Association of Prehospital Advanced Airway Management With Neurologic Outcome and Survival in Patients With Out-of-Hospital Cardiac Arrest

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Objective To test the hypothesis that prehospital advanced airway management is associated with favorable outcome after adult OHCA.

Design, Setting, and Participants Prospective, nationwide, population-based study (All-Japan Utstein Registry) involving 649,654 consecutive adult patients in Japan who had an OHCA and in whom resuscitation was attempted by emergency responders with subsequent transport to medical institutions from January 2005 through December 2010.

Main Outcome Measures Favorable neurological outcome 1 month after an OHCA, defined as cerebral performance category 1 or 2.

Results Of the eligible 649,359 patients with OHCA, 367,837 (57%) underwent bag-valve-mask ventilation and 281,522 (43%) advanced airway management, including 41,972 (6%) with endotracheal intubation and 239,550 (37%) with use of supraglottic airways. In the full cohort, the advanced airway group incurred a lower rate of favorable neurological outcome compared with the bag-valve-mask group (1.1% vs 2.9%; odds ratio [OR], 0.38; 95% CI, 0.37-0.39). In multivariable logistic regression, advanced airway management had an OR for favorable neurological outcome of 0.38 (95% CI, 0.37-0.40) after adjusting for age, sex, etiology of arrest, first documented rhythm, witnessed status, type of bystander cardiopulmonary resuscitation, use of public access automated external defibrillator, epinephrine administration, and time intervals. Similarly, the odds of neurologically favorable survival were significantly lower both for endotracheal intubation (adjusted OR, 0.41; 95% CI, 0.37-0.45) and for supraglottic airways (adjusted OR, 0.38; 95% CI, 0.36-0.40). In a propensity score–matched cohort (357,228 patients), the adjusted odds of neurologically favorable survival were significantly lower both for endotracheal intubation (adjusted OR, 0.45; 95% CI, 0.37-0.55) and for use of supraglottic airways (adjusted OR, 0.36; 95% CI, 0.33-0.39). Both endotracheal intubation and use of supraglottic airways were similarly associated with decreased odds of neurologically favorable survival.

Conclusion and Relevance Among adult patients with OHCA, any type of advanced airway management was independently associated with decreased odds of neurologically favorable survival compared with conventional bag-valve-mask ventilation.

Importance It is unclear whether advanced airway management such as endotracheal intubation or use of supraglottic airway devices in the prehospital setting improves outcomes following out-of-hospital cardiac arrest (OHCA) compared with conventional bag-valve-mask ventilation.
METHODS
Study Design and Participants
The All-Japan Utstein Registry of the Fire and Disaster Management Agency (FDMA) is a prospective, nationwide, population-based registry system of OHCA in adults and children, with Utstein-style data collection. This study enrolled all adults aged 18 years or older who had OHCA and for whom resuscitation was attempted by EMS personnel with subsequent transport to medical institutions from January 1, 2005, to December 31, 2010. Patients were excluded from the analysis if out-of-hospital airway management or age was not documented. Cardiac arrest was defined as the end of cardiac mechanical activity determined by the absence of signs of circulation. The ethics committees of Kinki University Faculty of Medicine and Massachusetts General Hospital approved the study with a waiver of informed consent.

Study Setting
The population of Japan was roughly 128 million in 2010, with approximately 107 million people aged 18 years or older. The EMS system in Japan has been described previously. Briefly, in Japan, municipal governments provided EMS through 802 fire stations with dispatch centers. All EMS personnel performed CPR according to the Japanese CPR guidelines, which are based on the American Heart Association and the International Liaison Committee on Resuscitation. In most cases, an ambulance crew consisted of 3 EMS personnel, including at least 1 emergency lifesaving technician who had completed extensive training. These technicians were authorized to insert an intravenous line, to use semiautomated external defibrillators, and to lead CPR. In 1991, emergency lifesaving technicians were also permitted to use supraglottic airway devices (laryngeal mask airway, laryngeal tube, and esophageal-tracheal twin-lumen airway device) for patients with OHCA under medical control direction. Beginning in 2004, endotracheal intubation could be performed by specially trained emergency lifesaving technicians who had completed an additional 62 hours of training sessions and performed 30 supervised successful intubations in operating rooms.

