Effect of a Strategy of Initial Laryngeal Tube Insertion vs Endotracheal Intubation on 72-Hour Survival in Adults With Out-of-Hospital Cardiac Arrest
A Randomized Clinical Trial

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IMPORTANCE Emergency medical services (EMS) commonly perform endotracheal intubation (ETI) or insertion of supraglottic airways, such as the laryngeal tube (LT), on patients with out-of-hospital cardiac arrest (OHCA). The optimal method for OHCA advanced airway management is unknown.

OBJECTIVE To compare the effectiveness of a strategy of initial LT insertion vs initial ETI in adults with OHCA.

DESIGN, SETTING, AND PARTICIPANTS Multicenter pragmatic cluster-crossover clinical trial involving EMS agencies from the Resuscitation Outcomes Consortium. The trial included 3004 adults with OHCA and anticipated need for advanced airway management who were enrolled from December 1, 2015, to November 4, 2017. The final date of follow-up was November 10, 2017.

INTERVENTIONS Twenty-seven EMS agencies were randomized in 13 clusters to initial airway management strategy with LT (n = 1505 patients) or ETI (n = 1499 patients), with crossover to the alternate strategy at 3- to 5-month intervals.

MAIN OUTCOMES AND MEASURES The primary outcome was 72-hour survival. Secondary outcomes included return of spontaneous circulation, survival to hospital discharge, favorable neurological status at hospital discharge (Modified Rankin Scale score ≤3), and key adverse events.

RESULTS Among 3004 enrolled patients (median [interquartile range] age, 64 [53-76] years, 1829 [60.9%] men), 3000 were included in the primary analysis. Rates of initial airway success were 90.3% with LT and 51.6% with ETI. Seventy-two hour survival was 18.3% in the LT group vs 15.4% in the ETI group (adjusted difference, 2.9% [95% CI, 0.2%-5.6%]; *P* = .04). Secondary outcomes in the LT group vs ETI group were return of spontaneous circulation (27.9% vs 24.3%; adjusted difference, 3.6% [95% CI, 0.3%-6.8%]; *P* = .03); hospital survival (10.8% vs 8.1%; adjusted difference, 2.7% [95% CI, 0.6%-4.8%]; *P* = .01); and favorable neurological status at discharge (7.1% vs 5.0%; adjusted difference, 2.1% [95% CI, 0.3%-3.8%]; *P* = .02). There were no significant differences in oropharyngeal or hypopharyngeal injury (0.2% vs 0.3%), airway swelling (1.1% vs 1.0%), or pneumonia or pneumonitis (26.1% vs 22.3%).

CONCLUSIONS AND RELEVANCE Among adults with OHCA, a strategy of initial LT insertion was associated with significantly greater 72-hour survival compared with a strategy of initial ETI. These findings suggest that LT insertion may be considered as an initial airway management strategy in patients with OHCA, but limitations of the pragmatic design, practice setting, and ETI performance characteristics suggest that further research is warranted.

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Out-of-hospital cardiopulmonary arrest (OHCA) affects more than 350 000 adults in the United States each year, with less than 10% surviving to hospital discharge in 2016.[1] In the United States and countries with advanced emergency medical services (EMS) systems, paramedics commonly perform endotracheal intubation (ETI) on patients with cardiac arrest to provide a direct conduit to the lungs, facilitate controlled oxygenation, and protect the lungs from aspiration of vomitus.

ETI plays a central but controversial role in contemporary EMS care. More than 30 years ago, ETI became a standard US paramedic practice under the assumption that it would improve OHCA outcomes. However, numerous studies have highlighted the challenges of paramedic ETI, including significant rates of unrecognized tube misplacement or dislodgement, need for multiple ETI attempts, and ETI insertion failure.[2-4] ETI has also been associated with iatrogenic hyperventilation and chest compression interruptions.[5,6] Furthermore, opportunities for EMS ETI training and skills maintenance are limited in the United States, with many paramedics performing only 1 live procedure annually.[7]

Alternatives to ETI include supraglottic airway (SGA) devices including the laryngeal mask airway, esophageal-tracheal combitube, i-gel, and laryngeal tube (LT). Compared with ETI, SGA insertion is rapid, simple, and requires less training, while offering ventilatory characteristics that are similar to ETI.[8] While traditionally reserved for contingency use in the event of unsuccessful ETI efforts, SGA insertion has been incorporated by many EMS agencies as the primary method of ventilation during OHCA resuscitation. However, multiple observational studies reported better outcomes associated with ETI compared with SGAs.[9-11]

To date, few randomized clinical trials have compared ETI with other airway techniques in OHCA.[12-14] This Resuscitation Outcomes Consortium Pragmatic Airway Resuscitation Trial (PART) compared the effectiveness of initial LT and initial ETI strategies on outcomes in adult OHCA.

