

## Temporal Differences in Out-of-Hospital Cardiac Arrest Incidence and Survival

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**Background**—Understanding temporal differences in the incidence and outcomes of out-of-hospital cardiac arrest (OHCA) has important implications for developing preventative strategies and optimizing systems for OHCA care.

**Methods and Results**—We studied 18 588 OHCA of presumed cardiac origin in patients aged  $\geq 18$  years who received resuscitative efforts by emergency medical services (EMS) and were enrolled in the Cardiac Arrest Registry to Enhance Survival (CARES) from October 1, 2005, to December 31, 2010. We evaluated temporal variability in OHCA incidence and survival to hospital discharge. There was significant variability in the frequency of OHCA by hour of the day ( $P < 0.001$ ), day of the week ( $P < 0.001$ ), and month of the year ( $P < 0.001$ ), with the highest incidence occurring during the daytime, from Friday to Monday, in December. Survival to hospital discharge was lowest for OHCA that occurred overnight (from 11:01 PM to 7 AM; 7.1%) versus daytime (7:01 AM to 3 PM; 10.8%) or evening (3:01 PM to 11 PM; 11.3%;  $P < 0.001$ ) and during the winter (8.8%) versus spring (11.1%), summer (11.0%), or fall (10.0%;  $P < 0.001$ ). There was no difference in survival to hospital discharge between OHCA that occurred on weekends and weekdays (9.5% versus 10.4%,  $P = 0.06$ ). After multivariable adjustment for age, sex, race, witness status, layperson resuscitation, first monitored cardiac rhythm, and emergency medical services response time, compared with daytime and spring, survival to hospital discharge remained lowest for OHCA that occurred overnight (odds ratio, 0.81; 95% confidence interval, 0.70–0.95;  $P = 0.008$ ) and during the winter (odds ratio, 0.81; 95% confidence interval, 0.70–0.94;  $P = 0.006$ ), respectively.

**Conclusions**—There is significant temporal variability in the incidence of and survival after OHCA. The relative contribution of patient pathophysiology, likelihood of the OHCA being observed, and prehospital and hospital-based resuscitative factors deserves further exploration. (*Circulation*. 2013;128:2595–2602.)

**Key Words:** epidemiology ■ heart arrest ■ mortality ■ out-of-hospital cardiac arrest

Out-of-hospital cardiac arrest (OHCA) occurs in  $>300\,000$  individuals in the United States each year and remains associated with very high mortality and morbidity.<sup>1,2</sup> 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), defibrillation as appropriate, advanced life support measures, and postresuscitation care in the receiving hospital.<sup>3</sup> Prior studies have suggested temporal variability in OHCA occurrence,<sup>4–10</sup> and a few have suggested temporal differences in survival<sup>8,11,12</sup>; however, mechanisms for these findings are poorly understood. These epidemiological studies are limited by lack of details on patient and arrest characteristics, as well

as on prehospital care and outcomes. Further understanding of the temporal variability of OHCA occurrence and outcomes is important to develop preventative strategies and optimize resource planning for prehospital and in-hospital response to cardiac arrest, with the aim of improving patient survival.

### Clinical Perspective on p 2602

In the present study, we used OHCA data from the Cardiac Arrest Registry to Enhance Survival (CARES), which is a large, diverse US population surveillance database of OHCA episodes. We investigated temporal variability by time of day, day of week, and month of year in the incidence and outcomes of OHCA. We also explored potential mechanisms that may explain this variability.

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## Methods

### Study Population

CARES is a central repository of OHCA data from >70 EMS agencies and 340 hospitals throughout the United States (Figure 1). The registry serves as a quality improvement project and allows EMS agencies to compare key performance indicators to improve OHCA care. Methods for data collection and a complete description of the registry population have been reported previously.<sup>13,14</sup> In brief, CARES includes data on people who have an OHCA event of a presumed cardiac origin (based on the care provider's clinical judgment) and who receive resuscitative efforts (eg, CPR or defibrillation) by EMS. Patients with obvious signs of death (eg, rigor mortis or dependent lividity) or for whom a "do not resuscitate" order is respected are not included. Noncardiac causes (eg, trauma, drowning, overdose, asphyxia, electrocution, primary respiratory arrest, or other noncardiac causes) are also excluded from enrollment in CARES.

The present study population included all OHCA events that occurred in patients  $\geq 18$  years old enrolled in CARES with a recorded 9-1-1 call date and time between October 1, 2005, and December 31, 2010 ( $n=22\,146$ ). Events that occurred in nursing homes or other healthcare institutions were not included ( $n=3558$ ), given that these were thought to represent a population distinct from the majority of OHCA cases. The final sample for the present analysis consisted of 18 588 OHCA events. The CARES study was approved by the Emory University institutional review board. Because the data are used primarily at the local sites for quality improvement, sites are granted a waiver of informed consent under the common rule. Analysis of aggregate deidentified data was performed at the Duke Clinical Research Institute in Durham, NC.

