Neurological outcome of chest compression-only bystander CPR in asphyxial and non-asphyxial out-of-hospital cardiac arrest: an observational study.

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Abstract

Background: According to guidelines and bystander skill, two different methods of cardiopulmonary resuscitation (CPR) are feasible: standard CPR (S-CPR) with mouth-to-mouth ventilations and chest compression-only CPR (CO-CPR) without rescue breathing. CO-CPR appears to be most effective for cardiac causes, but there is a lack of evidence for asphyxial causes of out-of-hospital cardiac arrest (OHCA). Thus, the aim of our study was to compare CO-CPR versus S-CPR in adult OHCA from medical etiologies and assess neurologic outcome in asphyxial and non-asphyxial causes.

Methods: Using the French National OHCA Registry (RéAC), we performed a multicenter retrospective study over a five-year period (2013 to 2017). All adult-witnessed OHCA who had benefited from either S-CPR or CO-CPR by bystanders were included. Non-medical causes as well as professional rescuers as witnesses were excluded. The primary end point was 30-day neurological outcome in a weighted population for all medical causes, and then for asphyxial, non-asphyxial and cardiac causes.

Results: Of the 8 619 subjects included for all medical causes, 6 742 had a non-asphyxial etiology, including 5 904 of cardiac causes, and 1 710 had an asphyxial OHCA. 8.6%; 95% CI [8.1-9.3] of subjects had a good neurological outcome (i.e. cerebral performance category of 1 or 2). Bystanders who performed S-CPR began more often immediately (89.0%; 95% CI [87.3-90.5] versus 78.2%; 95% CI [77.2-79.2]) and in younger subjects (64.1 years versus 65.7; $p < 0.001$). In the weighted population, subjects receiving bystander-initiated CO-CPR had an adjusted relative risk (aRR) of 1.04; 95% CI [0.79-1.38] of having a good neurological outcome at 30 days for all medical causes, 1.28; 95% CI [0.92-1.77] for asphyxial etiologies, 1.08; 95% CI [0.80-1.46] for non-asphyxial etiologies and 1.09; 95% CI [0.93-1.28] for cardiac-related OHCA.

Conclusions: We observed no significant difference in neurological outcome when lay bystanders of OHCA initiated CO-CPR or S-CPR, whether the cause was asphyxial or not. CO-CPR should probably be promoted in adults because it has many advantages (easier to learn and lower infection risk).

Background

Early initiated bystander cardiopulmonary resuscitation (CPR) during out-of-hospital cardiac arrest (OHCA) is pivotal with regard to successful outcomes.[1,2] In Europe, since 2010, two different methods of on-scene CPR have been feasible depending on lay rescuer skills: standard CPR (S-CPR) for trained rescuers and chest compression-only CPR (CO-CPR).[3] S-CPR consists of administering two mouth-to-mouth ventilations every 30 chest compressions (30:2). During CO-CPR, continuous chest compressions are performed without rescue breathing. This technique is easily performed by naïve rescuers guided by a dispatcher and avoids decreases in blood flow secondary to the interruption of chest compressions.[4,5] The three randomized studies comparing S-CPR and CO-CPR performed by lay bystanders showed no differences in survival after OHCA.[6–8] However, meta-analyses of these randomized studies showed that CO-CPR was associated with improved survival.[9,10] Only the randomized study by Rea et al. focused on neurological outcome, which was not different between the S-CPR and CO-CPR groups, except in the cardiac cause subgroup where CO-CPR was better.[7] The results of observational studies have been heterogeneous with regard to neurological outcome.[2,11–16] Some have reported contradictory results on apparently similar populations,[12,16] while others excluded asphyxial causes of cardiac arrest.[7,11,14,16] Failure to provide bystander ventilation for CPR of asphyxial cardiac arrest has not yet been evaluated. Thus, the aim of our study was to compare CO-CPR versus S-CPR in adult OHCA from medical etiologies and assess neurologic outcomes in subgroups of asphyxial and non-asphyxial causes.