Methods

Design
We conducted a multicenter cluster-crossover randomized trial. The trial methods have been previously reported, and the trial protocol is available in Supplement 1.[15] The institutional review boards of the participating institutions approved the trial under federal rules for conduct of emergency research under Exception From Informed Consent (21 CFR 50.24). Participating sites satisfied all requirements for this, including community consultation, public disclosure, and notification of patient, family members, or legally authorized representatives of enrollment.

Funding
The trial was funded by a National Heart, Lung, and Blood Institute (NHLBI) program supporting large-scale, low-cost pragmatic clinical trials.[16] This required following stipulated

Key Points

Question What is the effect of an initial airway management strategy using laryngeal tube insertion, compared with endotracheal intubation, on survival among adults with out-of-hospital cardiac arrest?

Findings In this cluster-crossover randomized trial of 3004 adults with out-of-hospital cardiac arrest, 72-hour survival was 18.3% for laryngeal tube insertion and 15.4% for endotracheal intubation, a significant difference.

Meaning A strategy of initial laryngeal tube insertion, compared with endotracheal intubation, was associated with greater likelihood of 72-hour survival, but given limitations in study design and findings, additional research is warranted.

pragmatic trial principles, the use of existing research infrastructure, adherence as much as possible to existing clinical practice, and focus on describing outcomes rather than explanatory mechanisms. The Pragmatic-Explanatory Continuum Indicator Summary 2 (PRECIS-2)[17] wheel for the trial is provided in eAppendix 1 in Supplement 2. The capped funding amount constrained the potential number of enrolled patients.

Data and Safety Monitoring
A trial-appointed study monitoring committee monitored EMS agency and regional center protocol compliance and data reporting. An NHLBI-appointed data and safety monitoring board approved the protocol, monitored the safety and interim results of the trial, and made recommendations for its continuation or suspension.

Study Setting and Organization
The trial included 27 EMS agencies associated with US sites of the Resuscitation Outcomes Consortium, a North American multicenter network funded by the NHLBI to conduct clinical trials of therapies for OHCA and major trauma (eTable 1 in Supplement 2). The University of Alabama at Birmingham and the University of Washington Clinical Trials Center functioned as the respective clinical and data coordinating centers for the trial.

Selection of Patients
The trial included adults (age ≥18 years or per local interpretation) with nontraumatic OHCA treated by participating EMS agencies and requiring anticipated ventilatory support or advanced airway management (eAppendix 2 in Supplement 2). Patients who received initial clinical care by EMS agencies with ETI or SGA insertion capabilities and that were not affiliated with the trial were excluded.

Interventions
The trial randomized EMS agencies to either of 2 initial advanced airway management strategies: initial LT insertion or initial orotracheal ETI (eFigure 1 in Supplement 2). Although a variety of SGA devices are available, only LT insertion was allowed because it is the most commonly

used SGA in the United States. The protocol allowed the use of neuromuscular blocking agents or video laryngoscopy but not other techniques (eg, nasotracheal intubation) for initial intubation efforts.

The protocol did not prescribe or limit the number of initial LT or ETI insertion attempts. If the initial LT/ETI insertion efforts were unsuccessful, EMS personnel performed rescue airway management using any available airway technique, including bag-valve-mask (BVM) ventilation, ETI (including alternate ETI techniques such as nasal or digital intubation), insertion of LT or another SGA device, or needle jet ventilation or cricothyroidotomy. EMS personnel followed local protocols for confirmation of airway placement and management of OHCA, including field termination of resuscitation efforts. Patients receiving BVM ventilation only (without any LT or ETI attempts) were retained in their assigned treatment group per intention-to-treat principles. The trial did not prescribe clinical care at the receiving hospitals, including the use or replacement of the EMS airway, the provision of targeted temperature management, percutaneous coronary intervention, or the timing of withdrawal of life-sustaining therapy.[18]

While ETI is almost exclusively an advanced life support skill, basic life support clinicians at the Milwaukee and Portland sites had been trained in LT insertion.[19,20] When these EMS agencies were assigned to LT, select basic life support–only clinicians performed initial LT insertion. When assigned to ETI, these clinicians performed BVM ventilation until advanced life support arrival.

