Determinants of unfavorable prognosis for out-of-hospital sudden cardiac arrest in Bielsko-Biala district

Dariusz Gach¹, Jolanta U. Nowak², Łukasz J. Krzych³

¹Department of Cardiology, Regional Hospital, Bielsko-Biala, Poland
²3rd Department of Cardiology, School of Medicine with the Division of Dentistry in Zabrze, Medical University of Silesia in Katowice, Silesian Center for Heart Diseases, Zabrze, Poland
³Department of Anesthesiology, Intensive Care, and Emergency Medicine, Medical University of Silesia in Katowice, Department of Cardiac Anesthesia and Intensive Therapy, Silesian Center for Heart Diseases, Zabrze, Poland

Abstract

Introduction: The prognosis in out-of-hospital sudden cardiac arrest (OHCA) remains unfavorable and depends on a number of demographic and clinical variables, the reversibility of its causes and its mechanisms.

Aim: To investigate the risk factors of prehospital death in patients with OHCA in Bielsko County.

Material and methods: The study analyzed all dispatch cards of the National Emergency Medical Services (EMS) teams in Bielsko-Biala for the year 2013 (n = 23 400). Only the cards related to sudden cardiac arrest in adults were ultimately included in the study (n = 272; 190 men, 82 women; median age: 71 years).

Results: Sixty-seven victims (45 men, 22 women) were pronounced dead upon the arrival of the EMS team, and cardiopulmonary resuscitation (CPR) was not undertaken. In the remaining group of 205 subjects, CPR was commenced but was ineffective in 141 patients (97 male, 44 female). Although univariate analysis indicated 6 predictors of prehospital death, including OHCA without the presence of witnesses (odds ratio (OR) = 4.2), OHCA occurring in a public place (OR = 3.1), no bystander CPR (OR = 9.7), no bystander cardiac massage (OR = 13.1), initial diagnosis of non-shockable cardiac rhythm (OR = 7.0), and the amount of drugs used for CPR (OR = 0.4), logistic regression confirmed that only the lack of bystander cardiac massage (OR = 6.5) and non-shockable rhythm (OR = 4.6) were independent determinants of prehospital death (area under ROC curve = 0.801).

Conclusions: Non-shockable rhythm of cardiac arrest and lack of bystander cardiac massage are independent determinants of prehospital death in Bielsko-Biala inhabitants suffering from OHCA.

Key words: out-of-hospital cardiac arrest, prognosis, risk factors.

Streszczenie

Wprowadzenie: Rokowanie w pozaszpitalnym nagłym zatrzymaniu krążenia (PNZK) jest niekorzystne i zależy od licznych zmiennych demograficznych i klinicznych, okoliczności zdarzenia, odwracalności przyczyn oraz jego mechanizmów.

Cel: Próba wytypowania czynników ryzyka zgonu przedszpitalnego u chorych po PNZK w powiecie bielskim.

Materiał i metody: Analizie poddano ujednolicone karty wyjazdowe zespołów Państwowego Ratownictwa Medycznego (ZRM) za 2013 r. (n = 23 400). Ocenie poddano te, które dotyczyły wezwań do nagłego zatrzymania krążenia u osób dorosłych (n = 272; 190 mężczyzn, 82 kobiety; mediana wieku 71 lat).