Under medical control direction in the placement of an advanced airway device, the choice of either endotracheal intubation or supraglottic airway was at the discretion of each specially trained emergency lifesaving technician. Advanced airway management was performed, with efforts limited to a total of 2 attempts, after checking initial rhythm and using defibrillation when appropriate, along with chest compression and bag-valve-mask ventilation. Advanced airway device placement with successful ventilation was confirmed by an esophageal detection device and/or an end-tidal carbon dioxide monitor (quantitative or colorimetric). The performance of CPR including prehospital advanced airway management was reviewed by local medical control committees.

Data Collection and Quality Control
Data were collected prospectively with an Utstein-style data form that included sex, age, etiology of arrest, bystander witness status, first documented cardiac rhythm, presence and type of CPR by bystander, administration of epinephrine by EMS personnel, and technique of airway management. A series of EMS times of call receipt, vehicle arrival at the scene, contact with patients, initiation of CPR, and hospital arrival were recorded based on the clock used by each EMS system. Outcome measures included return of spontaneous circulation before hospital arrival, 1-month survival, and neurological status 1 month after the event. To collect 1-month follow-up data, the EMS personnel in charge of each patient with OHCA queried the medical control director at the hospital. Patient neurological status was determined by the treating physician; the EMS received a written response. If the patient was not at the hospital, the EMS personnel conducted a follow-up search.

Data forms were completed by the EMS personnel caring for the patients, and the data were integrated into the Utstein registry system on the FDMA database server. Forms were logically checked by the computer system and were confirmed by the FDMA. If the data form was incomplete, the FDMA returned it to the respective fire station and the data were reconfirmed.

Study End Points
The primary end point was favorable neurological outcome 1 month after cardiac arrest, defined a priori as Glasgow-Pittsburgh cerebral performance category 1 (good performance) or 2 (moderate disability). The other categories—3 (severe cerebral disability), 4 (vegetative state), and 5 (death)—were regarded as unfavorable neurological outcomes. Secondary outcome measures were return of spontaneous circulation before hospital arrival and 1-month survival.

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PREHOSPITAL ADVANCED AIRWAY MANAGEMENT FOR OUT-OF-HOSPITAL CARDIAC ARREST

Statistical Analysis

We compared outcomes between any advanced airway management and bag-valve-mask ventilation for all adult OHCA. Then, we compared outcomes between either advanced airway technique (endotracheal intubation or supraglottic airways) and bag-valve-mask ventilation. With the full cohort, 3 unconditional logistic regression models (unadjusted, adjusted for selected variables, and adjusted for all covariates) were fit using each of the 3 end points as a dependent variable. A set of potential confounders was chosen a priori based on biological plausibility and a priori knowledge. These selected variables included age, sex, cause of cardiac arrest, first documented rhythm, witnessed status, type of bystander CPR, use of a public access automated external defibrillator, epinephrine administration, and time intervals from receipt of call to CPR by EMS and from receipt of call to hospital arrival. All covariates included the selected variables above and year, lifesaving technician presence, physician presence in ambulance, defibrillation by EMS personnel, insertion of intravenous line, and prefecture.

Our data derive from 367,837 patients who underwent bag-valve-mask ventilation and 281,522 who underwent advanced airway management. On the assumption of an incidence of 3.0% favorable neurological outcomes in the bag-valve-mask group, the study has 90% power to detect a difference as small as 0.16% between the groups for a 2-sided significance level of 0.05.

Prehospital advanced airway management was not randomly assigned in the study population; therefore, we used a propensity score approach to condition on potential selection bias and confounding. With a multivariable logistic regression model that did not take end points into account, we computed the propensity score, which represented the probability that a patient with cardiac arrest would undergo prehospital advanced airway management. Specifically, a full nonparsimonious model was fit with advanced airway management as the dependent variable, which included the variables in Table 1 in addition to dummy variables for the 47 prefectures in Japan as the independent variables. To maximize the efficacy of propensity score matching, missing values for categori-
cal variables included in the propensity score model (bystander witness status, bystander CPR, use of a public access automated external defibrillator, use of epinephrine, defibrillation by EMS, and insertion of intravenous line) were dummy coded using the missing indicator method (eTable 1; available at http://www.jama.com).