### Data Definitions

The time of the OHCA was defined as the time the 9-1-1 call was received. All events were stratified by timing of occurrence into the following categories: (1) Daytime (7:01 AM to 3 PM), evening (3:01 PM to 11 PM), or overnight (11:01 PM to 7 AM); (2) weekday (Monday to Friday) or weekend (Saturday and Sunday); and (3) winter (December to February), spring (March to May), summer (June to August), or fall (September to November).

## Outcomes

Temporal variability by time of day, day of week, and month of year in the incidence of OHCA and rate of survival to hospital discharge was evaluated. Among patients who survived to hospital discharge, temporal variability in the rate of favorable neurological function (defined as cerebral performance categories 1 and 2)<sup>15</sup> was also determined. A cerebral performance category score of 1 denotes mild or no neurological disability, and 2 denotes moderate neurological disability.<sup>16</sup>

## Statistical Analysis

Descriptive statistics are summarized as medians with interquartile ranges (25th, 75th percentile) for continuous variables and counts (percentages) for categorical variables. The hourly, daily, and monthly frequency of OHCA incidence and rates of survival to hospital discharge are shown graphically and were compared with  $\chi^2$  goodness-of-fit tests. Patient and event characteristics and outcomes were compared between time blocks with the Kruskal-Wallis test for continuous variables and the  $\chi^2$  test for categorical variables. To equalize the assessed number of month and season time periods, the study period was limited to January 1, 2006, to December 31, 2010, for the analyses of month and season; as a result, 119 OHCA events (0.6%) were excluded.

Logistic regression modeling was used to examine the association between the time of OHCA (evening and overnight compared with daytime) and survival to hospital discharge after adjustment for patient age, sex, race (white versus others), first monitored cardiac rhythm (shockable versus nonshockable), witness status (witnessed versus unwitnessed arrest), layperson resuscitation (CPR or automated external defibrillator application), and EMS response time (time from 9-1-1 call received at dispatch to EMS arrival at scene). Shockable first cardiac rhythm included ventricular fibrillation, ventricular tachycardia, and unknown shockable rhythm. Nonshockable first cardiac rhythm included asystole, pulseless electrical activity, and unknown nonshockable rhythm. Continuous covariates were tested for linearity, and nonlinear adjustment covariates were transformed with spline functions or truncated, as appropriate. Rate of missingness was <1% for all covariates; patients with any missing covariate ( $n=179$ , 0.96%) were excluded, and imputation was not



**Figure 1.** Geographic origin of study patients. The map represents regions participating in the Cardiac Arrest Registry to Enhance Survival (CARES). State sites depict states participating in statewide data collection. Current sites depict regions participating in CARES.

performed. Thus, the analysis population for logistic regression modeling was 18 409 OHCA events. Results are presented as odds ratios with 95% confidence intervals. Logistic regression modeling was also used to examine the association between the occurrence of OHCA on weekends (compared with weekdays) and survival to hospital discharge and the association between the occurrence of OHCA in the summer, fall, or winter (compared with spring) and survival to hospital discharge. The same list of adjustment covariates was used in the models.

Given that the 9-1-1 call time may variably be delayed from the actual time of OHCA occurrence (particularly among unwitnessed arrests), we repeated the analyses in the following 2 prespecified subpopulations: (1) Witnessed arrest with shockable first cardiac rhythm, because the 9-1-1 call time in this group most closely reflects the actual time of cardiac arrest and because the probability of survival is highest, with interventions most likely to improve outcomes; and (2) unwitnessed arrest with nonshockable first cardiac rhythm, because the 9-1-1 call time in this group least accurately reflects the actual time of cardiac arrest and because the probability of survival is the lowest, with interventions least likely to improve outcomes. All analyses were performed with SAS software version 9.2 (SAS Institute, Cary, NC). All *P* values <0.05 were interpreted as statistically significant.

