Effect of Time of Day on Prehospital Care and Outcomes after Out-of-Hospital Cardiac Arrest

Running title: Wallace et al.; Time of day and OHCA outcomes

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Journal Subject Code: Treatment:[25] CPR and emergency cardiac care
Abstract:

Background—Over 300,000 out-of-hospital cardiac arrests (OHCA) occur each year in the United States. The relationship between time of day and OHCA outcomes in the prehospital setting is unknown. Any such association may have important implications for Emergency Medical Services (EMS) resource allocation.

Methods and Results—We performed a retrospective review of cardiac arrest data from a large, urban EMS system. Included were OHCA occurring in adults from January 2008 to February 2012. Excluded were traumatic arrests and cases where resuscitation measures were not performed. Day was defined as 8:00am to 7:59pm, and night as 8:00pm to 7:59am. A relative risk regression model was used to evaluate the association between time of day and prehospital return of spontaneous circulation (ROSC) and 30-day survival, adjusting for clinically relevant predictors of survival. Among the 4,789 included cases, 1,962 (41.0%) occurred at night. Mean age was 63.8 (SD 17.4) years; 54.5% were male. Patients with an OHCA occurring at night did not have significantly lower rates of prehospital ROSC compared to daytime arrests (11.6% vs. 12.8%, p=0.20). However, rates of 30-day survival were significantly lower at night (8.56% vs. 10.9%, p=0.02). After adjusting for demographics, presenting rhythm, field termination, duration of call, dispatch-to-scene interval, automated external defibrillator application, bystander cardiopulmonary resuscitation, and location, 30-day survival remained significantly higher following daytime OHCA, with a relative risk of 1.10 (95% CI 1.02-1.18).

Conclusions—Rates of 30-day survival were significantly higher for OHCA occurring during the day compared to night, even after adjustment for patient, event, and prehospital care differences.

Key words: heart arrest, cardiac arrest, resuscitation, cardiopulmonary resuscitation, emergency medical services, emergency, emergency medicine, emergency department
Background

Out-of-hospital cardiac arrest (OHCA) is a public health problem affecting nearly 300,000 individuals each year in the United States. Survival rates from OHCA are generally poor, with one large US registry study documenting an eight percent rate of survival to hospital discharge. Successful resuscitation requires implementing a “chain of survival” with both prehospital and hospital-based links, including activation of the Emergency Medical Services (EMS) system, early cardiopulmonary resuscitation (CPR) with an emphasis on high quality chest compressions, defibrillation as appropriate, advanced life support measures, and post-resuscitation care in the receiving hospital.

The detection and treatment of OHCA at night may be less effective due to differences in patient characteristics, event characteristics, and therapeutic measures. Previous work has shown that in-hospital cardiac arrest (IHCA) survival rates exhibit temporal variability, with both return of spontaneous circulation (ROSC) and survival to hospital discharge occurring less frequently during nighttime hours, even after adjustment for multiple potential confounders including illness category. Likewise, a recent analysis of witnessed OHCA in Japan demonstrated that nighttime hospital admissions are associated with worsened clinical outcomes than daytime admissions. However, no study to date has evaluated the association between time of day and OHCA outcomes and care measures in the immediate prehospital setting. Any such association would have important implications for EMS staffing, training, and resource allocation.

In this investigation, we sought to evaluate variability in prehospital ROSC by time of day among adults with OHCA. We hypothesized that outcomes after OHCA would be worse at night, even when adjusted for potentially confounding patient, event, and therapeutic characteristics.
Methods

Setting and Design

This investigation was an observational, retrospective study of OHCA patients treated by the Philadelphia Fire Department (PFD). In addition to fire suppression responsibilities, the PFD is the exclusive public provider of emergency, prehospital care and transportation for individuals in metropolitan Philadelphia. It responds to approximately 270,000 medical emergencies per year, serving a population of over 1.5 million via a universal emergency access phone number (9-1-1). The PFD operates a tiered EMS system with 36 advanced life support (ALS) ambulances, each staffed by two paramedics or one paramedic and one firefighter-emergency medical technician (EMT); and 14 basic life support (BLS) ambulances, staffed with two firefighter-EMTs. It also utilizes 59 engine companies and 29 ladder companies as basic life support (BLS) first responders, each staffed with at least one firefighter-EMT. These first responder companies are equipped with automated external defibrillators (AEDs) and oxygen, among other life support materials.