Wyniki: W 67 przypadkach (45 mężczyzn, 22 kobiety) stwierdzono zgon po przybyciu zespołu ratownictwa medycznego (ZRM) i nie podejmowano resuscytacji krążeniowo-oddechowej (RKO). W pozostałych 205 przypadkach podjęto RKO, która była nieskuteczna u 141 osób (97 mężczyzn, 44 kobiety). Choć w analizach jednoczynnikowych predyktorami zgonu przedszpitalnego były: PNZK bez obecności świadków (OR = 4,2; 95% CI: 2,1–8,5), PNZK występujące w miejscu publicznym (OR = 3,1; 95% CI: 1,6–6,0), brak RKO przez świadka (OR = 9,7; 95% CI: 4,2–22,2), niepodjęcie masażu serca przez świadka zdarzenia (OR = 13,1; 95% CI: 5,4–31,6), stwierdzono początkowo niedefibrylacyjny rytm serca (OR = 7,0; 95% CI: 3,7–13,1) oraz ilość leków użytąch do RKO (OR = 0,4; 95% CI: 0,2–0,7), to w modelu regresji logistycznej jedynie niepodjęcie masażu serca przez świadka (OR = 6,5; 95% CI: 2,1–18,0) i rytm niedefibrylacyjny (OR = 4,6; 95% CI: 2,2–10,0) okazały się niezależnymi determinantami zgonu (AUROC = 0,801; 95% CI: 0,742–0,851).

Wnioski: Niezależnymi od siebie czynnikami ryzyka zgonu przedszpitalnego u mieszkańców powiatu bielskiego po PNZK są niedefibrylacyjny rytm zatrzymania krążenia i brak podjęcia masażu serca przez świadka zdarzenia.

Słowa kluczowe: pozaszpitalne zatrzymanie krążenia, rokowanie, czynniki ryzyka.
Introduction

Sudden cardiac arrest (SCA) is an important medical, social, and economic problem. It exerts a significant burden on the health care system and its various elements, requiring multifaceted action and financial expenditure [1]. Depending on the location in which it occurs, SCA can be classified as out-of-hospital (OHCA) or in-hospital (IHCA). These separate nosological entities are often associated with different etiology, prevalence, management, and prognosis [1].

Despite the progress made in the field of cardiopulmonary resuscitation (CPR), the prognosis for OHCA remains unfavorable and depends on many demographic and clinical variables as well as on the circumstances of the SCA, its mechanisms, and its reversibility [2]. The extent of action taken to prevent post-resuscitation syndrome is also not without bearing [2].

In view of international reports, the established predictors of CPR success and variables improving SCA prognosis include male sex, a shockable cardiac rhythm, the presence of a witness, prompt CPR, short duration of CPR, restoration of consciousness, and the lack of signs of shock or multiple organ dysfunction syndrome [1, 2]. However, the amount of current national data on the subject is unsatisfactory.

Aim

The study aims to identify the risk factors for prehospital death in patients after OHCA in Bielsko County.

Material and methods

Ambulance dispatch cards used by the Emergency Medical Services (EMS) teams in Bielsko-Biała in 2013 (n = 23 400) were analyzed retrospectively. The study included dispatch cards pertaining to cases of SCA (n = 276). Patients below 18 years of age were excluded from the study (n = 4). Ultimately, 272 dispatch cards were analyzed. During the analyzed period, the county featured 7 EMS substations serving the city of Bielsko-Biała and the following communes: Bestwina, Buczkowice, Czechowice-Dziedzice, Jasienica, Jaworze, Kozy, Porabka, Szczyrk, Wilamowice, and Wilkowice. The EMS stations maintain 6 specialized and 5 standard ambulances in a state of around-the-clock readiness.

The information was gathered based on standard dispatch cards issued to the EMS teams. The potential mortality risk factors included basic demographic characteristics, variables associated with the circumstances, potential cause, and mechanism (the initially diagnosed rhythm) of OHCA, actions taken by witnesses (presence of witnesses at the scene, bystander CPR, the use of an automatic external defibrillator) and by the EMS team (ambulance response time, actions taken at the scene, duration of CPR, result of CPR). The primary endpoint was prehospital death defined as death diagnosed after the EMS team’s arrival without CPR or the failure of CPR performed by the EMS team after arriving at the scene.