Methods

Study design

We performed a retrospective cohort study analysis based on data extracted from the French National OHCA Registry (RéAC) from January 1 2013 to December 31 2017. Only centers that were checked for completeness of OHCA inclusions and data quality regularly controlled were selected for this study. There were 57 of 94 centers meeting this requirement. RéAC is a cohort which includes all OHCA managed by mobile intensive care units (MICU) in France. A MICU consists of an ambulance driver, a nurse and a senior emergency physician as a minimum team. A detailed description of the emergency medical system in France has been previously published.[17] Briefly, the regional medical dispatching centers (SAMU) receive emergency calls, coordinate the emergency services and assist CPR by telephone. It is a two-tiered pre-hospital system with a fire department ambulance (first professional aid provider) available for prompt intervention and basic life support (BLS), and a mobile emergency and resuscitation service (MERS) including a MICU for advanced life support (ALS). The RéAC form meets the requirements of the French Emergency Medical Service organizations and is structured according to the Utstein universal style.[18] Data is entered in the secured RéAC database (www.registreac.org).[19] Several quality controls were performed on this database (online and offline tests).

The present study was approved by the French Advisory Committee on Information Processing in Health Research (CCTIRS) and the French National Data Protection Commission (CNIL, authorization no. 910946). It was approved as a medical assessment registry without requirement for patient consent.[19]

Patient population

We selected in the RéAC database all witnessed OHCA in adults (≥ 18 years of age) with lay bystander-initiated cardiopulmonary resuscitation (CPR) before the arrival of professional first responders. Exclusion criteria were unwitnessed OHCA, CPR without chest compressions (ventilation only), OHCA in the presence of professional rescuers and traumatic OHCA. We assessed all medical etiologies of OHCA and classified them in asphyxial and non-asphyxial etiologies, including a subgroup of cardiac causes. The OHCA etiology was determined by the MICU physician in charge of the patient. Subjects were also classified in two groups, according to the bystander-initiated CPR method: chest compression only (CO-CPR) and chest compression with mouth-to-mouth ventilation (i.e. S-CPR).

Endpoints

The primary endpoint was the Glasgow-Pittsburgh Cerebral Performance Categories (CPC) at day 30. Favorable neurological outcome was defined by CPC scores of ≤ 2.[20] The secondary endpoint was D-30 survival. Outcomes were collected by blinded assessors.

Statistical analyses

Continuous variables were reported as means with standard deviation (SD) and categorical variables were summed as percentages and 95% confidence interval (95% CI).

In order to obtain unbiased estimations of the average intervention effects, we used inverse probability of treatment weighting (IPTW). This method was performed in two steps: first, an estimation of the propensity score of intervention (CO-CPR) with a logistic model, and then an estimation of the effect on D-30 neurological outcome, weighted on the propensity score. Covariates included in the model were selected using a univariate analysis of their impact on intervention assignation and on D-30 neurological outcome. Indeed, the inclusion of variables not or weakly correlated to the outcome increases the variance of the effect and is related to low reduction of bias.[21] The variables included for the propensity score were therefore limited to variables related to the outcome, i.e. whether or not related to exposure (CO-CPR or S-CPR). For each analysis (main and in subgroups), we constructed a different propensity score. In order to minimize the impact of missing data, we performed multiple imputation using chained equations (MICE) with predictive mean matching for continuous data (only one variable included in the propensity score with missing data was imputed: “Time between the emergency call and arrival of first professional rescuers at the scene” with 19.8% of missing data).

The primary endpoint was assessed with a logistic regression model adjusted on the previously calculated propensity score. Results are expressed as adjusted relative risks with 95% CI. Significance was set at $P < 0.05$ and all associations were determined through two-sided testing. Analyses were performed using the R environment (version 3.4.4) in Rstudio software (version 1.2.1335) with the packages mice (version 3.6.0), survey (version 3.35-1) and twang (version 1.5).

