CHEST

Comparative Effectiveness of Amiodarone and Lidocaine for the Treatment of In-Hospital Cardiac Arrest

Deborah Wagner, PharmD; S. L. Kronick, MD; H. Nawer, PharmD; J. A. Cranford, PhD; S. M. Bradley, MD, PhD; and R. W. Neumar, MD, PhD

BACKGROUND: American Heart Association Advanced Cardiac Life Support (ACLS) guidelines support the use of either amiodarone or lidocaine for cardiac arrest caused by ventricular tachycardia or ventricular fibrillation (VT/VF) based on studies of out-of-hospital cardiac arrest. Studies comparing amiodarone and lidocaine in adult populations with in-hospital VT/VF arrest are lacking.

RESEARCH QUESTION: Does treatment with amiodarone vs lidocaine therapy have differential associations with outcomes among adult patients with in-hospital cardiac arrest from VT/VF?

STUDY DESIGN AND METHODS: This retrospective cohort study of adult patients receiving amiodarone or lidocaine for VT/VF in-hospital cardiac arrest refractory to CPR and defibrillation between January 1, 2000, and December 31, 2014, was conducted within American Heart Association Get With the Guidelines-Resuscitation participating hospitals. The primary outcome was return of spontaneous circulation (ROSC). Secondary outcomes were 24 h survival, survival to hospital discharge, and favorable neurologic outcome.

RESULTS: Among 14,630 patients with in-hospital VT/VF arrest, 68.7% (n = 10,058) were treated with amiodarone and 31.3% (n = 4,572) with lidocaine. When all covariates were statistically controlled, compared with amiodarone, lidocaine was associated with statistically significantly higher odds of the following: (1) ROSC (adjusted OR [aOR], 1.15, $P = .01$; average marginal effect [AME], 2.3; 95% CI, .5-4.2); (2) 24 h survival (aOR, 1.16; $P = .004$; AME, 3.0; 95% CI, 0.9-5.1); (3) survival to discharge (aOR, 1.19; $P < .001$; AME, 3.3; 95% CI, 1.5-5.2); and (4) favorable neurologic outcome at hospital discharge (aOR, 1.18; $P < .001$; AME, 3.1; 95% CI, 1.3-4.9). Results using propensity score methods were similar to those from multivariable logistic regression analyses.

INTERPRETATION: Compared with amiodarone, lidocaine therapy among adult patients with in-hospital cardiac arrest from VT/VF was associated with statistically significantly higher rates of ROSC, 24 h survival, survival to hospital discharge, and favorable neurologic outcome.

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KEY WORDS: cardiology; cardiopulmonary arrest; cardiopulmonary resuscitation; drugs; guidelines

ABBREVIATIONS: AME = average marginal effect; GWTG-R = Get With the Guidelines-Resuscitation; IHCA = in-hospital cardiac arrest; IPTW = inverse probability of treatment weighting; OHCA = out-of-hospital cardiac arrest; PSM = propensity score method; ROSC = return of spontaneous circulation; VF = ventricular fibrillation; VT = ventricular tachycardia

AFFILIATIONS: From the Department of Pharmacy (D. W. and H. N.) and Department of Emergency Medicine (S. L. K., J. A. C., and R. W. N.), Michigan Medicine, and Allina Health (S. M. B.).

CORRESPONDENCE TO: Deborah Wagner, PharmD; email: debbiew@umich.edu

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Take-home Points

Study question: Do the data in the GWTG-R provide evidence to support the use of lidocaine in adult IHCA?

Results: Reconsideration for the use of lidocaine as a preferred agent in adult IHCA should be considered based on the results of this study showing that lidocaine was associated with statistically significant higher rates of ROSC, 24 h survival, survival to hospital discharge, and favorable neurologic outcome.

Interpretation: The influence of lidocaine on neurologic outcome should be a major consideration for use in adult IHCA.

Sudden cardiac death claims > 350,000 lives annually in the United States.[1] Nearly equal proportions of cardiac arrests occur out-of-hospital and in-hospital,[2] but studies of out-of-hospital cardiac arrest (OHCA) dominate guideline recommendations for management. Differences in the patient populations and characteristics of in-hospital cardiac arrest (IHCA) may influence the effectiveness of therapies recommended based on the management of patients with OHCA. Recommended treatments for cardiac arrest caused by ventricular tachycardia or ventricular fibrillation (VT/VF) incorporate the use of defibrillation, vasopressors, and antiarrhythmic drugs that include amiodarone and lidocaine.