Using the match algorithm by Parsons,25 based on propensity score, a subgroup of patients with cardiac arrest requiring advanced airway management were matched with unique control patients who underwent bag-valve-mask ventilation. Then, 3 conditional logistic regression models (unadjusted, adjusted for selected variables, and adjusted for all covariates) were fit with each of the 3 end points as a dependent variable.

All statistical analyses were performed with SAS statistical software, version 9.3 (SAS Institute Inc). All statistical tests were 2-tailed. The chosen type I error rate was P<.05, except when testing the subgroup of patients with endotracheal intubation or supraglottic airways for which a Bonferroni adjustment for multiplicity was used (P<.025).

RESULTS

A total of 658,829 adult patients with OHCA were documented. Among 649,654 resuscitation attempts, 295 arrests with unknown airway management status were excluded (Figure 1). Of the remaining 649,359 patients, 367,837 (56.7%; 95% CI, 56.5%-56.8%) underwent bag-valve-mask and 281,522 (43.4%; 95% CI, 43.2%-43.5%) underwent advanced airway management, including 41,972 (6.5%; 95% CI, 6.4%-6.5%) with endotracheal intubation and 239,550 (36.9%; 95% CI, 36.8%-37.0%) with supraglottic airways.

Table 1 shows the demographic characteristics for adult OHCA by type of care. The mean age of all patients was 73 years; the majority were male. Table 2 summarizes survival outcomes by airway management among all patients. Overall, rates of return of spontaneous circulation, 1-month survival, and neurologically favorable survival were 6.5% (95% CI, 6.5%-6.6%), 4.7% (95% CI, 4.7%-4.8%), and 2.2% (95% CI, 2.1%-2.2%), respectively. The rates of neurologically favorable survival were 1.0% (95% CI, 0.9%-1.1%) in the endotracheal intubation group, 1.1% (95% CI, 1.1%-1.2%) in the supraglottic airway group, and 2.9% (95% CI, 2.9%-3.0%) in the bag-valve-mask ventilation group. The unadjusted model using the full cohort demonstrated significant negative associations between any advanced airway management and the 3 end-point measures (P<.001 for all) (Table 2). Similarly, in the adjusted model using the selected variables and all variables, both advanced airway techniques (endotracheal intubation and supraglottic airways) were independent negative predictor of all 3 outcomes (P<.001 for all; Table 2).

To assess the robustness of the results, we performed a series of sensitivity analyses (Table 3). First, in an analysis of patients lost to follow-up, when assuming that all missing patients in the bag-valve-mask group (n=444) had an unfavorable neurological outcome and all missing patients in the advanced airway group (n=366) had a favorable outcome, advanced airway management was still a significant negative predictor of favorable neurological outcome after adjusting for selected variables (adjusted odds ratio [OR], 0.43; 95% CI, 0.42-0.45). When adjusting for achievement of return of spontaneous circulation in addition to the selected variables, the adjusted association of endotracheal intubation and supraglottic airways with poor neurological outcome persisted (OR, 0.51 [95% CI, 0.45-0.56] and OR, 0.52 [95% CI, 0.49-0.54], respectively) (Table 3). Similarly, the adjusted association persisted with stratification by achievement of return of spontaneous circulation, etiology of cardiac arrest, first documented rhythm, and type of witness status (Table 3).

Demographic characteristics were similar between the propensity-matched groups (Table 4). Figure 2 and eTable 2 summarize survival outcomes by airway management among propensity-matched patients. The unadjusted model showed significant negative associations between advanced airway management, regardless of its technique, and the 3 end-
point measures (P < .001 for all). In the multivariable models using selected and all variables, significant negative associations were detected between any type of advanced airway management and the 3 outcome measures (Figure 2). In particular, the adjusted OR for neurologically favorable survival was 0.45 (95% CI, 0.37-0.55; P < .001) for endotracheal intubation and 0.36 (95% CI, 0.33-0.39; P < .001) for supraglottic airways compared with bag-valve-mask ventilation after controlling for the selected variables.

