Impact of Changes in Resuscitation Practice on Survival and Neurological Outcome after Out-of-Hospital Cardiac Arrest Resulting From Non-Shockable Arrhythmias

**Running title:** Kudenchuk et al.; Non-shockable arrhythmias

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Abstract:

**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 implementing American Heart Association resuscitation guidelines that eliminated “stacked” shocks and emphasized chest compressions. “Non-shockable” rhythms are now the predominant presentation of OHCA, upon which the benefit of such treatments is uncertain.

**Methods and Results** - We studied 3960 patients with nontraumatic OHCA from non-shockable initial rhythms treated by pre-hospital providers in King County, WA over a 10 year period. Outcomes during a 5 year intervention period after adoption of new resuscitation guidelines were compared to the previous 5 year historical control period. The primary outcome was 1-year survival. Patient demographics and resuscitation characteristics were similar between control (n=1774) and intervention (n=2186) groups, among whom 471/1774 (27%) versus 742/2186 patients (34%), respectively, achieved return of circulation (ROSC); 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 adjusting for potential confounders, the intervention period was associated with an improved odds of 1.50 (95% confidence interval (CI) 1.29, 1.74) for ROSC; 1.53 (CI 1.14, 2.05) for hospital survival, 1.56 (CI 1.11, 2.18) for favorable neurological status; 1.54 (CI 1.14, 2.10) for 1-month survival, and 1.85 (CI 1.29, 2.66) for 1-year survival.

**Conclusions** - Outcomes from OHCA due to non-shockable rhythms, though poor by comparison with shockable rhythm presentations, improved significantly after implementing resuscitation guideline changes, suggesting their potential to benefit all presentations of OHCA.

**Key words:** cardiac arrest, cardiopulmonary resuscitation, heart arrest, mortality, resuscitation
Introduction

Cardiovascular disease accounts for 30% of global mortality, or about 17 million deaths annually, nearly half of which are from sudden and unexpected cardiac arrest. Resuscitation from out-of-hospital cardiac arrest (OHCA) requires a coordinated, time-critical set of interventions termed “links in the chain of survival”. Despite this approach, outcomes following OHCA are poor with overall survival estimated between 5-10%. In an effort to improve survival, the International Liaison Committee on Resuscitation (ILCOR) and American Heart Association (AHA) Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care were changed in 2005 and reiterated in 2010 to increase the proportion of time devoted to chest compressions during resuscitation. Changes included reducing the initial number of back-to-back rhythm analyses and shocks, eliminating rhythm and pulse checks immediately after each shock, increasing the ratio of chest compressions to ventilation from 15:2 to 30:2, and doubling the required period of CPR between successive rhythm evaluations.

Some communities have reported a significant increase in survival from OHCA following implementation of this protocol among patients presenting with shockable cardiac arrest due to ventricular fibrillation or tachycardia (VF/VT), and described an association between fewer interruptions in chest compressions and outcome.

While 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 non-shockable arrhythmias – asystole and pulseless electrical activity (PEA) - from which survival is especially poor and 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 non-shockable OHCA is...
uncertain.\textsuperscript{10,11} Also at issue is whether treatments that benefit VF/VT, might be less beneficial for non-shockable arrests. For example, chest compressions are believed to have greater importance than ventilations in VF/VT,\textsuperscript{18} but the converse could be true when resuscitating non-shockable arrest, if due to respiratory failure. We hypothesized that the predominant effect from guideline changes would be beneficial so that protocols which prioritize chest compressions would be associated with improved survival in OHCA due to non-shockable arrhythmias.

\section*{Methods}

\subsection*{Study Design and Setting}

We performed a retrospective cohort study of all non-traumatic cardiac arrests due to a non-shockable rhythm that were treated by emergency medical service (EMS) providers from King County, Washington over approximately 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 approximately 2000 square miles and a population of 1.3 million residents. The EMS of King County is a two-tiered system comprised of basic life support provided by emergency medical technician (EMT)-trained firefighters equipped with automated external defibrillators (AED) and advanced life support 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 approximately 5 and 10 minutes, respectively.\textsuperscript{7}
**Intervention**