Results

Patient characteristics

During the five-year study period, 51 638 OHCAs were registered in the database from 57 centers. There were 35.1% unwitnessed OHCA, the bystanders were professional rescuers in 22.7% of cases and in 22.7% of the cases no resuscitation was undertaken by non-professional witnesses. Finally, 8 619 patients were included, of which 6 742 had a non-asphyxial etiology (including 5 904 cardiac causes), and 1 710 had an asphyxial OHCA etiology (Fig. 1). The main characteristics of the patients are reported in Table 1. Compared to CO-CPR, S-CPR began more often immediately (89.0%; 95% CI [87.3–90.5] versus 78.2%; 95% CI [77.2–79.2]) and in younger subjects (64.1 years versus 65.7; $p < 0.001$). CPR was dispatcher-assisted in 64.5% 95% CI [61.1–67.7] for S-CPR and 77.1% for CO-CPR 95% CI [75.8–78.4]. In the non-asphyxial OHCA group, 17.5%; 95% CI [16.6–18.5] subjects received S-CPR compared to 20.1%; 95% CI [18.3–22.1] in the asphyxial OHCA group. The main baseline characteristics of the sub-groups of patients are reported in **Table I in the supplemental material**. The proportion bystander-initiated S-CPR was higher at the beginning of the period (linear regression, $P < 0.001$; $R^2 = 0.44$) (Fig. 2); the same trend was observed in other subgroups (**Figure I in the supplementary material**). Simultaneously, the rate of good neurological outcome increased over time (linear regression, $P = 0.001$; $R^2 = 0.17$) (Fig. 2). In **Table II in the supplemental material** we reported characteristics of subjects according to neurological outcome and the etiology of OHCA. From some of these variables, we constructed the propensity scores for each group.

Table 1
Characteristics of patients according to cardiac arrest management by bystanders

Characteristic	S-CPR (n = 1544)	CO-CPR (n = 6997)	*P* value
Age, mean (SD), y	64.1 (16.7)	65.7 (15.8)	< 0.001
Male, n (%)	1057 (68.5)	4924 (70.4)	0.14
Location, n (%)			< 0.001
Home/Private place	1047 (67.8)	5052 (72.2)	
Public place	272 (17.6)	1211 (17.3)	
Workplace	56 (3.6)	183 (2.6)	
Other	169 (11.0)	551 (7.9)	
Known medical history, n (%)			
Cardiovascular disease	655 (42.4)	3019 (43.1)	0.60
Respiratory disease	186 (12.0)	838 (12.0)	0.94
Diabetes	212 (13.7)	903 (12.9)	0.38
Cancer	104 (6.7)	515 (7.4)	0.39
Alcoholic abuse	29 (1.9)	188 (2.7)	0.07
Psychiatric disorder	58 (3.8)	183 (2.6)	0.01
Immediate CPR by bystander, n (%)	1374 (89.0)	5474 (78.2)	< 0.001
Time between emergency call and first professional rescuers arrival at the scene, mean (SD), min	10.8 (6.3)	10.9 (5.9)	0.43
Initial shockable cardiac rhythm, n (%)	448 (29.0)	2260 (32.3)	0.01
Presence of gasps, n (%)	135 (8.7)	504 (7.2)	0.04
Intraosseous injection route during CPR, n (%)	66 (4.3)	319 (4.6)	0.63
Epinephrine dose during CPR, mean (SD), mg	5.1 (4.8)	4.7 (4.5)	0.005

Abbreviations: CPR: cardiopulmonary resuscitation; MICU: mobile intensive care unit; ECMO, extracorporeal membrane oxygenation. *P* values were calculated by using the χ^2 test or Student's t-test.

Characteristic	S-CPR (n = 1544)	CO-CPR (n = 6997)	*P* value
Inotropic support, n (%)	261 (16.9)	1148 (16.4)	0.63
Impossible endotracheal intubation by MICU, n (%)	31 (2.0)	77 (1.1)	0.004
ECMO, n (%)	25 (1.6)	167 (2.4)	0.07
Targeted temperature management, n (%)	200 (13.0)	956 (13.7)	0.46
D-0 survival, n (%)	501 (32.4)	2333 (33.3)	0.50
D-30 survival, n (%)	154 (10.0)	706 (10.1)	0.89
Good neurological outcome at d-30, n (%)	134 (8.7)	604 (8.6)	0.95
Organ donation, n (%)	15 (1.0)	113 (1.6)	0.01
Abbreviations: CPR: cardiopulmonary resuscitation; MICU: mobile intensive care unit; ECMO, extracorporeal membrane oxygenation. *P* values were calculated by using the χ^2 test or Student's t-test.			