**COMMENT**

In this nationwide population-based cohort study of patients with OHCA, we found that CPR with advanced airway management was a significant predictor of poor neurological outcome compared with conventional bag-valve-mask ventilation. Unlike an earlier study that was underpowered to identify this clinically important association,\(^1\) our study was sufficiently large to clearly demonstrate the negative association between advanced airway management and neurologically favorable survival after cardiac arrest. Furthermore, both endotracheal intubation and supraglottic airways were similarly associated with a decreased chance of favorable neurological outcome. The observed associations were large and persisted across different analytic assumptions.

Our clinical data are consistent with findings from several studies in trauma and pediatric patients.\(^7\) These studies have suggested that prehospital endotracheal intubation may lead to a decreased rate of favorable neurological outcome, and only a few studies have demonstrated benefit from endotracheal intubation.\(^7\) Additionally, several studies of OHCA have demonstrated the association between endotracheal intubation and decreased survival to hospital discharge.\(^6\) An important unanswered question regards the mechanism connecting endotracheal intubation with poor outcomes. It has been well documented that prehospital intubation is a complex psychomotor task and that EMS personnel have difficulty gaining and maintaining competency in this skill.\(^7\) Endotracheal intubation by unskilled practitioners can produce ad-

<table>
<thead>
<tr>
<th>Model</th>
<th>Total No. of Patients</th>
<th>Bag-Valve-Mask Ventilation, No. (%)</th>
<th>Overall</th>
<th>Endotracheal Intubation</th>
<th>Supraglottic Airway</th>
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<td></td>
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<td>OR (95% CI) vs Bag-Valve-Mask(^a)</td>
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<tr>
<td>Total</td>
<td>649 859</td>
<td>367 837 (56.7)</td>
<td>281 522 (43.4)</td>
<td>41 972 (6.5)</td>
<td>239 550</td>
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<td></td>
<td>1.0 (1.0)</td>
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Abbreviation: OR, odds ratio.

\(^a\)P < .001 for all.

\(^b\)Selected variables are a predefined set of potential confounders including age, sex, cause of cardiac arrest, first documented rhythm, bystander witness, type of cardiopulmonary resuscitation (CPR) initiated by bystander, use of a public access automated external defibrillator by bystander, epinephrine administration, time from receipt of call to CPR by emergency medical service, and time from receipt of call to hospital arrival.

\(^c\)Adjustment for all variables included in Table 1 and dummy variables for the 47 prefectures in Japan.

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verse events, such as unrecognized esophageal intubation, tube dislodge-
ment, iatrogenic hypoxemia, and bradycardia.26 Furthermore, prehospital in-
tubation may influence patient outcome by affecting the execution of simulta-
neous basic life support procedures, result-
ing in ineffective chest compres-
sions with significant interruptions.7

Most studies of prehospital airway management using supraglottic air-
ways have focused on process mea-
sures, such as success rates and speed
of placement. Most of these found
higher success rates and faster place-
ment for the supraglottic airways.27-29

From a physiological perspective, one
might expect this to translate into bet-
ter outcomes because of fewer inter-
ruptions of chest compressions. How-
ever, we observed that not only endotracheal intubation but also
supraglottic airways were indepen-
dently associated with a lower rate of
neurologically favorable survival. Our
finding is consistent with a recent
study that failed to demonstrate a sur-
vival advantage with supraglottic air-
ways in patients with OHCA.12

Assuming the validity of our study, a
more secure airway, regardless of its
technique, would be detrimental. Pre-
vious studies have shown that inadvertent hyperventilation after
advanced airway management can
cause increased intrathoracic pressure,
leading to decreased coronary and
cerebral perfusion pressure among
intubated patients with OHCA.30,31

The literature has also reported that
hyperoxia among patients following
resuscitation from cardiac arrest was
associated with increased mortal-
ity.32,33 These unanticipated physi-
ologic effects may offset the potential
benefits of proper advanced airway
management.

High-quality prospective clinical
trials of prehospital airway manage-
ment would be instrumental in reveal-
ing causality between airway manage-
ment and outcome. A broad array of
methods for analyzing the associa-
tion between advanced airway
management and neurologic outcome
was used in our study. We compared
the associations of supraglottic air-
ways with outcomes adjusting for
age, sex, cause of cardiac arrest, first
documented rhythm, bystander witness,
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tion, time from receipt of call to CPR by EMS,
and time from receipt of call to hospital arrival.

