Impact of in or out of office hours at admission time on outcome in out-of-hospital cardiac arrest patients

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Background In out-of-hospital cardiac arrest (OHCA), neurological outcome is determined by the severity of neurological injury, early percutaneous coronary intervention, and application of neuroprotective temperature management. As this is a very time-intensive and manpower-intensive protocol, we hypothesized that there would be a difference in outcome between OHCA patients admitted during and out of office hours.

Methods We prospectively collected demographic data of OHCA patients in two hospitals. All patients included were treated at 33°C for 24 h, followed by a rewarming phase until 36.6°C. During office hours were defined as arriving between 8:00 a.m. and 5:00 p.m. on weekdays. Neurological outcome at 180 days was assessed following the Cerebral Performance Category scale.

Results Forty-seven (31%) patients were admitted during office hours and 105 (69%) out of office hours ($P = 0.199$). Patients admitted during office hours were significantly older, respectively, 66 ± 14 and 59 ± 15 years ($P = 0.014$). There was no significant difference between both groups in the number of patients who underwent coronary angiography, door to angiography time, and number of affected vessels. The median time spent in the target range of PaO$_2$, PaCO$_2$, and lactate was also not significantly different. We found no significant difference in survival until 180 days between both groups ($P = 0.599$), even after adjustment for age (95% confidence interval: 0.44–1.90, hazard ratio: 0.912).

Conclusion Survival until 180 days between OHCA patients admitted during office hours or out of office hours was not significantly different in two hospitals with a fixed protocol for neuroprotection and 24/7 streamlined access to coronary angiography. European Journal of Emergency Medicine 00:000–000 Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

Keywords: diurnal variation, outcome, out-of-hospital cardiac arrest

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Introduction

In out-of-hospital cardiac arrest (OHCA) patients, neurological outcome in the postresuscitation phase is determined by the severity of neurological injury induced by flow and/or pressure deficit during cardiopulmonary resuscitation (CPR) and by the quality of postresuscitation care \cite{1,2}. In addition, this outcome relies on the implementation of a chain of survival where both prehospital and hospital-based care need to be adequate. A strict protocol includes an accurate activation of the emergency medical services, early CPR with high-quality chest compressions and defibrillation, early percutaneous coronary intervention (PCI) where indicated, and eventually intensive care management with optimal hemodynamic treatment, the application of temperature management, and neuromonitoring \cite{1,3,4}. Several medical disciplines, nurses, ambulance workers, and technicians are involved in this intensive treatment of the (post-)resuscitation patient.

The treatment of post-OHCA patients may be less effective at night because of a combination of patient, event, hospital, staffing, and response factors and the intensity of the treatment. Indeed, a previous study suggested a better 30-day survival for OHCA patients admitted during the day \cite{5}. Similarly, a Japanese analysis of witnessed OHCA showed that night-time hospital admissions were associated with worsened clinical outcomes compared with daytime admissions \cite{6}. Other studies reported that even in-hospital cardiac arrest (CA) survival rates show temporal variability describing a less frequent occurrence of return of spontaneous circulation (ROSC) and survival to hospital discharge during night-time hours \cite{7–9}. This result remained even after adjustment for multiple potential confounders, including illness category and event location.

We studied the survival, the differences in emergency coronary angiography (ECA) findings, and demographic factors associated with survival in patients presenting with OHCA in two hospitals during office hours and out of office hours in a 1:2 case-control matched analysis in the period 2009–2013.

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characteristics between comatose OHCA patients admitted during and out of office hours in two large hospitals with a very strict and fixed protocol for neuroprotection. As the treatment of postresuscitation patients is very labor-intensive and multidisciplinary, we hypothesized that there would still be a difference in outcome between OHCA patients admitted during and out of office hours.

