Bayesian Analysis of the Pragmatic Airway Resuscitation Trial

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Study objective: Intubation and laryngeal tube insertion are common airway management strategies in out-of-hospital cardiac arrest. Bayesian analysis offers an alternate statistical approach to assess the results of a trial. We use Bayesian analysis to compare the effectiveness of initial laryngeal tube versus initial intubation strategies on outcomes after out-of-hospital cardiac arrest in the Pragmatic Airway Resuscitation Trial.

Methods: We performed a post hoc Bayesian analysis of the Pragmatic Airway Resuscitation Trial. We defined prior distributions representing neutral or skeptical estimates of laryngeal tube benefit. Using Bayesian log binomial models, we fit models for 72-hour survival, hospital survival, and hospital survival with favorable neurologic status. We estimated the posterior probability (the probability of observing an effect difference between treatment groups) of the benefit of laryngeal tube over intubation on out-of-hospital cardiac arrest outcomes.

Results: The parent trial enrolled 3,004 patients (1,505 laryngeal tube, 1,499 intubation). Under a neutral prior distribution (relative risk 1.0), laryngeal tube was better than intubation (72-hour survival risk difference 1.8% [95% credible interval {CrI} −0.9% to 4.5%], posterior probability 91%; hospital survival 1.4% [95% CrI −0.4% to 3.4%], posterior probability 93%; and hospital survival with favorable neurologic status 0.7% [95% CrI −0.5% to 2.1%], posterior probability 86%). Under a skeptical prior distribution (relative risk 0.83 to 0.92), laryngeal tube was also better than intubation (72-hour survival risk difference 1.7% [95% CrI −0.9% to 4.3%], posterior probability 89%; hospital survival 1.3% [95% CrI −0.5% to 3.3%], posterior probability 91%; and hospital survival with favorable neurologic status 0.6% [95% CrI −0.5% to 2.0%], posterior probability 82%).

Conclusion: Under various prior assumptions, post hoc Bayesian analysis of the Pragmatic Airway Resuscitation Trial confirmed better out-of-hospital cardiac arrest outcomes with a strategy of initial laryngeal tube than initial intubation. [Ann Emerg Med. 2019;74:809-817.]

Please see page 810 for the Editor's Capsule Summary of this article.

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INTRODUCTION

Background

Out-of-hospital cardiac arrest is a public health problem affecting greater than 350,000 adults in the United States and 275,000 in Europe each year.[1,2] Airway management is an important element of cardiac arrest resuscitation, ensuring a pathway for delivery of oxygen to the lungs for circulation to the body. For greater than 30 years, intubation has been the most common form of advanced airway management performed by paramedics in the United States and other countries with mature emergency medical services (EMS) systems. However, paramedic intubation has pitfalls, including unrecognized tube misplacement or dislodgement, the need for multiple intubation attempts, and chest compression interruptions.[3-5]

As an alternative to intubation, some EMS agencies have implemented the use of supraglottic airway devices such as the laryngeal mask airway, esophageal-tracheal Combitube, i-gel, and laryngeal tube to manage the airway. Retrospective analyses indicate worse out-of-hospital cardiac arrest outcomes with supraglottic airway than intubation.[6-9] However, the recent Pragmatic Airway Resuscitation Trial (PART), one of the first clinical trials of airway management in adult out-of-hospital cardiac arrest, found better out-of-hospital cardiac arrest outcomes with a strategy of initial laryngeal tube rather than initial intubation.[10]

Editor's Capsule Summary

What is already known on this topic

Laryngeal tubes were superior to intubation as initial airway management in a recent, large, randomized controlled trial of out-of-hospital cardiac arrest.

What question this study addressed

Does a Bayesian reanalysis corroborate the Pragmatic Airway Resuscitation Trial's frequentist findings?

What this study adds to our knowledge

In this randomized controlled trial of 3,004 subjects with cardiac arrest, the Bayesian analyses confirmed laryngeal tube superiority for 72-hour survival, survival to hospital discharge, and survival with good neurologic function.

How this is relevant to clinical practice

This Bayesian reanalysis corroborates the superiority of laryngeal tubes over intubation as initial airway management for out-of-hospital cardiac arrest.