Along with ongoing educational and training activities, each year, all EMTs in King County are required to demonstrate didactic and hands-on skills for CPR and AED competency as part of mandatory recertification. In 2004, EMT training incorporated major changes in the resuscitation protocol in advance of publication of the 2005 AHA Guidelines, based on the medical directors’ appraisal of the then known science. The previous protocol, derived from the 2000 AHA Guidelines, consisted of three serial (“stacked”) shocks for VF with an immediate rhythm reanalysis or post-defibrillation pulse check (if no shock was advised) between each shock, and one minute of prescribed CPR between sequential rhythm re-analyses 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 three to one, eliminated rhythm and pulse checks immediately after shocks and extended the time period for CPR between rhythm analyses from one to two 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 non-traumatic EMS-treated OHCA that occurred over approximately 10 years, from January 1, 2000 through March 31, 2010. Eligible cases included persons treated by EMS for an initially non-shockable, non-traumatic OHCA that occurred prior to their arrival. Cardiac arrest as the result of drowning or smoke inhalation and patients less than 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 such that 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.\textsuperscript{20} 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.\textsuperscript{21} The dataset includes demographic information, EMS response intervals, resuscitation characteristics, treatments and outcomes. Arrest etiology was determined from all available information including hospital records and death certificates. Neurological status at discharge was classified according to the Cerebral Performance Category (CPC) score and based on review of the hospital record.\textsuperscript{22}

A non-shockable initial rhythm was determined by a no-shock advisory from the AED and was further characterized by its description in the prehospital record, and, where available, by review of AED electrocardiogram (ECG) recordings.\textsuperscript{23} PEA was defined as any organized ventricular rhythm (exclusive of ventricular tachycardia) with an absent pulse, and asystole as absence of any ventricular electrical activity. In all cases rhythms could be consistently classified as shockable or non-shockable based on the AED shock advisory and confirmed by the rhythm’s description in the prehospital record; ECG recordings were available in 1058 of 1780 (59%) from the control period and 1414 of 2173 (65%) from the intervention period.

Outcomes
The primary outcome was survival at one year. Secondary endpoints included return of spontaneous circulation (ROSC) at hospital arrival (demarcating the end of EMS care), survival to hospital discharge, favorable neurological status (CPC score 1-2) at hospital discharge, and one-month (30 day) survival. Long-term survival was ascertained through use of Washington State Vital Statistics records and the United States Social Security Death Index. However, for persons discharged alive from the hospital between January-March 2010, one-month and one-year survival status were ascertained using 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 Chi-square test statistic to compare categorical variables and continuous variables by the nonparametric Wilcoxon rank sum test. If missing, BLS and ALS response time values were imputed using 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 (CI), with multivariable analyses adjusting for Utstein elements, including age, gender, 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), arrest etiology, 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 post-discharge
characteristics, we evaluated the relationship of long-term outcomes contingent upon 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 arrest etiology and initial rhythm to determine if the change in protocol might have differential effects in these subgroups. 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 gender, 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, USA).

The study was approved by the University of Washington Human Subjects Review Committee. The authors had full access to the data, take full responsibility for its integrity, 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 non-traumatic arrest prior to EMS arrival (**Figure 1**). The proportion excluded because of traumatic etiology or age < 18 was similar between the 2 time periods (12%). The proportion of
patients with non-shockable 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 non-shockable rhythm, 1774 (45%) treated prior to the protocol change, and 2186 (55%) after (Figure 1). Among patients with non-shockable rhythms, the distribution of asystole (65%) and PEA (35%) was similar between the two periods.

Patient demographics and resuscitation characteristics in the two time periods were comparable with respect to age, gender, location of arrest, whether the arrest was bystander-witnessed, and EMS response interval (Table 1). The provision of bystander CPR was lower in the control period (48% versus 57%, p<0.001), whereas the proportion of cardiac arrests ascribed to a cardiac etiology was higher (59% versus 54%, p<0.001).

**Outcome**

As presented in Table 2, each outcome was better during the intervention than control period. For example, for the primary outcome, 1-year survival improved from 2.7% (48 of 1774 patients) to 4.9% (106 of 2186 patients) between the control and intervention period (p= 0.001). Similarly, between control and intervention periods ROSC at hospital arrival improved from 26.6% to 33.9% of patients (p<0.001); survival to hospital discharge from 4.6% to 6.8% (p=0.004); neurologically favorable survival at discharge from 3.4% to 5.1% (p=0.005), and survival at one-month from 4.1% to 6.2% of patients (p=0.004). Furthermore, the intervention period retained a beneficial outcome association after adjustment for Utstein elements (Table 2). For example, the odds ratio (95% confidence interval) of 1-year survival for the intervention compared to control period was 1.85 (1.29, 2.66) after multivariable adjustment. Comparably significant odds ratios were observed for all secondary outcomes.