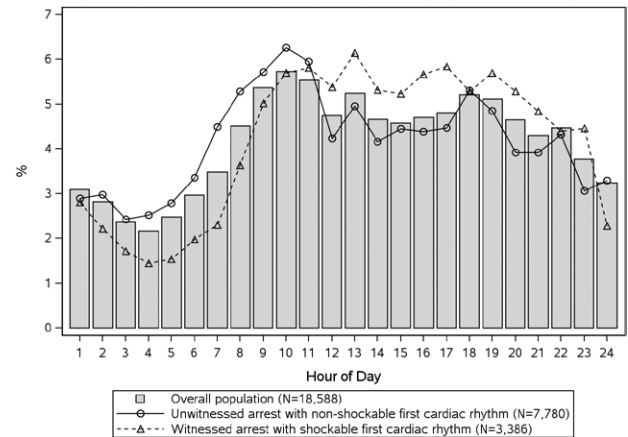
## Results

### Characteristics of the Study Cohort

Of the 18 588 OHCA events that comprised the present study cohort, the median (25th, 75th percentile) patient age was 63 (52, 76) years; 11 782 events (63.4%) occurred in male patients; 14 616 events (78.6%) occurred at home; 9203 events (49.5%) were witnessed; 4963 events (26.7%) had a shockable first cardiac rhythm; 3386 events (18.2%) were witnessed arrests with a shockable first cardiac rhythm; 7780 events (41.9%) were unwitnessed and had a nonshockable first cardiac rhythm; CPR was performed by a layperson in 4888 events (26.3%); and an automated external defibrillator was applied by a layperson in 410 events (2.2%). The median (25th, 75th percentile) time from 9-1-1 call received to EMS arrival at the scene was 6.8 (5.0, 9.0) minutes. Survival to hospital discharge occurred in 1885 events (10.1%); survival to hospital discharge was 32.7% among events that were witnessed and had a shockable first cardiac rhythm and 2.0% among unwitnessed events with a nonshockable first cardiac rhythm. Among survivors to hospital discharge, 1507 (80.0%) had a favorable neurological outcome.

### Circadian Variability in OHCA Incidence and Outcomes

9-1-1 calls for OHCA occurred more frequently during the daytime (*n*=7503 [40.4%]) and evening (*n*=6883 [37.0%]) than at night (*n*=4202 [22.6%]; *P*<0.001), with a large peak in occurrence from 8 to 11 AM and a smaller secondary peak from 5 to 7 PM (Figure 2). The morning and early evening peaks in 9-1-1 calls were observed only for unwitnessed arrests with a nonshockable first cardiac rhythm and not for witnessed arrests with a shockable first cardiac rhythm (Figure 2). Overnight arrests were more likely to occur at home, to be unwitnessed, and to have a nonshockable first cardiac rhythm and were less likely to receive layperson CPR or automated external defibrillator application (Table). Time from 9-1-1 call to EMS arrival on scene was longest at night.



**Figure 2.** Distribution of occurrence of out-of-hospital cardiac arrest by hour of the day. *P*<0.001 for  $\chi^2$  goodness of fit across all hours of the day for the overall population, patients with unwitnessed arrest and nonshockable first cardiac rhythm, and patients with witnessed arrest and shockable first cardiac rhythm.

Rates of return of spontaneous circulation and survival to hospital admission were lowest for OHCA that occurred at night (Table). Overall and among patients admitted to the hospital, survival to hospital discharge was also lowest for OHCA that occurred overnight (Figure 3). Among the cohort of witnessed arrests with shockable first cardiac rhythm, survival to hospital discharge was 26.1% for arrests that occurred overnight compared with 34.4% for daytime arrests and 33.5% for evening arrests (*P*=0.001). There was no difference in survival to hospital discharge by time of day among unwitnessed arrests with nonshockable first cardiac rhythms (*P*=0.34). After multivariable adjustment, compared with daytime OHCA, overnight OHCA (adjusted odds ratio, 0.81; 95% confidence interval, 0.70–0.95; *P*=0.008) but not evening OHCA (adjusted odds ratio, 1.01; 95% confidence interval, 0.90–1.13; *P*=0.92) were associated with lower survival to hospital discharge. Rates of favorable neurological outcomes among index hospitalization survivors were similar in the 3 time blocks (*P*=0.24; Table).

### Circaseptan Variability in OHCA Incidence and Outcomes

There is circaseptan variability in the incidence of OHCA, with greatest occurrence on Saturday and lowest occurrence on Tuesday (*P*<0.001; Figure 4). This variability was observed for unwitnessed arrests with nonshockable first cardiac rhythm (*P*<0.001) but not for witnessed arrests with shockable first cardiac rhythm (*P*=0.18). Overall, 13 015 (70.0%) of the OHCA events occurred on weekdays compared with 5573 (30.0%) on the weekend. When weighed for the inverse of days (5 for weekdays and 2 for weekend), there was no difference in incidence of OHCA on weekdays versus weekends (*P*=0.27). Compared with OHCA that occurred on weekdays, cardiac arrest on weekends was more likely to occur at home (80.9% versus 77.7%, *P*<0.001) and less likely to be treated with layperson application of an automated external defibrillator (1.7% versus 2.4%, *P*=0.002). Rates of