Data used in the present study were derived from an electronic database of ALS and BLS patient care reports, which were provided by the PFD to the University of Pennsylvania investigative team. Patient care reports are generated for all EMS responses. They summarize the events of the medical emergency as well as treatments provided. OHCA events were extracted by the investigators from this database using a consistent approach with available data. Specifically, cases where CPR, defibrillation, and/or epinephrine (1:10,000 dilution) were provided as treatments were extracted, as these therapies are specific for OHCA. Additional cases were extracted based on EMS personnel “Impression” of the case as a ‘cardiac arrest’ or ‘code blue’, these diagnoses having been selected from a drop-down menu upon generation of
the patient care report.

Multiple verification steps were performed by authors SKW and FSS to validate this case identification algorithm and to evaluate for missed OHCA. To assess for false positives, we randomly selected 500 cases meeting our extraction criteria for examination. Hand review of the written case narratives revealed no false positives. All patients had suffered cardiac arrests. To assess for missed cases of OHCA, we reviewed an exploratory set of cases not meeting extraction criteria where the EMS personnel “Impression” of the patient was ‘unconscious/unresponsive’, ‘hypotension’, or ‘cardiac rhythm disturbance’. Of the 7815 exploratory cases identified, 32 possible false negatives were found, with only 12 of these being true OHCA in progress upon EMS arrival. Based on this data, the sensitivity of our original identification algorithm was 99.3%, and the specificity 100%.

The patient care reports included nearly 500 different patient and provider level variables including patient gender, age, and race; event address; time interval between dispatch, arrival at patient location, and delivery to a receiving hospital or field termination; initial cardiac rhythm as shockable (ventricular fibrillation or ventricular tachycardia) vs. non shockable (pulseless electrical activity or asystole); bystander CPR use (yes/no); arrest location (public or private); AED use by a bystander or first responder (yes/no); defibrillation (yes/no); epinephrine use (yes/no); field termination status (yes/no); and a free-form, written case narrative.

Due to the lack of a dedicated collection variable, bystander CPR was derived via hand extraction following review of the written case narratives by one investigator (AKA). Our estimate is therefore conservative as it depends upon mention of the bystander in the written summary of the emergency. We were not able to distinguish between public access AED use by a bystander and AED use by a first responder (for example, PFD engine or ladder company).
This study was approved by the Institutional Review Boards of the Hospital of the University of Pennsylvania, the City of Philadelphia Department of Public Health, and the Commonwealth of Pennsylvania Bureau of EMS.

Study Sample

Our study population included all EMS-treated adult patients (≥18 years of age) who suffered an OHCA of presumed cardiac etiology between January 1, 2008 and February 20, 2012 (n=4789). Resuscitation efforts had to be performed in order for a patient to be included in the study. Patients with “do not resuscitate” orders were excluded. Likewise, patients found to be dead on arrival were also excluded from analysis. In this way, biases in the threshold for resuscitation efforts by time of day were minimized. Traumatic arrests, including those caused by firearm injuries and motor vehicle collisions, were excluded via an iterative keyword search of the written case narratives. We also excluded patients whose names and date of birth were unknown, as survival status would be impossible to determine for these individuals (n=152). Such cases without name or birth date represented only 3.1% of the cohort, and their distribution between day and night was not significantly different (p=0.35; data not shown).

Measurement

Time of day was defined by the time at which the PFD was dispatched to the OHCA event. In this study, day was defined as 8:00am to 7:59pm, while night was defined as 8:00pm to 7:59am. These periods were selected to reflect the 12-hour shift schedule followed during the study period by EMS personnel working for the PFD.

Our prospectively selected primary outcome measure was prehospital ROSC, which was hand extracted from the written case narratives by two investigators (SKW, AKA). Our secondary outcome measure was 30-day survival as determined via the United States Social
Security Death Index, in conjunction with death statistics provided by the Pennsylvania Department of Health and an online obituary search using the patient’s name. We defined 30-day survival as living ≥30 calendar days from the EMS cardiac arrest event date, generated at the time of dispatch. Survivors were confirmed via a public records search on LexisNexis (LexisNexis Group, Dayton, OH). We were not able to determine 30-day survival in 768 patients (16.0%) using these resources, meaning they could be found in neither death indexes nor public records. There was no significant difference in the distribution of these patients between day and night (15.2% unknown 30-day survival status among the night cohort vs. 17.2% unknown 30-day survival status among the day cohort, p=0.06). Information pertaining to the neurological status of surviving patients was not available.