Primary and secondary endpoints

Unweighted population

On day 30, 8.6%; 95% CI [8.1–9.3] of subjects had a good neurological outcome. The details of the CPC are presented in Fig. 3 **and Figure II in the supplemental material** for the subgroups. There was no significant difference in outcomes between subjects receiving S-CPR or CO-CPR (Table 1 **and Table I in the supplemental material** for the subgroups).

Weighted population

The population was successfully weighted (i.e. standardized mean difference < 0.1) for the main analysis and the subgroups analysis (**Figure III in the supplemental material**). Subjects receiving bystander-initiated CO-CPR had an adjusted relative risk (aRR) of 1.04; 95% CI [0.79–1.38] of having a good neurological outcome at 30 days (Table 2). The aRR for D-30 survival was 1.04; 95% CI [0.79–1.36]. The aRR of the other subgroups are detailed in the Table 2 and for other variables in the **Figure IV in the supplemental material**. There was no statistical difference between the two different methods of bystander-initiated CPR for neurological outcome and D-30 survival, whatever the cause of the OHCA.

Table 2
Adjusted relative risks [95% CI] of CO-CPR on the weighted population

	D-30 survival	Good neurological outcome
All medical causes	1.04 [0.79–1.36]	1.04 [0.79–1.38]
Asphyxial causes	1.21 [0.88–1.68]	1.28 [0.92–1.77]
Non-asphyxial causes	1.06 [0.79–1.42]	1.08 [0.80–1.46]
Cardiac causes	1.06 [0.90–1.24]	1.09 [0.93–1.28]
CO-CPR: chest compression-only cardiopulmonary resuscitation		

Discussion

From a French OHCA prospective cohort, we evaluated the impact of bystander-initiated CO-CPR on the neurological outcome. We did not observe significant differences in neurological outcomes according to the CPR method performed (S-CPR or CO-CPR), whatever the cause of OHCA (asphyxial or non-asphyxial). These results are consistent with the observations of SOS-KANTO and Rea *et al.*, who did not find differences between CO-CPR and S-CPR in medical OHCAs.[2,7] Similar results were reported by Panchal *et al.* in OHCA secondary to non-cardiac causes.[13] In contrast, Ogawa *et al.* found that S-CPR was beneficial in OHCA secondary to non-cardiac causes, but not in OHCA secondary to cardiac causes.[12] Several studies have reported better neurological outcome in subjects who received bystander-initiated CO-CPR when the etiology of OHCA was a cardiac cause.[2,7,11,14] Kitamura *et al.* in a large population showed that CO-CPR was beneficial for medical OHCA (excluding some causes: asphyxia, electrocution, drowning and drug overdose) after one-to-one propensity score matching.[16] However, they were unable to adjust the results on targeted temperature management (hypothermia), as in other observational studies.[2,12–15] Nevertheless, it has been clearly established that there is a strong link between this therapy and the neurological outcome, whether or not the rhythm of cardiac arrest is shockable.[22–24] Here, we were able to adjust the population on this variable, as well as other numerous factors influencing the outcome. Recently Riva *et al*. found there was an almost a 2-fold higher rate of CPR before EMS arrival and a concomitant 6-fold higher rate of CO-CPR over time but did not collect neurological outcome at day 30.[25]

Lay bystanders are more and more often performing CO-CPR

From 2013 to 2017, we observed a clear decrease in S-CPR by lay bystanders to the benefit of CO-CPR (reduction of 50%). The same trends were observed in Sweden during the same period,[25] and it has also been observed in other countries.[11,15,16] Indeed, since 2010, the International Consensus on

Cardiopulmonary Resuscitation has been encouraging untrained people to carry out CO-CPR, and EMS dispatchers must provide CO-CPR instructions by telephone.[26] Indeed, in our study there were more dispatcher-assisted CPR in the CO-CPR group and fewer CO-CPR patients received immediate bystander CPR, as it would take time for the dispatcher to explain the mechanics of performing CPR to a bystander. At the end of our study period, there were fewer than 15% of bystanders performing S-CPR. S-CPR can maybe initiate more frequently without delay as public awareness by movies, and television promote early S-CPR more than CO-CPR.