Statistical analysis

Statistical analysis was conducted based on procedures available in the licensed software MedCalc (v14). Quantitative variables are presented as medians (and interquartile ranges; IQR, 25th–75th percentile). Qualitative variables are presented as absolute values and percentages. Differences in quantitative variables between the groups were examined with parametric (Student’s t) or nonparametric (Mann-Whitney U) tests based on the type of variable distribution. The distribution was verified with the Kolmogorov-Smirnov test. A χ² test or Fisher’s exact test was used for qualitative variables. Odds ratios (OR) with 95% confidence intervals (95% CI) were used to assess the relationships between qualitative variables. In order to assess the risk of prehospital mortality, the results of basic analyses were repeated in multivariate analysis, using forward stepwise logistic regression. Variables with p < 0.1 in intergroup comparisons were included. Logistic odds ratios (logOR) and their 95% confidence intervals were estimated. The model’s diagnostic accuracy was verified based on the area under the receiver operating characteristic curve (AUROC) and its statistical significance. The ultimately accepted criterion of significance was p < 0.05.

Results

Out of the 272 analyzed calls, in 67 cases (45 men, 22 women), death was pronounced after the arrival of the EMS team, and CPR was not attempted. In the remaining 205 cases, CPR was conducted; it was unsuccessful in 141 individuals (97 men, 44 women).

The potential risk factors for death without CPR (i.e., in the group of 67 victims) are presented in Table I. The duration of bystander CPR (p = 0.5) (Fig. 1) and ambulance response time (p = 0.2) (Fig. 2) had no bearing on the results. The CPR failure (in the group of 205 victims who underwent CPR) was more frequent when the OHCA occurred without the presence of witnesses (OR = 2.5; 95% CI: 1.2–5.2; p = 0.01) or in a public place (OR = 2.95; 95% CI: 1.5–6.0; p = 0.003), when no bystander CPR was provided (OR = 5.0; 95% CI: 2.1–11.9; p = 0.01), no cardiac massage was attempted (OR = 5.8; 95% CI: 2.4–14.4; p < 0.001), and the initial rhythm was non-shockable (OR = 3.8; 95% CI: 2.0–7.4; p < 0.001). Individuals receiving more CPR medications had a higher chance of being resuscitated (OR = 0.4; 95% CI: 0.2–0.7; p = 0.001). The duration of CPR conducted by a witness (p = 0.4) (Fig. 3) or the EMS team (p = 0.6) (Fig. 4) and ambulance response time (p = 0.2) (Fig. 5) had no bearing on the results. The potential risk factors for the failure of CPR attempted by the EMS team after arriving at the scene are presented in Table II.

In short, the prehospital mortality risk factors (i.e., in 272 patients) included: OHCA without witnesses (OR = 4.2; 95% CI: 2.1–8.5; p < 0.001), OHCA in a public place (OR = 3.1; 95% CI: 1.6–6.0; p < 0.001), no bystander CPR (OR = 9.7; 95% CI: 4.2–22.2; p < 0.001), no bystander cardiac massage (OR = 13.1; 95% CI: 5.4–31.6; p < 0.001), and initial diagnosis of a non-shockable cardiac rhythm (OR = 7.0;
Tab. I. Potential risk factors for death with no CPR attempted by the EMS team after arriving at the scene (in 67 vs. 205 victims)

