Lay-Cardiopulmonary resuscitation after out-of-hospital cardiac arrest in aneurysmal subarachnoid hemorrhage patients - a retrospective multi-centric study

Tobias Pantel (tobiasfabian.pantel@uke.de)
University Medical Center Hamburg-Eppendorf
Axel Neulen
University Medical Center of the Johannes Gutenberg University Mainz
Marius Mader
University Medical Center Hamburg-Eppendorf
Elena Kurz
University Medical Center of the Johannes Gutenberg University Mainz
Verena Fassl
University Medical Center of the Johannes Gutenberg University Mainz
Manfred Westphal
University Medical Center Hamburg-Eppendorf
Florian Ringel
University Medical Center of the Johannes Gutenberg University Mainz
Patrick Czorlich
University Medical Center Hamburg-Eppendorf

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Abstract

Introduction

Aneurysmal subarachnoid hemorrhage (SAH) may be associated with sudden cardiac arrest (CA). Since there are many data on the positive impact of lay resuscitation on patient survival, but data are rare for SAH patients, our study aimed to investigate this aspect.

Methods

In this multi-center retrospective analysis, we reviewed the local SAH databases for OHCA and CPR from 01/2011 to 12/2020. Data on CPR were extracted from the ambulance and emergency room (ER) reports. Information on clinical management after hospital admission were gathered from the institutional health records. Collected data were correlated with patient survival as defined outcome parameter.

Results

We screened 1120 patients with SAH and identified 38 patients with SAH, OHCA and CPR (3.4%). Our cohort showed a high proportion of posterior circulation aneurysms (n = 17, 44.7%). Lay CPR was performed in 20 patients. Time to CPR was significantly shorter for lay CPR ($p < 0.001$). 17 patients (44.7%) were not initially assigned to CCT, resulting in a significantly prolonged time interval (154 ± 58 vs. 40 ± 23 min; $p < 0.033$). Overall survival rate of patients with OHCA and CPR was 29.7% (11 patients). However, pre-hospital lay CPR ($p = 0.632$) and shorter duration to the initial CCT after admission ($p = 0.065$) did not influence the outcome.

Conclusions

Sudden OHCA occurs regularly in patients with SAH. A timely initiated and high-quality CPR is crucial to facilitate patient's initial survival. Although prolonged time to CCT does not affect survival, SAH should be considered as a cause of CA and CCT should be integrated into the diagnostic algorithm.

Introduction

Aneurysmal subarachnoid hemorrhage (SAH) is a devastating type of intracranial hemorrhage and associated with relevant short- and long-term morbidity and mortality [1–3]. In addition to acute neurological symptoms, complications in other organ systems may occur at the moment of aneurysm rupture [4]. Within the last couple of years growing evidence of impaired cardiac function in the acute phase of SAH was made [5, 6]. In current studies, the cause is not primarily seen in a cardiac problem but rather in a dysregulation of the neuro-cardiac axis [7]. Possible consequences include neurogenic stress cardiomyopathy (NSC), which, depending on severity, can cause impaired cardiac function and,

consecutively, cerebral hypoperfusion [6, 8]. In addition, there is a widely accepted assumption that SAH is one of the most relevant noncardiac causes of sudden cardiac arrest (CA) [5]. Although there have been several studies focusing on this, the rate of occurrence remains unclear and ranges from 3–11%, which is most likely due to the fact that an unknown number of patients died before hospital admission [9–11].

To enable survival and improve neurological outcome for the affected patients, immediate initiation of high-quality cardio-pulmonary resuscitation (CPR) after the onset of cardiac arrest is mandatory [12–14]. In case of return of spontaneous circulation (ROSC), rapid transport of the patient to a hospital is necessary for further diagnosis and treatment of the underlying cause [13, 15]. Even though great advances in emergency care and intensive care treatment have been made within the last years, overall survival and outcome in patients with CA is still unfavorable with high mortality rates and impaired neurological outcome in case of survival [13, 16]. Especially the lack of immediate CPR and the resulting delay in the start of adequate resuscitation is seen as a major factor contributing to the severity of persisting neurologic deficits [17]. Many studies have demonstrated the critical role and the positive impact of immediate resuscitation on patient's survival, independent of the underlying disease [18, 19]. Thus, patients who were resuscitated immediately are reported to have a higher overall survival compared to those who were not resuscitated immediately (17% vs. 9%), which underlines the importance of lay CPR [20].