Learning

CO-CPR is considered easier to learn and perform. Indeed, at a distance from resuscitation training, the performance of CO-CPR declines only slightly compared to S-CPR.[27] In addition, a shorter CO-CPR learning program leads to better performance on chest compressions for the general public.[28] Moreover, the learning of mouth-to-mouth during the COVID-19 pandemic period is an issue. Indeed, the risk of contamination via mannequins is real when mouth-to-mouth is performed by all learners.[29] Trained people begin CPR more often, resulting in improved OHCA survival.[30] CO-CPR teaching must therefore be preferred and recognized as sufficient to obtain a BLS certificate.[29]

Infectious risk

Mouth-to-mouth ventilation is a hindrance to the initiation of CPR because of the risk of disease transmission.[31,32] Even though cases of transmission of infectious diseases are rare (less than 1/200 000), they can occur: *Neisseria meningitidis*, *Mycobacterium tuberculosis*, enteric pathogens, herpes simplex virus and probably even severe acute respiratory syndrome-associated coronavirus (SARS-CoV).[33–35] It seems logical that mouth-to-mouth ventilation increases the risk of transmission of SARS-CoV-2 compared to chest compressions. However, there is no clear evidence that chest compressions result in the generation of aerosol and transmission of infection.[36]

International Liaison Committee on Resuscitation (ILCOR) and the American Heart Association (AHA) suggest that, as long as the COVID-19 pandemic persists, lay rescuers should consider CO-CPR in adult cardiac arrest.[37,38] Furthermore, in the case of non-household bystander, a face mask or cloth covering the mouth and nose of the rescuer and/or victim should be also considered.[37] However, COVID-19 may be responsible for acute respiratory distress syndrome (ARDS) requiring mechanical ventilation or even extracorporeal membrane oxygenation (ECMO).[39,40] As a result, the incidence of asphyxial OHCA is expected to increase significantly. It is precisely in these situations where the administration of early rescue breaths was thought to be beneficial, but our study suggested that CO-CPR performed by lay bystanders in asphyxial OHCA seemed to be at least equivalent to S-CPR with regard to neurological outcomes.

Non-cardiac cause

We did not find improved neurological outcome with S-CPR as opposed to CO-CPR and point-estimate indicates possible better outcome for CO-CPR. The results of previous studies on these non-cardiac causes are discordant. Some did not find a difference between CO-CPR and S-CPR,[7,13] while others showed a superiority of S-CPR.[2] Another study based on drowning, i.e. hypoxic cardiac arrest, also found no difference between CO-CPR and S-CPR.[41] Cause of OHCA was classified by physician in charge of patient during prehospital care with history, clinical, and electric information available. The Utstein style consensus define medical cause as cases in which the cause of the cardiac arrest is presumed to be cardiac, other medical cause (eg, anaphylaxis, asthma, gastro-intestinal bleed), and in which there is no obvious cause of the cardiac arrest and asphyxia causes as external causes of asphyxia, such as foreign-body airway obstruction, hanging, or strangulation.[18] But mechanisms of OHCA can be challenged by this categorization as patient who collapse secondary to hypoxemia related to acute left ventricular congestive heart failure will be categorized as “cardiac” whereas “asphyxia” is the determinant of OHCA and ventilation maybe the first therapeutic option.[42]

Based on our results and previous studies, it can be considered that CO-CPR has many advantages over S-CPR and that it seems logical to continue this CPR practice only in adults, regardless of the cause of medical OHCA, even beyond the COVID-19 pandemic.

Limitations

First of all, S-CPR and CO-CPR were not assigned by random allocation. In our prospective cohort, we performed an IPTW analysis and made some adjustments for selection bias and confounding factors. Under these conditions, the measured effect was as close as possible to randomized trials.[43]

Second, an inherent limitation of this type of registry analysis is the lack of completeness of data which may have resulted in not being completely exhaustive in the selection of the population. In order to overcome this bias, as explained above, we have only included centers with high quality data. For example, only 0.9% of the subjects included could not be analyzed due to a lack of neurological outcome (CPC).

Third, the classification of the cause of OHCA was done by the MMT emergency physician. The autopsy data was not available in our registry. This may have led to misclassification of some patients because the causes of OHCA are sometimes difficult to define at an early stage.[44]

Lastly, the quality of bystander-initiated CPR could not be monitored, and we suppose that those who performed S-CPR were more experienced because we observed a higher rate of immediate resuscitation initiation. Moreover, in the case of inexperienced bystanders, the guidelines recommend that medical dispatchers guide the CO-CPR.