| Variable                                      | Death (n/N) | OR (95% CI)      | P-value |
|-----------------------------------------------|-------------|------------------|---------|
| Male sex                                      | Yes 45/190  | 1.18 (0.60–2.06) | 0.6     |
|                                               | No 22/82    |                  |         |
| Age [in whole years]                          |             |                  |         |
| +                                             | 79 (66–86)  | 1.04 (1.01–1.06) | 0.002   |
| –                                             | 68 (60–77)  |                  |         |
| OHCA during the weekend                       | Yes 20/79   | 1.05 (0.58–1.93) | 0.9     |
|                                               | No 47/193   |                  |         |
| OHCA in a public place                        | Yes 8/49    | 0.54 (0.24–1.22) | 0.1     |
|                                               | No 59/223   |                  |         |
| Ambulance called by a family member           | Yes 51/210  | 1.07 (0.52–2.21) | 0.9     |
|                                               | No 12/47    |                  |         |
| OHCA without the presence of witnesses        | Yes 49/108  | 6.74 (3.63–12.51)| < 0.001 |
|                                               | No 18/146   |                  |         |
| No bystander CPR                              | Yes 144/152 | 17.41 (7.85–38.62)| < 0.001 |
|                                               | No 61/120   |                  |         |
| No bystander defibrillation                   | Yes 67/271  | 0.99 (0.04–24.60)| 0.99    |
|                                               | No 0/1      |                  |         |
| No bystander cardiac massage                  | Yes 66/125  | 327.47 (19.94–5377.21)| < 0.001    |
|                                               | No 0/146    |                  |         |
| No bystander ventilation                      | Yes 0       | −                 | −       |
|                                               | No 0        |                  |         |
| Non-shockable rhythm                          | Yes 67/166  | 145.0 (8.83–2365.53)| < 0.001    |
|                                               | No 0/106    |                  |         |

*Impossible to assess. OHCA – out-of-hospital sudden cardiac arrest, CPR – cardiopulmonary resuscitation

95% CI: 3.7–13.1; p < 0.001). Individuals receiving more CPR medications had a higher chance of being resuscitated (OR = 0.4; 95% CI: 0.2–0.7; p = 0.001) (Table III). The individuals whose resuscitation failed were older (median: 72 years, IQR: 61–82) than the ones who were transferred to the hospital after successful CPR (median: 65 years, IQR: 58–77) (p = 0.06) (Fig. 6).

Ultimately, in logistic regression, only the lack of cardiac massage (logOR = 6.5; 95% CI: 2.1–18.0; p < 0.001) and non-shockable rhythm (logOR = 4.6; 95% CI: 2.2–10.0;
Determinants of unfavorable prognosis for out-of-hospital sudden cardiac arrest in Bielsko-Biala district

Fig. 3. Duration of bystander cardiopulmonary resuscitation (CPR) vs. CPR failure. The diagram presents the median and interquartile range (box), dispersion (whiskers), outlying values (small circles), and extreme values (small squares)

Fig. 4. Duration of cardiopulmonary resuscitation (CPR) by the emergency medical services (EMS) team vs. CPR failure. The diagram presents the median and interquartile range (box), and dispersion (whiskers)

Fig. 5. Ambulance response time vs. cardiopulmonary resuscitation (CPR) failure. The diagram presents the median and interquartile range (box), dispersion (whiskers), outlying values (small circles), and extreme values (small squares)

\[
p < 0.001
\]

\[
p = 0.4
\]

\[
p = 0.6
\]

\[
p < 0.001
\]

Discussion

An important step in improving the still unfavorable prognosis of OHCA is to identify its potential predictors. In our material, they were ultimately identified as: no cardiac massage by witnesses/bystanders and non-shockable rhythm of SCA. These two variables alone enabled the prediction of prehospital death in as many as 80% of cases.

These observations are in accordance with the data from the relevant Polish literature. Rudner et al. [3] demonstrated in a population of Katowice inhabitants that individuals in whom OHCA occurred in the presence of witnesses had a two times higher chance of being admitted to a hospital (OR = 2.2; 95% CI: 1.1–4.6) and an almost four times higher chance of being discharged from the hospital (OR = 3.9; 95% CI: 0.9–18). Furthermore, the performance of CPR by a bystander was associated with a 3-fold increase in the chance of CPR success (OR = 3.2; 95% CI: 1.4–4.5) and hospital discharge (OR = 2.7; 95% CI: 1.1–5.3), while shockable cardiac rhythm was associated with a 4-fold increase in the chance of survival until hospital admission after OHCA (OR = 3.9; 95% CI: 1.9–7.7) and hospital discharge (OR = 3.5; 95% CI: 1.2–10.3), regardless of the extent of neurological injury [3]. On the other hand, in a study conducted among the adult population of Szczecin by Jankowski [4], the success of prehospital resuscitation depended only on its duration, while the presence of witnesses and their participation in CPR had no significant effect on survival; this was explained by the small percentage of cases in which the witnesses provided aid to the SCA victims.

