Retrospective cohort study of hospital variation in airway management during in-hospital cardiac arrest and the association with patient survival: insights from Get With The Guidelines-Resuscitation

Steven M. Bradley1*, Yunshu Zhou2, Satya Krishna Ramachandran3, Milo Engoren4, Michael Donnino3 and Saket Girotra2

Abstract

**Importance:** The optimal approach to airway management during in-hospital cardiac arrest is unknown.

**Objective:** To describe hospital-level variation in endotracheal intubation during cardiopulmonary resuscitation (CPR) for in-hospital cardiac arrest and the association between hospital use of endotracheal intubation and arrest survival.

**Design, setting, participants:** Retrospective cohort study of adult patients suffering in-hospital cardiac arrest at Get With The Guidelines-Resuscitation participating hospitals between January, 2000, and December, 2016. Hospitals were categorized into quartiles based on the proportion of in-hospital cardiac arrest patients managed with endotracheal intubation during CPR. Risk-adjusted mixed models with random intercepts were created to assess the association between hospital quartile of in-hospital arrests managed with endotracheal intubation during CPR and survival to hospital discharge.

**Exposure:** Hospital rate of endotracheal intubation during CPR for in-hospital arrest

**Main outcomes and measures:** Survival to hospital discharge

**Results:** Among 155,252 patients suffering in-hospital cardiac arrest at 656 hospitals, 69.7% of patients received endotracheal intubation during CPR and overall survival to discharge was 24.8%. At the hospital level, the median rate of endotracheal intubation use was 71.2% (interquartile range, 63.6 to 78.1%; range, 26.6 to 100%). We found a strong inverse association between hospital rate of endotracheal intubation and survival to discharge (risk-adjusted odds ratio comparing highest intubation quartile vs. lowest intubation quartile, 0.81; 95% confidence interval (CI), 0.74 to 0.90; \( p \) value < .001). This association was modified by the presence of respiratory failure prior to arrest (\( p \) for interaction < .001) and stratified analyses demonstrated lower patient survival at hospitals with higher rates of endotracheal intubation was limited to patients without respiratory failure prior to cardiac arrest.

(Continued on next page)
Conclusion: In a national sample of patients suffering IHCA, the use of endotracheal intubation during CPR varied across hospitals. We found a strong inverse association between hospital use of endotracheal intubation during CPR and survival to discharge, but this association was confined to patients without respiratory failure prior to arrest. Identifying the optimal approach to airway management for in-hospital cardiac arrest may have a significant impact on patient survival.

Keywords: Resuscitation, Intubation, Cardiac arrest

Background
More than 200,000 patients suffer in-hospital cardiac arrest (IHCA) annually in the USA with an in-hospital mortality that approaches 80% [1, 2]. Airway management is a central component of resuscitation care, but it is unclear if endotracheal intubation improves patient survival. As the process of tracheal intubation often requires cessation of chest compressions [3, 4] and may result in delays in timely defibrillation or epinephrine administration [5, 6], avoiding intubation may minimize interruptions in aspects of high-quality resuscitation care [7]. In fact, studies from both the in- and out-of-hospital setting have associated resuscitation strategies that delay or minimize intubation with improved patient survival [8–12]. Resuscitation guidelines now support either invasive or non-invasive approaches to ventilation and oxygenation in the management of cardiac arrest [13].

Although prior patient-level studies of IHCA suggest a negative association between endotracheal intubation and patient survival [12], less is known about hospital practices in airway management during CPR and the association without outcomes. Given clinical uncertainty about the optimal approach to airway management in resuscitation care, variation may exist in the use of tracheal intubation during cardiac arrest. Evaluating rates of hospital use of intubation during cardiac arrest and the association with patient outcomes may provide insights on resuscitation practices with the potential to improve patient survival.

Accordingly, we analyzed data from the Get With The Guidelines-Resuscitation (GWTG-R) registry to describe hospital rates of endotracheal intubation during IHCA and evaluated the association between hospital rates of intubation and survival outcomes. We hypothesized that hospitals with lower rates of intubation during IHCA would be associated with greater survival. Prior studies suggest the association between intubation and arrest outcomes may be modified by the presence of respiratory failure and arrest rhythm, with greater potential harm of intubation with ventricular tachycardia or ventricular fibrillation (VT/VF) arrest or non-respiratory arrest. Accordingly, we also assessed for modification of the association between airway management and patient outcomes by initial arrest rhythm and the presence or absence of respiratory failure. We hypothesized that the inverse association between hospital rates of intubation and patient outcomes would be stronger for VT/VF arrests and non-respiratory arrests.

Methods
Data source
We analyzed data from the GWTG-R registry, an American Heart Association sponsored prospective, multi-site registry of in-hospital cardiac arrest events. The GWTG-R has been described previously in detail [9]. Briefly, an IHCA event is defined in the registry as a pulseless cardiac arrest that requires chest compressions and/or defibrillation. Data abstraction for each IHCA is performed by trained personnel at each participating institution [8]. Data integrity and accuracy is ensured through use of standardized reporting software and certification of data entry personnel [10].