Importance

Clinical trial results are commonly analyzed with frequentist statistical techniques, which focus on the likelihood of the observed results assuming that the null hypothesis is true, resulting in the binary interpretation of the trial results as "positive" or "negative."[11] Important limitations of frequentist analytic approaches include the inability to express the probability of the observed results, misinterpretation of the analytic framework, failure to identify differences because of flawed assumptions about the assumed effect, and the inability to incorporate existing knowledge or opinion about an intervention.

An alternative statistical approach, Bayesian analysis offers important advantages over frequentist techniques.[12-15] It can incorporate information from previous studies, providing results that reflect the influence of existing knowledge or assumptions of effect; this may be particularly important when previous evidence is opposing or conflicting. Bayesian inference provides direct estimates of the probability of an observed treatment effect, a measure that is not obtainable from frequentist approaches. Bayesian results are also expressed in a manner potentially more meaningful in clinical application. Bayesian analysis can yield important new perspectives to complement frequentist-based clinical trial findings.

Goals of This Investigation

We conducted a post hoc Bayesian analysis to assess the effect of paramedic airway management strategy on 72-hour survival, return of spontaneous circulation, hospital survival, and hospital survival with good neurologic outcome after adult out-of-hospital cardiac arrest in PART.

MATERIALS AND METHODS

Study Design

We conducted a post hoc analysis of data from PART, using Bayesian analytic techniques. The institutional review boards of the participating institutions approved the parent PART study under federal rules for conduct of emergency research under exception from informed consent (21 CFR 50.24).

Setting

We previously reported the trial methods for PART.[16] The trial included 27 EMS agencies associated with the Birmingham, AL; Dallas–Fort Worth; Milwaukee; Pittsburgh; and Portland, OR, sites of the Resuscitation Outcomes Consortium. The configuration of study EMS agencies varied, with some providing exclusively advanced life support (ALS) care and others providing tiered basic life support and ALS care. The EMS agencies primarily served urban and suburban settings, with select agencies also serving rural populations.

Selection of Participants

We included all subjects enrolled in the parent trial. PART included adults aged 18 years or older (or per local interpretation) with out-of-hospital cardiac arrest and requiring advanced airway management or bag-valve-mask ventilation. Key exclusion criteria included pregnant women, prisoners, obvious traumatic cause of arrest, and initial airway management by a nonstudy advanced EMS unit. The trial enrolled patients from December 1, 2015, through November 4, 2017.

Interventions

The interventions of PART included strategies of initial advanced airway management with laryngeal tube or intubation. EMS agencies followed local protocols for all other aspects of care. In the event of failed initial airway insertion, EMS agencies were allowed to rescue with any available airway technique. The 27 EMS agencies were organized into 13 randomization clusters, with assigned airway intervention alternating on an a priori–defined schedule of 3- to 5-month intervals.

Outcome Measures

For this analysis, we focused on the primary outcome of the trial (survival to 72 hours after the index arrest), as well as key secondary outcomes: return of spontaneous circulation (presence of palpable pulses on emergency department [ED] arrival), survival to hospital discharge, and favorable neurologic status on hospital discharge (modified Rankin Scale score $\leq$3).

Bayesian analysis incorporates existing knowledge into the estimates of treatment effects, typically from previously published studies.[12,13] We considered data from a meta-analysis by Benoit et al[6] that summarized supraglottic airway and intubation use in out-of-hospital cardiac arrest patients across 10 studies (Table E1, available online at http://www.annemergmed.com). All of the included studies were retrospective, pooled all supraglottic airway devices into a single group, and found better or similar outcomes for intubation compared with supraglottic airway.[6,7,9] We also included results from the REVIVE–Airways trial (the pilot study that preceded the larger Airways-2 trial), which randomized 615 adults with out-of-hospital cardiac arrest to intubation, i-gel, or laryngeal mask airway, observing hospital survival rates of 9.1%, 10.3%, and 8.0%, respectively.[17,18] We did not incorporate the findings of the trial by Gausche et al,[19] which compared bag-valve-mask ventilation and intubation, because the study did not include supraglottic airway use and focused on children. Consistent with Bayesian principles in defining prior probabilities, we also did not incorporate estimates from the Airways-2 trial because those results were not available at PART enrollment.[20]