Our results are also in accordance with international observations reported in studies from Sweden [5], Denmark [6], Korea [7], Australia [8], Japan [9], Spain [10], Canada [11], France [12], Singapore [13], and Austria [14]. The reports cited above primarily underscored the role of early bystander CPR before the arrival of emergency teams, including bystander defibrillation [5–7, 9–11, 13, 14].

In this context, it is worthwhile to note that, in multivariate analysis, it was the lack of cardiac massage (and not necessarily other types of resuscitation) that was a predictor of prognosis, regardless of the SCA mechanism. This can be most likely attributed to the marginal number of cases in which the witnesses used automatic defibrillators (only one documented case) [15]. This confirms that patient management after OHCA requires multidisciplinary action and goes far beyond the activities of medical services alone. Each element of the aid provided to the victim is equally important, as the final outcome may depend on the
**Tab. II.** Potential risk factors for the failure of CPR attempted by the EMS team after arriving at the scene (in 205 vs. 272 victims)

| Variable | Death (n/N) | OR (95% CI) | P-value |
|----------|-------------|-------------|---------|
| Male sex | Yes 97/145  | 1.36 (0.70–2.66) | 0.4 |
|          | No 44/60     |             |         |
| Age [in whole years] | + 69 (61–77) | 1.01 (0.99–1.03) | 0.4 |
|          | – 65 (58–77) |             |         |
| OHCA during the weekend | Yes 39/59 | 1.19 (0.62–2.26) | 0.6 |
|          | No 102/146   |             |         |
| OHCA in a public place | Yes 20/41  | 2.95 (1.50–6.0) | 0.003 |
|          | No 121/164   |             |         |
| Ambulance called by a family member | Yes 111/159 | 0.51 (0.24–1.08) | 0.08 |
|          | No 19.35     |             |         |
| OHCA without the presence of witnesses | Yes 48/59 | 2.49 (1.19–5.20) | 0.01 |
|          | No 93/146    |             |         |
| No bystander CPR | Yes 54/61  | 5.05 (2.15–11.89) | < 0.001 |
|          | No 87/144    |             |         |
| No bystander defibrillation | Yes 141/204 | 6.68 (0.27–166.37) | 0.2 |
|          | No 0/1       |             |         |
| No bystander cardiac massage | Yes 53/59  | 5.82 (2.35–14.42) | < 0.001 |
|          | No 88/146    |             |         |
| No bystander ventilation | Yes 1/13   | 5.14 (0.58–45.69) | 0.1 |
|          | No 9/30      |             |         |
| Non-shockable rhythm | Yes 82/99  | 3.84 (2.01–7.36) | < 0.001 |
|          | No 59/106    |             |         |
| Number of administered CPR medications [per medication type] | + 2 (1–2) | 0.40 (0.23–0.70) | 0.001 |
|          | – 2 (2–2)    |             |         |