Conclusion

From our weighted population analysis, we observed no significant differences in neurological outcome when lay bystanders of OHCA initiated CO-CPR or S-CPR. We also specifically analyzed non-asphyxial and asphyxial causes of OHCA, and even in the latter cases mouth-to-mouth ventilation did not improve the outcome. Bystanders should be encouraged to practice CPR, but because of the many advantages of CO-CPR (learning, infection risk), we believe that CO-CPR should probably be promoted.

Abbreviations

CPR: cardiopulmonary resuscitation; S-CPR: standard CPR; CO-CPR: compression-only CPR; OHCA: out-of-hospital cardiac arrest; RéAC: French National OHCA Registry; CI: confidence interval; CPC: cerebral performance category; aRR: adjusted relative risk; MICU: mobile intensive care unit; BLS: basic life support; MERS: mobile emergency and resuscitation service; ALS: advanced life support; SD: standard deviation; IPTW: inverse probability of treatment weighting; MICE: multiple imputation using chained equations; SARS-CoV: severe acute respiratory syndrome-associated coronavirus; ILCOR: International Liaison Committee on Resuscitation; AHA: American Heart Association; ARDS: acute respiratory distress syndrome; ECMO: extracorporeal membrane oxygenation

Declarations

Ethics approval and consent to participate

This study was approved as a medical registry assessment by the French Advisory Committee on Information Processing in Health Research (CCTIRS), and by the French National Data Protection Commission (CNIL, authorisation number; 910946). This study was approved as a medical registry assessment without the requirement for patient consent.

Consent for publication

Not applicable

Availability of data and materials

Data are available on request to the corresponding author.

Competing interests

The authors declare that they have no competing interests.

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(MGEN), the University of Lille and the Institute of Health Engineering of Lille.

Authors' contributions

FJ and QLB had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. FJ and QLB elaborated the conception and design of the study. HH and VB collected the data. FJ, JR, ND, CLC and QLB contributed to the analysis and interpretation of the data. FJ wrote the first draft of the paper, with all other authors making important critical revisions. All authors have read and approved the final version of the manuscript.