Patient population
We included patients aged 18 years or older who experienced IHCA at a GWTG-R participating hospital from January 1, 2000, to December 31, 2016. If a patient had multiple IHCA, we excluded data from subsequent episodes to focus on the index event. Patients with pre-existing invasive ventilation prior to the arrest were excluded from the analysis. We also excluded patients with missing data on airway management, first pulseless rhythm, or survival outcomes. As our analyses were conducted at the hospital level, we excluded hospitals with fewer than 10 arrests to avoid inflation of variation due to small sample sizes.

Primary exposure
We identified patients who underwent placement of an endotracheal tube during CPR. Use of a bag valve mask, nasal mask, mouth-to-mouth ventilation, or a laryngeal mask airway during CPR was considered non-tracheal intubation approaches to airway management and not included in the exposure group.
Study outcomes
The primary outcome measure was survival to hospital discharge. The secondary outcomes included return of spontaneous circulation and survival to 24 h.

Statistical analysis
We determined the proportion of patients treated with endotracheal intubation during CPR at GWTG-R participating hospitals. We then categorized hospitals into quartiles based on the proportion of patients who received tracheal intubation during CPR. We compared patient and hospital-level characteristics across hospital quartile of intubation during CPR using Cochrane-Armitage test for categorical variables and simple linear regression for continuous variables.

We next constructed a two-level hierarchical multivariable model to evaluate the risk-adjusted association between the hospital quartile of intubation during CPR and our primary and secondary outcomes. In these models, hospital site was added as a random effect and we adjusted for patient-level variables and hospital quartile of endotracheal intubation as fixed effects. Patient-level covariates for risk adjustment were chosen from previously validated survival models [11] using the GWTG-R database and included age, sex, race category (white, black, other), initial arrest rhythm (asystole, pulseless electrical activity, ventricular fibrillation, and ventricular tachycardia), hospital location of arrest (intensive care unit, monitored ward, non-monitored ward, procedural area/emergency department, other), witnessed arrest, time of arrest (daytime [7 A.M. to 10:59 P.M.], night [11 P.M. to 6:59 A.M.], day of the week [weekday-Monday-Friday], weekend [Saturday or Sunday]), use of a hospital-wide code alert, pre-existing medical conditions (heart failure during current or prior admission, myocardial infarction during current or prior admission, hypotension, respiratory failure, renal insufficiency, hepatic insufficiency, metabolic or electrolyte abnormality, diabetes mellitus, baseline depression in central nervous system function, acute stroke, pneumonia septicemia, major trauma, and cancer), and interventions in place at prior to the arrest (use of intravenous vasoactive agents, intra-arterial catheter, and dialysis).

We evaluated the association between quartiles of hospital intubation rates and study outcomes using hierarchical logistic regression models with hospital-specific random intercepts. We also examined for effect modification (interaction) of the association between hospital intubation rates and patient outcomes by initial arrest rhythm and the presence or absence of respiratory failure. Further stratified analyses were planned if the interaction term was significantly associated with survival to discharge, stratified by presence or absence of ventricular tachycardia or ventricular fibrillation as the initial presenting rhythm and presence or absence of respiratory failure prior to arrest. For all analyses, the null hypothesis was evaluated at a two-sided significance level of 0.05. SAS Software Version 9.4 (SAS Institute Inc., Cary, NC).

Results
We identified 155,252 index IHCA at 656 hospitals (Fig. 1). Endotracheal intubation was used during CPR in 108,221 (69.7%) patients overall, 17,422 (55.1%) patients with an initial presenting rhythm of VT/VF, 90,799 (73.5%) patients with PEA or asystolic arrests, 35,850 (68.4%) patients with respiratory failure, and 72,371 (70.4%) patients without respiratory failure. There was substantial variation in hospital intubation rates during CPR, with a median of 71.2% and a range of 26.6 to 100.0% (Fig. 2).

Table 1 displays the baseline differences among patients across the intubation rate quartile hospitals. Compared with patients at hospitals in the lowest quartile of intubation rates, patients at hospitals in the highest quartile of intubation were more likely to be black (24.8% vs 17.5%), arrest in a non-monitored unit (27.2% vs 19.8%), and have a hospital-wide code activated (80.8% vs 74.2%). Other statistically significant but clinically small differences were noted among many characteristics given the large size of the study cohort.

A total of 38,435 (24.8%) of patients survived to hospital discharge. The unadjusted discharge survival decreased from 27.2% in the hospital quartile with the lowest intubation rate to 22.4% in the hospital quartile with the highest intubation rate (Table 2). Compared with hospitals in the lowest quartile of intubation use, risk-adjusted survival to discharge was lower in all quartiles with higher intubation use and lowest in the hospital quartile with highest intubation use (odds ratio [OR], 0.81; 95% confidence interval [CI], 0.74 to 0.90, p ≤ .0001). Similar trends were observed for our secondary outcomes of ROSC and survival to 24 h (Table 2).