We used the constituent studies of the meta-analysis by Benoit et al[6] and the REVIVE–Airways trial as the basis for defining skeptical prior distributions. Using meta-analytic techniques, we estimated pooled relative risks (RRs) of 0.83, 0.92, and 0.90 for return of spontaneous circulation, survival to hospital discharge, and neurologically intact survival to hospital discharge, respectively. We centered the skeptical prior distributions on these point estimates. To reflect the uncertainty about these estimates, we used 95% credible intervals (CrIs) ranging from half to double the assumed RR (SD 0.35 in the log RR scale; ie, 0.4 to 1.6 and 0.45 to 1.8). Because the constituent studies did not assess the 72-hour survival (the primary outcome of PART), we used the RR for survival to hospital discharge (0.92) as a surrogate.

Because the constituent studies of the meta-analysis by Benoit et al[6] all used observational designs, we were concerned that confounding by indication may have obscured the potential superiority of supraglottic airways. Furthermore, the single published randomized trial suggested higher hospital survival with i-gel than intubation (but not laryngeal mask airway).[18] Therefore, we defined a neutral prior probability distribution centered at an RR of 1.0 (eg, previous evidence suggests no difference between supraglottic airway and intubation), with a 95% CrI of 0.5 to 2.0 that excluded implausible large treatment effects (SD 0.35 in the log RR scale).[21] Because of the absence of data suggesting better outcomes with supraglottic airway than intubation, we opted not to define an optimistic prior distribution.

Primary Data Analysis

We used Bayesian log binomial models to analyze each outcome (72-hour survival, return of spontaneous circulation, hospital survival, and hospital survival with good neurologic outcome). The intervention group (laryngeal tube versus intubation) was the primary independent variable. We incorporated randomization cluster as a random effect. We developed estimates of the RR (laryngeal tube versus intubation), risk difference (laryngeal tube–intubation), and corresponding 95% CrIs for each outcome. We also estimated the posterior probability of laryngeal tube benefit (ie, probability that laryngeal tube is associated with better outcomes compared with intubation) for each model. We conducted the analyses with both neutral and skeptical prior probability distributions.

We conducted 2 sensitivity analyses to test the robustness of the findings. First, the parent trial observed slight imbalances in subject allocation between the laryngeal tube and intubation arms in select randomization clusters. Thus, we repeated the analyses with multivariate adjustment for age, sex, bystander cardiopulmonary resuscitation (CPR), bystander- or EMS-witnessed arrest, and initial ECG rhythm. Second, to test the effect of the selected prior probability thresholds, we repeated the assessment of 72-hour survival, using "highly skeptical" and "extremely skeptical" prior probabilities, centered at RRs of 0.7 and 0.6, respectively, in accordance with the studies with the largest effect favoring intubation. These latter prior probabilities were based on the most extreme RR observed in previous studies (ie, the estimate for return of spontaneous circulation by Tanabe et al[8]) and on investigator consensus to represent more extreme estimates.

We implemented the Bayesian analyses with Markov chain Monte Carlo methods. For each analysis, we ran 3 Markov chain Monte Carlo analyses with random starting values. We implemented a burn-in of 3,000 iterations, with sampling from a further 10,000 iterations for each chain. To monitor convergence, we used trace plots and the

Gelman-Rubin convergence diagnostic (Rhat) for all parameters.[22] We conducted all analyses in R (R Foundation, Vienna, Austria), using rstan and rstanarm packages.

RESULTS

The parent trial screened 3,840 patients and enrolled 3,004, including 1,505 with laryngeal tube and 1,499 with intubation. Patient characteristics between laryngeal tube and intubation were similar (Table 1). Protocol compliance for the laryngeal tube and intubation arms was 95.5% and 90.7%, respectively. Elapsed time from first EMS arrival to airway start was shorter for laryngeal tube than intubation. Initial laryngeal tube and intubation success (excluding bag-valve-mask ventilation) was 89.9% and 51.3%. Overall laryngeal tube and intubation airway success (initial+rescue airway attempts) was 94.2% and 91.5%. A total of 352 patients received only bag-valve-mask ventilation without any advanced airway insertion efforts. The proportion of patients transported to the hospital was similar between treatment groups.