A limitation of the study is the
missing data in the OHCA Registry
database. Some patients may have
been transported to the hospital in
the presence of paramedics who
were not the initial responders.
Additionally, some patients may
have died before they were eval-
uated by paramedics.

Table 3. Sensitivity and Stratified Analyses of Multivariable Associations With Neurologically Favorable Survival and Airway Management in the Total Patient Population

<table>
<thead>
<tr>
<th>Model</th>
<th>Total No. of Patients</th>
<th>Bag-Valve-Mask</th>
<th>OR (95% CI) vs Bag-Valve-Mask</th>
<th>No. (%</th>
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<th>No. (%</th>
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<th>No. (%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity analysis Including loss to follow-up</td>
<td>649359</td>
<td>10759 (2.0)</td>
<td>3522 (1.3)</td>
<td>0.43 (0.42-0.45)</td>
<td>457 (1.1)</td>
<td>0.44 (0.39-0.48)</td>
<td>3065 (1.3)</td>
<td>0.43 (0.41-0.45)</td>
</tr>
<tr>
<td>Adjusted for ROSC</td>
<td>648517</td>
<td>10759 (2.9)</td>
<td>3516 (1.1)</td>
<td>0.51 (0.45-0.56)</td>
<td>432 (1.0)</td>
<td>0.51 (0.45-0.56)</td>
<td>2724 (1.1)</td>
<td>0.52 (0.49-0.54)</td>
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<tr>
<td>Stratification by achievement of ROSC prior to hospital arrival</td>
<td>42203</td>
<td>8660 (33.5)</td>
<td>2184 (13.4)</td>
<td>0.61 (0.57-0.65)</td>
<td>297 (8.5)</td>
<td>0.65 (0.57-0.75)</td>
<td>1887 (14.5)</td>
<td>0.60 (0.56-0.64)</td>
</tr>
<tr>
<td>No ROSC</td>
<td>607123</td>
<td>2098 (0.6)</td>
<td>969 (0.4)</td>
<td>0.65 (0.60-0.71)</td>
<td>134 (0.4)</td>
<td>0.71 (0.59-0.85)</td>
<td>835 (0.4)</td>
<td>0.65 (0.59-0.73)</td>
</tr>
<tr>
<td>Stratification by etiology Cardiac origin</td>
<td>359733</td>
<td>8199 (4.2)</td>
<td>2410 (1.5)</td>
<td>0.36 (0.34-0.38)</td>
<td>293 (1.3)</td>
<td>0.36 (0.32-0.41)</td>
<td>2117 (1.5)</td>
<td>0.36 (0.34-0.39)</td>
</tr>
<tr>
<td>Noncardiac origin</td>
<td>289626</td>
<td>2560 (1.5)</td>
<td>746 (0.6)</td>
<td>0.46 (0.42-0.50)</td>
<td>139 (0.7)</td>
<td>0.51 (0.43-0.61)</td>
<td>607 (0.6)</td>
<td>0.45 (0.41-0.49)</td>
</tr>
<tr>
<td>Stratification by initial rhythm Ventricular fibrillation or ventricular tachycardia</td>
<td>48233</td>
<td>5296 (20.1)</td>
<td>1697 (7.8)</td>
<td>0.36 (0.34-0.39)</td>
<td>189 (6.6)</td>
<td>0.34 (0.29-0.40)</td>
<td>1508 (8.0)</td>
<td>0.37 (0.34-0.39)</td>
</tr>
<tr>
<td>Pulsless electrical activity/asystole</td>
<td>601126</td>
<td>5463 (1.6)</td>
<td>1459 (0.6)</td>
<td>0.40 (0.38-0.43)</td>
<td>243 (0.6)</td>
<td>0.47 (0.42-0.54)</td>
<td>1216 (0.6)</td>
<td>0.39 (0.37-0.42)</td>
</tr>
<tr>
<td>Stratification by witness status Not witnessed</td>
<td>367363</td>
<td>1635 (0.8)</td>
<td>665 (0.4)</td>
<td>0.49 (0.44-0.53)</td>
<td>80 (0.4)</td>
<td>0.47 (0.37-0.59)</td>
<td>585 (0.4)</td>
<td>0.49 (0.44-0.54)</td>
</tr>
<tr>
<td>Witnessed by layperson</td>
<td>212639</td>
<td>5690 (5.1)</td>
<td>2068 (2.0)</td>
<td>0.39 (0.37-0.41)</td>
<td>303 (1.8)</td>
<td>0.43 (0.38-0.49)</td>
<td>1765 (2.1)</td>
<td>0.38 (0.36-0.43)</td>
</tr>
<tr>
<td>Witnessed by EMS</td>
<td>52893</td>
<td>3383 (8.8)</td>
<td>383 (2.7)</td>
<td>0.29 (0.26-0.32)</td>
<td>43 (2.3)</td>
<td>0.27 (0.20-0.37)</td>
<td>340 (2.8)</td>
<td>0.29 (0.26-0.33)</td>
</tr>
</tbody>
</table>