Overall rates of intubation differed by the presence or absence of respiratory failure (68.4% with respiratory failure present, 70.4% when respiratory failure absent; p < .0001) and presenting arrest rhythm (55.1% with VT/VF, 73.5% with asystole/PEA; p < .0001). The association between hospital endotracheal intubation use and outcomes was modified by the presence of respiratory failure (P for interaction < .0001 for all outcomes) but not presenting rhythm (P = 0.30). Stratified on the absence or presence of respiratory failure, patients without respiratory failure were more likely to survive IHCA at hospitals with low rates of tracheal intubation use, but no association was observed between hospital rates of tracheal intubation use and survival of IHCA among patients with respiratory failure (Table 3). The inverse association between hospital
intubation rates and survival was observed for both VT/VF and PEA/asystolic arrests (Table 4).

Discussion
In a national registry of more than 150,000 IHCA and more than 650 hospitals, we described variation in the use of endotracheal intubation during resuscitation efforts and the association between hospital rates of tracheal intubation use and patient outcomes. Use of endotracheal intubation was common with 70% of patients receiving a tracheal intubation during CPR. However, hospital rates of tracheal intubation use varied from 27 to 100%. Compared to hospitals with more frequent use of tracheal intubation, hospitals with lower rates of tracheal intubation use were associated with better patient survival. This association was modified by
Table 1 Patient and hospital characteristics by hospital quartiles of endotracheal intubation during CPR

| Patient characteristics | All patients | 1—lowest (n = 32,825) | 2 (n = 44,535) | 3 (n = 47,480) | 4—highest (n = 30,412) | P value for trend |
|-------------------------|-------------|-----------------------|----------------|----------------|------------------------|-----------------|
| Median intubation rate during CPR, % (IQR) | 71.4 (64.7, 76.7) | 57.6 (50.0, 61.3) | 67.5 (65.6, 69.0) | 75.0 (72.8, 76.4) | 80.4 (79.5, 83.1) | < .001 |
| Patient demographics | | | | | | |
| Age, mean (SD) | 67.17 (15.3) | 66.01 (15.5) | 67.02 (15.3) | 67.69 (15.1) | 67.85 (15.3) | < .001 |
| Black race | 32,044 (20.6) | 5752 (17.5) | 8721 (19.6) | 10,032 (21.1) | 7539 (24.8) | < .001 |
| Female sex | 64,369 (41.5) | 13,342 (40.7) | 18,576 (41.7) | 19,516 (41.1) | 12,935 (42.5) | < .001 |
| Cardiac arrest characteristics | | | | | | |
| Initial cardiac-arrest rhythm—no. (%) | | | | | | < .001 |
| Asystole | 52,250 (33.7) | 10,088 (30.7) | 14,887 (33.4) | 16,231 (34.2) | 11,044 (36.3) | |
| Pulseless electrical activity | 71,370 (46.0) | 15,437 (47.0) | 20,283 (45.5) | 21,891 (46.1) | 13,759 (45.2) | |
| Pulseless ventricular tachycardia | 11,512 (7.4) | 2705 (8.2) | 3463 (7.8) | 3345 (7.1) | 1999 (6.6) | |
| Ventricular fibrillation | 20,120 (13.0) | 4595 (14.0) | 5902 (13.3) | 6013 (12.7) | 3610 (11.9) | |
| Hospital location of arrest—no. (%) | | | | | | < .001 |
| Intensive care unit | 53,274 (34.3) | 12,494 (38.1) | 16,269 (36.5) | 15,463 (32.6) | 9048 (30.0) | |
| Monitored unit | 35,249 (22.7) | 6513 (19.8) | 9691 (21.8) | 11,476 (24.2) | 7569 (24.9) | |
| Non-monitored unit | 35,611 (22.9) | 6500 (19.8) | 9685 (21.8) | 11,170 (23.5) | 8256 (27.2) | |
| Procedural areas/OR/ED | 28,749 (18.5) | 6914 (21.1) | 8231 (18.5) | 8530 (18.0) | 5074 (16.7) | |
| Other | 2369 (1.5) | 404 (1.2) | 659 (1.5) | 841 (1.8) | 465 (1.5) | |
| Arrest at night (11 P.M. to 7 A.M.)—no./total no. (%) | 49,611 (32.0) | 10,104 (30.8) | 14,161 (31.8) | 15,401 (32.4) | 9945 (32.7) | < .001 |
| Arrest on weekend—no. (%) | 47,933 (30.9) | 10,104 (30.8) | 13,713 (30.8) | 14,746 (31.1) | 9370 (30.8) | 0.68 |
| Hospital-wide response activated—no. (%) | 125,741 (81.0) | 24,342 (74.2) | 36,713 (82.4) | 40,103 (84.5) | 24,583 (80.8) | < .001 |
| Preexisting conditions | | | | | | |
| Heart failure, this admission—no. (%) | 26,227 (16.9) | 5185 (15.8) | 6717 (15.1) | 8345 (17.6) | 5980 (19.7) | < .001 |
| Previous heart failure—no. (%) | 35,040 (22.6) | 7322 (22.3) | 9691 (21.8) | 11,476 (24.2) | 7569 (24.9) | < .001 |
| Myocardial infarction, this admission—no. (%) | 25,132 (16.2) | 5312 (16.2) | 6979 (15.7) | 7516 (15.8) | 5325 (17.5) | < .001 |
| Previous myocardial infarction—no. (%) | 25,137 (16.2) | 4948 (15.1) | 6561 (14.7) | 7533 (15.9) | 6095 (20.0) | < .001 |
| Hypotension—no. (%) | 30,309 (19.5) | 6913 (21.1) | 9691 (21.8) | 11,476 (24.2) | 7569 (24.9) | < .001 |
| Respiratory failure—no. (%) | 52,430 (33.8) | 11,011 (33.5) | 14,960 (33.6) | 15,938 (33.6) | 10,521 (34.6) | 0.01 |
| Renal insufficiency—no. (%) | 51,151 (33.0) | 10,037 (30.6) | 14,588 (32.8) | 15,707 (33.1) | 10,819 (35.6) | < .001 |
| Hepatic insufficiency—no. (%) | 9913 (6.4) | 1901 (5.8) | 2822 (6.3) | 2922 (6.2) | 2268 (7.5) | < .001 |
| Metabolic or electrolyte abnormality—no. (%) | 22,673 (14.6) | 5119 (15.6) | 6015 (13.5) | 6483 (13.6) | 5056 (16.6) | 0.002 |
| Diabetes mellitus—no. (%) | 50,550 (32.6) | 10,431 (31.8) | 14,159 (31.8) | 15,547 (32.7) | 10,413 (34.2) | < .001 |
| Baseline depression in CNS function—no. (%) | 15,097 (9.7) | 2954 (9.0) | 3841 (8.6) | 4640 (9.8) | 3662 (12.0) | < .001 |
| Interventions in place before the arrest | | | | | | |
| Intravenous vasopressor medication—no. (%) | 21,813 (14.1) | 5587 (17.0) | 6611 (14.8) | 6030 (12.7) | 3585 (11.8) | < .001 |
| Dialysis—no. (%) | 3823 (2.5) | 783 (2.4) | 1094 (2.5) | 1010 (2.1) | 936 (3.1) | < .001 |
Table 1 Patient and hospital characteristics by hospital quartiles of endotracheal intubation during CPR (Continued)

