Impact of Changes in Resuscitation Practice on Survival and Neurological Outcome After Out-of-Hospital Cardiac Arrest Resulting From Nonshockable Arrhythmias

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Background—Out-of-hospital cardiac arrest (OHCA) claims millions of lives worldwide each year. OHCA survival from shockable arrhythmias (ventricular fibrillation/tachycardia) improved in several communities after implementation of American Heart Association resuscitation guidelines that eliminated “stacked” shocks and emphasized chest compressions. “Nonshockable” rhythms are now the predominant presentation of OHCA; the benefit of such treatments on nonshockable rhythms is uncertain.

Methods and Results—We studied 3960 patients with nontraumatic OHCA from nonshockable initial rhythms treated by prehospital providers in King County, Washington, over a 10-year period. Outcomes during a 5-year intervention period after adoption of new resuscitation guidelines were compared with the previous 5-year historical control period. The primary outcome was 1-year survival. Patient demographics and resuscitation characteristics were similar between the control (n=1774) and intervention (n=2186) groups, among whom 471 of 1774 patients (27%) versus 742 of 2186 patients (34%), respectively, achieved return of spontaneous circulation; 82 (4.6%) versus 149 (6.8%) were discharged from hospital, 60 (3.4%) versus 112 (5.1%) with favorable neurological outcome; 73 (4.1%) versus 135 (6.2%) survived 1 month; and 48 (2.7%) versus 106 patients (4.9%) survived 1 year (all \( P < 0.005 \)). After adjustment for potential confounders, the intervention period was associated with an improved odds of 1.50 (95% confidence interval, 1.29–1.74) for return of spontaneous circulation, 1.53 (95% confidence interval, 1.14–2.05) for hospital survival, 1.56 (95% confidence interval, 1.11–2.18) for favorable neurological status, 1.54 (95% confidence interval, 1.14–2.10) for 1-month survival, and 1.85 (95% confidence interval, 1.29–2.66) for 1-year survival.

Conclusion—Outcomes from OHCA resulting from nonshockable rhythms, although poor by comparison with shockable rhythm presentations, improved significantly after implementation of resuscitation guideline changes, suggesting their potential to benefit all presentations of OHCA. (Circulation. 2012;125:1787-1794.)

Key Words: cardiopulmonary resuscitation ■ heart arrest ■ mortality ■ out-of-hospital cardiac arrest ■ resuscitation
Although such progress is encouraging, the incidence of shockable cardiac arrest is diminishing and currently accounts for only about one quarter of all OHCA. At present, OHCA is largely attributable to nonshockable arrhythmias—asystole and pulseless electric activity—from which survival is especially poor and for which few if any interventions are effective. In particular, the impact of community-wide treatment strategies incorporating changes in CPR guidelines for what is now a majority of patients with nonshockable OHCA is uncertain. Also at issue is whether treatments that benefit ventricular fibrillation/tachycardia might be less beneficial for nonshockable arrests. For example, chest compressions are believed to have greater importance than ventilations in ventricular fibrillation/tachycardia, but the converse could be true during resuscitation of nonshockable arrest if caused by respiratory failure. We hypothesized that the predominant effect from guideline changes would be beneficial so that protocols that prioritize chest compressions would be associated with improved survival in OHCA resulting from nonshockable arrhythmias.

Methods

Study Design and Setting

We performed a retrospective cohort study of all nontraumatic cardiac arrests resulting from a nonshockable rhythm that were treated by emergency medical service (EMS) providers from King County, Washington, over ∼10 years. The investigation compares a control period of 5 consecutive years during which the 2000 guidelines were practiced against a subsequent intervention period of similar duration when the EMS CPR protocol prioritized chest compression consistent with the 2005 guidelines. King County (excluding the city of Seattle) has an area of 2000 square miles and a population of 1.3 million residents. The EMS of King County is a 2-tiered system comprising basic life support provided by emergency medical technician–trained firefighters equipped with automated external defibrillators (AEDs) and advanced life support provided by paramedics who are trained in rhythm recognition and provide intubation, manual defibrillation, and intravenous medications. Both tiers of response are activated simultaneously for cardiac arrest; the mean times from receipt of an emergency call to basic and advanced life support on-scene arrival are ∼5 and 10 minutes, respectively.