Current guidelines for VT/VF arrest recommend use of either amiodarone or lidocaine, with no indication of preference.[3] These recommendations are based on three large randomized controlled trials comparing lidocaine and amiodarone in the management of out-of-hospital VT/VF arrest,[4] ALIVE,[5] and the Resuscitation Outcomes Consortium Amiodarone, Lidocaine, or Placebo Study (ROC-ALPS).[6] Compared with placebo, there was evidence of improved survival to admission with use of either amiodarone or lidocaine. There were no differences in survival to admission when comparing lidocaine vs amiodarone.

Cardiac arrests occurring in the out-of-hospital setting are often unwitnessed, with associated delay between recognition of arrest, initiation of CPR, and pharmacologic therapy. In comparison, IHCAs are often witnessed or monitored, with resulting rapid initiation of CPR and management. It is unknown if these differences influence the relative effectiveness of amiodarone and lidocaine for patients with IHCA, and prior studies of antiarrhythmic medication use for IHCA are lacking. Accordingly, using a large US national registry of IHCA, our goal was to compare outcomes of patients with IHCA caused by VT/VF treated with amiodarone or lidocaine.

Study Design and Methods

Data Source and Patient Population

The American Heart Association's Get With the Guidelines-Resuscitation (GWTG-R) inpatient registry is a national, multicenter, prospective registry and quality improvement program for IHCA. Hospitals participating in the registry submit clinical information regarding the medical history, hospital care, and outcomes of consecutive patients hospitalized for cardiac arrest using an online, interactive case report form and Patient Management Tool (IQVIA). At participating hospitals, in-hospital adult resuscitation events for which an emergency resuscitation response was initiated and a resuscitation record was completed are included in the database.[7] The variables used in the database are based on the Utstein-Style Guidelines for Uniform Reporting of Laboratory CPR Research, and all data are evaluated for accuracy and compliance with guidelines via data entry software and training and certification of data entry personnel.[8] For data prior to October 1, 2010, IQVIA serves as the data collection (through their Patient Management Tool) and coordination center for the American Heart Association/American Stroke Association GWTG programs. The University of Pennsylvania serves as the data analytic center and has an agreement to prepare the data for research purposes.

Within GWTG-R from January 2000 to December 2014, a total of 39,089 adult patients (≥ 18 years of age) who experienced VT/VF IHCA were identified. We excluded 159 patients with an arrest that began in an outpatient or ambulatory care setting; 3,598 patients who did not receive defibrillation (standard treatment includes defibrillation for cardiac arrest caused by VT/VF); 14,827 patients who did not receive amiodarone or lidocaine; 4,522 patients who received both antiarrhythmic therapies, as we would not be able to determine which antiarrhythmic was administered first or to which antiarrhythmic the patient had or had not ultimately responded; 247 patients with missing data on amiodarone and lidocaine treatment; and 1,106 patients with incomplete documentation. Our final analytic cohort included 14,630 patients with IHCA secondary to VT/VF who received defibrillation and either lidocaine or amiodarone (Fig 1).

The primary outcome in this study was return of spontaneous circulation (ROSC). Secondary outcomes included 24 h survival postarrest, survival to hospital discharge, and favorable neurologic outcome. Favorable neurologic outcome was defined as cerebral performance category at hospital discharge = good cerebral performance (conscious, alert, able to work, might have mild neurologic or psychologic deficit) or moderate cerebral disability (conscious, sufficient cerebral function for independent activities of daily life; able to work in sheltered environment).

Patient, event, and treatment characteristics were compared according to use of amiodarone and lidocaine using independent-group *t* tests