Abbreviations: EMS, emergency medical service; OR, odds ratio; ROSC, return of spontaneous circulation.

2Unconditional logistic regression models adjusted for selected variables including age, sex, cause of cardiac arrest, first documented rhythm, bystander witness, type of cardiopulmonary resuscitation (CPR) initiated by bystander, use of a public access automated external defibrillator by bystander, epinephrine administration, time from receipt of call to CPR by EMS, and time from receipt of call to hospital arrival.

3P<.001 for all.

4Adjusted for achievement of ROSC in addition to the above selected variables.

5Adjusted for time from cardiopulmonary resuscitation by EMS to ROSC in addition to the above selected variables.
ment and outcomes. However, such trials are logistically and methodologically difficult in this clinical setting. Additionally, as trials are often designed to address specific questions in select groups, the characteristics of trial populations may differ significantly from those of the general population. As an alternative, our prospective nationwide cohort data reflect the effectiveness of prehospital airway management in the natural setting of a “real” population and current clinical practice, therefore enhancing the potential generalizability of the findings. In addition, multiple studies arrived at similar conclusions despite differing populations, disease groups, and designs. There are plausible mechanisms to support this conclusion. Thus, our data lend significant support to the concept that prehospital intubation and its alternatives are less effective, or even harmful, than was previously believed.

Should clinicians avoid advanced airway management during CPR based on the best available observational evidence? Although one option would be to remove advanced airway management from the skill set of all out-of-hospital rescuers, that approach would disregard situations in which advanced airway management would be expected to be efficacious, especially for long-distance transfers and respiratory failure not yet with cardiac arrest. Future research will need to identify whether there are subsets of patients for whom prehospital advanced airway management is beneficial. In addition, as observational studies cannot establish causal relationships in the way that randomized trials can, a rigorously conducted and adequately powered clinical trial evaluating this criterion standard in patients with OHCA now seems timely and necessary. While awaiting results of such a trial, we believe that decision makers for communities and national organizations should rethink the approach to prehospital airway management and need to invest more resources in optimizing the first 3 links in the chain of survival for the promotion of better outcomes among patients with OHCA.