Intervention

Along with ongoing educational and training activities, each year, all emergency medical technicians in King County are required to demonstrate didactic and hands-on skills for CPR and AED competency as part of mandatory recertification. In 2004, emergency medical technician training incorporated major changes in the resuscitation protocol in advance of publication of the 2005 AHA guidelines, which were based on the medical directors’ appraisal of the then-known science. The previous protocol, derived from the 2000 AHA guidelines, consisted of 3 serial (“stacked”) shocks for ventricular fibrillation with an immediate rhythm reanalysis or postdefibrillation pulse check (if no shock was advised) between each shock and 1 minute of prescribed CPR between sequential rhythm reanalyses if no shock was indicated. The new protocol (implemented on January 1, 2005) reduced the initial set of sequential rhythm analyses with stacked shocks from 3 to 1, eliminated rhythm and pulse checks immediately after shocks, and extended the time period for CPR between rhythm analyses from 1 to 2 minutes, mirroring the changes that would be forthcoming in the 2005 guidelines. Notably, a ratio of 15 chest compressions to 2 ventilations (15:2) was maintained during the initial year of the new protocol (consistent with prior guidelines) until new guidelines were released in December 2005, at which time the ratio changed to 30:2. All AEDs were reconfigured to facilitate this change in protocol.

Study Population

The study population was drawn from all nontraumatic EMS-treated OHCA that occurred over ∼10 years, from January 1, 2000, through March 31, 2010. Eligible cases included persons treated by EMS for an initially nonshockable, nontraumatic OHCA that occurred before their arrival. Patients with cardiac arrest caused by drowning or smoke inhalation and patients <18 years of age were excluded. The control period (before implementation of the new protocol) included all eligible cases from January 1, 2000, through December 31, 2004. The protocol change was implemented simultaneously throughout King County on January 1, 2005, so the intervention period included all eligible cases from that time through March 31, 2010.

Data Collection and Definitions

Since 1976, the EMS Division of King County has maintained an ongoing registry of all cardiac arrests in which EMS resuscitation was attempted. EMS incident report forms, AED rhythm and audio recordings, dispatch data, hospital records, and death certificates were collected to form a consecutive case series that adhered to the Utstein guidelines for reporting OHCA. The data set includes demographic information, EMS response intervals, resuscitation characteristics, treatments, and outcomes. The cause of the arrest was determined from all available information, including hospital records and death certificates. Neurological status at discharge was classified according to the Cerebral Performance Category score and was based on review of the hospital record.

A nonshockable initial rhythm was determined by a no-shock advisory from the AED and was further characterized by its description in the prehospital record and, when available, by review of AED ECG recordings. Pulseless electric activity was defined as any organized ventricular rhythm (exclusive of ventricular tachycardia) with an absent pulse; asystole was defined as the absence of any ventricular electric activity. In all cases, rhythms could be consistently classified as shockable or nonshockable on the basis of the AED shock advisory and confirmed by the description of the rhythm in the prehospital record; ECG recordings were available in 1058 of 1780 patients (59%) from the control period and 1414 of 2173 patients (65%) from the intervention period.

Outcomes

The primary outcome was survival at 1 year. Secondary end points included return of spontaneous circulation at hospital arrival (demarcating the end of EMS care), survival to hospital discharge, favorable neurological status (Cerebral Performance Category score 1–2) at hospital discharge, and 1-month (30-day) survival. Long-term survival was ascertained through the use of Washington State Vital Statistics records and the US Social Security Death Index. However, for persons discharged alive from the hospital between January and March 2010, 1-month and 1-year survival status was ascertained from only the Social Security Death Index because Washington State Vital Statistics records had not yet been completed for 2011. Exclusion of this 2010 portion of the cohort did not change the reported results.

Analysis

We used descriptive statistics to compare characteristics by study period, the χ2 test statistic to compare categorical variables, and the nonparametric Wilcoxon rank-sum test to compare continuous variables. If missing, basic and advanced life support response time values were imputed from the median response time for each study period. This was required for ∼18% of response intervals during the control period and a comparable proportion of 12% during the intervention period. Logistic regression was used to calculate individual and adjusted odds ratios and 95% confidence intervals, with multivariable analyses adjusting for Utstein elements, including age,
sex, location of arrest, provision of bystander CPR, EMS response interval (minutes from call receipt at the dispatch center to the earliest EMS arrival on scene), cause of the arrest, witnessed status, and initial rhythm. We also evaluated the potential for generalized temporal trends to account for the study period association by using segmented regression analysis of interrupted time series data.25,26

To help evaluate the potential contributions of hospital-based care and postdischarge characteristics, we evaluated the relationship of long-term outcomes contingent on achieving spontaneous circulation at the end of EMS care and survival to hospital discharge. We performed these contingent analyses by restricting the cohort to those who achieved pulses at the end of EMS care and then to those who survived to hospital discharge.