Methods

We prospectively collected demographic data of comatose OHCA patients in two hospitals: one university hospital (University Hospitals Leuven) between May 2010 and September 2013 and one tertiary hospital (Ziekenhuis Oost-Limburg) between March 2011 and November 2013. All included patients had ROSC at arrival at the emergency department (ED). OHCA patients without ROSC were not included in this study. The study protocol was approved by the local medical ethics committees. Baseline characteristics were prospectively collected from Utstein templates, using standardized definitions, and emergency medical charts [10,11]. All included patients had no obvious noncardiac cause of arrest. The emergency medical team provided advanced life support in accordance with the European Resuscitation Council Guidelines 2010 [12]. Out of office hours were defined as arriving between 5:00 p.m. and 8:00 a.m. and during the weekend or on official holidays. We will use the term out of office and during office hours in the rest of this paper.

Therapeutic hypothermia protocol and patient management

All included patients, in both hospitals, were treated with therapeutic hypothermia (endovascular or surface cooling). Cold saline (4°C, 30 ml/kg) was administered immediately at hospital admission before ECA. Therapeutic hypothermia was further mechanically induced and maintained by endovascular (Icy-Catheter, CoolGard 3000; Alsius, Irvine, California, USA) or surface cooling (ArcticGel Pads, Arctic Sun 5000; Medivance, Louisville, Colorado, USA; Emcools Flex.Pad; EMCOOLS, Vienna, Austria) at arrival at the coronary care unit after ECA. All systems were provided with a feedback loop controlling target temperature using an esophageal temperature probe to control the initiating of cooling and rewarming of the patient. Patients were cooled to a target temperature of 33°C for 24 h, followed by an active rewarming phase (0.3°C/h) until 36.6°C. After rewarming, sedation was titrated toward patients' comfort with efforts toward minimizing sedation. Resuscitation target recommended in the guidelines were used: mean arterial pressure more than 65 mmHg, systolic blood pressure more than 90 mm Hg, SVO2 more than 70%, lactate less than 2.2 mmol/L, and urine output more than 0.5 ml/kg/h [3]. Ventilation was adjusted to maintain mild hypocapnia (PaCO2 between 32 and 38 mmHg, pH-stat approach) and normoxia (PaO2 between 70 and 150 mmHg, pH-stat approach).

Electrocardiography analysis

ECG analysis was retrospectively carried out on the first 12-lead ECG after ROSC by two investigators E.V. and C.G. This ECG could be obtained prehospital or at admission at the ED before coronary angiography was carried out. Both E.V. and C.G. were blinded for coronary angiographic findings during the interpretation of these ECGs. The following characteristics of ECG were assessed: ST-segment elevation, ST-segment depression, presence of left bundle branch block, presence of right bundle branch block, presence of intraventricular block, nonspecific ST-T changes, QTc prolongation, pacemaker rhythm, or normal ECG. These ECG findings were compared with previous ECGs if available. ST-segment elevation was defined as an elevation of at least 1 mm in two contiguous standard leads and at least 2 mm in precordial leads. An ST-segment depression was defined as a decrease of at least 0.5 mm in two contiguous leads.

Emergency coronary angiography analysis

The decision for ECA was left to the attending cardiologist. This decision was influenced by conservative treatment by the presence of known multiple comorbidities or unfavorable CA settings for future neurologic recovery. Obstructive coronary artery disease was defined as diameter stenosis of 50% or more in the left main coronary artery or stenosis of 70% or more in a major epicardial vessel. Culprit lesions were defined as coronary lesions suggestive of ruptured plaques or thrombotic lesions. TIMI classification was used to assess the coronary artery flow. PCI was considered successful if it resulted in less than 30% stenosis and TIMI flow more than 2 in the culprit vessel.

Neurological outcome

Neurological outcome at hospital discharge was assessed following the Cerebral Performance Category (CPC) scale [13,14]. According to the scale classification, CPC 1 indicates good cerebral performance, CPC 2 specifies moderate disability (sufficient for independent activities toward minimizing sedation). CPC 3 indicates severe disability (dependent on others), CPC 4 implies coma or vegetative state, and CPC 5 represents death.

Statistical analysis

Patients’ characteristics were compared using a Student’s t-test if normally distributed and a Mann–Whitney test if not normally distributed and expressed as respectively mean±SD or median with first and third quartile. Normality was tested using a Shapiro–Wilk test. The χ²-test and Fisher’s exact test were used to compare categorical variables. A P-value less than 0.05 was considered statistically significant. All tests were performed using SPSS (20.00; SPSS Inc., Chicago, Illinois, USA).