**Statistical Analysis**

Data were downloaded into a statistical software package (Stata 11.2, StataCorp LP, College Station, TX) for analysis. Descriptive statistics were used to characterize the study population. We used histograms to graphically check if continuous variables were normally distributed. Numerically, we looked at skewness and kurtosis. For normally distributed continuous variables, we calculated group means and standard deviations and applied t-tests to assess significant differences between groups. Results are presented as means and 95% confidence intervals (CI). For non-normal continuous variables, such as our time interval measures, we calculated medians and interquartile ranges (IQR) and used the Wilcoxon-Mann-Whitney test to assess significant differences between groups. For categorical variables, we tested for significant differences between groups using chi-square tests.

A relative risk regression model was used to evaluate the association between time of day and our outcome measures, adjusting for prospectively designated, clinically relevant predictors.
of survival. These included age, gender, race, presenting rhythm (shockable vs. non-shockable), field termination status, total duration of call (dispatch to arrival at hospital or field termination), time interval from dispatch to arrival at the scene, AED application by a bystander or first responder, bystander CPR performance, and location of the arrest (public or private). Gaussian error and robust standard error estimates were used. Relative risks with 95% CIs are presented; a relative risk greater than 1 indicates an improved likelihood of ROSC or 30-day survival compared to the reference group. Adjusted associations were likewise explored between several measures of prehospital care and time of day. A p-value less than 0.05 was considered statistically significant.

Results

The Philadelphia Fire Department responded to 4789 OHCA cases from January 1, 2008 through February 20, 2012 that met our inclusion criteria. Among these, 2827 cases occurred during the day (59.0%), compared to 1962 cases at night (41.0%). Patient demographics are shown in Table 1. The mean age of the cohort was 63.8 (SD 17.4) years. Males represented 54.5% of the group (n=2607). Patients suffering an OHCA at night were significantly younger (62.8 [SD 17.5] years) than daytime cases (64.4 [SD 17.4] years) (p=0.002). Patient gender and race did not vary significantly by time of day. The cohort was majority Black (52.1%) or White (35.9%). Other races represented included Asian (1.3%), Hispanic (4.9%), South Indian (0.6%), other (0.4%), and unknown (4.8%).

Arrest event characteristics stratified by time of day are displayed in Table 2. OHCA events occurring during the night were less likely to present in a shockable initial rhythm than daytime events (24.5% vs. 28.3%, p=0.003). Night OHCA cases also had significantly longer
median total call times, defined as time from dispatch to arrival at the hospital or field termination (30 minutes, IQR 23-38 minutes), compared to day cases (28 minutes, IQR 22-36 minutes) (p=0.01). Dispatch-to-scene time intervals were also significantly different by time of day when evaluated using a non-parametric test, though the median value was the same for both groups at six minutes (0<0.001). The application of an AED by a bystander or first responder was less likely to occur at night (47.0% vs. 50.1%, p=0.04). Finally, rates of bystander CPR were significantly lower at night compared to the day (7.59% vs. 12.7%, p<0.001). The rate of field termination did not differ by time of day, nor did arrest location.

Average prehospital ROSC rates and 30-day survival rates partitioned by hour of the day are shown in Figures 1a and 1b. Patients with an OHCA occurring at night did not have a significantly lower rate of prehospital ROSC compared to patients who arrested during the day (11.6% vs. 12.8%, p=0.20). However, rates of 30-day survival were significantly lower at night compared to the day (8.56% vs. 10.9%, p=0.02). After adjusting for potential confounders including age, gender, race, presenting rhythm (shockable vs. non-shockable), field termination status, duration of call, dispatch-to-scene interval, AED application by a bystander or first responder, bystander CPR performance, and arrest location – 30-day survival remained significantly higher following daytime OHCA, with a relative risk of 1.10 (95% CI 1.03-1.18) (Table 3).

