



## Article Appraisal

**Article:** 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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### Background and Study Objective(s):

The optimal choice of advanced airway for out-of-hospital cardiac arrest (OHCA) remains unclear as a growing body of evidence suggests potential harms associated with endotracheal intubation (ETI), and an equivalence of survival outcomes with supraglottic airway (SGA) use. The aim of this study was to compare the effects of initial airway strategy with a laryngeal tube (LT) vs. ETI on survival among adults with OHCA.

As an interesting aside, the same August 2018 edition of JAMA also published a similar cluster RCT performed in the UK, the AIRWAYS-2 trial, which studied adults with OHCA receiving initial iGel vs ETI, and reported no statistically significant difference in the outcomes of modified Rankin Score at time of hospital discharge or at 30 days in hospital.

### Study Design:

This Resuscitation Outcomes Consortium (ROC) multi-centre, cluster-crossover, randomized controlled trial enrolled 3004 adult, non-traumatic, OHCA patients across 6 American states via 27 EMS agencies from December 2015 to January 2017. The study was pragmatic in design and as such focused on existing emergency medical services (EMS) structures and practices and describing outcomes without seeking to explain. Excluded patients were those with known pregnancy; major facial trauma, bleeding or exsanguination; prior insertion of ETI or LT by a non-trial EMS agency; pre-existing tracheostomy; obvious asphyxia-related cardiac arrest; pre-existing do not resuscitate orders; inter-facility transports; or presence of left ventricular assist devices or total artificial hearts. EMS agencies were randomized into 13 clusters and treatment assignments within each cluster were computer-randomized in blocks of 2. Cluster randomization periods enrolled EMS agencies to either an initial LT strategy or an initial ETI strategy. Crossover between study groups was planned a priori in 3-5 month intervals.

The primary outcome was 72 hour survival. Secondary outcomes included ROSC, survival to hospital discharge, favourable neurological status at discharge defined as a modified Rankin Score  $\leq 3$ , and key adverse events including oropharyngeal/hypopharyngeal injury, airway swelling, pneumonia/pneumonitis, pneumothorax, inadequate ventilation, and airway displacement or dislodgment. Patients were blinded to the treatment assignment; however, EMS personnel were not blinded to the interventions, allocation, crossover timings, or outcomes ascertainment. A

clear protocol for out-of-hospital airway insertion was outlined in the study appendix, and in-hospital care was left to the discretion of treating physicians. Statistical analysis was performed via an intention-to-treat approach, as well as per-protocol, and a post hoc generalized estimating equation (GEE) analysis was carried out to assess the potential effects of unbalanced randomization and other issues within clusters.

## Results:

The primary outcome of 72-hour survival occurred in 18.3% of patients with LT vs 15.4% of patients with ETI in both ITT and per-protocol analyses. The 2.9% difference was statistically significant ( $p=0.04$ ) with a 95% CI of 0.2-5.6%. Patients with LT insertion also had statistically significant improvement in most secondary outcomes compared with patients with ETI, including ROSC (27.9 vs 24.3%, 3.6% difference with 95% CI 0.3-6.8%,  $p 0.03$ ), survival to hospital discharge (10.8 vs 8.1%, 2.7% difference with 95% CI 0.6-4.8%,  $p 0.01$ ), and favourable neurological status at discharge (7.1 vs 5.0%, 2.1% difference with 95% CI 0.3-3.8%,  $p 0.02$ ). Patients with ETI had increased adverse events compared to patients with LT, including unsuccessful initial airway insertion (44.1 vs 11.8%), requirement of 3 or more airway insertion attempts (18.9 vs 4.5%), unrecognized airway displacement or dislodgment (1.8 vs 0.7%), pneumothorax (7.0 vs 3.5%), and rib fractures (7.0 vs 3.3%). Patients with LT insertion had slightly increased incidences of inadequate ventilation compared to patients with ETI (1.8 vs 0.6%). There were no significant differences in oropharyngeal/hypopharyngeal injury, airway swelling, pneumonia, or pneumonitis. The time from EMS arrival to first airway attempt was 2.7 minutes shorter in the LT group than ETI, suggesting a greater rapidity of use with the LT. After adjustment with the post-hoc GEE analysis, however, no statistically significant differences were found with regard to primary and secondary outcomes in both ITT and per protocol analyses.

## Validity of Results:

The consensus of Journal Club attendees was that this study had a strong design with a clearly defined question. Its choices of primary and secondary outcomes were appropriate and its intervention protocol and execution were both exemplary. However, the necessity of a cluster-crossover design led to methodologic challenges that are challenging to adjust for, even with sophisticated techniques such as the GEE performed. Moreover, the significant differences that were found were very small, had confidence intervals approaching zero, and were not robust. The GEE analysis results (although post hoc, and thus with that caveat) suggest imbalances between the treatment and control arms may account for at least some of the findings. Of note, too, was the finding that treatment effect seemed to vary between randomization clusters, and showed a tendency towards favouring LT only in clusters with a lower baseline ETI survival. Potential confounders included the quality of chest compressions and the quality of ventilation, as chest compressions and ventilation are known to affect survival in OHCA but could not be measured in this study due to its pragmatic design.

## Generalizability of Results:

The large sample sizes and multicentre urban context of this study make the results generalizable to many other North American centres with similar access to resources and protocols for OHCA. Laryngeal tubes such as those used in this study are used throughout BCEHS, specifically the King Tube. Similarly, trial paramedics are not expected to have significantly different ETI training, equipment, or medications. Notable exceptions to these similarities are the availability of video laryngoscopy on Canadian EHS ambulances and the ability of paramedics to use paralytics, which were available to some of the study paramedics. Another potential limitation in applicability of this study to British Columbia is our province's unique tiered EHS system, whereby virtually all OHCA cases are attended by an Advanced Life Support (ALS) unit comprised of advanced care paramedics (ACPs) with significant experience. These ACPs almost certainly have more intubation expertise than the average EMS crew involved in this study, a situation with the potential to result in a different baseline OHCA ETI first pass success rate and better outcomes with ETI than those observed in the study.

## The Bottom Line:

The consensus amongst Journal Club attendees was that interpreting this study with a Bayesian approach (that is one that is informed by the other analogous literature on the potential harmful effects of ETI and equivalence or superiority of BVM or SGA) was warranted. The findings of this impressively performed and large-scale study weakly suggest use of LT in OHCA is associated with greater 72 hour survival, as well as survival to hospital discharge and favourable neurological status at hospital discharge, compared with initial ETI. Although the results are not robust, and limitations exist from this study's design and applicability to tiered EHS systems, the findings join a growing body

of evidence, including the recent AIRWAYS-2 trial, that gives strength to the conclusion that in selected EMS agencies, such as those with low OHCA volumes and less experienced providers, an “SGA first” strategy may be optimal. In at least some areas of BC where providers have lower volumes and resultingly lower experience, LT insertion seems to be a reasonable alternative to ETI for the first attempt to secure an airway.