Randomization

The trial used cluster randomization with crossover. We grouped the 27 EMS agencies into 13 randomization clusters. Each cluster selected an a priori crossover interval of 3 or 5 months. Based on each cluster's selected crossover interval and projected duration of trial participation, the lead statistician created a detailed a priori randomization plan (complete with crossover dates and assigned interventions), with the goal of achieving balance within and across sites at the end of the trial. Within each cluster, treatment assignments for consecutive intervals were computer-randomized in blocks of 2 to ensure balanced exposure to both airway groups. Crossovers between study groups could occur more than once.

Practical factors influenced the execution of the randomization. We provided crossover notifications to each cluster at least 1 month prior to the scheduled crossover date, aiming to initiate crossovers on the first day of a calendar month. We allowed EMS agencies to align crossover dates with training sessions, avoid weekends, and avoid crossovers during the last month of the trial. Some clusters experienced delays in start-up, which required adjustments of planned crossover dates (but not randomization groups). If clinicians from more than 1 participating EMS agency were present on scene, the first arriving unit determined the study treatment assignment.

Among the 56 random cluster treatment group assignments, we made 2 crossover adjustments to achieve balanced enrollment between study groups. Enrollment in 1 cluster exceeded projections; we instructed this cluster to carry out 1 additional crossover. One agency ended participation in the trial prior to study completion; to compensate, we instructed another cluster to defer its final crossover. These decisions regarding changes to cluster crossover timings were made without knowledge of outcome data by randomization cluster.

Outcomes

The primary outcome was survival to 72 hours after the index arrest, determined from hospital or (in cases of field termination of resuscitation) EMS records (eTable 2 in Supplement 2). We chose this outcome because it requires a smaller sample size than traditional outcomes (eg, survival to hospital discharge) and accommodated key elements of standard postarrest care such as therapeutic hypothermia (targeted temperature management), early percutaneous coronary intervention, and delay of neurological assessment.[18,21] Secondary trial outcomes included (1) return of spontaneous circulation (presence of palpable pulses on emergency department arrival), (2) survival to hospital discharge, and (3) favorable neurological status on hospital discharge (Modified Rankin Scale score ≤3). Other secondary outcomes included EMS airway management course and hospital adverse events. Research coordinators ascertaining clinical outcomes were not blinded to the study intervention.

While postulated mechanisms influencing OHCA outcomes following advanced airway management include chest compression interruptions and hyperventilation, the pragmatic nature of the trial precluded the formal collection and analysis of chest compression and ventilation data.[6,22,23]

Study Compliance Benchmarks

Benchmarks used by the study monitoring committee for assessing EMS agency performance in the trial are listed in eAppendix 3 in Supplement 2.

Data Analysis

We estimated the sample size based on the expected frequency of 72-hour survival (eAppendix 4 in Supplement 2). Because we could not identify any prior reports of 72-hour survival after OHCA, we used data from the ROC PRIMED trial.[24,25] After limiting this analysis to US sites with active use of SGA, we estimated baseline 72-hour survival rates of 16.2% for ETI and 11.1% for SGA, suggesting a potential effect size of 5.1%. By study team consensus, we selected a more conservative value of 4.5% as the difference to power the study.

To account for patients receiving BVM only, we increased the baseline LT survival rate to 13.7%. We designed the trial to have 85% power to detect a 4.5% difference in 72-hour survival, assuming an overall 2-sided α = .05, adjusting for number of analyses (3 interim and 1 final) and accommodating up to a 5% loss of precision due to cluster randomization with crossover. While the projected minimum sample size was 2612 patients (1306 per group) to

allow for exclusions, loss to follow-up, and patients treated with BVM only, we aimed to enroll a total of 3000 patients. Trial-stopping boundaries followed asymmetric 2-sided designs based on the unified family of group sequential stopping rules.[26,27]

We analyzed the primary and secondary outcomes on intention-to-treat bases. In cases where rescuers used only BVM (without ETI or LT insertion), we retained the patient in their assigned randomization. To quantify the treatment effect, we used generalized estimating equations (GEEs) with an identity link and robust standard errors, accounting for randomization cluster and number of interim analyses.

We assessed whether the association of airway management strategy with the primary outcome differed by a priori–defined subgroups, including initial cardiac rhythm, bystander-witnessed arrest, EMS response time, basic life support unit capability of LT insertion, time of airway placement after first rescuer arrival on scene, use of neuromuscular blocking agents before or during airway insertion efforts, age, use of video laryngoscopy, use of BVM ventilation only, and airway placement after return of spontaneous circulation. We assessed the influence of these factors by evaluating each (intervention by subgroup) interaction term in the primary model.

To assess the effect of deviations from random assignment, we conducted a per-protocol analysis, retaining only cases in compliance with their assigned airway group (eg, assigned to ETI and received ETI or BVM). We considered instances of BVM only to be compliant with the protocol because the expected course of airway management may entail BVM ventilation.