**Tab. III.** Potential risk factors for prehospital death (in 272 victims)

| Variable | Death (n/N) | OR (95% CI) | P-value |
|----------|-------------|-------------|---------|
| Male sex | Yes 142/190 | 1.39 (0.74–2.64) | 0.3 |
|          | No 66/82    |             |         |
| Age [in whole years] | + 72 (61–82) | 1.02 (0.99–1.04) | 0.09 |
|          | – 65 (58–77) |             |         |
| OHCA during the weekend | Yes 59/79 | 1.15 (0.62–2.11) | 0.7 |
|          | No 149/193  |             |         |
| OHCA in a public place | Yes 28/49  | 3.14 (1.63–6.05) | < 0.001 |
|          | No 180/223  |             |         |
| Ambulance called by a family member | Yes 162/210 | 0.57 (0.29–1.14) | 0.1 |
|          | No 31/47    |             |         |
| OHCA without the presence of witnesses | Yes 97/108 | 4.21 (2.08–8.51) | < 0.001 |
|          | No 111/164  |             |         |
| No bystander CPR | Yes 113/120 | 9.69 (4.22–22.24) | < 0.001 |
|          | No 95/152   |             |         |
| No bystander defibrillation | Yes 208/271 | 9.85 (0.40–244.81) | 0.2 |
|          | No 0/1      |             |         |
| No bystander cardiac massage | Yes 119/125 | 13.07 (5.40–31.66) | < 0.001 |
|          | No 88/146   |             |         |
| No bystander ventilation | Yes 1/13    | 5.14 (0.58–45.65) | 0.1 |
|          | No 9/30     |             |         |
| Non-shockable rhythm | Yes 149/166 | 6.98 (3.72–13.13) | < 0.001 |
|          | No 59/106   |             |         |
| Number of administered CPR medications [per medication type] | + 2 (1–2) | 0.40 (0.23–0.70) | 0.001 |
|          | – 2 (2–2)   |             |         |

**OHCA** – out-of-hospital sudden cardiac arrest, CPR – cardiopulmonary resuscitation
Determinants of unfavorable prognosis for out-of-hospital sudden cardiac arrest in Bielsko-Biała district

Fig. 6. Age vs. prehospital death. The diagram presents the median and interquartile range (box), dispersion (whiskers), and outlying values (small circles)

weakest link in the “chain of survival”. The assessment of the circumstances of OHCA translates directly into taking proper resuscitation measures and directing further specialized lifesaving action. Therefore, improving the frequency with which aid is provided to SCA victims by witnesses is of great importance for improving the victims’ survival.

Interestingly, the risk of death was observed to be increased when OHCA occurred in public places, which was in contrast with the relevant literature [6–9, 11, 12, 14]. It appears to be associated with the higher likelihood of CPR being performed by family members when the SCA occurred at home. Moreover, this relationship was not confirmed by multivariate analysis.

Another variable which was found to have statistical significance for the prognosis (though only in basic analyses) was the number of agents used during resuscitation (adrenaline alone = 1 agent, adrenaline + sodium = 2 agents, adrenaline + amiodarone = 2 agents, adrenaline + sodium + amiodarone = 3 agents, etc.). Individuals who received a higher number of agents had a higher chance of surviving until being transferred to a hospital. This issue has been discussed in the literature on several occasions [4, 12, 16, 17]. In the study by Jankowski [4], higher mortality risk was observed among patients receiving adrenaline (OR = 5.63 regardless of dosage). In a study by Dumas et al. [16] the use of adrenaline was also associated with worse prognosis (OR = 2.1 for the probability of death for a dose of 1 mg, OR = 3.3 for a dose of 2-5 mg, and OR = 4.4 for doses > 5 mg). Aschauer et al. [17] also created a prediction model for unfavorable SCA prognosis based on only 4 variables: older age, non-shockable cardiac rhythm, longer CPR duration required to restore spontaneous circulation, and larger dose of administered adrenaline. Finally, a study conducted among the inhabitants of Paris demonstrated that the necessity to use more than 3 mg of adrenaline during CPR was associated with a 20-fold increase in the mortality risk [12]. However, other authors suggest that patients who require the administration of adrenaline during CPR have a higher chance of achieving a return of spontaneous circulation, which does not necessarily influence long-term neurological functioning (e.g., according to the CPC scale) or the risk of long-term mortality [18, 19]. Repeating adrenaline doses after the cessation of circulation impairs microcirculatory perfusion in the central nervous system and exacerbates already existing metabolic disturbances [20]. This has been reflected in the current guidelines for resuscitation: their authors advise caution when considering the administration of adrenaline [1]. The discrepancy is difficult to explain, but it can be speculated that, in this study, a return of spontaneous circulation during CPR was less likely when cardiac massage and defibrillation were used alone without the need for administrating medication. Also, it is understandable that prognosis is better when the return of hemodynamically sufficient circulation occurs quickly and the CPR is shorter (e.g., when a bystander performs early defibrillation). Formulating more rational conclusions would have been easier if the dispatch cards (the standard Polish emergency medical action cards) contained information about the time between the SCA diagnosis and the administration of adrenaline. This would, however, require systemic action consisting in changing the current forms.