**Table. Patient Demographics, Arrest Characteristics, and Clinical Outcomes by Time of 9-1-1 Call Received**

|   | Total, n=18 588   | Time 9-1-1 Call Received             |                                       |   | P Value |
|---|-------------------|--------------------------------------|---------------------------------------|---|---------|
|   |                   | Daytime (7:01 AM to 3 PM),<br>n=7503 | Evening (3:01 PM to 11 PM),<br>n=6883 | Overnight (11:01 PM to 7 AM),<br>n=4202 |         |
| Patient demographics  |                   |                                      |                                       |   |         |
| Age, y  | 63 (52, 76)       | 64 (53, 77)                          | 63 (53, 76)                           | 61 (50, 74)                             | <0.001  |
| Male sex  | 11 782 (63.4%)    | 4764 (63.5%)                         | 4395 (63.9%)                          | 2623 (62.4%)                            | 0.30    |
| Race: white   | 7766 (41.8%)      | 3216 (42.9%)                         | 2936 (42.7%)                          | 1614 (38.4%)                            | <0.001  |
| Arrest characteristics  |                   |                                      |                                       |   |         |
| Location of arrest, home  | 14 616 (78.6%)    | 5608 (74.7%)                         | 5368 (78.0%)                          | 3640 (86.6%)                            | <0.001  |
| Witness status: witnessed arrest                                    | 9203 (49.5%)      | 3685 (49.1%)                         | 3599 (52.3%)                          | 1919 (45.7%)                            | <0.001  |
| Bystander resuscitation   |                   |                                      |                                       |   |         |
| Layperson CPR   | 4888 (26.3%)      | 2052 (27.4%)                         | 1798 (26.1%)                          | 1038 (24.7%)                            | 0.01    |
| Layperson AED application   | 410 (2.2%)        | 199 (2.7%)                           | 149 (2.2%)                            | 62 (1.5%)                               | <0.001  |
| Shockable first cardiac rhythm*                                     | 4963 (26.7%)      | 2036 (27.1%)                         | 2025 (29.4%)                          | 902 (21.5%)                             | <0.001  |
| Time from receipt of 9-1-1 call to EMS arrival at scene, min        | 7.0 (5.3, 9.3)    | 6.7 (5.0, 9.0)                       | 6.7 (5.0, 9.0)                        | 7.0 (5.4, 9.5)                          | <0.001  |
| Clinical outcomes   |                   |                                      |                                       |   |         |
| Overall survival to hospital discharge                              | 1885 (10.1%)      | 808 (10.8%)                          | 777 (11.3%)                           | 300 (7.1%)                              | <0.001  |
| Return of spontaneous circulation                                   | 6207 (33.4%)      | 2540 (33.9%)                         | 2428 (35.3%)                          | 1239 (29.5%)                            | <0.001  |
| Admission to hospital   | 4941 (26.6%)      | 1987 (26.5%)                         | 1980 (28.8%)                          | 974 (23.2%)                             | <0.001  |
| Survival to hospital discharge among patients admitted to hospital† | 1885/4941 (38.2%) | 808/1987 (40.7%)                     | 777/1980 (39.2%)                      | 300/974 (30.8%)                         | <0.001  |
| Favorable neurological outcomes‡                                    | 1507/1885 (80.0%) | 644/808 (79.7%)                      | 630/777 (81.1%)                       | 233/300 (77.7%)                         | 0.24    |

Data are presented as counts (%) for categorical variables and medians (25th, 75th percentiles) for continuous variables. AED indicates automated external defibrillator; CPR, cardiopulmonary resuscitation; and EMS, emergency medical service.

\*Shockable first cardiac rhythm includes ventricular fibrillation, ventricular tachycardia, and unknown shockable rhythm.

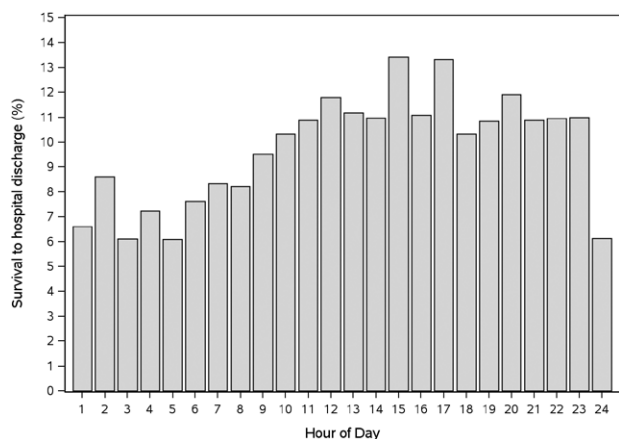
†Among patients admitted to hospital.