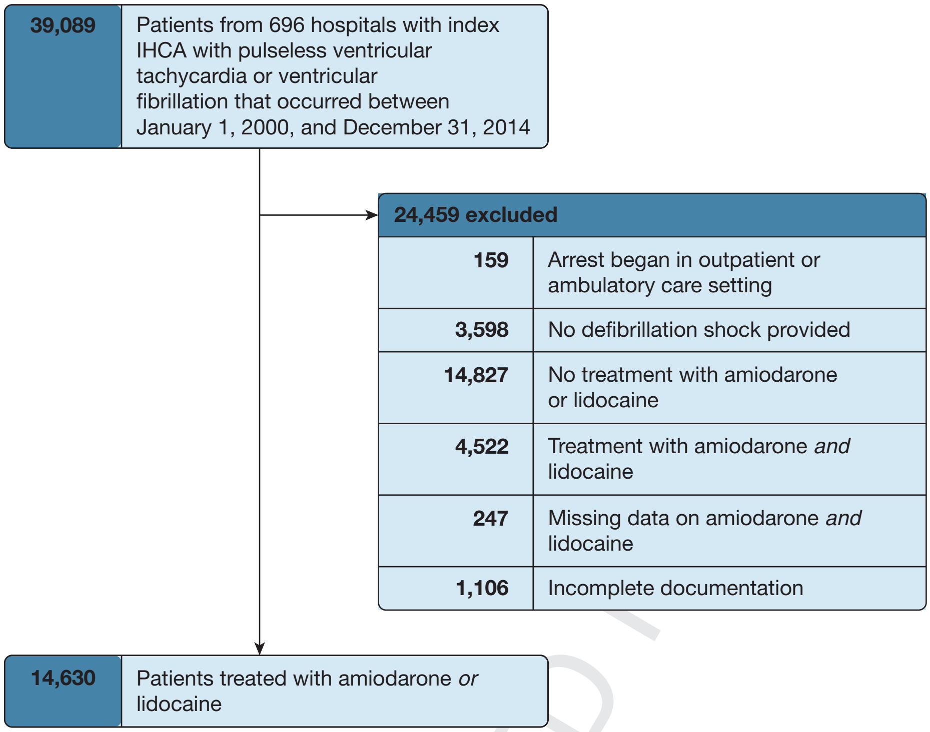

Figure 1 – *IHCA = in-hospital cardiac arrest.*

(for continuous variables) and χ^2 analysis (for binary variables). Unadjusted comparisons of ROSC, 24 h survival, survival to hospital discharge, and favorable neurologic outcome at hospital discharge were assessed with χ^2 analysis. Multivariable logistic regression analysis and propensity score methods (PSMs) were used to test for associations between treatment drug (ie, amiodarone vs lidocaine) and ROSC, 24 h survival, survival to hospital discharge, and favorable neurologic outcome at hospital discharge when other covariates Table 3) were statistically controlled. Consistent with previous studies based on the GWTG-R data, covariates in the risk-adjusted analysis included age at admission, sex, race/ethnicity,[9,10] preexisting conditions, event location, illness category, time of event (weekend vs weekday, daytime vs nighttime),[7,11] event witnessed, interventions already in place at the time of arrest (ECG; pulse oximetry), and time to defibrillation. Average marginal effects (AMEs) of treatment, defined as the average difference between the amiodarone and lidocaine groups in the predicted probability of a given outcome with other covariates held constant, were calculated and converted to percentages to gain perspective on the magnitude of treatment group differences.

PSMs were used in addition to multivariable logistic regression analysis.[12,13] The PS was defined as "the conditional probability of assignment to a particular treatment given a vector of observed covariates."[12] PSM can potentially facilitate causal inference from observational (ie, nonrandomized) studies by balancing the distribution of covariates between treatment groups.[14] In the PSM literature, the AME (ie, the risk difference between two groups) is referred to as the average treatment effect (ATE). Austin[15] reviewed PSMs and their relative performance in scenarios such as the current one in which the outcome variable is binary and the risk differences are the ATEs of interest. Results from simulations indicated that estimates of risk differences using inverse probability of treatment weighting (IPTW) with the PS showed lower SEs, approximately correct CIs, and correct type I error rates compared with PS matching, PS stratification, and covariate adjustment using the PS score. Based on the results of Austin, IPTW was used to estimate risk differences between lidocaine and amiodarone on ROSC, 24 h survival, survival to hospital discharge, and favorable neurologic outcomes. IPTW using the PS requires specification of a model for the propensity score and a model for the treatment outcome, and we included all covariates in both models to facilitate comparisons with results from multivariable logistic regression analysis.

An alpha level of 0.05 was used for all analyses, all hypothesis tests were two-sided, and *P* values for all test statistics were based on SEs adjusted for within-hospital nonindependence.[16] Analyses were conducted with the 2017 Stata (Stata Corp) software package.

Results

Among 14,630 patients with VT/VF IHCA, 68.7% (n = 10,058) were treated with amiodarone and 31.3% (n = 4,572) were treated with lidocaine. Patients treated with lidocaine were less likely to be male and more likely to be White; had lower rates of several preexisting conditions (including diabetes mellitus, hepatic insufficiency, metabolic or electrolyte abnormality, metastatic or hematologic cancer, renal insufficiency, respiratory insufficiency, and septicemia); were less likely to have events in the adult ICU and more likely to have events in the ED, general inpatient area, and