| Intra-arterial catheter | 6652 (4.3) | 1958 (6.0) | 1966 (4.4) | 1493 (3.1) | 1235 (4.1) | < .001 |
|-------------------------|------------|------------|------------|------------|------------|--------|
| Witnessed               | 122,016 (78.6) | 26,509 (80.8) | 35,904 (80.6) | 36,711 (77.3) | 22,892 (75.3) | < .001 |
| Hospital characteristics | All hospitals | N = 656 | 1—lowest (n = 165) | 2 (n = 164) | 3 (n = 163) | 4—highest (n = 164) | P value for trend 0.66 |
| Geographic census region, number (%) | Northeast | 101 (15.4) | 26 (15.8) | 29 (17.7) | 22 (13.5) | 24 (14.6) |
| | Midwest | 134 (20.4) | 36 (21.8) | 37 (22.6) | 28 (17.2) | 33 (20.1) |
| | West | 111 (16.9) | 43 (26.1) | 30 (18.3) | 28 (17.2) | 10 (6.1) |
| | South | 264 (40.2) | 39 (23.6) | 60 (36.6) | 81 (49.7) | 84 (51.2) |
| | Unknown | 46 (7.0) | 21 (12.7) | 8 (4.9) | 4 (2.5) | 13 (7.9) |
| Type of hospital, number (%) | Teaching hospital | 319 (48.6) | 81 (49.1) | 85 (51.8) | 78 (47.9) | 75 (45.7) |
| | Non-teaching hospital | 286 (43.6) | 62 (37.6) | 71 (43.3) | 80 (49.1) | 73 (44.5) |
| | Unknown | 51 (7.8) | 22 (13.3) | 8 (4.9) | 5 (3.1) | 16 (9.8) |
| Location, number (%) | Urban | 538 (82.0) | 125 (75.8) | 142 (86.6) | 139 (85.3) | 132 (80.5) |
| | Rural | 67 (10.2) | 18 (10.9) | 14 (8.5) | 19 (11.7) | 16 (9.8) |
| | Unknown | 51 (7.8) | 22 (13.3) | 8 (4.9) | 5 (3.1) | 16 (9.8) |
| Ownership | Private | 99 (15.1) | 20 (12.1) | 22 (13.4) | 26 (16.0) | 31 (18.9) |
| | Public | 511 (77.9) | 124 (75.2) | 134 (81.7) | 133 (81.6) | 120 (73.2) |
| | Unknown | 51 (7.8) | 22 (13.3) | 8 (4.9) | 5 (3.1) | 16 (9.8) |
| Bed size, number (%) | < 100 | 57 (8.7) | 22 (13.3) | 9 (5.5) | 13 (8.0) | 13 (7.9) |
| | 100–499 | 414 (63.1) | 92 (55.8) | 114 (69.5) | 109 (66.9) | 99 (60.4) |
| | ≥ 500 | 130 (19.8) | 30 (18.2) | 30 (18.3) | 33 (20.3) | 37 (22.6) |
| | Unknown | 55 (8.4) | 21 (12.7) | 11 (6.7) | 8 (4.9) | 15 (9.2) |