The present study is not free from limitations. Firstly, result generalization is limited by the relatively short time of observation and the lack of territorial differentiation of the victims. Secondly, it is a retrospective observational study and is, therefore, prone to systematic error. Thirdly, the lack of information concerning the potential causes of the cardiac arrest precludes more precise analysis going beyond a typical epidemiological description of the event. Finally, as we have no access to information concerning the course of hospital treatment, no outcomes of patients after their transfer to the Admission Room or the Emergency Room are available.

Conclusions

Non-shockable rhythm of cardiac arrest and no cardiac massage by bystanders constitute mutually independent predictors of prehospital mortality risk in inhabitants of Bielsko County after episodes of sudden cardiac arrest.

Disclosure

Authors report no conflict of interest.

References

1. Monsieurs KG, Nolan JP, Bossaert LL, Greif R, Macaonachie IK, Nikolaou NI, Perkins GD, Soar J, Truňář A, Wylie J, Zideman DA; ERC Guidelines 2015 Writing Group. European Resuscitation Council Guidelines for Resuscitation 2015: Section 1. Executive summary. Resuscitation 2015; 95: 1-80.
2. Krzych Ł, Knapiński P; Zespół poręszękcytacyjny. Kardiologia po Dyplomie 2015; 14: 34-41.
3. Rudner R, Łatowiecki P, Wartak M, Marciniak R, ByrcekJ. Ocena wybranych czynników wpływających na wyniki postępowania reanimacyjnego w pozaszpitalnych zatrzymanach krążenia. Anest Int Ter 2005; 3: 174-180.
4. Jankowski D. Nagle zatrzymanie krążenia poza szpitalem w populacji dorosłych miasta Szczecina w latach 2002-2003. Roczniki Pomorskiej Akademii Medycznej w Szczecinie 2007; 53: 33-42.
5. Hasselqvist-Ax I, Riva G, Herlitz J, Rosenqvist M, Hollenberg J, Nordberg P, Ringh M, Jonsson M, Axellsson C, Lindqvist J, Karlsson T, Svensson L. Early cardiopulmonary resuscitation in out-of-hospital cardiac arrest. N Engl J Med 2015; 372: 2307-2315.

6. Søholm H, Hassager C, Lippert F, Winther-Jensen M, Thomsen JH, Friberg H, Bro-Jepsen J, Køber L, Kjærgaard J. Factors associated with successful resuscitation after out-of-hospital cardiac arrest and temporal trends in survival and comorbidity. Ann Emerg Med 2015; 65: 523-531.

7. Yang HJ, Kim GW, Kim H, Cho JS, Rho TH, Yoon HD, Lee MJ; NEDIS-CA Consortium. Epidemiology and outcomes in out-of-hospital cardiac arrest: a report from the NEDIS-based cardiac arrest registry in Korea. J Korean Med Sci 2015; 30: 95-103.

8. Nehme Z, Andrew E, Bray JE, Cameron P, Bernard S, Meredith IT, Smith K. The significance of pre-arrest factors in out-of-hospital cardiac arrests witnessed by emergency medical services: a report from the Victorian Ambulance Cardiac Arrest Registry. Resuscitation 2015; 88: 35-42.