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TABLE 1] ■■■

	Treated With Lidocaine (n = 4,572)	Treated With Amiodarone (n = 10,058)	*P* Value
Age at admission, mean ± SD, y	65.7 ± 14.7	65.2 ± 14.3	.09
Male	2,868 (62.7%)	6,478 (64.4%)	.05
Race/ethnicity (White)	3,553 (77.7%)	7,541 (75.0%)	.03
Preexisting conditions			
Acute CNS nonstroke event	245 (5.4%)	537 (5.3%)	.98
Acute stroke	148 (3.2%)	325 (3.2%)	.99
Baseline depression in CNS function	389 (8.5%)	845 (8.4%)	.88
Diabetes mellitus	1,240 (27.1%)	3,093 (30.8%)	< .001
Heart failure this admission	892 (19.5%)	2,102 (21.8%)	.13
Heart failure prior to this admission	1,023 (22.4%)	2,402 (23.9%)	.09
Hepatic insufficiency	176 (3.9%)	494 (4.9%)	.01
Hypotension or hypofusion	950 (20.8%)	2,224 (22.2%)	.15
Major trauma	92 (2.0)	229 (2.3%)	.39
Metabolic or electrolyte abnormality	557 (12.2%)	1,372 (13.7%)	.04
Metastatic or hematologic cancer	284 (6.2)	750 (7.5%)	.02
MI this admission	1,537 (33.6%)	3,218 (32.1%)	.18
MI prior to admission	1,107 (24.2%)	2,281 (22.7%)	.13
Pneumonia	371 (8.1)	911 (9.1%)	.007
Renal insufficiency or dialysis	1,044 (22.9)	2,908 (29.0%)	< .001
Respiratory insufficiency	1,374 (30.1)	3,451 (34.4%)	< .001
Septicemia	349 (7.6)	1,053 (10.5%)	< .001
Event location[a]			
Adult ICU	1,973 (43.2%)	5,091 (50.6%)	< .001
Interventional area	325 (7.1%)	622 (6.2%)	.09
ED	897 (19.6%)	1,404 (14.0%)	< .001
General inpatient area, telemetry, or step-down unit	1,044 (22.8%)	2,569 (25.5%)	.005
Operating room	162 (3.5%)	127 (1.3%)	< .001
Other	171 (3.7%)	242 (2.4%)	< .001
Illness category[b] (cardiac)	3,060 (66.9%)	6,650 (66.2%)	.45
Event occurred on weekend[c] (yes)	1,398 (30.6%)	2,971 (29.5%)	.23
Event witnessed[d] (yes)	4,007 (87.7%)	8,804 (87.5%)	.86
Time of cardiac arrest: daytime	3,158 (70.0%)	7,160 (71.7%)	.03
ECG monitoring[e] (yes)	3,933 (86.0%)	8,794 (87.4%)	.09
Pulse oximetry monitoring[e] (yes)	3,020 (66.1%)	7,219 (71.8%)	< .001
Continuous vasopressor (yes)	1,196 (26.2%)	3,309 (32.9%)	< .001
Mechanical ventilation (yes)	1,223 (26.8%)	3,118 (31.0%)	< .001
Time to defibrillation, min	2.2 (3.9)	2.4 (4.2)	.002

MI = myocardial ischemia/infarction.
[a]For the "event location" variable: Adult ICU includes the locations "Adult Coronary Care Unit (CCU)," "Adult ICU (includes medical, surgical, cardiovascular, trauma, and burn ICUs)," and "All ICUs." Interventional area includes the locations "Cardiac Catheterization Laboratory," "Diagnostic/Intervention Area," and "Diagnostic/Intervention Area Including Catheter Lab."
Other includes the locations "Delivery Suite," "Neonatal ICU," "Pediatric ICU," "Post-Anesthesia Recovery Room (PACU)," "Rehab, Skilled Nursing or Mental Health Unit/Facility," "Same-day Surgical Area," "Pediatric Cardiac Intensive Care Unit (PCICU)," "Unknown/Not Documented," and "Other."
[b]For the "Illness category" variable, "Cardiac" includes "Medical-Cardiac" and "Surgical-Cardiac." "Non-cardiac" includes "Medical-Noncardiac," "Surgical-Noncardiac," "Obstetric," "Trauma," and "Other."
[c]Weekend was defined as the period from 11:00 PM Friday to 6:59 AM Monday.
[d]In response to the question "Was the onset of the cardiopulmonary arrest directly observed by someone (family, lay bystander, employee, or health care professional)?"
[e]In response to the item "Intervention(s) ALREADY IN PLACE when the need for chest compressions and/or defibrillation was first recognized."