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Figures

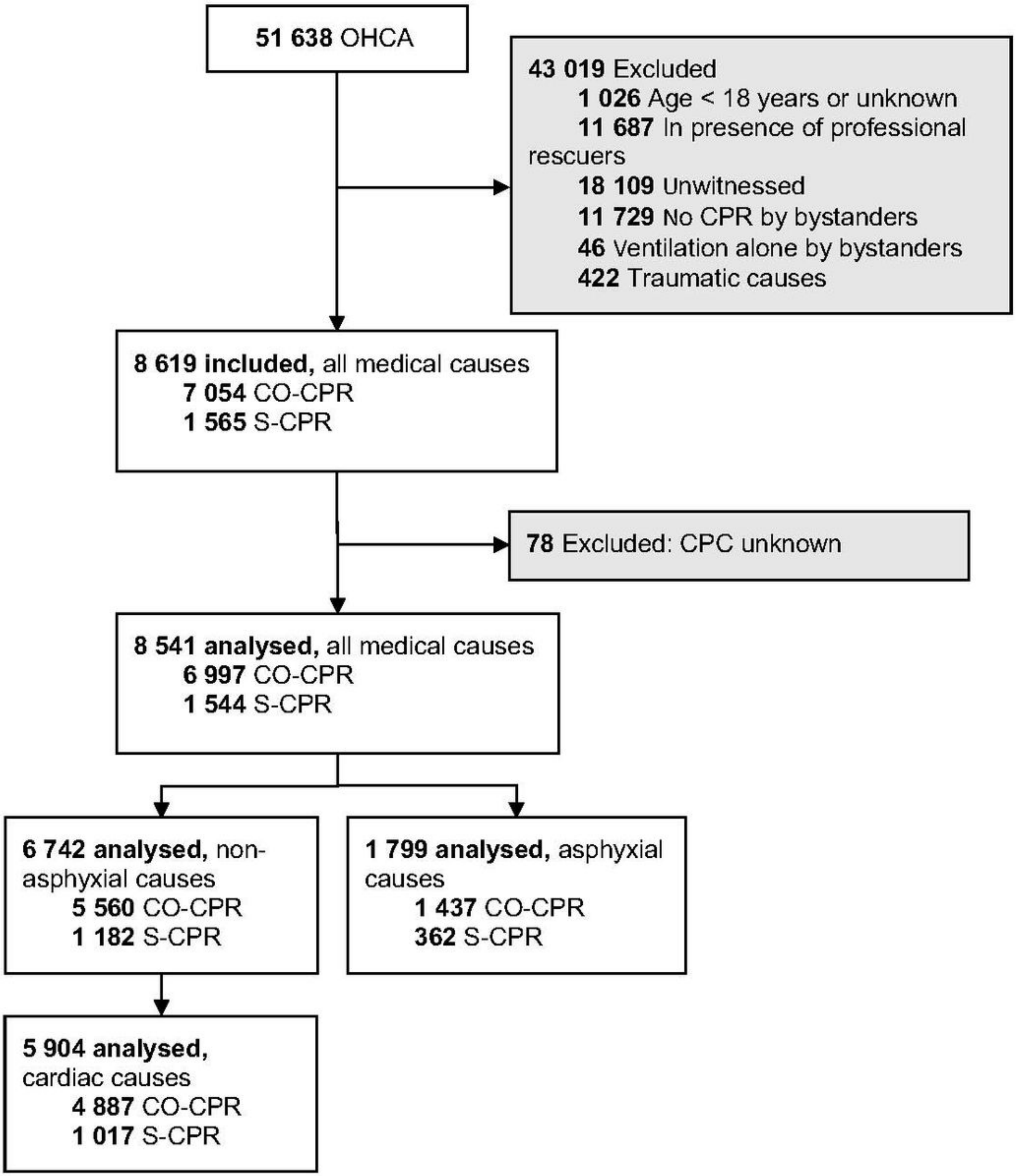

Figure 1

Flow chart of patient inclusion OHCA, out-of-hospital cardiac arrest; CO-CPR, chest compression-only cardiopulmonary resuscitation; S-CPR standard cardiopulmonary resuscitation; CPC, Cerebral Performance Categories