To assess the effect of unbalanced randomization within clusters, we conducted post hoc GEE analyses of the intention-to-treat and per-protocol populations, adjusting for age, sex, bystander- or EMS-witnessed arrest, time to EMS arrival, bystander chest compressions, and initial cardiac rhythm. We repeated post hoc analysis of the intention-to-treat population with a hierarchical model (patients nested within EMS agency and EMS agency nested within randomization cluster) and a model with randomization cluster as a fixed effect. We examined the effect of randomization order (LT first vs ETI first) by fitting a treatment by order interaction term. We also conducted as-treated analyses, classifying each case to 1 of 3 groups according to airway technique received: LT, ETI, and BVM or other. We limited as-treated comparisons to LT vs ETI.

Missing data were flagged on data entry and reviewed by data entry staff for accuracy. We treated "unknown" variable categories as informative and included these as separate factors in the GEE models. We considered missing baseline data to be missing completely at random for post hoc GEE models; we did not impute values. Patients with missing data in any of the adjustment variables were excluded from the model. We used 2-sided tests with an α of .05 as the threshold for statistical significance. We conducted all analyses using the statistical package R version 3.2.5 (The R Foundation).

Results

Patient Characteristics
The trial enrolled patients from December 1, 2015, through November 4, 2017. The duration of enrollment for each cluster ranged from 11 to 23 months (eFigure 2 in Supplement 2). Enrollment clusters crossed over between interventions 1 to 6 times. Of 3840 screened patients, 3004 were included; 1505 assigned to initial LT and 1499 assigned to initial ETI (Figure). The proportion of LT and ETI assignments varied across randomization clusters (eFigure 3 in Supplement 2).

Baseline patient and airway management characteristics are provided in Table 1 and eTable 3 in Supplement 2. LT and ETI protocol compliance (initial attempt with assigned airway or use of BVM only) were 95.5% and 90.7%, respectively. Elapsed time from first EMS arrival to airway start was shorter for LT than ETI (median, 9.8 vs 12.5 minutes). Initial LT and ETI success rates (excluding BVM) were 90.3% and 51.6%. Overall LT and ETI airway success rates (initial + rescue airway attempts) were 94.2% and 91.5%, respectively. Clinicians at receiving emergency departments converted 64.4% of EMS LT to ETI. Among patients receiving successful EMS ETI, emergency department clinicians performed repeat ETI in 33.1%. Outcomes of initial and rescue airway interventions are presented in eFigure 4 in Supplement 2.

A total of 352 patients received BVM only without any advanced airway insertion efforts. Reported reasons for the use of BVM only included the patient regaining consciousness (29.3%), death prior to airway insertion attempts (14.2%), jaw clenching (trismus, 11.9%), adequate ventilation with BVM (9.9%), arrival at emergency department prior to airway insertion efforts (7.7%), and other (8.8%) (eTable 4 in Supplement 2).

Primary Outcome
Seventy-two–hour survival was unknown for 4 patients (0.1%). Among the remaining patients, 72-hour survival was 18.3% in the LT group vs 15.4% in the ETI group; accounting for randomization cluster and interim analyses, this difference was 2.9% (95% CI, 0.2%-5.6%; *P* = .04; relative risk, 1.19 [95% CI, 1.01-1.39]) (Table 2).

Secondary Outcomes
Secondary outcomes in the LT group vs ETI group were return of spontaneous circulation (27.9% vs 24.3%; adjusted difference, 3.6% [95% CI, 0.3%-6.8%]; *P* = .03), hospital survival (10.8% vs 8.1%; adjusted difference, 2.7% [95% CI, 0.6%-4.8%]; *P* = .01), and favorable neurological status at discharge (7.1% vs 5.0%; adjusted difference, 2.1% [95% CI, 0.3%-3.8%] *P* = .02). There were no statistically significant differences in treatment effects in 72-hour survival among a priori–defined subgroups (eFigure 5 in Supplement 2).

Additional Analyses
In the per-protocol group, 72-hour survival was greater for LT than ETI (18.3% vs 15.4%; risk difference, 2.9% [95% CI, 0.1%-5.7%]; *P* = .045).