TABLE 2] ■■■

	Treated With Lidocaine (n = 4,572)	Treated With Amiodarone (n = 10,058)	*P* Value
Return of spontaneous circulation[a] (yes)	3,3530 (77.3%)	7,700 (76.6%)	.47
24 h survival[b] (yes)	2,898 (63.4%)	5,937 (59.1%)	.001
Survival to hospital discharge[c] (yes)	2,168 (47.5%)	4,196 (42.0%)	< .001
Favorable neurologic outcome at hospital discharge[d]	1,681 (39.6%)	3,083 (33.3%)	< .001

[a]Was ANY documented return of adequate circulation [ROSC] (in the absence of ongoing chest compressions return of pulse/heart rate by palpation, auscultation, Doppler, arterial BP waveform, or documented BP) achieved during the event?
[b]Did patient survive 24 h from start of index CPA event?.
[c]Did patient survive to hospital discharge?.
[d]Defined as cerebral performance category at hospital discharge = *good cerebral performance* (conscious, alert, able to work, might have mild neurologic or psychologic deficit) or *moderate cerebral disability* (conscious, sufficient cerebral function for independent activities of daily life; able to work in sheltered environment). Due to missing data, the total sample size for this variable was 13,494 (n = 9,248 for treatment with amiodarone and n = 4,246 for treatment with lidocaine).

OR; were more likely to have events in the daytime; and were less likely to have pulse oximetry monitoring (Table 1).

Results from unadjusted comparisons between the lidocaine and amiodarone groups on the four outcomes (ROSC, 24 h survival, survival to discharge, and favorable neurologic outcome at hospital discharge [defined as cerebral performance category at hospital discharge = good cerebral performance (conscious, alert, able to work, might have mild neurologic or psychologic deficit) or moderate cerebral disability (conscious, sufficient cerebral function for independent activities of daily life; able to work in sheltered environment]) are presented in Table 2. There was no statistically significant difference between treatment groups on ROSC (absolute risk difference, 0.7; 95% CI, –1.2 to 2.7; *P* = .47). However, treatment with lidocaine was associated with statistically significantly higher rates of 24 h survival (absolute risk difference, 4.3; 95% CI, 2.2 to 6.5; *P* = .001), survival to hospital discharge (absolute risk difference, 5.5; 95% CI, 3.4 to 7.8; *P* < .001), and favorable neurologic outcome at hospital discharge (absolute risk difference, 6.3; 95% CI, 3.9 to 8.6; *P* < .001) (Fig 2).

The models were adjusted to minimize the influence of confounders from explaining the differences in outcome. Results from multivariable logistic regression analyses are presented in Table 3. In fully adjusted models, statistically significant correlates of lower odds of all four outcomes included age, several preexisting conditions (hypotension or hypoperfusion, metastatic or hematologic cancer, renal insufficiency or dialysis, sepsis, and continuous vasopressor), and time to defibrillation. Statistically significant correlates of higher odds of all four outcomes included White race, myocardial infarction this admission, cardiac illness category, ECG monitoring, and year admitted. With all covariates statistically controlled, compared with amiodarone, lidocaine was associated with statistically significantly higher odds of the following: (1) ROSC (aOR = 1.15; *P* = .01, AME, 2.3; 95% CI, .5-4.2); (2) 24 h survival (aOR, 1.16; *P* = .004; AME, 3.0; 95% CI, 0.9-5.1); (3) survival to discharge (aOR, 1.19; *P* < .001; AME, 3.3; 95% CI, 1.5-5.2); and (4) favorable neurologic outcome at hospital discharge (aOR, 1.18; *P* < .001; AME, 3.1; 95% CI, 1.3-4.9) (Fig 3).

Results from PSM analyses using IPTW were similar to original results using multivariable logistic regression analysis, although the risk differences from PSM analyses were smaller in magnitude across all four outcome measures. Compared with amiodarone, lidocaine was associated with statistically significantly higher rates of the following: (1) ROSC (ATE, 2.3; *P* = .04; 95% CI, .1 to 4.2); (2) 24 h survival (ATE, 2.3; *P* = .04; 95% CI, 0.1 to 4.5); (3) survival to discharge (ATE, 2.6; *P* = .02; 95% CI, 0.5-4.6); and (4) favorable neurologic outcome at hospital discharge (ATE, 2.2; *P* = .04; 95% CI, 0.1-4.3). Our PSM results seem similar to those from other studies that found few differences between estimates of the ATE based on multivariable modeling vs PSM.[17,18]

Discussion

In a national cohort of nearly 15,000 patients with IHCA caused by VT/VF, patient outcomes were compared

Figure 2 – *ROSC = return to spontaneous circulation.*

according to treatment with lidocaine or amiodarone. Adjusted results showed that use of lidocaine was associated with statistically significantly higher rates of ROSC (AME, 2.3%), 24 h survival (AME, 3.0%), survival to discharge (AME, 3.3%), and favorable neurologic survival (AME, 3.1%). These observational findings warrant further investigation to ensure the optimal care of patients experiencing in-hospital VT/VF arrest. Amiodarone was introduced as the first-line antiarrhythmic to be used in VT and VF with the 2000