Adjusted associations were likewise explored between measures of prehospital care and time of day (Figure 2). Bystander CPR was more likely to occur during the day, even after multivariate adjustment (adjusted relative risk 1.20, 95% CI 1.13-1.28). Shockable initial rhythms including ventricular fibrillation and ventricular tachycardia were also more likely to present during the day (adjusted relative risk 1.07, 95% CI 1.01-1.13). Finally, the quintile of
dispatch-to-scene time was significantly shorter during the day compared to the night (adjusted relative risk 0.89, 95% CI 0.82-0.97).

Discussion

We found that rates of 30-day survival following OHCA were lower at night (defined as 8:00pm to 7:59am) compared to the day (defined as 8:00am to 7:59pm), even after adjustment for patient, arrest event, and prehospital care factors. This analysis represents the largest study to date of temporal variability in OHCA outcomes within the United States. The present work provides important insights into the prehospital patient and event characteristics that contribute to survival variability from OHCA by time of day.

Our findings are consistent with a recent analysis from Koike et al., 6 which found that adult OHCA patients admitted to Japanese receiving hospitals during the daytime had significantly higher rates of one-month survival (adjusted odds ratio 1.26, 95% CI 1.22-1.31). The investigators also found that nighttime OHCA admissions were younger on average and less likely to receive bystander CPR, consistent with our findings. This study was limited to witnessed cardiac arrests and looked only at post-admission survival outcomes. Peberdy et al. 5 found that survival-to-discharge rates from IHCA were lower at night even after multivariate adjustment (adjusted odds ratio 1.18, 95% CI 1.12-1.23). The authors hypothesized that the mechanism for decreased survival at night was likely multifactorial, including physiological factors, hospital staffing, and operational differences.

Temporal variability in health care staff performance has been well documented in the clinical literature. Horwitz et al. 7 found that evening and night shift hospital workers were at greater risk of occupational injury than their daytime counterparts. Kuhn 8 has reviewed the
effects of shift work on the disruption of circadian rhythms in emergency medicine physicians, which include increased illness and poor mood. Smith-Coggins et al. ⁹ found that emergency medicine attending physicians were less effective at performing manual and cognitive tasks when working night shifts and sleeping during the day, as compared to working day shifts and sleeping during the night. Further research may be needed to determine if there is a biologic reason for lower OHCA survival at night, or if decreased physical and mental performance on the part of EMS providers and receiving hospital staff are contributing factors.

Indeed, it is possible that the quality of CPR and other resuscitation care measures by EMS workers at night may be an important, unmeasured contributing factor to the observed variability in OHCA survival by time of day. Studies have demonstrated that the quality of multiple parameters of CPR provided by health care staff can be inconsistent.¹⁰,¹¹ The use of innovative approaches, including debriefing sessions ¹² and rolling refreshers, ¹³ have been shown to enhance subsequent CPR performance quality and outcomes when imparted to health care workers who treat cardiac arrest. Translation of such strategies to the prehospital setting may be an important topic of future investigation.

We found significant variation in EMS response time by time of day. The interval from dispatch to scene was significantly longer at night, as was the interval from dispatch to hospital arrival or field termination. Though we controlled for these variables in our adjusted analysis, it remains possible that the decreased rate of survival observed at night is partially a factor of delayed response times, given the time sensitive nature of cardiac arrest and the reduced likelihood of life-saving bystander resuscitation measures during the nighttime hours. Whether delayed response times at night are due to staffing, performance, or transportation factors will be an important area of further study.
It is also important to consider other issues of survival variability from OHCA in light of our findings. Sasson et al.\textsuperscript{14} found differences in bystander CPR provision by neighborhood in Atlanta based on income level in a recent analysis. Likewise, Lerner et al.\textsuperscript{15} identified clusters of OHCA incidence as well as low bystander CPR in Rochester, New York. It is possible that certain geographic regions in Philadelphia are more sensitive to day and night differences in survival than others. Such neighborhoods might benefit from the placement of additional public access AEDs or trained first responders. Geographic analysis of survival patterns in Philadelphia is an important future research goal.

Finally, it is notable that we found no significant difference in immediate prehospital ROSC by time of day, but we did find a significant difference in 30-day mortality, even after adjustment for prehospital confounders. This finding may suggest that the reason for the observed difference lies in the hospital care provided to the patients during the day versus the night, as suggested by Koike et al.\textsuperscript{6} It is possible that some hospitals offer less comprehensive treatment during the nighttime, potentially affecting patient outcome. Corroborating citywide prehospital records with hospital charts from many different facilities is often not feasible; however, future studies may wish to consider the possibility in order to control for this factor.