When we restricted the analyses to patients who achieved spontaneous circulation at the
end of EMS care or who survived to hospital discharge, there was some evidence suggesting a greater likelihood of long-term survival among patients with successful field resuscitation or who survived to hospital discharge in the intervention period as compared with the control period (Table 2).

We did not observe temporal trends in outcome within the two study periods (Figure 2). Moreover, when segmented regression analysis was applied to account for a potential generalized temporal trend in survival, the association between outcome and intervention period changed only slightly. For example the odds ratio of 1 year survival associated with the study period changed from 1.85 in the main model to 1.86 (1.28, 2.69) when segmented regression analysis was applied. Similarly ROSC changed from 1.50 in the main model to 1.53 (1.31, 1.77) with segmented regression analysis.

We also evaluated the outcomes according to initial rhythm and arrest etiology. We found no evidence that the association between protocol period and outcome differed according to the initial rhythm (p-values for interaction ≥ 0.6) (Table 3). However the test for interaction suggested a potential difference according to arrest etiology, with the p-value for the interaction term near or less than < 0.05 for each of the 5 outcomes (Table 3). That is, the benefit associated with the protocol change was observed specifically among patients whose arrest was attributed to a cardiac etiology, whereas there was no evidence of such an association among those with arrests of non-cardiac etiology.

In the matched-pairs analyses to compare elements of CPR process between the two 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 as compared with control period, while the time spent performing rhythm analyses
decreased significantly (Table 4).

Discussion

In this cohort investigation, we observed a significant improvement in short and long-term survival and neurological outcome among patients with non-shockable 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, though there was no evidence of harm among arrests due to non-cardiac cause.

While cardiac arrest due to non-shockable rhythms has been previously characterized, a strategy that improves outcome in such patients has yet to be demonstrated. Overall, we observed a 2% absolute increase in 1-year survival after OHCA due to a non-shockable rhythm. Although seemingly modest, with a number needed to treat of approximately 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 upwards of 125,000 non-shockable OHCA events treated each year in North America. Consequently, the survival improvement observed in the current study potentially translates into an additional 2500 long-term survivors each year in North America alone, and upwards 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 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, but not definitively from non-shockable arrhythmias.\textsuperscript{13, 28} This greater emphasis on blood flow (chest compressions) may have accounted for the greater benefit seen when cardiac arrest was due to a cardiac etiology, while having less influence in arrests of non-cardiac etiology in whom 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 and specifically among those with non-cardiac etiology.

Though previously shown to principally benefit patients with shockable arrhythmias,\textsuperscript{7, 10, 11} the changes in the approach to resuscitation implemented during the intervention period are conceivably even more critical for patients with non-shockable OHCA, for whom defibrillation confers no known benefit,\textsuperscript{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, but rather a consistently better survival for each of the years after as compared to 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 non-shockable arrest were generally similar during both periods, as was the proportion of patients who presented with asystole versus PEA.

Other treatment protocols during the study periods could also account for the differences seen, such as those concurrently investigated by the Resuscitation Outcomes Consortium, and a dispatcher-assisted CPR trial. However these interventions were all randomized, did not change the fundamental components of the resuscitation protocol itself, nor were any found to improve outcome. In the dispatcher assisted CPR trial in particular, there was no difference in neurologically intact survival among patients with non-shockable cardiac arrest who received chest compression-only instruction from dispatchers as compared with instruction in chest compression with rescue breathing. A trial-related training or Hawthorne effect could also 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 as well as regular retraining exercises that have not substantively changed 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. While mechanistic aspects of bystander CPR were not specifically measured, notably 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, none of which specialize in post resuscitation 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.\textsuperscript{26, 31} Furthermore, the rate of ROSC 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 as compared with control period (Table 2). One interpretation of these findings is that these downstream hospital and post-discharge components contributed in part to the observed long-term survival. An alternative explanation is that the pre-hospital benefit afforded by the greater likelihood of ROSC at 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.\textsuperscript{32}

Finally, one must consider whether the study findings are generalizable, given its performance in a community with a mature EMS system. These limitations should be considered in the context of the investigation’s strengths. 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 due to non-shockable rhythms, including neurologically-favorable survival to hospital discharge and survival at one-year, though 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 condition’s changing epidemiology.