Results

One hundred and fifty-two OHCA patients were included in this study. In both hospitals, 76 consecutive
OHCA patients were included. Forty-seven (31%) OHCA patients were admitted during office hours and 105 (69%) OHCA patients were admitted out of office hours ($P=0.199$; Fig. 1). In the during office hours group, 37 (79%) were men, whereas in the out of office group, 72 (69%) were men ($P=0.199$). Patients were younger in the group admitted during out of office hours ($59\pm15$ years) compared with patients admitted during office hours ($66\pm14$ years) ($P=0.014$). Initial presenting rhythm, time to ROSC, and witnessed arrest were similar during or out of office hours (Table 1). We could not determine time of ROSC in 41 (27%) patients on the basis of medical charts and Utstein forms. There was no significant difference in the distribution of these patients based on medical charts and Utstein forms. There was no significant difference in the distribution of these patients admitted during office hours (23%) or out of office hours (29%) ($P=0.972$). No significant differences were found in comorbidities between both groups (Table 2). There was a tendency toward more active smokers presenting during office hours (41%) compared with patients admitted out of office hours (25%) ($P=0.076$).

Thirty-seven (79%) patients of the 47 admitted during office hours and 72 (69%) of the 105 patients admitted out of office hours (25%) ($P=0.067$). The median time was 51 min (23–74 min) in patients admitted during office hours and 54 min (30–91 min) in patients admitted out of office hours ($P=0.249$). The number of affected vessels and localization of injury during ECA as ECG findings was not different between both groups (Tables 3 and 4). Significantly more patients had been treated with surface cooling during office hours (41%) compared with patients admitted out of office hours (25%) ($P=0.067$). The median time spent in the target range of PaO2, PaCO2, and lactate was not significantly different during the first 24 h between both groups ($P=0.357, 0.245, \text{and} 0.750$, respectively).

Survival until 30 days was not significant between both groups. Fifty-seven percent of the patients admitted out of office hours and 51% of the patients admitted during office hours survived until 30 days ($P=0.486$; Table 5). There was no difference between both groups after adjustment for age (95% confidence interval: $-0.079$ to $-0.025$, hazard ratio: 0.053). Survival until 180 days was 51% in the out of office hours group and 47% in the office hours group ($P=0.599$). In addition, no significant difference was observed in the CPC score at 180 days after CA between both groups ($P=0.820$).

After adjustment for age, there was no difference between both groups (95% confidence interval: 0.44–1.90, hazard ratio: 0.912).

### Table 1 Demographic and cardiac arrest data

<table>
<thead>
<tr>
<th></th>
<th>Out of office hours</th>
<th>During office hours</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>105 (69)</td>
<td>47 (31)</td>
<td>0.199</td>
</tr>
<tr>
<td>Male [N (%)]</td>
<td>72 (69)</td>
<td>37 (79)</td>
<td>0.199</td>
</tr>
<tr>
<td>Age (mean \pm SD)</td>
<td>59 \pm 15</td>
<td>66 \pm 14</td>
<td>0.014</td>
</tr>
<tr>
<td>Initial rhythm [N (%)]</td>
<td>1 missing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
<td>68 (65)</td>
<td>29 (62)</td>
<td>0.854</td>
</tr>
<tr>
<td>Asystole</td>
<td>24 (23)</td>
<td>9 (16)</td>
<td>0.632</td>
</tr>
<tr>
<td>PEA</td>
<td>12 (11)</td>
<td>8 (17)</td>
<td>0.435</td>
</tr>
<tr>
<td>Time to ROSC [median (IQR) (min)]</td>
<td>24 (15–39)</td>
<td>23 (16.5–35)</td>
<td>0.972</td>
</tr>
<tr>
<td>Immediate CPR [N (%)]</td>
<td>59 (56)</td>
<td>26 (55) (2 missing)</td>
<td>0.906</td>
</tr>
<tr>
<td>Witnessed arrest [N (%)]</td>
<td>92 (88)</td>
<td>39 (83)</td>
<td>0.357</td>
</tr>
</tbody>
</table>

CPR, cardiopulmonary resuscitation; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation.