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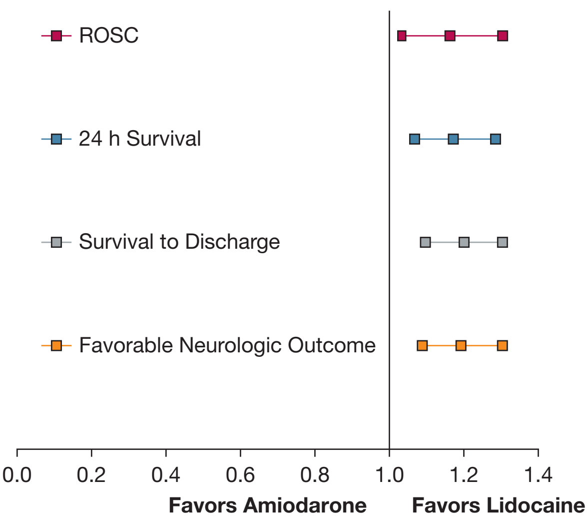

Figure 3 – *ROSC = return to spontaneous circulation.*

update to the America Heart Association Advanced Cardiac Life Support guidelines,[19] replacing prior recommendations for lidocaine as first-line therapy.[20-23] Until revised guidelines in 2018, which suggested that either amiodarone or lidocaine may be used,[3] amiodarone remained a preferred therapy. This preference was evident in the current study of patients experiencing cardiac arrest between 2000 and 2014,[24-26] with 69% of patients receiving amiodarone and 31% lidocaine.

Although studies comparing lidocaine and amiodarone in the management of adults with IHCA are lacking, prior studies of pediatric populations have been completed. A 2014 study of IHCA in pediatric patients with VT/VF found that lidocaine was associated with improved ROSC and 24 h survival but not survival to discharge.[27] A more recent study by Holmberg et al[28] found no difference between agents when compared in a propensity-matched study, again creating a lack of consensus for superiority of one agent over another. There have been no extensive studies of antiarrhythmic use in adult patients with IHCA. A 2018 systematic review by Ali et al[29] included evidence for patients in any setting (in-hospital and out-of-hospital) for all ages. They found 14 randomized controlled trials and 18 observational studies, but only one observational pediatric study reviewed earlier looked at in-hospital data. There was no difference between either amiodarone or lidocaine compared with placebo relative to survival to discharge or good neurologic function. ROSC with lidocaine, however, was significantly better than placebo. Direct comparison between the two agents found no difference for any outcomes. The ROC-ALPS trial of OHCA using the polysorbate-free amiodarone also found no difference in survival to discharge or neurologic state compared with lidocaine.[6] ROSC, however, was higher in the lidocaine group. Currently, the IV nonpolysorbate amiodarone formulation is not available in the United States. To the best of our knowledge, the current study is the largest study to date of amiodarone and lidocaine use in adult patients with IHCA examining the outcomes of ROSC, 24 h survival, survival to hospital discharge, and neurologic outcome.

The current unadjusted analysis revealed no difference between treatment groups in terms of ROSC. Patients treated with lidocaine did have statistically significantly higher rates of survival to hospital discharge compared with patients treated with amiodarone. However, following extensive risk adjustment for potential confounders, lidocaine treatment was associated with statistically significantly higher odds of ROSC and continued to be associated with statistically significantly higher odds of 24 h survival and survival to discharge compared with amiodarone treatment. Our results differ from the only studies we discovered of in-hospital arrest from VT/VF. Neither Pollak et al[30] nor Rea et al[31] reported a difference for treatment with amiodarone compared with lidocaine for survival at 24 h or survival to discharge or ROSC or 24 h survival. These differences, however, may be due to the larger sample size used in our analysis. One must also consider that local responses to Code Blue alerts within various institutions may be directed by an institution-specific protocol for medication administration that may preferentially select one agent first over another.

Results also showed that lidocaine compared with amiodarone was associated with a statistically significantly higher rate of favorable neurologic outcome, as defined by the cerebral performance categories “good cerebral performance” and “moderate cerebral disability” at discharge. There are several potential mechanisms for a positive association between lidocaine post-ROSC outcomes in the absence of an association with ROSC itself. One possibility is