On Bayesian analysis with a neutral prior probability, the laryngeal tube group exhibited higher 72-hour survival than the intubation group (risk difference 1.8%; 95% CrI –0.9% to 4.5%); the posterior probability for this relationship was high (91%) (Figure, Table 2). Under the assumption of a skeptical prior probability, the posterior probability for the risk difference between laryngeal tube

Table 1. Baseline characteristics of subjects enrolled in the PART.

Characteristic	Laryngeal Tube, N=1,505	Intubation, N=1,499
Age, median (IQR), y	64 (53–76)	64 (53–76)
Men, n/N (%)	928/1,503 (61.7)	901/1,499 (60.1)
Witnessed arrest, n/N (%)		
EMS	180/1,357 (13.3)	179/1,399 (12.8)
Bystander	511/1,357 (37.7)	529/1,399 (37.8)
None	666/1,357 (49.1)	691/1,399 (49.4)
Unknown*	148/1,505 (9.8)	100/1,499 (6.7)
Bystander chest compressions, n/N (%)		
Yes	698/1,258 (55.5)	709/1,279 (55.4)
No	560/1,258 (44.5)	570/1,279 (44.6)
Unknown*	247/1,505 (16.4)	220/1,499 (14.7)
Time from dispatch to first arrival of EMS, min		
Median (IQR)	5.0 (3.9–6.3)	5.3 (4.1–6.8)
≤4, n/N (%)	409/1,444 (28.3)	305/1,405 (21.7)
Unknown	61/1,505 (4.1)	94/1,499 (6.3)
First ECG rhythm, n/N (%)		
Shockable rhythm (ventricular fibrillation, ventricular tachycardia, or delivery of AED shock)	301/1,505 (20.0)	270/1,499 (18.0)
Nonshockable (asystole, pulseless electrical activity, or AED nonshockable)	1,160/1,505 (77.1)	1,197/1,499 (79.9)
Other	44/1,505 (2.9)	32/1,499 (2.1)
Compliance with assigned airway intervention,† n/N (%)	1,437/1,505 (95.5)	1,360/1,499 (90.7)
Elapsed times for airway placement, median (IQR) [N], min		
EMS arrival to start of first airway attempt	9.8 (7.0–13.2) [1,122]	12.5 (9.0–16.8) [1,038]
EMS arrival to successful or abandoned airway insertion	10.6 (7.7–14.0) [1,200]	13.4 (9.8–17.8) [1,038]
Start of first airway attempt to successful or abandoned airway insertion	0.5 (0.0–1.0) [1,092]	0.9 (0.0–1.1) [952]
Transported to hospital, n/N (%)	906/1,505 (60.2)	889/1,499 (59.3)

*For "unknown" values, the denominator is total patients in the group.
†Episodes were classified as compliant if the randomized airway was initially attempted or if only bag-valve-mask ventilation was used. Episodes were classified as noncompliant if another airway device was used.