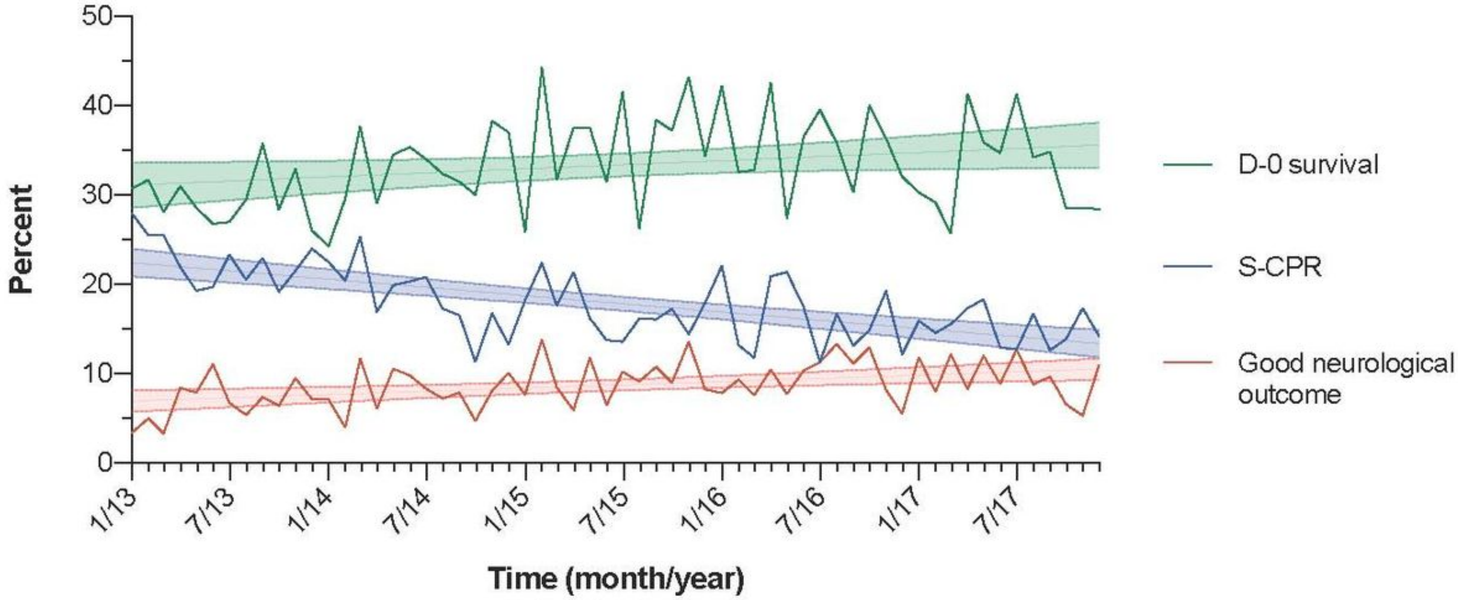

Figure 2

Percentage and linear regression (95% confidence interval) of S-CPR, D0-survival and D-30 neurological outcome, by month CO-CPR, chest compression-only cardiopulmonary resuscitation; S-CPR standard cardiopulmonary resuscitation. Favorable neurologic outcome was defined as a CPC score of 1 (good cerebral performance or minor disability) or 2 (moderate disability)

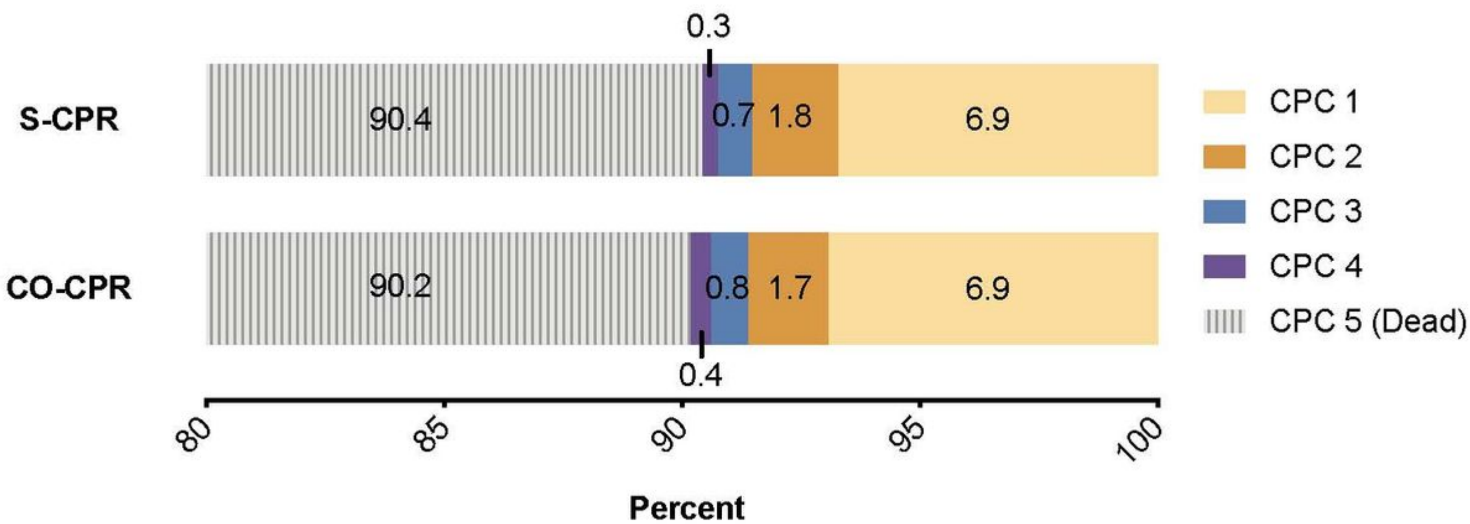

Figure 3

Distribution of Cerebral Performance Categories on day 30 after cardiac arrest (all medical causes). CO-CPR, chest compression-only cardiopulmonary resuscitation; S-CPR standard cardiopulmonary resuscitation; CPC, Cerebral Performance Categories (favorable neurologic outcome was defined as a CPC score of 1 (good cerebral performance or minor disability) or 2 (moderate disability))

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