Another point addressed by recent studies, is the influence of emergency room management after hospital admission on the further clinical course of these patients. Patients with post-resuscitation conditions are routinely managed by an internal medicine ER team [15]. The focus is primarily on cardiac and internal diseases, which are statistically the most likely underlying cause of CA. However, in case of doubt, this can lead to neurological causes being considered only subsequently, and the patient is therefore transferred to CCT imaging and further therapy with delay. The importance of an optimal ER management and its negative influence on patient's survival and outcome has already been demonstrated for trauma and also for SAH patients [21].

Hence in this study we set out to investigate both the impact of lay CPR and the initial ER management in patients with cardiac arrest and SAH with regard to survival and neurological outcome.

Materials And Methods

Patient data

The study was reported to the responsible Ethics Committees (local ethical review board of Hamburg, Germany and Ethics Committee of the Rhineland-Palatinate Medical Association, (WF-010/21)) and was performed in accordance with the ethical standards laid down in the Declaration of Helsinki and its latter amendments. Because the data were anonymized, and the study was retrospective, informed consent was waived.

Data acquisition

An analysis of all patients treated with an SAH in our both tertiary medical centers from 01/2011 to 12/2020 was performed. Aneurysmal nature of SAH was verified by cerebral digital subtraction angiography (DSA), computed tomography angiography (CTA) or magnetic resonance angiography (MRA). Radiologically proven aneurysms were classified according to their location of the anterior or posterior circulation. All patients were further evaluated with respect to OHCA, which was the inclusion criterion for this study. Patients with unclear or ambiguous information about CA or with in-hospital CA (IHCA) were excluded (see Fig. 1). Focus was made on prognostic data including Glasgow Coma Scale (GCS), World Federations of Neurosurgical Societies (WFNS) scale and Fisher grade which were gathered from patient's health records. The WFNS score was classified according to the GCS and/or neurological status at the arrival of the emergency service, which corresponds to the time of cardiac arrest. In addition, the cardiac rhythm at time of the first electrocardiogram (ECG) was obtained (Table 1).

Table 1
Population characteristics for patients with SAH and out-of-hospital cardiac arrest (OHCA). [1]World Federation of Neurosurgical Societies scale.

Feature	OHCA (n = 38)
Age [years], mean (SD)	55.1 (13.9)
Female, n (%)	20 (52.6)
First documented cardiac rhythm	
Asystole	14 (36.7)
Ventricular fibrillation	2 (5.3)
Pulseless electrical activity	11 (29)
ROSC / unknown	11 (29)
WFNS scale[1], n (%)	
5	38 (100)
Fisher score, n (%)	
3	3 (7.9)
4	35 (92.1)
Aneurysm location, n (%)	
Anterior circulation	21 (55.3)
Posterior circulation	17 (44.7)
Aneurysm multiplicity, n (%)	5 (13.2)
Aneurysm diameter [mm], mean (SD)	10 (7.6)

Patients' emergency protocols were screened with respect to CPR information, such as CPR type, duration to initiation of CPR, initial cardiac rhythm and duration to ROSC, presented in Table 2. In the case of lay CPR, the duration until the start of CPR was assumed to be immediate (time value set as 0 minutes). In cases of professional resuscitation, the time from the receipt of the emergency call to the arrival of the emergency service was taken, which could be extracted from the emergency service protocols.

Table 2
Resuscitation features and emergency room handling for patients who survived OHCA and those who did not. [1] Information on neurological status at discharge were missing in two cases, resulting in an overall patient number of 36 cases for this part.

Feature	Survivor (n = 12)	Non-Survivor (n = 26)	P value
Age [years], mean (SD)	48.2 (4.2)	58.3 (2.6)	p < 0.001
Fisher score, n (%)			
3	1 (8.3)	2 (7.7)	
4	11 (91.7)	24 (92.3)	
Type of CPR, n (%)			
Lay CPR	7 (58.3)	13 (50)	p = 0.632
Professional CPR	5 (41.7)	13 (50)	
Time to CPR [min], mean (SD)	0.73 (2.1)	3.2 (4.8)	p = 0.193
Time to ROSC [min], mean (SD)	5 (4.5)	11.6 (8.1)	p = 0.013
Emergency room handling in presence of a neurologist/neurosurgeon, n (%)	8 (66.7)	15 (57.7)	p = 0.163
Time to cranial CT [min], mean (SD)	45.7 (11.7)	107.6 (36.8)	P = 0.317
mRS at discharge [1], n (%)			
0	0 (0)	0 (0)	
1	2 (20)	0 (0)	
2	0 (0)	0 (0)	
3	2 (20)	0 (0)	
4	3 (30)	0 (0)	
5	3 (30)	0 (0)	
6	0 (0)	26 (100)	