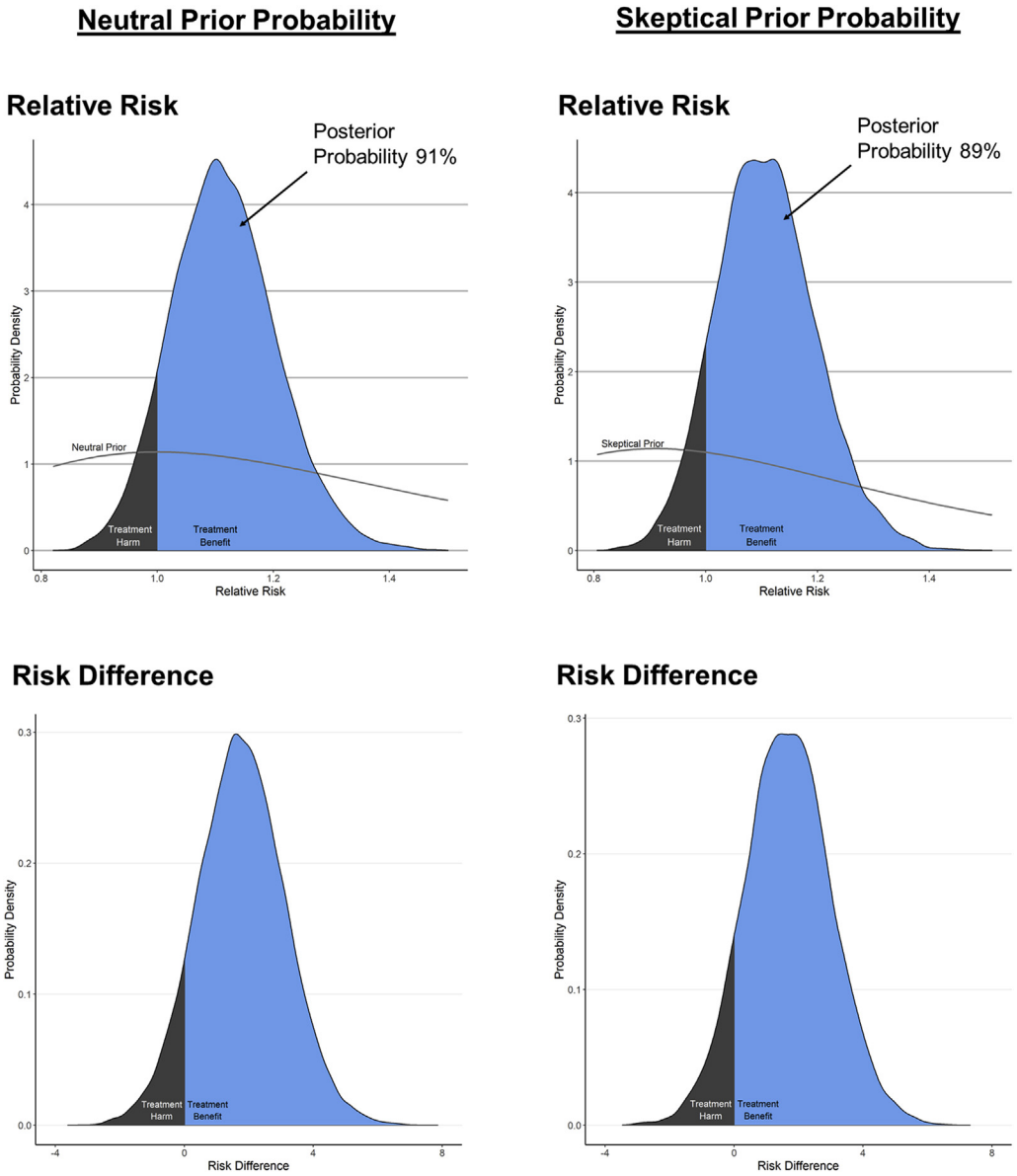

Figure. Bayesian posterior probability of effect of airway management strategy (initial laryngeal tube versus initial intubation) on 72-hour survival. The blue-shaded areas represent the posterior probability of increased 72-hour survival with laryngeal tube compared with intubation for each model. The sum of the area under each probability density curve equals 1.

and intubation remained high (89%). Rates of return of spontaneous circulation, survival to hospital discharge, and favorable neurologic status on discharge favored laryngeal tube over intubation. The observed posterior probabilities for these associations remained high across both neutral and skeptical prior probabilities (posterior probabilities 86% to 93% and 82% to 91%, respectively).

After adjustment for age, sex, witnessed arrest, bystander CPR, and initial ECG rhythm, laryngeal tube exhibited higher 72-hour survival than intubation under both neutral prior probabilities (adjusted risk difference 4.4%; 95% CrI –1.2% to 10.5%; posterior probability 94%) and skeptical prior probabilities (adjusted risk difference 4.1%; 95% CrI –1.4% to 10.1%; posterior probability 93%) (Table E2, available online at http://www.annemergmed.com). Similar associations were observed for return of spontaneous circulation, survival to hospital discharge, and favorable neurologic status at hospital discharge. Under the assumption of a highly skeptical prior probability (RR=0.7), the higher 72-hour survival for laryngeal tube persisted (risk difference 1.4%; 95% CrI –1.1% to 4.1%; posterior probability 86%) (Table E3, available online at http://www.

Table 2. Bayesian analysis of the PART.