This study has several limitations. First, as with any observational study, the negative association between any type of out-of-hospital advanced airway management and favorable neurological outcome does not necessarily prove causality and might be confounded by unmeasured factors. Despite a rigorous adjustment for confounding factors with a propensity score–matched analysis, there are other variables that may have contributed for which our study was unable to control or that were not collected a priori. Examples of potential confounding variables include rural or urban distinction, location of cardiac arrest, time interval from cardiac arrest onset to CPR among unwitnessed cardiac arrests, individual rescuer training levels, hospital-level variables, and postresuscitation care such as induced hypothermia therapy. Additionally, one might surmise that patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Advanced Airway Management (n = 178,614)</th>
<th>Bag-Valve-Mask Ventilation (n = 178,614)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients per year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>27,058 (15.1)</td>
<td>27,795 (15.6)</td>
</tr>
<tr>
<td>2006</td>
<td>28,002 (15.7)</td>
<td>28,367 (15.9)</td>
</tr>
<tr>
<td>2007</td>
<td>28,448 (15.9)</td>
<td>28,494 (16.0)</td>
</tr>
<tr>
<td>2008</td>
<td>30,771 (17.2)</td>
<td>30,284 (17.0)</td>
</tr>
<tr>
<td>2009</td>
<td>31,294 (17.5)</td>
<td>30,784 (17.2)</td>
</tr>
<tr>
<td>2010</td>
<td>33,041 (18.5)</td>
<td>32,892 (18.4)</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>72.9 (15.8)</td>
<td>72.9 (16.8)</td>
</tr>
<tr>
<td>Male sex</td>
<td>104,427 (58.5)</td>
<td>104,575 (58.5)</td>
</tr>
<tr>
<td>Etiology of cardiac arrest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>99,383 (55.6)</td>
<td>99,586 (55.8)</td>
</tr>
<tr>
<td>Noncardiac</td>
<td>79,231 (44.4)</td>
<td>79,028 (44.2)</td>
</tr>
<tr>
<td>Initial cardiac rhythm</td>
<td></td>
<td></td>
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<tr>
<td>Ventricular fibrillation or tachycardia</td>
<td>13,519 (7.6)</td>
<td>13,557 (7.6)</td>
</tr>
<tr>
<td>Pulseless electrical activity/asystole</td>
<td>165,065 (92.4)</td>
<td>165,057 (92.4)</td>
</tr>
<tr>
<td>Bystander witness status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No witness</td>
<td>102,437 (57.4)</td>
<td>102,435 (57.3)</td>
</tr>
<tr>
<td>Layperson</td>
<td>60,143 (33.7)</td>
<td>60,581 (33.9)</td>
</tr>
<tr>
<td>Health care practitioner</td>
<td>11,704 (6.6)</td>
<td>11,149 (6.2)</td>
</tr>
<tr>
<td>CPR by bystander</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No bystander CPR</td>
<td>106,591 (59.7)</td>
<td>105,753 (59.2)</td>
</tr>
<tr>
<td>Compression-only CPR</td>
<td>46,814 (26.2)</td>
<td>47,290 (26.5)</td>
</tr>
<tr>
<td>Conventional CPR</td>
<td>22,850 (12.8)</td>
<td>23,224 (13.0)</td>
</tr>
<tr>
<td>Use of public access AED by bystander</td>
<td>921 (0.5)</td>
<td>924 (0.5)</td>
</tr>
</tbody>
</table>

Abbreviations: AED, automated external defibrillator; CPR, cardiopulmonary resuscitation; IQR, interquartile range.
with return of spontaneous circulation prior to any airway management would have subsequently received bag-valve-mask ventilation rather than advanced airway management. These patients may have had neurologically favorable survival more frequently because of early return of spontaneous circulation rather than choice of airway management. However, the subgroup analysis limited to patients who achieved return of spontaneous circulation prior to hospital arrival demonstrated that advanced airway management, regardless of its type, still remained a significant negative predictor for the outcome even after adjusting for time interval from CPR to return of spontaneous circulation. Similarly, in the subgroup analysis of patients who did not achieve return of spontaneous circulation, the adjusted association of advanced airway management with poor neurological outcome persisted. Both suggest that this choice of airway management is the important variable.

Our study is also limited by the absence of information regarding the process of intubation. Indeed, up to 20% of out-of-hospital tracheal intubation efforts may fail.36 However, we defined advanced airway management as suc-

**Figure 2.** Results of Conditional Logistic Regression Models Using One of the End Points as a Dependent Variable With Propensity-Matched Patients