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Conflict of Interest Disclosures: This research study had no direct commercial sponsorship, and none of the 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 (NHLBI) in their roles as co-investigators in the Resuscitation Outcomes Consortium. While 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:


Table 1. Resuscitation characteristics of patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control Period</th>
<th>Intervention Period</th>
<th>p*</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>2000-2004 (n=1774)</td>
<td>2005-2010 (n=2186)</td>
<td></td>
</tr>
<tr>
<td>Initial rhythm PEA, % (n)</td>
<td>35.3 (627)</td>
<td>34.8 (760)</td>
<td></td>
</tr>
<tr>
<td>Age in years, mean (SD), median (Q1 to Q3)</td>
<td>67 (17.0), 71 (55-80)</td>
<td>66.6 (17.0), 68 (55-80)</td>
<td></td>
</tr>
<tr>
<td>Male gender, % (n)</td>
<td>59.4 (1054)</td>
<td>58.8 (1285)</td>
<td></td>
</tr>
<tr>
<td>Cardiac etiology, % (n)</td>
<td>59.4 (1054)</td>
<td>53.8 (1175)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Witnessed arrest, % (n)</td>
<td>38.6 (684)</td>
<td>38.9 (850)</td>
<td></td>
</tr>
<tr>
<td>Public arrest location, % (n)</td>
<td>9.6 (171)</td>
<td>9.3 (204)</td>
<td></td>
</tr>
<tr>
<td>Bystander CPR, % (n)</td>
<td>47.9 (850)</td>
<td>56.7 (1239)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean interval from emergency call to 1st responding unit arrival, mean (SD), median (Q1 to Q3)</td>
<td>5.4 (2.3), 5 (4-6)</td>
<td>5.5 (2.3), 5 (4-6)</td>
<td></td>
</tr>
<tr>
<td>Abbreviations: PEA= pulseless electrical activity, CPR = cardiopulmonary resuscitation, SD = standard deviation, Q1 to Q3= interquartile range (Q1- Q3)</td>
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</table>

*p > 0.05 except where indicated

Table 2. Unadjusted and adjusted odds ratios for study outcomes associated with the intervention as compared with the control protocol period

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Period 2000-2004</th>
<th>Period 2005-2010</th>
<th>Odds Ratio (95% confidence intervals)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2000-2004 (n=1774)</td>
<td>2005-2010 (n=2186)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td>Unadjusted p-value Adjusted† p-value</td>
</tr>
<tr>
<td>ROSC at hospital arrival, n (%)</td>
<td>471 (26.6)</td>
<td>742 (33.9)</td>
<td>1.42 (1.24, 1.63)</td>
</tr>
<tr>
<td>Survival to hospital discharge, n (%)</td>
<td>82 (4.6)</td>
<td>149 (6.8)</td>
<td>1.51 (1.14, 1.99)</td>
</tr>
<tr>
<td>Good neurological outcome, n (%)</td>
<td>60 (3.4)</td>
<td>112 (5.1)</td>
<td>1.59 (1.15, 2.20)</td>
</tr>
<tr>
<td>1 month survival, n (%)</td>
<td>73 (4.1)</td>
<td>135 (6.2)</td>
<td>1.53 (1.14, 2.05)</td>
</tr>
<tr>
<td>1 year survival, n (%)</td>
<td>48 (2.7)</td>
<td>106 (4.9)</td>
<td>1.83 (1.29, 2.59)</td>
</tr>
<tr>
<td>Patients who survived to hospital discharge</td>
<td></td>
<td></td>
<td>Unadjusted p-value Adjusted† p-value</td>
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<tr>
<td>Survival to hospital discharge</td>
<td></td>
<td></td>
<td>1.19 (0.88, 1.61)</td>
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<tr>
<td>Good neurological outcome*</td>
<td></td>
<td></td>
<td>1.21 (0.86, 1.70)</td>
</tr>
<tr>
<td>1 month survival</td>
<td></td>
<td></td>
<td>1.22 (0.89, 1.66)</td>
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<tr>
<td>1 year survival</td>
<td></td>
<td></td>
<td>1.47 (1.02, 2.11)</td>
</tr>
<tr>
<td>Patients who survived to hospital discharge</td>
<td>82</td>
<td>149</td>
<td>1.19 (0.49, 2.88)</td>
</tr>
<tr>
<td>1 month survival</td>
<td></td>
<td></td>
<td>1.75 (1.0, 3.07)</td>
</tr>
</tbody>
</table>