Limitations

Our study has several limitations. The analysis was specific to Philadelphia and may not be generalizable to other cities with different EMS systems and patient populations. Nonetheless, Philadelphia represents a large and diverse metropolitan area with a fire department-based EMS system, common in many American cities. The PFD is large, accounting for over one third of all EMS runs in the state of Pennsylvania and covering a heterogeneous, but geographically unified population. In fact, the advantage of limiting our study to Philadelphia is that the city is served
by one EMS system; thus, no differences among EMS agencies serve as confounders in the present work.

An additional limitation to this study is that our prehospital database was not linked to inpatient records from the 27 adult receiving hospitals in Philadelphia. Thus, specific details about hospital course, post-resuscitation care, and survival to discharge were not available. However, by using the United States Social Security Death Index in conjunction with Pennsylvania State Vital Statistics and an online obituary search, 30-day survival status was obtained for the majority of patients. Thirty-day survival is a robust clinical outcome and its use is consistent with other published OHCA studies.16-18

No data were obtained for 30-day survival in 768 patients (16.0% of the cohort). However, there was no significant difference in the distribution of these patients between day and night, making the chance of bias in our analysis unlikely (15.2% unknown 30-day survival status among the night cohort vs. 17.2% in the day cohort, p=0.06).

Conclusion

We observed that rates of 30-day survival were significantly lower for cases of OHCA occurring at night compared to the day, even after adjustment for patient, event, and care differences. We also found significant differences in the rates of bystander CPR, AED use, and response time intervals by time of day. There are likely several factors contributing to the observed survival variability by time of day, including biologic differences in the patients themselves, variation in the quality of CPR parameters, staffing and operational factors, and response time. These data suggest the need to further study nighttime EMS resuscitation quality and system processes to improve patient safety and survival after OHCA.
Acknowledgments: We would like to acknowledge the hard work and dedication of the Philadelphia Fire Department in providing high-quality emergency medical care to the citizens of Philadelphia.

Funding Sources: This work was supported by a grant from the Doris Duke Charitable Foundation to the University of Pennsylvania to fund Clinical Research Fellow Sarah K. Wallace and by a Thomas B. and Jeannette E. Laws McCabe Fund Institutional Grant awarded to Roger A. Band.

Conflict of Interest Disclosures: Dr. Abella reports research funding from the Medtronic Foundation, Philips Healthcare, the Doris Duke Foundation, and the National Heart, Lung, and Blood Institute. Dr. Becker reports research funding from the Medtronic Foundation, Philips Healthcare, Zoll Medical, Abbott Point of Care Diagnostics, BeneChill, and the National Heart, Lung, and Blood Institute.

References:


Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Day OHCA 8:00am-7:59pm (n=2827)</th>
<th>Night OHCA 8:00pm-7:59am (n=1962)</th>
<th>Total (n=4789)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (SD) in Years</td>
<td>64.4 (17.4)</td>
<td>62.8 (17.5)</td>
<td>63.8 (17.4)</td>
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<td>Male Gender (%)</td>
<td>1539 (54.6%)</td>
<td>1068 (54.4%)</td>
<td>2607 (54.5%)</td>
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<td>Black Race (%)</td>
<td>1446 (51.2%)</td>
<td>1050 (53.5%)</td>
<td>2496 (52.1%)</td>
<td>0.11</td>
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Table 2. Event characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Day OHCA 8:00am-7:59pm (n=2827)</th>
<th>Night OHCA 8:00pm-7:59am (n=1962)</th>
<th>Total (n=4789)</th>
<th>P Value</th>
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<tbody>
<tr>
<td>Shockable Initial Rhythm (%)</td>
<td>801 (28.3%)</td>
<td>481 (24.5%)</td>
<td>1282 (26.8%)</td>
<td>0.003</td>
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<td>Resuscitation Terminated in Field (%)</td>
<td>177 (6.26%)</td>
<td>148 (7.54%)</td>
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<td>Median Total Call Time (IQR) in HH:MM</td>
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<td>(00:22-00:37)</td>
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<td>Median Dispatch-to-Scene Time (IQR) in HH:MM</td>
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<td>(00:04-00:09)</td>
<td>(00:04-00:09)</td>
<td>&lt;0.001</td>
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<td>AED Application (%)</td>
<td>1415 (50.1%)</td>
<td>922 (47.0%)</td>
<td>2337 (48.8%)</td>
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<tr>
<td>Bystander CPR (%)</td>
<td>359 (12.7%)</td>
<td>149 (7.59%)</td>
<td>508 (10.6%)</td>
<td>&lt;0.001</td>
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<td>Private arrest location (%)</td>
<td>2365 (83.7%)</td>
<td>1644 (83.8%)</td>
<td>4009 (83.7%)</td>
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<td>Prehospital ROSC (%)</td>
<td>362 (12.8%)</td>
<td>227 (11.6%)</td>
<td>589 (12.3%)</td>
<td>0.20</td>
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<td>30-Day Survival (%)*</td>
<td>260 (10.9%)</td>
<td>139 (8.56%)</td>
<td>399 (9.92%)</td>
<td>0.02</td>
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* 30-day survival was available for n=4021 patients
Table 3. OHCA outcomes by day vs. night