*We don’t have the initial rhythm of one person.

### Table 2 Cooling data

<table>
<thead>
<tr>
<th></th>
<th>Out of office hours</th>
<th>During office hours</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coolgard (endovascular cooling) [%]</td>
<td>80 (76)</td>
<td>29 (62)</td>
<td>0.067</td>
</tr>
<tr>
<td>Arctic Sun (surface cooling) [%]</td>
<td>19 (18)</td>
<td>17 (36)</td>
<td>0.015</td>
</tr>
<tr>
<td>EMCOOLS pads (surface cooling) [%]</td>
<td>4 (4)</td>
<td>1 (2)</td>
<td>0.591</td>
</tr>
<tr>
<td>% of time of first 24 h spent between target [median (IQR)]</td>
<td>87.5 (62.5–100)</td>
<td>87.5 (55.6–100)</td>
<td>0.357</td>
</tr>
<tr>
<td>PaO2</td>
<td>67.5 (62.5–100)</td>
<td>67.5 (55.6–100)</td>
<td>0.357</td>
</tr>
<tr>
<td>PaCO2</td>
<td>98.8 (60–78)</td>
<td>98.8 (60–78)</td>
<td>0.245</td>
</tr>
<tr>
<td>Lactate</td>
<td>65.1 (0–100)</td>
<td>62.5 (0–100)</td>
<td>0.750</td>
</tr>
</tbody>
</table>

Diurnal outcome in OHCA patients Genbrugge et al. 3

![Fig. 1](image-url)

Distribution of out-of-hospital cardiac arrest (OHCA) patients admissions at the emergency department (ED) during and out of office hours. (a) Distribution of OHCA patient admission at the ED during office hours: rate of admission of OHCA patients at the ED by hour of the day admitted during office hours. (b) Distribution of OHCA patient admission at the ED during nights, weekends, and official holidays: rate of admission of OHCA patients at the ED by hour of the day admitted out of office hours (night, weekend, and official holidays).
hours (from 5:01 p.m. to 7:59 a.m.), even after adjustment for age. Although OHCA patients admitted during out of office hours were significantly younger, no additional significant differences in overall patient characteristics, ECG, and angiographic findings were observed. Despite the limited power of this study, it was found that with a fixed post-CA protocol, continuous access to coronary angiography, and good multidisciplinary collaboration, it is possible to abolish survival differences between during and out of office hours. These findings should be confirmed by prospective or even randomized larger trials.

Because previous studies are heterogeneous in terms of patient inclusion criteria and endpoints, it is difficult to compare our findings with the available data. Because of these different inclusion criteria and endpoints, most of these studies included a much larger number of patients. Three large studies observed a significantly higher 30-day survival rate in OHCA patients during daytime, with a 30-day survival rate of 11% during the day and 9% during the night in the study of Wallace et al. [5], 10% during the day and 9% during the night in the study of Koike et al. [6], and 8% during the day and 3% during the night in the study of Karlsson et al. [15]. Even after adjustment for prehospital care factors between day and night, a significantly lower survival rate was observed during the night. Therefore, the better survival rate during the day may be attributed to a difference in postresuscitation hospital care [5,6]. Unlike our study, these studies included all OHCA patients, with or without ROSC [16–18]. This also explains the higher survival rates in our study, in which we included only OHCA patients with ROSC in contrast to the others, who included all OHCA patients irrespective of whether the patient achieved ROSC or not.

In our study, OHCA patients admitted during out of office hours were significantly younger compared with admissions during office hours, which is consistent with previously described studies [5,6,15]. In contrast, Thakur et al. [17] and Soo et al. [18] found no difference in circadian variation between OHCA patients using a cut-off of 70 years. A possible explanation could be that older patients who still live alone and have a CA during the night are found later, with the consequence that they do not achieve ROSC. Nevertheless, the previously described studies included OHCA patients irrespective of whether ROSC was achieved and found the same age difference [16–18]. As such, the reason for this difference remains unclear.

