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.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT02419573

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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.

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.

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 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 $\alpha = .05$, 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