In addition, we conducted subgroup analyses according to the cause of the arrest and initial rhythm to determine whether the change in protocol might have differential effects in these subgroups.20 An interaction term was added to the primary model to test whether the association differed according to subgroup. Finally, to help assess for potential mechanisms of how guidelines changes might have influenced outcomes, we compared CPR process information during the first 5 minutes of EMS resuscitation using AED recordings from a representative sample of 25 cases before and 25 cases after the protocol change that were matched by sex, age, initial rhythm, and EMS agency. We used the paired t test to compare total chest compressions, chest compression fraction (the proportion of resuscitation time with chest compressions in the absence of spontaneous circulation), and duration of rhythm analyses (seconds). All analyses were conducted with STATA/SE 11.0 software (College Station, TX).

The study was approved by the University of Washington Human Subjects Review Committee. The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript.

Results

In total, 6713 patients had an OHCA during the study period, of whom 5909 were adults with a nontraumatic arrest before EMS arrival (Figure 1). The proportions excluded because of traumatic origin or age <18 years were similar between the 2 time periods (12%). The proportion of patients with nonshockable initial rhythms increased from 1774 of 2758 patients (64%) during the control period to 2186 of 3151 (69%) during the intervention period (P<0.001). A total of 3960 patients had an initially nonshockable rhythm, 1774 (45%) treated before and 2186 (55%) treated after the protocol change (Figure 1). Among patients with nonshockable rhythms, the distributions of asystole (65%) and pulseless electric activity (35%) were similar between the 2 periods.

Patient demographics and resuscitation characteristics in the 2 time periods were comparable with respect to age, sex, location of arrest, whether the arrest was witnessed by bystander, and EMS response interval (Table 1). The provi-
Cardiac cause, % (n) 59.4 (1054) 53.8 (1175)

Male sex, % (n) 59.4 (1054) 58.8 (1285)

Age, mean (SD), y 67 (17.0) 66.6 (17.0)

Initial rhythm PEA, % (n) 35.3 (627) 34.8 (760)

Witnessed arrest, % (n) 38.6 (684) 38.9 (850)

Public arrest location, % (n) 9.6 (171) 9.3 (204)

Bystander CPR, % (n) 47.9 (850) 56.7 (1239)

Mean interval from emergency call to first responding unit arrival, mean (SD), min 5.4 (2.3) 5.5 (2.3)

Median (Q1–Q3) 71 (55–80) 68 (55–80)

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Table 1. Resuscitation Characteristics of Patients

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Table 2. Unadjusted and Adjusted Odds Ratios for Study Outcomes Associated With the Intervention Compared With the Control Protocol Period

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control Period, 2000–2004 (n=1774)</th>
<th>Intervention Period, 2005–2010 (n=2186)</th>
<th>Odds Ratio (95% Confidence Interval)</th>
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<tr>
<td>Overall</td>
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<td>ROSC at hospital arrival, n (%)</td>
<td>471 (26.6)</td>
<td>742 (33.9)</td>
<td>1.42 (1.24–1.63) &lt;0.001 1.50 (1.29–1.74) &lt;0.001</td>
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<td>Survival to hospital discharge, n (%)</td>
<td>82 (4.6)</td>
<td>149 (6.8)</td>
<td>1.51 (1.14–1.99) 0.004 1.53 (1.14–2.05) 0.004</td>
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<td>Good neurological outcome, n (%)†</td>
<td>60 (3.4)</td>
<td>112 (5.1)</td>
<td>1.59 (1.15–2.20) 0.005 1.56 (1.11–2.18) 0.01</td>
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<td>1-mo survival, n (%)</td>
<td>73 (4.1)</td>
<td>135 (6.2)</td>
<td>1.53 (1.14–2.05) 0.004 1.54 (1.14–2.10) 0.006</td>
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<td>1-y survival, n (%)</td>
<td>48 (2.7)</td>
<td>106 (4.9)</td>
<td>1.83 (1.29–2.59) 0.001 1.85 (1.29–2.66) 0.001</td>
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<td>Patients with ROSC at hospital arrival</td>
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<td>149</td>
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ROSC indicates return of spontaneous circulation.

*Adjusted for age, sex, location of arrest, provision of bystander cardiopulmonary resuscitation, emergency medical service response interval (minutes from call receipt at the dispatch center to the earliest emergency medical service arrival on scene), cause of arrest, witnessed arrest, and initial rhythm.