Abbreviations: CPR cardiopulmonary resuscitation, IQR interquartile range, SD standard deviation, OR operating room, ED emergency department, no. number

Table 2 Survival outcomes by hospital quartile of endotracheal intubation during CPR

| All patients | Hospital quartile of intubation rate during CPR |
|--------------|-----------------------------------------------|
| Unadjusted rate, N (%) | 38,435 (24.8) | 8926 (27.2) | 11,432 (25.7) | 11,265 (23.7) | 6812 (22.4) |
| Adjusted odds ratio, (95% CI) | Reference | 0.95 (0.86, 1.04) | 0.86 (0.78, 0.94) | 0.81 (0.74, 0.90) | \( P < .001 \) |
| **ROSC** | | | | | |
| Unadjusted rate, N (%) | 99,881 (64.4) | 22,283 (67.9) | 28,657 (64.4) | 29,910 (63.0) | 19,031 (62.6) |
| Adjusted odds ratio, (95% CI) | Reference | 0.91 (0.81, 1.01) | 0.84 (0.75, 0.94) | 0.83 (0.74, 0.93) | \( P = .001 \) |
| Survival to 24 h | | | | | |
| Unadjusted rate, N (%) | 65,739 (42.3) | 14,419 (43.9) | 19,066 (42.8) | 19,792 (41.7) | 12,462 (41.0) |
| Adjusted odds ratio, (95% CI) | Reference | 0.96 (0.88, 1.04) | 0.89 (0.82, 0.97) | 0.87 (0.80, 0.95) | \( P = .001 \) |

Abbreviations: N number, CI confidence interval, CPR cardiopulmonary resuscitation
the presence or absence of respiratory failure, with the association between lower rates of tracheal intubation use and better survival being limited to patients without respiratory failure. These findings are consistent with prior patient-level analyses and highlight the importance of further investigation to define the optimal approach to tracheal intubation use in the management of patients suffering in-hospital arrest.

Prior studies of cardiac arrest have suggested the potential for reduced use of intubation during CPR to improve patient outcomes [8–10, 12]. For example, in several pre-post studies of a resuscitation strategy that included non-tracheal intubation management, an approach that minimized use of intubation was associated with improved survival in out-of-hospital cardiac arrest [8–10]. However, several modifications were made to the CPR algorithm in these studies and the relative contribution of tracheal intubation use on patient outcomes was unclear. Subsequently, a propensity-matched analysis from GWTG-R demonstrated intubation within the first 15 min of CPR compared with no intubation to be associated with lower survival [12]. However, while this prior analysis adjusted for confounding due to indication by matching patients who underwent endotracheal intubation at a given minute during resuscitation with control patients who had received CPR for the same duration, potential for unmeasured confounding still remains [14]. Therefore, our findings of a strong association between rates of endotracheal intubation during in-hospital cardiac arrest and survival at a hospital-level lends further support to the findings of prior patient-level studies.

Use of tracheal intubation during resuscitation efforts has several mechanisms by which it could contribute to patient outcomes [15]. Attempts at tracheal intubation may result in delays to timely defibrillation [5], epinephrine administration [6], or interruption of chest compressions [16]. Studies of pre-hospital CPR have noted tracheal intubation placement is associated with a median 46-s interruption in chest compressions and
nearly a third of interruptions exceeded 1 min [3]. Endotracheal intubation may also facilitate greater ease of ventilation and thereby potentiate excessive ventilation and oxygenation, both contributors to poor patient outcomes [17, 18].

Despite these potential drawbacks, it is important to recognize scenarios where use of tracheal intubation may have particular benefit. Animal model studies have suggested the importance of ventilation in scenarios that simulate respiratory arrest [19]. Accordingly, several pre-post studies evaluating delayed use of tracheal intubation have limited this change in practice to patients with arrest of presumed cardiac origin and a shockable arrest rhythm [8, 9]. In a prior observational study of IHCA from GWTG-R, intubation was not associated with worse survival among patients with preceding respiratory failure [12]. As such, the relative importance of tracheal intubation use to optimize patient outcomes may depend on the arrest etiology and presenting rhythm. These prior studies informed our decision to evaluate for effect modification on initial arrest rhythm and the presence or absence of respiratory failure. Our study findings further support a differential importance of tracheal intubation in resuscitation care depending on arrest etiology, with the inverse association between intubation use and patient outcomes being strongest in patients without respiratory failure prior to arrest. Survival outcomes in patients with respiratory insufficiency prior to arrest were similar across hospital intubation quartiles. These findings also highlight that our exposure is not a surrogate for resuscitation quality, as patient outcomes were not uniformly better for all patient populations at hospitals with lower intubation rates.