‡Among hospital survivors, cerebral performance categories 1 and 2.

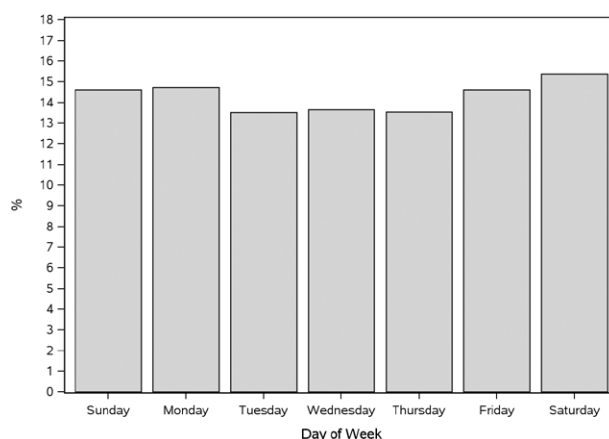
layperson CPR and time from 9-1-1 call to EMS arrival on scene were similar on weekends and weekdays.

Rates of return of spontaneous circulation (33.2% versus 33.5%,  $P=0.74$ ) and survival to hospital admission (21.5% versus 21.2%,  $P=0.54$ ) were similar on weekends and weekdays; however, among those admitted to the hospital, survival to hospital discharge was lower for OHCA on weekends than on weekdays (44.9% versus 47.1%,  $P=0.04$ ). Overall, there was no difference in survival to discharge as a function of the

day of the week ( $P=0.32$ ; Figure 5) or when stratified by weekends versus weekdays (9.5% versus 10.4%,  $P=0.06$ ). Among witnessed arrests with shockable first cardiac rhythm, survival was lower for arrests that occurred on weekends than on weekdays (29.5% versus 34.0%,  $P=0.01$ ), but among unwitnessed arrests with nonshockable first cardiac rhythms, there was no difference in survival between arrests that occurred on weekends or weekdays (2.2% versus 2.0%,  $P=0.64$ ). Among survivors to hospital discharge, there was no difference in

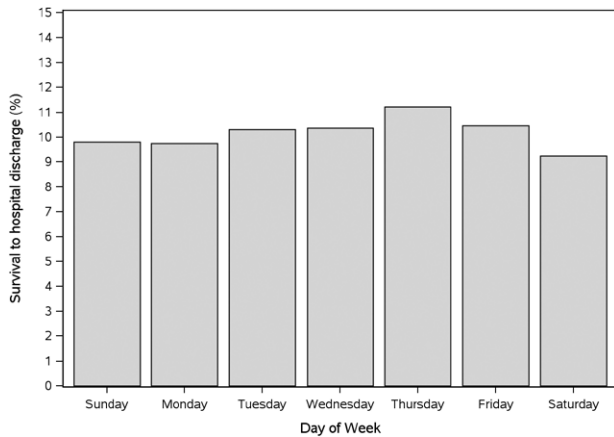


**Figure 3.** Distribution of survival to hospital discharge by hour of the day.  $P<0.001$  for  $\chi^2$  goodness of fit across all hours of the day.



**Figure 4.** Distribution of out-of-hospital cardiac arrest by day of the week.  $P<0.001$  for  $\chi^2$  goodness of fit across all days of the week.





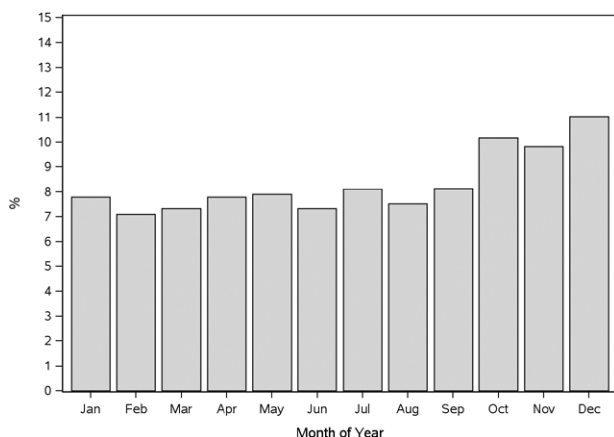
**Figure 5.** Distribution of survival to hospital discharge by day of the week.  $P=0.32$  for  $\chi^2$  goodness of fit across all days of the week.

favorable neurological outcomes between OHCA episodes that occurred on weekends or weekdays ( $P=0.57$ ).