Despite the younger age in the CA population during out of office hours, we did not observe any difference in the survival and the number of affected coronary arteries between both groups. One would expect a higher survival rate in a younger population and more one coronary vessel disease (ST-elevation myocardial infarction) in contrast to multivessel disease in the elderly [19].

**Discussion**

In the present study, no difference was found in survival until 180 days after CA between OHCA patients admitted at the ED during office hours (from 8:00 a.m. to 5:00 p.m.) compared with patients admitted during out of office hours (from 5:01 p.m. to 7:59 a.m.), even after adjustment for age. Although OHCA patients admitted during out of office hours were significantly younger, no additional significant differences in overall patient characteristics, ECG, and angiographic findings were observed. Despite the limited power of this study, it was found that with a fixed post-CA protocol, continuous access to coronary angiography, and good multidisciplinary collaboration, it is possible to abolish survival differences between during and out of office hours. These findings should be confirmed by prospective or even randomized larger trials.

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Soo et al. [18] reported a clear circadian variation in OHCA patients admitted alive at the ED. Patients admitted during the day presented more frequently with ventricular fibrillation as the initial rhythm. As their data showed a low number of bystander CPR after midnight, they suggested that the survival of these patients could be affected by the availability of bystander CPR and the speed of ambulance response. However, we could not confirm these findings in our study as the number of witnessed arrest patients and the initiation of immediate bystander CPR were equally distributed. This discordance could be attributed to the manner in which we defined our groups, which was not in line with other studies; we included only patients who achieved ROSC.

In agreement with the findings of Zahn et al. [20], this study showed no circadian differences in clinical events and mortality between patients undergoing PCI. However, others did report worse outcomes in OHCA patients admitted outside working hours, whether PCI was performed or not [21]. Possible reasons that may worsen the outcome of these patients admitted out of office hours are the presence of a smaller staff, less extensive diagnostics, and postresuscitation care [7]. As process of care is mostly different at these time points, it was suggested that adequate staffing and provided service protocols, as given in an ED and ICU, can improve survival [7].

The diagnostic and therapeutic measures were similar in the two patient groups without differences in witnessed arrest, time to ROSC, ECA and door to ECA time, PCI, placement of intra-aortic balloon pump, and urgent coronary artery bypass graft. Moreover, no significant differences could be observed in PaO₂, PaCO₂, and lactate during the first 24 h, with equal distributions in the targeted range both during and out of office hours. We found a significant difference in the use of surface cooling between both groups, with more use of surface cooling during out of office hours. Both systems use a feedback mechanism. These findings suggest the need for a similar and multidisciplinary treatment both during and out of office hours. Furthermore, this study also stresses the importance of centralizing the care of OHCA patients to experienced centers, with a 24/7 interventional cardiology service, ICU, possibility of target therapeutic hypothermia, and on-site cardiac and vascular surgery [22,23]. To conclude, a well-trained team and a standardized treatment approach with a clear fixed protocol may lead to the improvement of outcome in OHCA patients so that the temporal variability in healthcare staff performance can be minimized.

The results of this study should be interpreted in the context of several limitations. First, the analysis was specific to the patient population of ZOL Genk and UZ Leuven and may not be generalizable to other hospitals. The time points 8:00 a.m. and 5:00 p.m. were chosen because from 5:00 p.m., the coronary angiography ward started in both hospitals until 7:59 a.m. It is possible that these time points are different in other hospitals and therefore not suitable. A second limitation is the observational nature of our study. Third, this study has a rather small sample size that can be too small to observe small differences between both groups. Fourth, because of the inclusion of only OHCA patients who achieved ROSC, our data are difficult to compare with the current literature.

**Conclusion**

Survival and CPC score until 180 days between patients admitted during office hours and out of office hours were not significantly different in two large tertiary care centers with a fixed protocol for neuroprotection and 24/7 streamlined access to coronary angiography. In this rather small study, we found that a good post-CA protocol and multidisciplinary care for the post-CA patient can abolish the survival difference between during and out of office hours. These findings need to be confirmed in larger studies.

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**Conflicts of interest**

There are no conflicts of interest.

**References**