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TABLE 3] ■■■

	ROSC		24 h Survival		Survival to Hospital Discharge		Favorable Neurologic Outcome	
	aOR (95% CI)	*P* Value	aOR (95% CI)	*P* Value	aOR (95% CI)	*P* Value	aOR (95% CI)	*P* Value
Age at admission	.97 (.96 to.99)	.001	.95 (.94 to .97)	< .001	.91 (.89 to .92)	< .001	.90 (.89 to .92)	< .001
Female	1.18 (1.07 to 1.30)	.001	1.04 (.96 to 1.12)	.38	1.00 (.92 to 1.09)	.94	.99 (.91 to 1.08)	.87
Race/ethnicity (white)	1.35 (1.22 to 1.49)	< .001	1.34 (1.22 to 1.47)	< .001	1.43 (1.29 to 1.59)	< .001	1.40 (1.26 to 1.57)	< .001
Preexisting conditions								
Acute CNS nonstroke event	.97 (.80 to 1.17)	.62	.92 (.79 to 1.08)	.34	.95 (.78 to 1.15)	.58	.83 (.69 to 1.01)	.06
Acute stroke	1.08 (.86 to 1.36)	.51	.76 (.61 to .93)	.009	.73 (.59 to .91)	.006	.54 (.42 to .69)	< .001
Baseline depression in CNS function	.99 (.86 to 1.14)	.93	.99 (.88 to 1.12)	.88	.81 (.70 to .94)	.007	.53 (.44 to .63)	< .001
Diabetes mellitus	1.02 (.94 to 1.12)	.60	1.00 (.92 to 1.08)	.99	.96 (.88 to 1.05)	.36	.94 (.86 to 1.02)	.15
Heart failure this admission	.99 (.89 to 1.11)	.74	1.00 (.90 to 1.11)	.96	.97 (.88 to 1.08)	.63	.95 (.85 to 1.06)	.34
Heart failure prior to this admission	.92 (.82 to 1.03)	.15	.91 (.83 to 1.01)	.08	.87 (.79 to .96)	.006	.85 (.76 to .94)	.002
Hepatic insufficiency	.84 (.69 to 1.01)	.07	.80 (.67 to .95)	.01	.73 (.51 to .79)	<.001	.63 (.50 to .79)	< .001
Hypotension or hypofusion	.69 (.62 to .77)	< .001	.60 (.55 to .66)	<.001	.57 (.51 to .63)	< .001	.57 (.51 to .64)	< .001
Major trauma	.89 (.68 to 1.17)	.42	.66 (.52 to .84)	.001	.53 (.39 to .71)	< .001	.52 (.37 to .73)	< .001
Metabolic or electrolyte abnormality	1.14 (1.00 to 1.29)	.046	1.01 (.91 to 1.14)	.73	.95 (.84 to 1.08)	.44	.94 (.82 to 1.07)	.35
Metastatic or hematologic cancer	.84 (.71 to .98)	.03	.71 (.62 to .81)	< .001	.65 (.56 to .75)	< .001	.61 (.52 to .71)	< .001
MI this admission	1.62 (1.46 to 1.80)	< .001	1.49 (1.37 to 1.63)	< .001	1.45 (1.33 to 1.58)	< .001	1.43 (1.30 to 1.57)	< .001
MI prior to admission	1.05 (.95 to 1.17)	.34	1.05 (.95 to 1.16)	.32	1.05 (.95 to 1.16)	.33	1.01 (.91 to 1.12)	.81
Pneumonia	1.12 (.98 to 1.28)	.11	1.18 (1.03 to 1.35)	.02	1.08 (.93 to 1.25)	.32	.93 (.80 to 1.09)	.38
Renal insufficiency or dialysis	.85 (.77 to .93)	<.001	.71 (.66 to .77)	< .001	.55 (.51 to .60)	<.001	.56 (.51 to .61)	< .001
Preexisting conditions								
Respiratory insufficiency	.97 (.88 to 1.07)	.52	.90 (.83 to .99)	.03	.82 (.75 to .91)	< .001	.76 (.69 to .85)	< .001
Septicemia	.87 (.76 to .99)	.04	.83 (.73 to .95)	.006	.69 (.59 to .80)	< .001	.70 (.59 to .82)	< .001
Event location								
Adult ICU	...		...		...		...	
Interventional area	.80 (.66 to .99)	.03	0.85 (0.73 to 1.00)	.05	1.00 (.86 to 1.17)	.99	.95 (.81 to 1.12)	.55
ED	1.00 (.87 to 1.16)	.96	.88 (0.78 to .99)	.03	1.21 (1.08 to 1.36)	.001	1.13 (1.01 to 1.27)	.03
General inpatient area	0.81 (.71 to .91)	.001	0.82 (0.72 to .94)	< .001	.94 (.84 to 1.05)	.28	.95 (.85 to 1.06)	.37
Operating room	.79 (.59 to 1.04)	.10	1.32 (1.02 to 1.70)	.04	1.64 (1.24 to 2.18)	.001	1.83 (1.27 to 2.45)	< .001
Other	1.00 (.77 to 1.30)	.99	1.18 (.93 to 1.51)	.17	1.39 (1.10 to 1.75)	.006	1.31 (1.03 to 1.65)	.02
Illness category: cardiac	1.62 (1.46 to 1.79)	<.001	1.91 (1.74 to 2.08)	< .001	1.97 (1.80 to 2.16)	<.001	2.06 (1.86 to 2.28)	<.001