Characteristic	Laryngeal Tube (%), N=1,505	Intubation (%), N=1,499	Bayesian Analysis Neutral Prior Probability: Prior Distribution ln(RR)	RR* (95% CrI)	Risk Difference, %† (95% CrI)	Posterior Probability,‡ %	Bayesian Analysis Skeptical Prior Probability: Prior Distribution ln(RR)	RR* (95% CrI)	Risk Difference, %† (95% CrI)	Posterior Probability,‡ %
Primary outcome										
Survival to 72 h (intention-to-treat population)	275/1,505 (18.3)	230/1,495 (15.4)	Normal (0 to 0.35) [RR=1.0]	1.11 (0.95 to 1.30)	1.8 (−0.9 to 4.5)	91	Normal (−0.094 to 0.35) [RR=0.92]	1.10 (0.94 to 1.29)	1.7 (−0.9 to 4.3)	89
Secondary outcomes										
Return of spontaneous circulation on ED arrival	420/1,505 (27.9)	365/1,499 (24.3)	Normal (0 to 0.35) [RR=1.0]	1.07 (0.95 to 1.21)	1.7 (−1.3 to 4.9)	88	Normal (−0.198 to 0.35) [RR=0.83]	1.07 (0.95 to 1.20)	1.6 (−1.4 to 4.7)	86
Survival to hospital discharge	163/1,504 (10.8)	121/1,495 (8.1)	Normal (0 to 0.35) [RR=1.0]	1.18 (0.95 to 1.46)	1.4 (−0.4 to 3.4)	93	Normal (−0.094 to 0.35) [RR=0.92]	1.16 (0.94 to 1.43)	1.3 (−0.5 to 3.3)	91
Favorable neurologic status at discharge (modified Rankin Scale score ≤3)	107/1,500 (7.1)	75/1,495 (5.0)	Normal (0 to 0.35) [RR=1.0]	1.17 (0.90 to 1.53)	0.7 (−0.5 to 2.1)	86	Normal (−0.105 to 0.35) [RR=0.90]	1.14 (0.88 to 1.50)	0.6 (−0.5 to 2.0)	82

Results of unadjusted analyses. Models account for clustering by randomization block.
*Laryngeal tube versus intubation.
†Laryngeal tube–intubation.
‡Posterior probability of treatment benefit from laryngeal tube.

annemergmed.com). Under the assumption of an extremely skeptical prior probability (RR=0.6), the higher 72-hour survival for laryngeal tube persisted (risk difference 1.3%; 95% CrI –1.3% to 4.0%; posterior probability 84%). High posterior probabilities also persisted for the other out-of-hospital cardiac arrest endpoints under the more extreme prior probability assumptions.

LIMITATIONS

Limitations of the parent PART include its pragmatic approach using existing clinical practice methods and protocols, a low airway insertion success rate in the intubation arm (51.6%), slight imbalance in subject allocation in select randomization clusters, and mitigation of observed effects on multivariable adjustment. The parent trial also did not analyze chest compression and ventilation data.[23-25] The current Bayesian analysis does not overcome these limitations. Rather, our results offer alternate analytic perspectives that complement the parent frequentist analysis.

Our Bayesian findings are based on post hoc analyses and should be interpreted with caution. The quality of previous studies influences the quality of prior distributions. We based prior probability estimates on published studies that were largely observational and retrospective; there were few clinical trials to guide estimates of prior probabilities. We excluded an enthusiastic prior probability because of the absence of existing data favoring supraglottic airway over intubation, but additional future studies could shift existing knowledge. The previous studies also pooled supraglottic airways; we assumed that these figures would provide a reasonable basis for our analysis of laryngeal tube. To account for the possibility that we were too conservative in baseline assumptions, we tested the models with highly and extremely skeptical scenarios, attaining largely similar results.

We did not include the results of the Airways-2 trial in the formulation of prior probabilities.[20] However, Airways-2 observed no difference in hospital survival between i-gel insertion and intubation, and therefore we expect that this study would reinforce a neutral prior probability distribution. We did not try to elicit prior probabilities from expert clinician opinion. None of the previous studies evaluated 72-hour survival; our use of survival to hospital discharge as the basis for 72-hour survival may have overestimated this parameter.

Because of the post hoc nature of this analysis, we opted to focus on the primary outcomes of the trial. We chose not to evaluate other secondary trial outcomes such as EMS airway management course and hospital adverse events.