<table>
<thead>
<tr>
<th>A</th>
<th>Endotracheal intubation vs bag-valve-mask ventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. (%)</strong></td>
<td><strong>Odds Ratio (95% CI)</strong></td>
</tr>
<tr>
<td><strong>Model</strong></td>
<td><strong>Total No. of Patients</strong></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Return of spontaneous circulation</td>
<td>357228</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>26019 (7.3)</td>
</tr>
<tr>
<td>Adjusted for selected variables</td>
<td>357228</td>
</tr>
<tr>
<td>Adjusted for all variables</td>
<td>357228</td>
</tr>
<tr>
<td>1-month survival</td>
<td>357228</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>357228</td>
</tr>
<tr>
<td>Adjusted for selected variables</td>
<td>357228</td>
</tr>
<tr>
<td>Adjusted for all variables</td>
<td>357228</td>
</tr>
<tr>
<td>Neurologically favorable survival</td>
<td>357228</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>357228</td>
</tr>
<tr>
<td>Adjusted for selected variables</td>
<td>357228</td>
</tr>
<tr>
<td>Adjusted for all variables</td>
<td>357228</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B</th>
<th>Supraglottic airway vs bag-valve-mask ventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. (%)</strong></td>
<td><strong>Odds Ratio (95% CI)</strong></td>
</tr>
<tr>
<td><strong>Model</strong></td>
<td><strong>Total No. of Patients</strong></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Return of spontaneous circulation</td>
<td>357228</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>152601 (42.7)</td>
</tr>
<tr>
<td>Adjusted for selected variables</td>
<td>357228</td>
</tr>
<tr>
<td>Adjusted for all variables</td>
<td>357228</td>
</tr>
<tr>
<td>1-month survival</td>
<td>357228</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>357228</td>
</tr>
<tr>
<td>Adjusted for selected variables</td>
<td>357228</td>
</tr>
<tr>
<td>Adjusted for all variables</td>
<td>357228</td>
</tr>
<tr>
<td>Neurologically favorable survival</td>
<td>357228</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>357228</td>
</tr>
<tr>
<td>Adjusted for selected variables</td>
<td>357228</td>
</tr>
<tr>
<td>Adjusted for all variables</td>
<td>357228</td>
</tr>
</tbody>
</table>

Full models for the primary outcome analysis are included in eTable 2.

4For all odds ratios, P < .001.

5Selected variables are a predefined set of potential confounders including age, sex, cause of cardiac arrest, first documented rhythm, bystander witness, type of cardiopulmonary resuscitation (CPR) initiated by a bystander, use of public access automated external defibrillator by bystander, epinephrine administration, time from receipt of call to CPR by emergency medical service, and time from receipt of call to hospital arrival.

6All variables included all covariates in Table 1 and variables for 47 prefectures in Japan.
cessful endotracheal intubation or supraglottic airway placement only. Thus, in our study, failed advanced airway management cases reverted to and were classified as bag-valve-mask ventilation cases. This would have biased our conclusions toward the null.

Another limitation is that our analysis of a nationwide population-based cohort describes that in Japan only. Similar studies with data from other countries may result in different findings. In particular, one might hypothesize that training of airway management for Japanese EMS personnel is relatively suboptimal, resulting in poor outcomes. However, the certification process for EMS personnel credentialed to perform endotracheal intubation in Japan is stricter than that in other countries. Indeed, the national paramedic curriculum in the United States requires students to perform 5 successful endotracheal intubations to graduate; 25 successful intubations are required in the United Kingdom and 30 are required in Japan. Further, existing literature suggests that intubation proficiency is attained by EMS personnel after 15 to 20 successful endotracheal intubations (predicted intubation success threshold of 90%). This would serve to reduce the potential generalizability of our inference to other settings.

Finally, as with all epidemiological studies, data integrity, validity, and ascertainment bias are potential limitations. The use of uniform data collection on the basis of Utstein-style guidelines for reporting cardiac arrest, large sample size, and a population-based design were intended to minimize these potential sources of bias. This large, nationwide, population-based cohort study showed that CPR with prehospital advanced airway management, whether endotracheal intubation or supraglottic airways, was independently associated with a decreased likelihood of favorable neurological outcome compared with conventional bag-valve-mask ventilation among adults with OHCA. Our observations contradict the assumption that aggressive airway intervention is associated with improved outcomes and provide an opportunity to reconsider the approach to prehospital airway management in this population.

**Author Contributions:** Dr Hasegawa had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Hasegawa, Brown.

Acquisition of data: Hasegawa, Hirade.

Analysis and interpretation of data: Hasegawa, Chang, Brown.

Drafting of the manuscript: Hasegawa.

Critical revision of the manuscript for important intellectual content: Hasegawa, Hirade, Chang, Brown.

Statistical analysis: Hasegawa, Chang.

Obtaining funding: Hirade.

Administrative, technical, or material support: Brown.

Study supervision: Hasegawa, Hirade, Chang, Brown.

Conflict of Interest Disclosures:** All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

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**Disclaimer:** The article contents are solely the responsibility of the authors and do not necessarily represent the official views of the Fire and Disaster Management Agency.

**Online-Only Material:** e Tables 1 and 2 are available at [www.jama.com](http://www.jama.com).

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