Figure. Flow of Patients in the Pragmatic Airway Resuscitation Trial
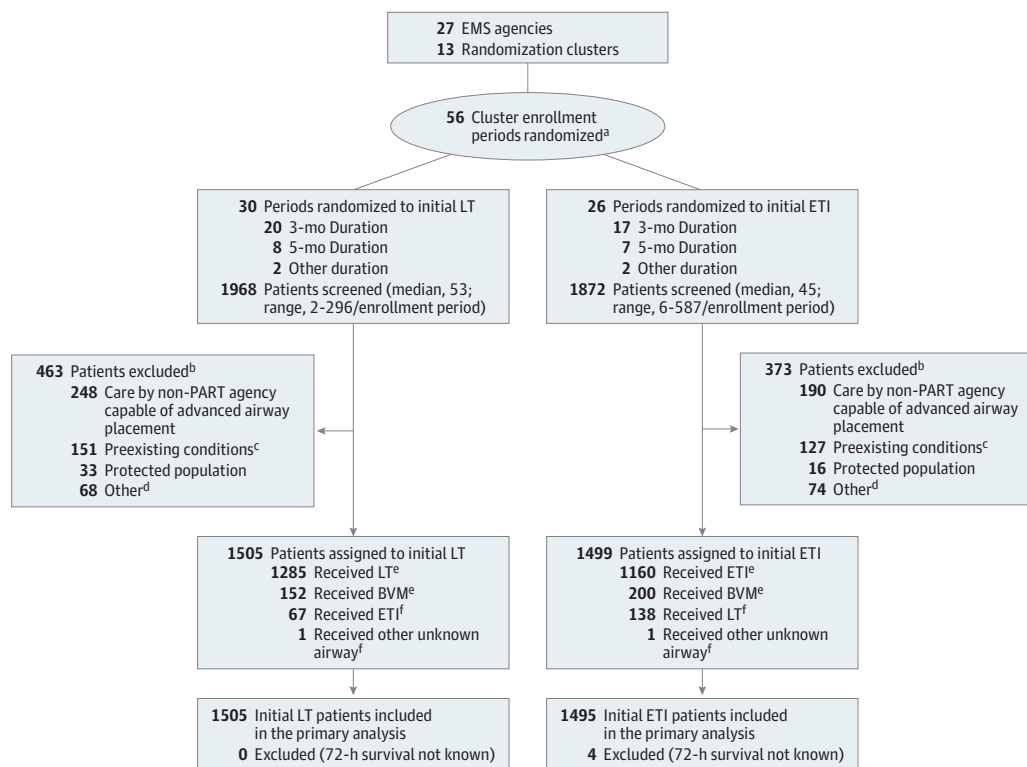
Randomization of clusters and screening and inclusion of patients in the trial. EMS indicates emergency medical services; ETI, endotracheal intubation; LT, laryngeal tube; PART, Pragmatic Airway Resuscitation Trial.

[a] Cluster enrollment periods depicted in eFigure 2 in Supplement 2. Twenty-seven EMS agencies were grouped into 13 randomization clusters, with each cluster selecting an a priori crossover interval of 3 or 5 months.

[b] Screened patients may have been excluded for more than 1 reason.

[c] Preexisting conditions include preexisting tracheostomy; preexisting

do-not-attempt-resuscitation orders; patient with advanced airway inserted prior to EMS arrival; patients with left ventricular assist device or total artificial heart; and patients with a do-not-enroll bracelet.

[d] Other exclusions include major bleeding or exsanguination, obvious asphyxial cardiac arrest, interfacility transports, and traumatic etiology of arrest.

[e] Protocol compliance.

[f] Protocol deviation.

Adverse events are summarized in **Table 3**. Compared with LT, patients in the ETI group were more likely to experience 3 or more airway insertion attempts (18.9% vs 4.5%). Unsuccessful initial airway insertion was higher for ETI than LT (44.1% vs 11.8%). Unrecognized airway misplacement or dislodgement was higher for ETI than LT (1.8% vs 0.7%). EMS personnel reported inadequate ventilation more often in LT than ETI (1.8% vs 0.6%). Pneumothoraces (7.0% vs 3.5%) and rib fractures (7.0% vs 3.3%) were more common with ETI than LT. There were no significant differences in oropharyngeal or hypopharyngeal injury (0.2% vs 0.3%), airway swelling (1.1% vs 1.0%), or pneumonia or pneumonitis (26.1% vs 22.3%) in the LT vs ETI groups.

Post-Hoc Analyses

In the intention-to-treat population, after post hoc adjustment for age, sex, initial cardiac rhythm, response time, witnessed status, and bystander chest compressions, the difference in 72-hour survival between LT and ETI was not

statistically significant (adjusted difference, 2.1% [95% CI, −0.5% to 4.8%]; $P = .11$; Table 2). In a hierarchical model with patients nested within agency and agency nested within randomization cluster and applying independent correlation structure, the difference in 72-hour survival between LT and ETI was 1.8% (95% CI, −0.9% to 4.5%). In a linear regression model with randomization cluster included as a fixed effect, the difference in 72-hour survival between LT and ETI was 1.5% (95% CI, −1.2% to 4.3%).