†Cerebral performance category 1 to 2 at hospital discharge calculated from available data: n=78 for the period of 2000 to 2004 and n=145 for the period of 2005 to 2010.
The changes first introduced in the 2005 guidelines have the potential to increase chest compressions but potentially at the cost of fewer ventilations. In the sampled analysis of matched pairs, we confirmed that the guideline changes resulted in a greater number of chest compressions, a higher proportion of resuscitation time with chest compressions, and less time devoted to rhythm analysis (Table 4). Previous work has shown a favorable association between the frequency of chest compressions and outcome in cardiac arrest from shockable arrhythmias but not definitively from nonshockable arrhythmias.\(^\text{13,28}\) This greater emphasis on blood flow (chest compressions) may have accounted for the greater benefit seen among patients whose arrest was attributed to a cardiac cause, whereas there was no evidence of such an association among those with arrests attributable to a noncardiac cause.

In the matched-pairs analyses comparing elements of CPR process between the 2 study periods, the number of chest compressions and proportion of time devoted to chest compressions during the initial 5 minutes of resuscitation increased significantly during the intervention compared with the control period, whereas the time spent performing rhythm analyses decreased significantly (Table 5).

### Discussion

In this cohort investigation, we observed a significant improvement in short- and long-term survival and neurological outcome among patients with nonshockable OHCA after implementation of a protocol consistent with CPR guidelines that prioritized chest compressions. This improvement was not attributable to temporal trends within the study periods but appeared to coincide with the change in protocol itself. These improvements were especially evident among arrests attributable to a cardiac cause, although there was no evidence of harm among arrests attributable to a noncardiac cause.

Although cardiac arrest resulting from nonshockable rhythms has previously been characterized,\(^\text{10,11}\) a strategy that improves outcome in such patients has yet to be demonstrated.\(^\text{10,11,27}\) Overall, we observed a \(\approx 2\%\) absolute increase (representing an \(\approx 81\%\) relative improvement) in 1-year survival after OHCA caused by a nonshockable rhythm. Although seemingly modest, with a number needed to treat of \(\approx 50\) for every additional life saved, this survival difference translates to a measurable improvement in public health from a widely applicable and comparatively low-cost intervention. Population-based estimates indicate upward of 125 000 nonshockable OHCA events treated each year in North America.\(^\text{3}\) Consequently, the survival improvement observed in the present study potentially translates into an additional 2500 long-term survivors each year in North America alone and upward of tens of thousands globally. Most of these patients were judged to have good functional outcome at hospital discharge, indicating that their survival could be considered both quantitatively and qualitatively meaningful.

### Mechanisms

The changes introduced in the 2005 guidelines have the potential to increase chest compressions but potentially at the cost of fewer ventilations. In the sampled analysis of matched pairs, we confirmed that the guideline changes resulted in a greater number of chest compressions, a higher proportion of resuscitation time with chest compressions, and less time devoted to rhythm analysis (Table 4). Previous work has shown a favorable association between the frequency of chest compressions and outcome in cardiac arrest from shockable arrhythmias but not definitively from nonshockable arrhythmias.\(^\text{13,28}\) This greater emphasis on blood flow (chest compressions) may have accounted for the greater benefit seen when cardiac arrest was due to cardiac causes while having less influence in arrests of noncardiac causes in which other aspects of care such as ventilation in patients with respiratory arrest might have greater relevance. Importantly, we saw no evidence of harm from the protocol change in any subgroup.

Although previously shown to principally benefit patients with shockable arrhythmias,\(^\text{7,10,11}\) the changes in the approach to resuscitation implemented during the intervention period are conceivably even more critical for patients with nonshockable OHCA, for whom defibrillation confers no known
benefit,29 whereas fewer interruptions for rhythm/shock analyses coupled with more chest compressions between analyses provide needed circulatory support until a potentially reversible cause is treated.

Limitations
This study was observational, not a randomized trial. Consequently, we cannot be certain that the survival improvement corresponding to the protocol change was causal. Temporal changes or other factors could confound the observed relationship between time period and outcome. However, we did not observe gradual temporal improvements in outcome when analyzed year by year by segmented regression; rather, we saw consistently better survival for each of the years after compared with before the protocol change (Figure 2). Moreover, multivariable adjustment for the Utstein elements to account for possible confounding did not alter the observed relationships. Although it is possible that EMS providers systematically attempted resuscitation in a more viable patient group in the latter than former time period, we believe this is unlikely given that the demographics of patients with nonshockable arrest were generally similar during both periods, as was the proportion of patients who presented with asystole versus pulseless electric activity.