(Continued)

TABLE 3] (*Continued*)

	ROSC		24 h Survival		Survival to Hospital Discharge		Favorable Neurologic Outcome	
	aOR (95% CI)	*P* Value	aOR (95% CI)	*P* Value	aOR (95% CI)	*P* Value	aOR (95% CI)	*P* Value
Event occurred weekend	.93 (.86 to 1.02)	.14	.93 (.86 to 1.00)	.05	.90 (.82 to .98)	.01	.91 (.83 to .99)	.04
Event witnessed	1.12 (.97 to 1.29)	.13	1.17 (1.03 to 1.34)	.02	1.35 (1.18 to 1.55)	< .001	1.43 (1.25 to 1.63)	< .001
Time of arrest: daytime	1.06 (.97 to 1.15)	.23	1.13 (1.05 to 1.23)	.002	1.15 (1.06 to 1.26)	.001	1.14 (1.04 to 1.24)	.003
ECG monitoring	1.24 (1.09 to 1.41)	.001	1.22 (1.08 to 1.39)	.001	1.41 (1.24 to 1.61)	< .001	1.51 (1.31 to 1.74)	< .001
Pulse oximetry monitoring	1.13 (1.02 to 1.26)	.02	1.05 (0.95 to 1.16)	.46	.98 (.89 to 1.08)	.72	.95 (.86 to 1.06)	.39
Continuous vasopressor	.85 (.78 to .94)	.001	.49 (.45 to .54)	< .001	.43 (.40 to .48)	< .001	.42 (.38 to .47)	< .001
Mechanical ventilation	.97 (.87 to 1.08)	.55	.74 (.67 to .81)	< .001	.60 (.54 to .66)	< .001	.57 (.52 to .64)	< .001
Year admitted	1.04 (1.02 to 1.05)	< .001	1.02 (1.00 to 1.03)	.01	1.02 (1.01 to 1.04)	< .001	1.03 (1.01 to 1.04)	< .001
Time to defibrillation	.94 (.93 to .95)	< .001	.91 (.90 to .93)	< .001	.89 (.88 to .91)	< .001	.89 (.88 to .90)	< .001
Treatment drug: lidocaine vs amiodarone	1.15 (1.03 to 1.30)	.01	1.16 (1.05 to 1.28)	.004	1.19 (1.08 to 1.30)	< .001	1.18 (1.07 to 1.30)	< .001

*Due to missing data on covariates, sample sizes for multivariable analysis were as follows: return of spontaneous circulation (ROSC; n = 13,953); 24 h survival (n = 13,957); survival to discharge (n = 13,957); and favorable neurologic outcome (n = 13,957). aOR = adjusted OR; MI = myocardial infarction.

that lidocaine could have been associated with earlier ROSC compared with amiodarone, which might translate into better post-ROSC outcomes overall. There is also evidence for neuroprotective effects of lidocaine in animal models. This may be due to lidocaine's sodium channel inhibition, preservation of adenosine triphosphate, and neuroinflammatory reduction protecting against hypoxia and ischemia.[32] However, it is not clear why the same apparent treatment effect was not observed in OHCA studies unless it is also dependent on time to treatment, which could be more delayed in OHCA.

Limitations of the current study include that it was an observational analysis with potential for residual confounding. The data used in the current study came only from hospitals participating in the GWTG-R registry and may not generalize to other patients at other hospitals due to lack of time stamps for administration. Also, data were not available on underlying reasons for hospital admission, etiology of the cardiac arrest, whether the cardiac arrest was medical or surgery related, duration of CPR, hemodynamic parameters at ROSC, Acute Physiology and Chronic Health Evaluation II score, targeted temperature management, or the amount of drug administered. In addition, data regarding preexisting administration of either lidocaine or amiodarone are not available within the GWTG-R reporting and cannot be ruled out as a possible contributing factor for either success or failure. For example, it is plausible that choice of treatment was dependent on certain conditions that respond better to that treatment drug, resulting in better outcomes. This is in addition to the lack of documentation or oral agents such as mexiletine or other antiarrhythmic agents prior to the event.

Interpretation

Among adult patients with IHCA secondary to VT/VF who received defibrillation, treatment with lidocaine was associated with differences in ROSC, 24 h survival, rates of survival to hospital discharge, and favorable neurologic outcomes compared vs treatment with amiodarone. Further study of treatment specific to IHCA is needed to inform optimal management and guidelines for cardiac arrest in this setting. In addition, data on underlying reasons for hospital admission may inform the treatment decisions undertaken by inpatient teams or underlying pathology leading to the arrest.

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