS-H score of 1 to 2), there was no statistically significant change in survival to hospital admission or discharge. Among patients with critical TBI (RSS-H score of 5 to 6), there was an improvement in survival to hospital admission and a decreased survival to hospital discharge. As with the main EPIC study,[18] the lack of improvement in the critical cohort is likely due to the Stocchetti effect.[18,27,58] That is, improvements in prehospital trauma care may lead to a paradoxical effect of improved prehospital survival but decreased hospital survival, because critical patients that previously died in the field now survive to hospital admission but die in-hospital from nonsurvivable injury.[18,27,58]

Limitations

This study has limitations. First, it was observational rather than randomized. Thus, while it was prospective and controlled, it could not prove cause and effect. As such, we cannot know conclusively that the improvements in outcome were directly caused by the EMS guideline implementation. However, the concurrent increase in survival to hospital admission, an outcome that is proximate to the prehospital care, is supportive of the conclusion that the prehospital interventions led to the improvements in final outcome as well.

Second, we have limited data regarding the details of airway management in the field (eg, number of attempts, devices used for advanced airways). Thus, we are not able to make conclusions regarding specific airway management strategies (eg, use of video laryngoscopy, bougie-assisted intubation).

Third, it is possible that over the 8-year study period, advances in hospital-based care resulted in improved survival. To evaluate this issue, outcomes were compared between 2 patient cohorts that were unaffected by the EPIC study: (1) those cared for by nonparticipating EMS agencies and (2) those transported to trauma centers by privately owned vehicle. These were compared across the early (January 2007 to December 2012) and late (January 2013 to June 2015) EPIC study periods. Neither analysis yielded any evidence of secular outcome improvement over time. Indeed, there was a trend toward somewhat worse outcomes in the late groups.[18]

Fourth, the EPIC study ended in 2015. However, we have created safeguards to prevent any morphing of the data as we continue to use the database to perform the preplanned secondary analyses. These safeguards include (1) the data were fixed in 2017 (no subsequent data changes have occurred), (2) the confounders used in the analyses have remained consistent, and (3) we have not altered the approach to risk adjustment or statistical modeling.

Fifth, we were not able to evaluate functional outcomes. While survival to hospital discharge was always the primary outcome for this study, we had to suspend our plan to obtain 12-month functional outcome (Glasgow Outcome Score–Extended) due to a reduction in funding.

Sixth, it is important to note that these findings do not answer the questions surrounding when patients with TBI ought to be intubated in the field. While there was a significant (and probably appropriate) reduction in the proportion of prehospital intubations, more than 70% of patients with PPV during the postimplementation phase still underwent ETI. While there was significant improvement in outcomes among intubated patients after implementation of guideline-based care, this does not answer the question of whether they should have been intubated in the first place.

Conclusions

Among patients with severe TBI and active airway management, guideline implementation was independently associated with dramatic improvement in survival to hospital admission and discharge. This was true, both of patients who received basic airway interventions and those with advanced airways. These findings support the concept that focusing on the aggressive prevention and correction of hypoxia and hyperventilation improves outcome in patients who require ventilatory support, regardless of which airway intervention is performed by EMS.

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Acquisition, analysis, or interpretation of data: Spaite, Barnhart, Chikani, Rice, Howard, Hu.
Drafting of the manuscript: Gaither, Chikani, Hu.
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