DISCUSSION

This post hoc Bayesian analysis provides important information to complement and support the findings of the parent PART study, affirming the superiority of initial laryngeal tube over initial intubation strategies in adult out-of-hospital cardiac arrest resuscitation across all major study endpoints (72-hour survival, hospital survival, and hospital survival with favorable neurologic status).[14] Although previous studies have suggested better outcomes with intubation than supraglottic airway, the current Bayesian analysis indicated strong posterior probabilities favoring laryngeal tube over intubation under a range of prior probability assumptions. The Bayesian associations persisted even after multivariable adjustment and consideration of more extreme prior probability distributions.

Bayesian analysis offers important advantages over traditional frequentist approaches.[12-15] The interpretation of trial results may be difficult if there is lack of clarity from previous studies or a divergence of existing opinion in regard to the effectiveness of an intervention. However, Bayesian approaches directly incorporate previous knowledge into the assessment of the current results, explicitly quantifying the influence of clinical judgment and previous beliefs on the inferences of the current trial.[14] For example, our Bayesian analysis of PART suggests that there is a strong positive association between the laryngeal tube strategy and improved out-of-hospital cardiac arrest outcomes, even though almost all previous observational studies favored intubation.[6] Concerns about the subjective nature of prior probability selection may be mitigated by exploration of a range of prior assumptions. For example, in the current analysis we found that the superiority of laryngeal tube over intubation persisted even after consideration of highly and extremely skeptical prior probabilities.

Bayesian estimates are often more intuitive, indicating the probability of the hypothesis, given the data, rather than the frequentist approach of estimating the probability of the data, given the hypothesis.[14] Bayesian analysis can also provide direct probability estimates for specific effect thresholds.[14] For example, the current analysis indicates that under neutral prior assumption, there is a 91% chance that laryngeal tube results in any 72-hour survival higher than that of intubation. However, clinicians might be interested in the likelihood of particular effect sizes. For example, in this case, the posterior probability of a greater than or equal to 1% difference in 72-hour survival is 71%. Similarly, the posterior probabilities for greater than or equal to 2% or greater than or equal to 3% differences in 72-hour survival are 43% and 18%, respectively.

Previous studies have similarly demonstrated the utility of post hoc Bayesian analyses in aiding the interpretation of

a parent frequentist trial.[14,26,27] For example, the Extracorporeal Membrane Oxygenation (ECMO) to Rescue Lung Injury in Severe Acute Respiratory Distress Syndrome (ARDS) trial reported no association between early ECMO and mortality in severe ARDS, but the trial was stopped early for futility and nearly reached statistical significance.[28] In addition, there was a wide divergence of preexisting opinion in regard to the benefit of ECMO. However, the Goligher et al[14] post hoc Bayesian analysis of the ECMO to Rescue Lung Injury in Severe ARDS trial suggested that ECMO may be beneficial under a range of prior probability assumptions. The post hoc Bayesian analysis by Brophy and Johnson[26] of the Global Utilization of Streptokinase and Tissue Plasminogen Activator in Occluded Arteries trial raised uncertainty about the superiority of tissue plasminogen activator over streptokinase observed on frequentist analysis.

An important question is whether a Bayesian framework might prove advantageous in future airway management studies. In addition to PART, 2 other recent clinical trials tested EMS airway management strategies in out-of-hospital cardiac arrest; Airways-2 compared i-gel with intubation, and the Cardiac Arrest Airway Management trial compared bag-valve-mask ventilation with intubation.[20,29] The results of these trials can now be incorporated as prior probability information in future Bayesian efforts. The decision to conduct a future clinical trial often hinges on the subjective assessments of the existing frequentist trial results; for example, judging that a study "almost reached statistical significance." Bayesian posterior probabilities provide better measures to guide these types of assessment. Bayesian designs may also result in lower sample size requirements than do frequentist approaches.[15] Future airway management trials may encompass direct comparison of supraglottic airway subtypes or the assessment of advanced airway management in trauma and pediatric populations. Strategies to reduce required sample size will enhance the feasibility of these trials.

In conclusion, under various prior assumptions of treatment effect, post hoc Bayesian analysis of PART confirmed better out-of-hospital cardiac arrest outcomes with initial laryngeal tube than initial intubation airway management strategies. Bayesian analysis offers an important and novel option for assessing the effects of out-of-hospital resuscitation interventions.

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