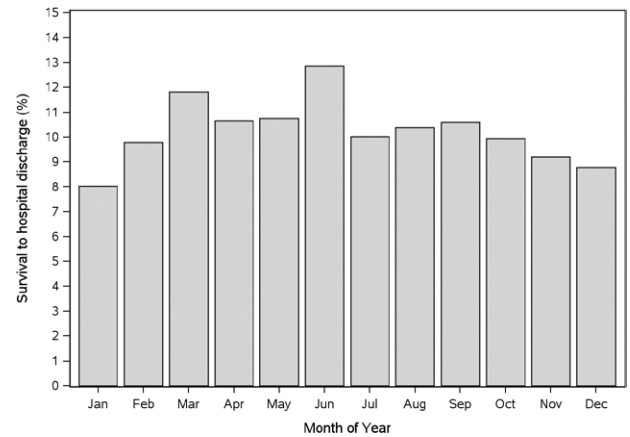
### Circannual Variability in OHCA Incidence and Outcomes

The highest incidence of OHCA occurred in December ( $P<0.001$ ; Figure 6), and results were similar for both witnessed arrests with shockable first cardiac rhythms ( $P<0.001$ ) and for unwitnessed arrests with nonshockable first cardiac rhythms ( $P<0.001$ ). When stratified by season, incidence of OHCA was greatest during the fall ( $P<0.001$ ). There were no significant differences in location of arrest, frequency of shockable first cardiac rhythm, or EMS response times between seasons, yet the proportion of witnessed arrests was greater during the summer ( $P=0.04$ ).

Rates of return of spontaneous circulation and survival to hospital admission were lowest during winter ( $P=0.003$  and  $0.005$ , respectively); however, among those admitted to a hospital, there was no difference in survival to discharge by season ( $P=0.11$ ). Overall survival to hospital discharge was highest in June (12.9%) and lowest in January (8.0%;  $P=0.002$ ; Figure 7). When stratified by season, survival was greatest during the spring (11.1%) and lowest during the winter (8.8%). After multivariable adjustment, compared with



**Figure 6.** Distribution of out-of-hospital cardiac arrest by month of the year.  $P<0.001$  for  $\chi^2$  goodness of fit across all months of the year.



**Figure 7.** Distribution of survival to hospital discharge by month of the year.  $P=0.002$  for  $\chi^2$  goodness of fit across all months of the year.

spring, survival to hospital discharge remained lower for OHCA that occurred during the winter (adjusted odds ratio, 0.81; 95% confidence interval, 0.70–0.94;  $P=0.006$ ), with similar survival during the summer ( $P=0.81$ ) or fall ( $P=0.28$ ). No difference in rates of favorable neurological outcomes was observed between seasons ( $P=0.31$ ).

### Discussion

In this large, population-based, multisite study of >18 000 OHCA events, several important findings emerged. First, the morning and early evening peaks in OHCA occurrence, as defined by the time the 9-1-1 call was received, were absent among witnessed arrests with shockable first cardiac rhythm and were observed only among unwitnessed arrests with nonshockable first cardiac rhythm. Second, the highest incidence of OHCA was observed between Friday and Monday and in December. Third, OHCA survival to hospital discharge was lowest overnight and during the winter. Finally, temporal variability in the rates of favorable neurological outcomes was not observed.

### Circadian Variability in OHCA Incidence and Outcomes

Over the past 3 decades, several<sup>4,5,7,8,10,17,18</sup> but not all<sup>19,20</sup> studies have demonstrated a circadian pattern in the incidence of OHCA, with a typical peak in occurrence during the early morning hours and a smaller secondary peak in the early evening. Evidence for circadian patterns in the incidence of acute myocardial infarction<sup>19,20</sup> with changes in potential physiological triggers, including blood pressure and heart rate, vascular tone, heart rate variability, blood viscosity, and platelet aggregation,<sup>5,21–23</sup> have been proposed to explain the morning peak in OHCA occurrence, with no explanation provided for the early evening peak. The task of determining the true time of OHCA is difficult, especially during the night, when there is an increased frequency of unwitnessed arrests. Early studies of temporal variability of OHCA used death certificates and hospital records<sup>4–6</sup> to determine the time of OHCA and were inaccurate given the delayed nature of the record keeping inherent in these circumstances. More recent studies have used the 9-1-1 call time as a surrogate for the time of cardiac arrest;

although not as vulnerable to the problems associated with the use of death certificates, this is also an imperfect measure, given that the probability of a cardiac arrest being witnessed or discovered shortly after onset is most likely variable over the course of the day because of human sleep/wake behavior.