Other treatment protocols during the study periods also could account for the differences seen such as those concurrently investigated by the Resuscitation Outcomes Consortium and a dispatcher-assisted CPR trial.3,30 However, these interventions were all randomized, did not change the fundamental components of the resuscitation protocol itself, and were not found to improve outcome. In the dispatcher-assisted CPR trial in particular, there was no difference in neurological intact survival among patients with nonshockable cardiac arrest who received chest compression–only instruction from dispatchers compared with instruction in chest compression with rescue breathing. A trial-related training or Hawthorne effect also could explain the observed survival benefit. However, the study community has a long history of participating in research, has consistently measured and reported outcomes from OHCA, and is accustomed to ongoing quality assurance activities and regular retraining exercises that have not changed substantively over the years regardless of trial participation.
One might consider whether unmeasured factors such as the characteristics of bystander CPR or hospital care were responsible for the survival benefit. Although mechanistic aspects of bystander CPR were not specifically measured, the favorable association between the intervention period and outcome persisted after adjustment for bystander CPR status. With respect to hospital care, patients were admitted to the same variety of nonacademic community hospitals during both study periods that do not specialize in postresuscitation care and uncommonly perform acute coronary interventions or administer hypothermia to patients with nonshockable cardiac arrest, given the paucity of evidence for benefit in this subgroup.26,31 Furthermore, the rate of return of spontaneous circulation at the end of EMS care, a measure directly attributable to prehospital rather than hospital care, was significantly higher during the intervention than control period. There was, however, some evidence that long-term prognosis among patients who achieved successful prehospital resuscitation or who survived to hospital discharge was better during the intervention compared with the control period (Table 2). One interpretation of these findings is that these downstream hospital and postdischarge components contributed in part to the observed long-term survival. An alternative explanation is that the prehospital benefit afforded by the greater likelihood of return of spontaneous circulation at the end of EMS care translated to improvement at later stages during recovery and convalescence. One of the tenets of resuscitation is that the later links in the chain of survival depend on the effectiveness of the earlier links, specifically CPR. This is evidenced, for example, by the association of early CPR with better long-term functional recovery from cardiac arrest.32

Finally, one must consider whether the findings of this study are generalizable, given that it was performed in a community with a mature EMS system. These limitations should be considered in the context of the strengths of the investigation. It took advantage of a robust population-based registry that related the guideline period to comprehensive short- and long-term outcomes and demonstrated what is achievable for a condition that remains a major public health burden.

Conclusions
Short- and long-term outcomes from OHCA resulting from nonshockable rhythms, including neurologically favorable survival to hospital discharge and survival at 1 year, although poor by comparison with shockable rhythm presentations, improved significantly after implementation of recent resuscitation guidelines that increased the proportion of resuscitation time devoted to chest compressions. These findings lend further evidence that resuscitation protocols aimed at increasing the basic provision of CPR have the potential to improve outcomes for all victims of cardiac arrest and are of particular importance in light of the changing epidemiology of the condition.

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Disclosures
This research study had no direct commercial sponsorship, and no authors have commercial conflicts of interest with respect to its content. Drs Kudenchuk and Rea both serve as volunteer contributors to the International Liaison Committee on Resuscitation and the American Heart Association for development of resuscitation guidelines and receive financial support from the National Heart Lung and Blood Institute in their roles as coinvestigators in the Resuscitation Outcomes Consortium. Although these organizations may have intellectual interest in the findings of this study, no funding was received from nor support sought from these sources for this study.

References
Although the overall incidence of out-of-hospital cardiac arrest has not changed in recent years, reports indicate that the proportion of arrests caused by shockable rhythms is diminishing. The vast majority of out-of-hospital cardiac arrests are now attributable to nonshockable arrhythmias—asystole and pulseless electrical activity—from which survival is especially poor and for which a treatment strategy that improves outcome has yet to be identified. In a number of communities, adoption of recent changes in cardiopulmonary resuscitation guidelines that prioritized the time devoted to chest compressions during resuscitation was associated with improved survival among patients with out-of-hospital cardiac arrest resulting from shockable rhythms. In this cohort investigation, we found that implementation of these guidelines was also associated with a significant improvement in short- and long-term survival and with favorable neurological outcomes, specifically among patients with nonshockable out-of-hospital cardiac arrest. After multivariable adjustment, the odds ratio of 1-year survival from nonshockable out-of-hospital cardiac arrest on implementation of these guideline changes compared with beforehand was 1.85 (95% confidence interval, 1.29–2.66). Comparably significant improvements were observed in return of spontaneous circulation, hospital admission rates, survival to hospital discharge, favorable neurological status at hospital discharge, and 1-month survival. These improvements could not be merely attributed to temporal trends within the study periods but appeared to coincide with the change in the cardiopulmonary resuscitation protocol itself. Our findings suggest that increasing the basic provision of cardiopulmonary resuscitation has the potential to improve outcomes for all victims of cardiac arrest and are of particular relevance and importance because of the changing epidemiology of the condition.

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