When stratifying by order of randomization (LT first or ETI first), the differences in 72-hour survival were 2.5% (95% CI, −0.9% to 5.9%) for LT first and 3.6% (95% CI, −0.9% to 8.2%) for ETI first (interaction $P = .69$). After post hoc multivariable adjustment, the difference in 72-hour survival in the perprotocol analysis was not statistically significant (adjusted difference, 2.3% [95% CI, −0.4% to 5.1%]; $P = .09$; Table 2).

In the as-treated analysis, the initial airway devices used on enrolled patients were ETI in 1224 patients, LT in 1423, and BVM or other in 354; there was no significant difference in

Table 1. Characteristics of Patients Included in Intention-to-Treat Population

Characteristic	Laryngeal Tube (n = 1505)	Endotracheal Intubation (n = 1499)
Age, median (IQR), y	64 (53-76)	64 (53-76)
Male, no./total No. (%)	928/1503 (61.7)	901/1499 (60.1)
Witnessed arrest, no./total No. (%)	n = 1357	n = 1399
EMS witnessed	180 (13.3)	179 (12.8)
Bystander witnessed	511 (37.7)	529 (37.8)
Not witnessed	666 (49.1)	691 (49.4)
Unknown[a]	148 (9.8)	100 (6.7)
Bystander chest compressions, no./No. (%)	n = 1258	n = 1279
Yes	698 (55.5)	709 (55.4)
No	560 (44.5)	570 (44.6)
Unknown[a]	247 (16.4)	220 (14.7)
Time from dispatch to first arrival of EMS		
Median (IQR), min	5.0 (3.9-6.3)	5.3 (4.1-6.8)
≤4 min, no./total No. (%)	408/1444 (28.3)	305/1405 (21.7)
Unknown	61 (4.1)	94 (6.3)
Time between EMS arrival and start of chest compressions		
Median (IQR), min	2.1 (1.1-3.8)	2.1 (1.0-3.7)
≤10 min, no./total No. (%)	1243/1347 (92.3)	1189/1279 (93.0)
First electrocardiogram rhythm, no./total No. (%)		
Shockable rhythm (ventricular fibrillation, ventricular tachycardia, or delivery of AED shock)	301 (20.0)	270 (18.0)
Nonshockable (asystole, pulseless electrical activity, or AED nonshockable)	1160 (77.1)	1197 (79.9)
Other	44 (2.9)	32 (2.1)
Epinephrine administered before hospital arrival, no./total No. (%)	1385 (92.0)	1405 (93.7)
Compliance with assigned airway intervention, no./total No. (%)[b]	1437 (95.5)	1360 (90.7)
Transported to hospital, no./total No. (%)	906 (60.2)	889 (59.3)
Hospital procedures, no./total No. (%)[c]		
Therapeutic hypothermia	242/460 (52.6)	185/400 (46.3)
Coronary catheterization	109/460 (23.7)	73/400 (18.3)
Patients per randomization cluster[d]		
Mean	116	115
Median (range)	94 (3-314)	66 (12-382)

Abbreviations: AED, automated external defibrillator; EMS, emergency medical services; IQR, interquartile range.

[a] For "unknown" values, denominator is total cases in group.

[b] Episodes were considered compliant if the randomized airway was initially attempted or if only bag-valve-mask was used. Episodes were considered noncompliant if another airway device was used.

[c] Percentage of those transported to hospital and survived for at least 1 hour.

[d] Total of 13 randomization clusters.

72-hour survival between those receiving initial LT and initial ETI (16.0% vs 13.5%; *P* = .07) (eTable 5 in Supplement 2).

Treatment effects varied among randomization clusters (eFigure 6 in Supplement 2) and EMS agencies (eFigure 7 in Supplement 2) and showed a tendency toward favoring LT only in clusters with lower baseline ETI survival.

The primary outcome (72-hour survival) was missing for 4 of 3004 enrolled patients (0.1%), all assigned to ETI. Because of the low number of missing cases, we did not apply multiple imputation. Among the 4 patients with missing 72-hour outcome, there were 16 possible combinations of 72-hour survival; only 1 (all 4 patients surviving to 72 hours) would have altered the primary trial results. Given the observed 15.4% 72-hour survival rate in the ETI group, the probability of all 4 cases surviving to 72 hours was 0.06%.