Consistent with previous literature, using the time of the 9-1-1 call as the surrogate for the time of cardiac arrest, we also observed a similar circadian pattern, with a large increase in 9-1-1 calls from 8 AM to 11 AM and a smaller secondary increase from 5 PM to 7 PM. Nonetheless, the large sample size and knowledge of witness status and first cardiac rhythm allowed us to further stratify the present study population according to events in which the timing of the 9-1-1 call was the most and least likely to represent the actual time of cardiac arrest. The striking absence of both peaks among witnessed arrests with shockable first cardiac rhythm, with presence only among unwitnessed arrests with nonshockable first cardiac rhythm, is a novel finding. This finding suggests a strong possibility that these peaks in 9-1-1 calls are attributable to finding patients in the morning who actually died during the night (thereby falsely classifying the deaths as having occurred in the morning) and to family members returning from work in the evening to find patients who actually died in the afternoon (thereby falsely classifying the deaths as having occurred in the evening). This explanation is further supported by additional post hoc analyses with the observation that these characteristic peaks occurred only among events that happened at home and not outside the home (data not shown).

Consistent with previous studies,<sup>12,24</sup> we found significant variability in survival to hospital discharge as a function of OHCA time or, more accurately, as a function of the 9-1-1 call time. Survival was lowest when the 9-1-1 call occurred between 11:01 PM and 7 AM. Patients who die overnight but are found in the morning are categorized into the daytime group, which further underestimates the temporal differences in survival. Patients who experience events at night are disadvantaged for a number of reasons. First, these patients have a greater likelihood of having an unwitnessed arrest during sleep, which results in delays in recognition and 9-1-1 call. Second, nighttime arrests are more likely to occur at home, where automated external defibrillator use is uncommon and the frequency of bystander CPR is lower. Third, EMS response times were slightly longer at night, perhaps because of decreased staffing or performance; nevertheless, this delay requires further study. Finally, the odds of survival remained 19% lower at night than during the day, even after adjustment for available patient and arrest characteristics, which suggests that temporal variability in other unmeasured factors may also be responsible for lower survival at night. Lower survival rate at night, both in admission to hospital and to discharge among those admitted to hospital, suggests that temporal variability both in prehospital and posthospital admission factors may contribute to differences in survival. Variability may include patient factors (eg, cause of cardiac arrest [primary arrhythmic or associated with myocardial infarction]), quality of resuscitation (eg, chest compressions), EMS and emergency department staffing, and access to interventions such as urgent coronary angiography and therapeutic hypothermia; however, these postulates require further study and confirmation.

It is possible that some hospitals offer less comprehensive treatment during the nighttime, potentially affecting patient outcomes.

### **Circaseptan Variability in Incidence and Outcomes**

We found an increase in the incidence of OHCA from Friday to Monday, which is consistent with other studies that found the greatest incidence of OHCA on Saturdays<sup>6,20</sup> and Mondays.<sup>9,10,25,26</sup> Although the reasons remain speculative, changes in behavior around weekends, including alcohol intake, sleep/wake cycle, and physical activity may partly explain this observation.<sup>27</sup> In contrast to previous studies,<sup>8</sup> we did not observe significant variability in survival after OHCA by day of week. Similar EMS response times and rates of return of spontaneous circulation and survival to hospital admission suggest that prehospital processes of OHCA care are comparable on weekends and weekdays, yet lower rate of survival to discharge among those admitted to the hospital on weekends suggests that in-hospital care for OHCA may be different on weekends compared with weekdays.

### **Circannual Variability in Incidence and Outcomes**

Seasonal variation in OHCA<sup>9,26</sup> and sudden cardiac death<sup>8</sup> have been described in several different populations, with exposure to cold considered to be one of the main factors influencing this variability. Nevertheless, it has been suggested that because seasonal variations of sudden death have also been found in areas with less extreme changes between summer and winter, such as Kuwait, the seasonal variation in sudden death may depend more on relative rather than absolute changes in the climate and may also be influenced by behavioral changes associated with the seasons.<sup>28</sup> Consistent with previous studies,<sup>9,29</sup> we also found OHCA to occur with greatest frequency in December. This finding was observed despite the inclusion of climatically varied sites. Stress during the winter holiday season or migration out of the city during the summer months may be other potential explanations for these findings.

Rates of survival to hospital discharge were  $\approx 40\%$  lower for OHCA that occurred during January than in June. We observed a greater proportion of witnessed arrests during the summer months, possibly because of the greater amount of time spent outside the house, which may account in part for increased survival during this time period; however, the odds of survival remained  $\approx 19\%$  lower during winter even after adjustment for known patient and event characteristics. Given that rates of return of spontaneous circulation and survival to hospital admission, but not rates of survival after hospital admission, were lower during the winter, unmeasured patient and prehospital care factors are likely responsible for seasonal differences in survival rates. Despite the observations of temporal differences in incidence and survival with OHCA, we found no evidence for temporal variability in favorable neurological outcomes among survivors.