Abbreviations: ROSC= return of spontaneous circulation
* Cerebral performance category 1-2 at hospital discharge, calculated from available data: n=78 for period 2000-2004 and n=145 for period 2005-2010
†Adjusted for age, gender, 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), arrest etiology, witnessed arrest and initial rhythm.
Table 3. Adjusted odds ratios for study outcomes associated with the intervention as compared with the control protocol period, stratified according to presenting arrest rhythm and cardiac arrest etiology.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Period 2000-2004</th>
<th>Period 2005-2010</th>
<th>Adjusted* OR (95% CI)</th>
<th>p value for interaction</th>
<th>Period 2000-2004</th>
<th>Period 2005-2010</th>
<th>Adjusted* OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presenting Arrest Rhythm</td>
<td></td>
<td></td>
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<tr>
<td>PEA</td>
<td>2000-2004</td>
<td>2005-2010</td>
<td>Adjusted* OR (95% CI)</td>
<td>p value for interaction</td>
<td>2000-2005</td>
<td>2005-2010</td>
<td>Adjusted* OR (95% CI)</td>
</tr>
<tr>
<td>ROSC at hospital arrival, n (%)</td>
<td>292 (46.6)</td>
<td>430 (56.6)</td>
<td>1.47 (1.18, 1.83)</td>
<td>0.93</td>
<td>179 (15.6)</td>
<td>312 (21.9)</td>
<td>1.51 (1.23, 1.86)</td>
</tr>
<tr>
<td>Survival to Discharge, n (%)</td>
<td>68 (10.9)</td>
<td>119 (15.7)</td>
<td>1.48 (1.07, 2.06)</td>
<td>0.73</td>
<td>14 (1.2)</td>
<td>30 (2.1)</td>
<td>1.69 (0.89, 3.21)</td>
</tr>
<tr>
<td>CPC 1-2 at discharge, n (%)</td>
<td>54 (8.7)</td>
<td>97 (12.8)</td>
<td>1.50 (1.04, 2.14)</td>
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<td>111 (14.6)</td>
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<td>24 (1.7)</td>
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<td>Survival to 1 year, n (%)</td>
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<td>87 (11.5)</td>
<td>1.90 (1.27, 2.85)</td>
<td>0.78</td>
<td>9 (0.8)</td>
<td>19 (1.3)</td>
<td>1.61 (0.72, 3.60)</td>
</tr>
<tr>
<td>Asystole</td>
<td>n=627</td>
<td>n=760</td>
<td></td>
<td></td>
<td>n=1147</td>
<td>n=1426</td>
<td></td>
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<tr>
<td>ROSC at hospital arrival, n (%)</td>
<td>292 (46.6)</td>
<td>430 (56.6)</td>
<td>1.47 (1.18, 1.83)</td>
<td>0.93</td>
<td>179 (15.6)</td>
<td>312 (21.9)</td>
<td>1.51 (1.23, 1.86)</td>
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<tr>
<td>Survival to Discharge, n (%)</td>
<td>68 (10.9)</td>
<td>119 (15.7)</td>
<td>1.48 (1.07, 2.06)</td>
<td>0.73</td>
<td>14 (1.2)</td>
<td>30 (2.1)</td>
<td>1.69 (0.89, 3.21)</td>
</tr>
<tr>
<td>CPC 1-2 at discharge, n (%)</td>
<td>54 (8.7)</td>
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<td>Arrest Etiology</td>
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<td>Cardiac Etiology</td>
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<tr>
<td>ROSC at hospital arrival, n (%)</td>
<td>236 (22.4)</td>
<td>359 (30.6)</td>
<td>1.69 (1.38, 2.08)</td>
<td>0.06</td>
<td>235 (32.6)</td>
<td>383 (37.9)</td>
<td>1.33 (1.07, 1.66)</td>
</tr>
<tr>
<td>Survival to Discharge, n (%)</td>
<td>25 (2.4)</td>
<td>61 (5.2)</td>
<td>2.54 (1.56, 4.14)</td>
<td>0.01</td>
<td>57 (7.9)</td>
<td>88 (8.7)</td>
<td>1.13 (0.78, 1.63)</td>
</tr>
<tr>
<td>CPC 1-2 at discharge, n (%)</td>
<td>17 (1.6)</td>
<td>46 (3.9)</td>
<td>2.91 (1.62, 5.20)</td>
<td>0.01</td>
<td>43 (6.0)</td>
<td>66 (6.5)</td>
<td>1.09 (0.72, 1.68)</td>
</tr>
<tr>
<td>Survival to 1 month, n (%)</td>
<td>21 (2.0)</td>
<td>53 (4.5)</td>
<td>2.63 (1.54, 4.45)</td>
<td>0.01</td>
<td>52 (7.2)</td>
<td>82 (8.1)</td>
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</tr>
<tr>
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<td>13 (1.2)</td>
<td>37 (3.2)</td>
<td>2.89 (1.50, 5.56)</td>
<td>0.11</td>
<td>35 (4.9)</td>
<td>69 (6.8)</td>
<td>1.49 (0.97, 2.31)</td>
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<tr>
<td>Non-Cardiac Etiology</td>
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<td>1.49 (0.97, 2.31)</td>
</tr>
</tbody>
</table>