Discussion

In this trial of 3004 adults with OHCA, a strategy of initial LT was associated with modest but significantly greater 72-hour survival than a strategy of initial ETI. There were also statistically significant associations with survival to hospital discharge and favorable neurological status at hospital discharge that favored the LT group. The trial offers preliminary observations that may potentially guide EMS airway management practices and serve as the basis for future research.

The trial demonstrated the effectiveness of an LT-based strategy of advanced airway management, not the efficacy of the LT airway device. OHCA resuscitation requires the careful

Table 2. Outcomes of Patients Included in the Primary and Secondary Analyses

	No. (%)			
Characteristic	Laryngeal Tube (n = 1505)	Endotracheal Intubation (n = 1499)	Difference, % (95% CI)[a]	P Value
Primary Outcome				
Survival to 72 h (intention-to-treat population)	275 (18.3)	230/1495 (15.4)	2.9 (0.2 to 5.6)	.04
Secondary Outcomes				
Return of spontaneous circulation on emergency department arrival	420 (27.9)	365 (24.3)	3.6 (0.3 to 6.8)	.03
Survival to hospital discharge	163/1504 (10.8)	121/1495 (8.1)	2.7 (0.6 to 4.8)	.01
Favorable neurologic status at discharge (Modified Rankin Scale score ≤3)	107/1500 (7.1)	75/1495 (5.0)	2.1 (0.3 to 3.8)	.02
Modified Rankin Scale score	n = 1500	n = 1495		
0-No symptoms	17 (1.1)	14 (0.9)		
1-No significant disability	32 (2.1)	29 (1.9)		
2-Slight disability	22 (1.5)	12 (0.8)		
3-Moderate disability	36 (2.4)	20 (1.3)		
4-Moderately severe disability	26 (1.7)	24 (1.6)		
5-Severe disability	26 (1.7)	22 (1.5)		
6-Dead	1341 (89.4)	1374 (91.9)		
Additional Analyses				
Per-protocol analysis-survival to 72 h	263/1437 (18.3)	209/1356 (15.4)	2.9 (0.1 to 5.7)	.045
Intention-to-treat post hoc adjusted analysis[b]			2.1 (−0.5 to 4.8)	.11
Per-protocol post hoc adjusted analysis[b]			2.3 (−0.4 to 5.1)	.09

[a] For the primary analysis, the estimated difference in 72-hour survival accounted for interim monitoring and clustering via robust standard errors. All other comparisons accounted for clustering.

[b] Post hoc analyses adjusted for age, sex, rhythm, response time, witness status, and bystander chest compressions. A total of 163 patients were omitted from post hoc models due to missing data.

Table 3. Out-of-Hospital and In-Hospital Adverse Events[a]

Characteristic	Laryngeal Tube (n = 1505)	Endotracheal Intubation (n = 1499)	Difference, % (95% CI)	P Value
Out-of-Hospital Adverse Events				
Multiple (≥3) insertion attempts[b]				
Initial airway	6/1353 (0.4)	18/1299 (1.4)	−0.9 (−1.7 to −0.2)	.01
Across all airways	61/1353 (4.5)	245/1299 (18.9)	−14.4 (−17.0 to −11.7)	<.001
Unsuccessful insertion[b]				
First airway technique	159/1353 (11.8)	573/1299 (44.1)	−32.4 (−35.6 to −29.1)	<.001
All airway techniques	78/1353 (5.8)	111/1299 (8.5)	−2.8 (−4.8 to −0.8)	.01
Unrecognized airway misplacement or airway dislodgement	10/1353 (0.7)	24/1299 (1.8)	−1.1 (−2.0 to −0.3)	.01
Inadequate ventilation	25/1353 (1.8)	8/1299 (0.6)	1.2 (0.3 to 2.1)	.01
In-Hospital Adverse Events				
Pneumothorax (first chest x-ray)[c]	17/485 (3.5)	30/428 (7.0)	−3.6 (−6.5 to −0.7)	.02
Rib fractures (first chest x-ray)[c]	16/485 (3.3)	30/428 (7.0)	−3.8 (−6.9 to −0.7)	.01
Oropharyngeal or hypopharyngeal injury (first 24 h)[d]	1/460 (0.2)	1/400 (0.3)	0 (−0.7 to 0.6)	.92
Airway swelling or edema (first 24 h)[d]	5/460 (1.1)	4/400 (1.0)	0.1 (−1.3 to 1.4)	.90
Pneumonia or aspiration pneumonitis (first 72 h)[d]	120/460 (26.1)	89/400 (22.3)	3.7 (−2.1 to 9.6)	.21

[a] Out-of-hospital adverse events were based on emergency medical services personnel reports. In-hospital adverse events were determined from review of medical records.