Randomized trials of invasive vs non-invasive intubation management for out-of-hospital cardiac arrest are ongoing [20]. However, significant differences in the arrest characteristic and management of in-hospital cardiac arrest present challenges in applying the findings from these trials to the inpatient setting. Unlike out-of-hospital cardiac arrest where half of events are

Table 4: Survival outcomes by hospital quartile of endotracheal intubation during CPR and stratified by presenting rhythm

|                      | All patients | Hospital quartile of intubation rate during CPR |          |          |          |          |          |
|----------------------|--------------|-----------------------------------------------|----------|----------|----------|----------|----------|
|                      |              | 1 (lowest) | 2 | 3 | 4 (highest) |
| VT/VF                |              |          |          |          |          |          |          |
| Survival to discharge|              |          |          |          |          |          |          |
| Unadjusted rate, N (%) | 14,898 (47.1) | 3677 (50.4) | 4436 (47.4) | 4345 (46.4) | 2440 (43.5) |
| Adjusted odds ratio (95% CI) | Reference | 0.94 (0.83, 1.06) | P = 0.29 | 0.88 (0.78, 0.99) | P = 0.03 | 0.82 (0.72, 0.93) | P = 0.002 |
| ROSC                 |              |          |          |          |          |          |          |
| Unadjusted rate, N (%) | 24,040 (76.0) | 5833 (80.0) | 7063 (75.5) | 7036 (75.2) | 4108 (73.3) |
| Adjusted odds ratio (95% CI) | Reference | 0.82 (0.72, 0.94) | P = 0.006 | 0.78 (0.68, 0.90) | P = 0.001 | 0.70 (0.60, 0.81) | P < .001 |
| Survival to 24 h     |              |          |          |          |          |          |          |
| Unadjusted rate, N (%) | 19,651 (62.1) | 4716 (64.6) | 5823 (62.2) | 5785 (61.8) | 3327 (59.3) |
| Adjusted odds ratio (95% CI) | Reference | 0.94 (0.84, 1.05) | P = 0.26 | 0.90 (0.80, 1.00) | P = 0.05 | 0.80 (0.71, 0.91) | P = 0.001 |
| PEA/asystole         |              |          |          |          |          |          |          |
| Survival to discharge|              |          |          |          |          |          |          |
| Unadjusted rate, N (%) | 23,537 (19.0) | 5249 (20.6) | 6996 (19.9) | 6920 (18.2) | 4372 (17.6) |
| Adjusted odds ratio (95% CI) | Reference | 0.95 (0.85, 1.05) | P = 0.30 | 0.84 (0.76, 0.94) | P = 0.002 | 0.82 (0.73, 0.91) | P < .001 |
| ROSC                 |              |          |          |          |          |          |          |
| Unadjusted rate, N (%) | 75,841 (61.4) | 16,450 (64.5) | 21,594 (61.4) | 22,874 (60.0) | 14,923 (60.2) |
| Adjusted odds ratio (95% CI) | Reference | 0.92 (0.82, 1.03) | P = 0.16 | 0.84 (0.75, 0.94) | P = 0.003 | 0.85 (0.76, 0.96) | P = 0.008 |
| Survival to 24 h     |              |          |          |          |          |          |          |
| Unadjusted rate, N (%) | 46,088 (37.3) | 9703 (38.0) | 13,243 (37.7) | 14,007 (36.7) | 9135 (36.8) |
| Adjusted odds ratio (95% CI) | Reference | 0.96 (0.88, 1.04) | P = 0.33 | 0.90 (0.82, 0.97) | P = 0.01 | 0.90 (0.82, 0.98) | P = 0.02 |

Abbreviations: N, number; CI, confidence interval; CPR, cardiopulmonary resuscitation.
unwitnessed and CPR is often delayed [21], the vast majority of in-hospital cardiac arrests occur in monitored settings with trained personnel to facilitate resuscitation care and minimal time to onset of resuscitation efforts [22]. These differences may influence the relative importance of endotracheal intubation during CPR. As such, further study focusing on the optimal approach to airway management of in-hospital arrest is needed.