Abbreviations: ROSC= return of spontaneous circulation; CPC= cerebral performance category; PEA= pulseless electrical activity; * Adjusted for age, gender, 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), arrest etiology, witnessed arrest and initial rhythm.

Table 4. Comparison of CPR characteristics according to protocol period during the initial 5 minutes of resuscitation.

<table>
<thead>
<tr>
<th></th>
<th>Period 2000-2004</th>
<th>Period 2005-2010</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=25*</td>
<td>n=25*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total number of chest compressions, mean (SD)</td>
<td>259 (101)</td>
<td>360 (87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Compression Ratio, mean (SD) †</td>
<td>53.7 (16.1)</td>
<td>66.8 (12.7)</td>
<td>0.008</td>
</tr>
<tr>
<td>Number of rhythm analyses, mean (SD)</td>
<td>2.9 (0.8)</td>
<td>2.4 (0.7)</td>
<td>0.01</td>
</tr>
<tr>
<td>Total time spent in rhythm analysis, seconds, mean(SD)</td>
<td>69 (26)</td>
<td>44 (19)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CPR= Cardio pulmonary resuscitation SD= standard deviation
* matched pairs based upon gender, age, initial cardiac arrest rhythm, and EMS agency providing care
† proportion of resuscitation time without spontaneous circulation during which chest compressions were administered
Figure Legends:

Figure 1. Selection of study population. The figure depicts the total number of patients treated for out-of-hospital cardiac arrest during the two study periods (January 1, 2000 through December 31, 2004, and January 1, 2005 through March 31, 2010), and the criteria used to identify those eligible for inclusion. Abbreviations: EMS = Emergency Medical Services, VF = Ventricular Tachycardia, VT = Ventricular Tachycardia, PEA = Pulseless Electrical Activity

Figure 2. Outcomes according to calendar year. The figure depicts the frequency of return of spontaneous circulation, survival to hospital discharge and 1-year survival during each year of the two protocol periods under evaluation, with 95% confidence intervals. No temporal trends were observed within the study periods as shown in the insert below (which provides the p for trend for each study outcome corresponding to the years that comprised the control and intervention periods). Rather, improved outcomes coincided with the change in protocol.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control Period 2000-2004</th>
<th>Intervention Period 2005-2010</th>
<th>p for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Return of spontaneous circulation at hospital arrival</td>
<td>0.78</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>Survival to hospital discharge</td>
<td>0.63</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>Cerebral Performance Category 1-2 at hospital discharge</td>
<td>0.84</td>
<td>0.64</td>
<td></td>
</tr>
<tr>
<td>1 month survival</td>
<td>0.79</td>
<td>0.51</td>
<td></td>
</tr>
<tr>
<td>1 year survival</td>
<td>0.53</td>
<td>0.29</td>
<td></td>
</tr>
</tbody>
</table>

ROSC = return of spontaneous circulation upon hospital arrival.
*Data for 2010 are shown through study end on March 31, 2010.
EMS treated cardiac arrest
1/2000-3/2010
N=6713

Period 2000-2004
N=3134

- Non eligible: N=376 (12%)
  - Age <18: 129
  - Trauma: 247

Eligible EMS cardiac arrest:
N= 2758 (88%)

- VF/VT
  N=984 (36%)

  - Non shockable:
    N= 1774 (64%)

    - PEA
      N= 627 (35%)

    - Asystole
      N= 1147 (65%)

- VF/VT
  N=965 (31%)

  - Non shockable:
    N= 2186 (69%)

    - PEA
      N= 760 (35%)

    - Asystole
      N= 1426 (65%)

Period 2005-2010
N=3579

- Non eligible: N=428 (12%)
  - Age <18: 163
  - Trauma: 265

Eligible EMS cardiac arrest:
N= 3151 (88%)
Impact of Changes in Resuscitation Practice on Survival and Neurological Outcome after Out-of-Hospital Cardiac Arrest Resulting From Non-Shockable Arrhythmias

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