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<th>Day OHCA 8:00am-7:59pm (n=2827)</th>
<th>Night OHCA 8:00pm-7:59am (n=1962)</th>
<th>Total (n=4789)</th>
<th>Unadjusted Relative Risk (95% CI) for Day vs. Night†</th>
<th>Adjusted Relative Risk (95% CI) for Day vs. Night *,‡</th>
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<tbody>
<tr>
<td>Prehospital ROSC (%)</td>
<td>362 (12.8%)</td>
<td>227 (11.6%)</td>
<td>589 (12.3%)</td>
<td>1.05 (0.98-1.12)</td>
<td>1.04 (0.97-1.12)</td>
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<table>
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<th></th>
<th>Day OHCA 8:00am-7:59pm (n=2397)</th>
<th>Night OHCA 8:00pm-7:59am (n=1624)</th>
<th>Total (n=4021)</th>
<th>Unadjusted Relative Risk (95% CI) for Day vs. Night§</th>
<th>Adjusted Relative Risk (95% CI) for Day vs. Night *,§</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-Day Survival (%)</td>
<td>260 (10.9%)</td>
<td>139 (8.56%)</td>
<td>399 (9.92%)</td>
<td>1.10 (1.02-1.19)</td>
<td>1.10 (1.02-1.18)</td>
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</table>

*Relative risk regression adjusted for age (quintile), gender, race, presenting rhythm (shockable vs. non-shockable), field termination status, total call time and call-to-scene time (quintiles), AED application by a bystander or first responder, bystander CPR performance, and arrest location
† p = 0.19 for day vs. night
‡ p = 0.23 for day vs. night
§ p ≤ 0.02 for day vs. night

Figure Legends:

**Figure 1.** (a) Rates of prehospital ROSC by hour of the day. Prehospital ROSC was 12.3% overall (solid line), 11.6% at night (dashed line), and 12.8% during the day (dotted line). The difference between night and day was not statistically significant (p=0.20). (b) Rates of 30-day survival by hour of the day. Thirty-day survival was 9.92% overall (solid line), 8.56% at night (dashed line), and 10.9% during the day (dotted line). The difference between night and day was statistically significant (p=0.02).

**Figure 2.** Adjusted relative risk of bystander CPR (yes/no), initial rhythm (shockable vs. non-shockable), and longer dispatch-to-scene interval (by quintile), day vs. night.
Figure 1A
Figure 1B
<table>
<thead>
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<th>Variable</th>
<th>Adjusted Relative Risk (95% CI) for Day vs. Night (n=4789)*</th>
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<tr>
<td>Bystander CPR</td>
<td>1.20 (1.13-1.28)</td>
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<tr>
<td>Shockable Initial Rhythm</td>
<td>1.07 (1.01-1.13)</td>
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<tr>
<td>Dispatch-to-Scene Interval (Quintile)</td>
<td>0.89 (0.82-0.97)</td>
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</table>

* Relative risk regression adjusted for all other variables in the model plus age (quintile), total call time (quintile), and AED application by a bystander or first responder
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Circulation. published online March 18, 2013;
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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