Our study findings should be interpreted in the context of several limitations. First, GWTG-R participating hospitals may not be representative of all US hospitals and therefore our findings may not be generalizable. Second, the GWTG-R does not collect data on the reasons for specific airway choices, the number of airway insertion attempts, and measures of difficult laryngoscopy or intubation that may have implications for the analysis. Third, use of laryngeal mask airways was low (<1%) such that subgroup analysis on different types of airways was not feasible. Fourth, we cannot exclude the potential for resuscitation time bias in which an exposure is more likely to occur the longer the cardiac arrest continues [23]. However, this concern is lessened a priori study that demonstrated higher patient survival at hospitals with longer median duration of resuscitation events [24]. Fifth, given the observational nature of our study, there is potential for confounding, although we performed robust risk adjustment to address this concern. Despite these limitations, our study provides insights into current practice and the potential importance of airway management protocols on patient survival.

Conclusions
Among more than 150,000 patients suffering in-hospital cardiac arrest at more than 650 hospitals, the rate of tracheal intubation use during resuscitation efforts varied from 27 to 100%. Hospitals with less frequent use of tracheal intubations during CPR were associated with better patient survival. This above association was modified by the presence or absence of respiratory failure with the apparent benefit of lower hospital rates of tracheal intubation use being limited to patients without respiratory failure. A better understanding of optimal airway management in the care of patients suffering in-hospital cardiac arrest is needed.

Acknowledgements
The American Heart Association Get with the Guidelines (formerly NRCPR) Investigators are Emilie Allen, Robert A. Berg, Scott Braithwaite, Paul S. Chan, Kathy Duncan, Dana Edelson, Brian Engel, Romerynko Geocadin, Elizabeth A. Hunt, Karl B. Kern, Tim Mader, Mary E. Mancini, Vinay M. Nadkarni, Grahm Nichol, Joseph P. Ornato, Mary Ann Peberdy, Cornilla Sasson, and Sam Warren.

Financial support
Dr. Girotra is supported by the NHLBI (K08HL122527). The American Heart Association (Dallas, TX) provided funding for the collection and management of the National Registry of Cardiopulmonary Resuscitation database.

Funding
Dr. Girotra is supported by the NHLBI (K08HL122527). The American Heart Association (Dallas, TX) provided funding for the collection and management of the National Registry of Cardiopulmonary Resuscitation database.

Availability of data and materials
The data that support the findings of this study are available from the American Heart Association, but restrictions apply to the availability of these data, which were used under license for the current study, and are not publicly available. With publication, data from the AHA GWTG-R program are available upon approval of a research request by the responsible GWTG-R research task force (https://www.heart.org/en/professional/quality-improvement/quality-research-and-publications/national-level-program-data-research-opportunities).

Authors’ contributions
SB and SR contributed to the study conception; SB, YZ, SR, and SG contributed to the study design; SB, YZ, SR, ME, MD, and SG contributed to the data acquisition, analysis, or interpretation; SB and SR contributed to the manuscript drafting; YZ, ME, MD, and SG contributed to the manuscript revision for important intellectual content; SB, YZ, SR, ME, MD, and SG approved the final version for publication and agreed to be accountable for all aspects of the work.

Ethics approval and consent to participate
The University of Iowa Institutional Review Board approved this study and a waiver of informed consent was granted.

Consent for publication
The Adult Research Task Force of GWTG-Resuscitation approved the study protocol and the final version of the manuscript.

Competing interests
The authors declare that they have no competing interests.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details
1Minneapolis Heart Institute and Minneapolis Heart Institute Foundation, 920 East 28th Street, Suite 300, Minneapolis, MN 55407, USA. 2University of Iowa Carver College of Medicine, Iowa City, IA, USA. 3Beth Israel Deaconess Medical Center, Boston, MA, USA. 4University of Michigan School of Medicine, Ann Arbor, MI, USA.

Received: 28 December 2018 Accepted: 9 April 2019
Published online: 06 May 2019

References
1. Merchant RM, Yang L, Becker LB, et al. Incidence of treated cardiac arrest in hospitalized patients in the United States. Crit Care Med. 2011;39(11):2401–6. https://doi.org/10.1097/CCM.0b013e3182257459.
2. Thompson LE, Chan PS, Tang F, et al. Long-term survival trends of Medicare patients after in-hospital cardiac arrest: insights from Get With The Guidelines-Resuscitation®. Resuscitation. 2018;123:58–64. https://doi.org/10.1016/j.resuscitation.2017.10.023.
3. Wang HE, Simeone SJ, Weaver MD, Callaway CW. Interruptions in cardiopulmonary resuscitation from paramedic endotracheal intubation. Ann Emerg Med. 2009;54(5):645–652.e1. https://doi.org/10.1016/j.annemergmed.2009.05.024.
4. Martin LD, Mhyre JM, Shanks AM, Temper KK, Kheterpal S. 3,423 emergency tracheal intubations at a university hospital: airway outcomes and complications. Anesthesiology. 2011;114(1):42–8. https://doi.org/10.1097/ALN.0b013e318201e415.
5. Chan PS, Krumholz HM, Nichol G, Nallamothu BK. American Heart Association National Registry of Cardiopulmonary Resuscitation Investigators. Delayed time to defibrillation after in-hospital cardiac arrest. N Engl J Med. 2008;358(1):9–17. https://doi.org/10.1056/NEJMoa0706467.
6. Doninno MW, Salciccioli JD, Howell MD, et al. Time to administration of epinephrine and outcome after in-hospital cardiac arrest with non-
shockable rhythms: retrospective analysis of large in-hospital data registry. BMJ. 2014;348:g3028.