9. Kitamura T, Kiyohara K, Sakai T, Iwami T, Nishiyama C, Kajino K, Nishiuchi T, Hayashi Y, Katayama Y, Yoshiya K, Shimazu T. Epidemiology and outcome of adult out-of-hospital cardiac arrest of non-cardiac origin in Osaka: a population-based study. BMJ Open 2014; 4: e006462.

10. Socias Crespi L, Ceniceros Rozalen MI, Rubio Roca P, Martinez Cuellar N, García Sánchez A, Ripoll Vera T, Lesmes Serrano A. Epidemiological characteristics of out-of-hospital cardiorespiratory arrest recorded by the 061 emergencies system (SAMA) in the Balearic Islands (Spain), 2009-2012. Med Intensiva 2015; 39: 199-206.

11. Drennan IR, Lin S, Sidikal DE, Morrison JJ. Survival rates in out-of-hospital cardiac arrest patients transported without prehospital return of spontaneous circulation: an observational cohort study. Resuscitation 2014; 85: 1488-1493.

12. Bougouin W, Lamhaut L, Marijon E, Jost D, Dumas F, Deye N, Beganton F, Emparan JP, Chazelle E, Carieu A, Jouven X. Characteristics and prognosis of sudden cardiac death in Greater Paris: population-based approach from the Paris Sudden Death Expertise Centre (Paris-SDEC). Intensive Care Med 2014; 40: 846-854.

13. Goh ES, Liang B, Fook-Chong S, Shahidah N, Soon SS, Yap S, Leong B, Gan HN, Foo D, Tham LP, Charles R, Ong ME. Effect of location of out-of-hospital cardiac arrest on survival outcomes. Ann Acad Med Singapore 2013; 42: 437-444.

14. Nürnberg A, Sterz F, Malzer R, Warenits A, Girs M, Stöckli M, Hlawin G, Magnat IA, Weiser C, Zajicek A, Glück H, Grave MS, Müller V, Benold N, Hubner P, Kaff A. Out of hospital cardiac arrest in Vienna: incidence and outcome. Resuscitation 2013; 84: 42-47.

15. Murakami Y, Iwami T, Kitamura T, Nishiyama C, Nishiuchi T, Hayashi Y, Kawamura T. Outcomes of out-of-hospital cardiac arrest by public location in the public-access defibrillation era. J Am Heart Assoc 2014; 3; e000533.

16. Dumas F, Bougouin W, Geri G, Lamhaut L, Bougle A, Daviaud F, Morichau-Beauchant T, Rosencher J, Marijon E, Carli P, Jouven X, Rea TD, Cariou A. Is epinephrine during cardiac arrest associated with worse outcomes in resuscitated patients? J Am Coll Cardiol 2014; 64: 2360-2367.

17. Aschauer S, Dorffner G, Sterz F, Erdogmus A, Laggner A. A prediction tool for initial out-of-hospital cardiac arrest survivors. Resuscitation 2014; 85: 1225-1231.

18. Loomba RS, Nijhawan K, Aggarwal S, Arora RR. Increased return of spontaneous circulation at the expense of neurologic outcomes: is prehospital epinephrine for out-of-hospital cardiac arrest really worth it? J Crit Care 2015; 30: 1376-1381.

19. Hubble MW, Johnson C, Blackwelder J, Collopy K, Houston S, Martin M, Wilkes D, Wiser J. Probability of return of spontaneous circulation as a function of timing of vasopressor administration in out-of-hospital cardiac Arrest. Prehosp Emerg Care 2015; 19: 457-463.

20. Hardig BM, Götberg M, Rundgren M, Götberg M, Zughait D, Kopotic R, Wagner H. Physiologic effect of repeated adrenaline (epinephrine) doses during cardiopulmonary resuscitation in the cath lab setting: a randomised porcine study. Resuscitation 2016; 101: 77-83.