The present findings have important implications from a public health and policy perspective for both prehospital and hospital-based OHCA care. Efforts are required to reduce diurnal variability and improve overall OHCA survival by increasing public knowledge of early cardiac arrest

recognition and enhancing public skills and readiness to perform CPR when necessary. Further reassessment of EMS and hospital resources and performance is recommended to evaluate for, and if present to eliminate, temporal disparity in staffing, dispatch procedures, number of vehicles able to respond, quality of CPR, and hospital-based interventions, including implementation of neuroprotective therapy and access to early cardiac interventions. These postulates, if confirmed, support advocacy and implementation of regional cardiac resuscitation systems of care that provide 24-7 (24 hours per day, 7 days per week) expert access to resuscitation-related services.<sup>30,31</sup> The rationale for such regional centers includes widespread underutilization of proven but logistically complex interventions and selective availability of specialized resources and expertise at specific centers. Furthermore, ongoing translational and clinical research is necessary to study novel strategies to efficiently deliver consistent and timely care to such patients.

### Study Limitations

Several issues merit consideration in the interpretation of the present study. First, the data are observational and registry based and therefore subject to unmeasured confounding and bias. We were unable to account for resuscitation-specific variables (eg, quality of chest compressions), the type of treating hospital (eg, academic versus community), or use of other treatments such as therapeutic hypothermia or urgent coronary angiography that may have contributed to the observed temporal variability in survival to hospital discharge. Second, voluntary participation in CARES may not generate representative samples of the OHCA patient population. Although the data were collected from numerous EMS sources that may have differences in record keeping of times, there should be no systematic differences in record keeping as a function of time. Third, it is unknown how the exclusion of OHCA events in which resuscitation was not attempted would affect the temporal variation in the incidence. Fourth, as discussed previously, the use of 9-1-1 call time as a surrogate for actual time of cardiac arrest can be inaccurate and thus has the potential for misclassification bias, for example, by falsely classifying patients who died at night to have arrested (and died) in the morning. Although assessment of the time of arrest from implantable cardiac defibrillator electrograms may be more accurate,<sup>32</sup> these have limited generalizability because of selection bias in the type of patients who tend to have these devices implanted. Fifth, we were unable to relate timing of cardiac arrest to patient behaviors such as wake time, physical activities, or medication compliance or to the type of cardiac arrest (eg, myocardial infarction or primarily arrhythmic). Finally, we undertook multiple comparisons, and findings should be interpreted with caution given the possibility of a type I error.

### Conclusions

In this large, geographically diverse, population-based study, we observed temporal differences in the incidence of and survival after OHCA. The frequency of OHCA was increased around the weekends and during the winter, and survival was lowest when OHCA occurred overnight and during the winter. Reasons for these findings are likely multifactorial,

including variability in biological processes in patients themselves and among all links in the “chain of survival.” Further study of immediate precipitants of cardiac arrest and temporal variability in prehospitalization and posthospitalization care is required to develop preventative strategies and optimize resource planning in an effort to improve OHCA outcomes.

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## CLINICAL PERSPECTIVE

Out-of-hospital cardiac arrest (OHCA) occurs in >300 000 individuals in the United States each year and remains associated with very high mortality. Successful resuscitation requires implementing a “chain of survival” with both prehospital and hospital-based links, including activation of emergency medical services, early cardiopulmonary resuscitation, defibrillation as appropriate, advanced life support measures, and postresuscitation care in the hospital. The association between the time of cardiac arrest and outcomes remains poorly understood. Understanding temporal differences in OHCA incidence and survival has important implications for developing preventative strategies and optimizing systems for care. We studied >18 000 OHCA events of presumed cardiac origin from the Cardiac Arrest Registry to Enhance Survival, a central repository of OHCA data from >70 emergency medical services agencies and 340 hospitals throughout the United States and found significant variability in the frequency of OHCA by hour of the day, day of the week, and month of the year, with the highest incidence during the daytime, on Saturday, and in December. We also found that survival to hospital discharge was lowest for OHCA that occurred overnight and during the winter, even after adjustment for patient, event, and prehospital care differences. Further exploration of the relative contribution of patient pathophysiology, likelihood of being observed, and prehospital and hospital-based resuscitative factors (including staffing, dispatch procedures, number of vehicles able to respond, quality of cardiopulmonary resuscitation, and use of neuroprotective therapy and cardiac investigations) is required in efforts to understand and mitigate this temporal disparity and improve overall OHCA outcomes.



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