[b] Excludes cases receiving bag-valve-mask ventilation only.

[c] Includes patients who were admitted to emergency department and underwent a chest x-ray.

[d] Includes patients who were admitted to emergency department and survived for at least 1 hour.

coordination of multiple interventions, including initiation and maintenance of chest compressions, controlled ventilation, vascular access, drug administration, and defibrillation. The simpler LT technique may better integrate with and facilitate these other treatments. Although the 2 groups reported similar procedural duration, the elapsed time from EMS arrival to first airway attempt was 2.7 minutes shorter in the LT than ETI group. Also, LT required fewer insertion attempts than ETI. This pragmatic trial did not assess mechanisms underlying the effect of airway type on chest compression quality (in particular, chest compression continuity), which may potentially influence OHCA outcomes.[5,28]

The ETI success rate of 51% observed in this trial is lower than the 90% success rate reported in a meta-analysis.[29] The reasons for this discordance are unclear. Prior reports of higher success rates may be susceptible to publication bias. Another possibility is that some medical directors encourage early rescue SGA use to avoid multiple unsuccessful intubation attempts and to minimize chest compression interruptions.[5] Few of the study EMS agencies had protocols limiting the number of allowed intubation attempts, so the ETI success rate was not the result of practice constraints. While the ETI proficiency of study clinicians might be questioned, the trial included a diverse range of EMS agencies and likely reflects current practice. It is not clear whether clinicians with more advanced ETI skills or experience would have altered these results. However, this pragmatic trial highlights the outcomes of care resulting from existing EMS airway clinical and training practices; supplementing the trial with specialized airway management training would have limited the generalizability of the findings.

Some limitations of a cluster-crossover design include imbalance in patient allocation, group baseline characteristics, and variations in within-cluster treatment effects. Post hoc adjustment for these factors influenced the observed associations with 72-hour survival, underscoring the importance of even small imbalances. Post hoc analyses also suggested that the benefit of LT may have been amplified in clusters with lower baseline ETI 72-hour survival. The reasons for these intercluster differences are unknown. Post hoc analyses are extremely difficult to interpret in the context of a clinical trial. While cluster-crossover designs have been successfully used in trials enrolling patients with OHCA, additional study must evaluate the nuances of this approach in the context of airway management.[24,30]

These results contrast with prior studies of OHCA airway management. Observational studies have reported higher survival with ETI than SGA, but they were nonrandomized, included a range of SGA types, and did not adjust for the timing of the airway intervention.[9,10,31-34] A trial of 830 children found no difference in survival or neurological outcomes between those randomized to BVM-only ventilation vs BVM+ETI, but the study occurred in 1994-1997, used clinicians who were newly trained in pediatric ETI, and included a range of medical conditions in addition to OHCA.[12] A recent trial of 2043 adult OHCA cases in France and Belgium found no OHCA survival differences between BVM and ETI, but care was rendered by physician-staffed EMS units, a model less common in the United States and countries with similar paramedic-based EMS systems.[35] In the United Kingdom, enrollment has been completed in Airways-2, a trial comparing i-gel SGA with ETI on OHCA outcomes.[36] The current trial focused on LT, which is more commonly used in the United States.

While prior studies suggest higher survival with BVM than with advanced airway devices, similar inferences should not be made based on the as-treated analysis of this trial. The BVM-only group exhibited higher rates of witnessed arrest, bystander chest compressions, and shockable rhythms than LT or ETI, and almost a third regained consciousness prior to advanced airway intervention, suggesting influence from resuscitation time bias.[37] These and other biases cannot be overcome by post hoc analytic techniques. A randomized trial comparing BVM and LT would be needed to assess their relative efficacy.

Limitations

This study has several limitations. First, the pragmatic trial evaluated strategies of LT and ETI under existing clinical protocols and educational practices without additional training or quality improvement monitoring. Second, the stipulations of the grant award influenced many elements of the study design such as limiting the available sample size. Third, the trial could not assess the influence of chest compression or ventilation quality. Fourth, the trial focused on LT use and not other SGAs. Fifth, many elements of the trial were not blinded, including the interventions, allocation, crossover timings, and outcomes ascertainment, and adjustments were made to the crossover plan to balance allocation. Sixth, these results pertain to the out-of-hospital environment and may not apply to the in-hospital setting.

Conclusions

Among adults with OHCA, a strategy of initial LT insertion was associated with significantly greater 72-hour survival compared with a strategy of initial ETI. These findings suggest that LT insertion may be considered as an initial airway management strategy in patients with OHCA, but limitations of the pragmatic design, practice setting, and ETI performance characteristics suggest that further research is warranted.

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