7. Kleinman ME, Brennan EE, Goldberger ZD, et al. Part 5: adult basic life support and cardiopulmonary resuscitation quality: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2015;132(18 Suppl 2):S414–35. https://doi.org/10.1161/CIR.0000000000000259.

8. Kellum MJ, Kennedy KW, Ewy GA. Cardiocerebral resuscitation improves survival of patients with out-of-hospital cardiac arrest. Am J Med. 2006;119(4):335–40. https://doi.org/10.1016/j.amjmed.2005.11.014.

9. Kellum MJ, Kennedy KW, Barney R, et al. Cardiocerebral resuscitation improves neurologically intact survival of patients with out-of-hospital cardiac arrest. Ann Emerg Med. 2008;52(3):244–52. https://doi.org/10.1016/j.annemergmed.2008.02.006.

10. Bobrow BJ, Clark LL, Ewy GA, et al. Minimally interrupted cardiac resuscitation by emergency medical services for out-of-hospital cardiac arrest. JAMA. 2008;299(10):1158–65. https://doi.org/10.1001/jama.299.10.1158.

11. Moser J, Itty A, Sanders A, et al. Cardiocerebral resuscitation is associated with improved survival and neurologic outcome from out-of-hospital cardiac arrest in elders. Acad Emerg Med Off J Soc Acad Emerg Med. 2010;17(3):269–75. https://doi.org/10.1111/j.1553-2712.2010.00689.x.

12. Andersen LW, Granfeldt A, Callaway CW, et al. Association between tracheal intubation during adult in-hospital cardiac arrest and survival. JAMA. 2017;317(3):349–506. https://doi.org/10.1001/jama.2016.1615.

13. Link MS, Berlow LC, Kudenchuk PJ, et al. Part 7: adult advanced cardiovascular life support: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2015;132(18 Suppl 2):S444–64. https://doi.org/10.1161/CIR.0000000000000261.

14. Angus DC. Whether to intubate during cardiopulmonary resuscitation: conventional wisdom vs big data. JAMA. 2017;317(5):477–8. https://doi.org/10.1001/jama.2016.20626.

15. Benoit JL, Prince DK, Wang HE. Mechanisms linking advanced airway management and cardiac arrest outcomes. Resuscitation. 2015;93:124–7. https://doi.org/10.1016/j.resuscitation.2015.06.005.

16. Souchtchenko SS, Benner JP, Allen JL, Brady WJ. A review of chest compression interruptions during out-of-hospital cardiac arrest and strategies for the future. J Emerg Med. 2013;45(3):458–66. https://doi.org/10.1016/j.jemermed.2013.01.023.

17. Aufderheide TP, Sigurdsson G, Pirrallo RG, et al. Hyperventilation-induced hypotension during cardiopulmonary resuscitation. Circulation. 2004;109(16):1960–5. https://doi.org/10.1161/01.CIR.0000126594.79136.61.

18. Kilgannon JH, Jones AE, Shapiro NI, et al. Association between arterial hypertension following resuscitation from cardiac arrest and in-hospital mortality. JAMA. 2010;303(21):2165–71. https://doi.org/10.1001/jama.2010.707.

19. Berg RA, Hillwig RW, Kern KB, Ewy GA. “Bystander” chest compressions and assisted ventilation independently improve outcome from piglet asphyxial pulseless “cardiac arrest”. Circulation. 2000;101(14):1743–8.

20. Wang HE, Prince DK, Stephens SW, et al. Design and implementation of the resuscitation outcomes consortium pragmatic airway resuscitation trial (PART). Resuscitation. 2016;101:57–64. https://doi.org/10.1016/j.resuscitation.2016.01.012.

21. Daya MR, Schmicker RH, Zive DM, et al. Out-of-hospital cardiac arrest survival improving over time: results from the Resuscitation Outcomes Consortium (ROC). Resuscitation. 2015;91:108–15. https://doi.org/10.1016/j.resuscitation.2015.02.003.

22. Girotra S, Nallamothu BK, Spertus JA, et al. Trends in survival after in-hospital cardiac arrest. N Engl J Med. 2012;367(20):1912–20. https://doi.org/10.1056/NEJMoa1109148.

23. Andersen LW, Grosssteurer AV, Donnino MW. “Resuscitation time bias”-a unique challenge for observational cardiac arrest research. Resuscitation. 2018;125:79–82. https://doi.org/10.1016/j.resuscitation.2018.02.006.

24. Goldberger ZD, Chan PS, Berg RA, et al. Duration of resuscitation efforts and survival after in-hospital cardiac arrest: an observational study. Lancet Lond Engl. 2012;380(9825):1473–81. https://doi.org/10.1016/S0140-6736(12)60862-9.