Information on the initial ER management following of each patient after ROSC and hospital admission were extracted from the patients' health records. Focus was made on the initially assigned department and the duration from hospital admission to first cranial computed tomography (CCT) scan. The treatment of the SAH patients in our study was performed in a specialized intensive care unit in accordance with the current international guidelines as well as with our institutional treatment protocols [22, 23].

All included patients were evaluated for short-term outcome, which was defined as in-hospital mortality. The modified Rankin scale (mRs) was used to assess the neurological status of these patients at discharge.

Statistical analysis

Data are displayed as mean ± standard deviation (sd) for continuous variables or absolute and relative numbers for categorical variables. Differences in continuous variables were analyzed with the Mann-Whitney U test, and differences in proportions were analyzed with the chi-square test or Fisher's exact test. A two-sided p-value less than 0.05 was considered as statistically significant. All analyses were performed using SPSS Inc. (Chicago, IL, USA).

Results

Patient cohort and general characteristics

Database analysis identified a total of 1120 patients treated for aneurysmal SAH at our tertiary medical centers between 01/2011 and 10/2020. In 45 (4.0%) of these patients, CA with following CPR was present. 38 (3.4%) patients had a clearly documented OHCA followed by CPR and were therefore included in this study (Fig. 1). The gender distribution of patients was homogeneous (female = 20, male = 18; p = 0.703), and the age of affected patients was 55.1 ± 13.9 years. SAH was classified Fisher 4 in 92.1%. In our OHCA cohort, diagnosed aneurysms were over proportionately localized at the posterior circulation (n = 17, 44.7%). In the overall cohort, the aneurysm distribution ratio for the anterior and posterior circulation was 84.3% vs 15.7%. The clinical characteristics of the patient cohort are shown in Table 1.

Resuscitation characteristics

Lay CPR was performed in 20 cases (52.6%), the remaining 18 patients (47.4%) were not resuscitated until arrival of the emergency service. The time taken to start CPR was prolonged for patients first treated by the emergency service (5.73 ± 1.6 min). In contrast, the time to ROSC after the start of resuscitation in these patients was 7.75 ± 1.5 min, which was unexpectedly shorter than in patients resuscitated by laypersons (12.4 ± 2.1 min), indicating a more affective CPR by trained emergency personal. However, this difference was not statistically significant (p = 0.075). Focusing on the patients who survived OHCA initially and were hospitalized, there was no statistically significant difference in the mode of

resuscitation. The vast majority of patients (65.7%) had non-cardiovertible cardiac rhythms (asystole or PEA) at the time of the first ECG. Five patients already had ROSC at this time, and in another six patients no reliable statement about the initial cardiac rhythm could be made from the records (see Table 1). Further evaluation was now carried out with a view to the patients who survived or did not survive their further hospital stay and could be discharged. Overall, 26 (70.3%) patients died during hospital stay, compared to those who survived (n = 12, 29.7%), they were significantly older (58.3 ± 2.6 (non-survivor) vs. 48.2 ± 4.2 (survivor), $p < 0.001$)). No difference between these two groups was detectable in terms of prognostic factors. The time to onset of CPR was without significant difference for both groups, but the time to return of ROSC was significantly prolonged for the patients who died during hospital stay (5.0 ± 4.5 min (survivor) vs. 11.6 ± 8.1 min (non-survivor); $p < 0.05$). A detailed overview is presented in Table 2.

Of all patients referred to a hospital after CPR, 17 (45.9%) patients were initially treated by an ER team without neurologist or neurosurgeon. The time to first CCT scan in these patients was 154.7 ± 57.9 minutes. Patients who were primarily co-managed by a neurologist or neurosurgeon received their first cranial CT scan after 40.2 ± 23 minutes. The time difference was statistically significant ($p = 0.033$). A difference in time to first cranial CT scan can further be demonstrated when patients are categorized into survivors and non-survivors (Table 2). However, a shorter duration to the initial CCT scan after hospital admission ($p = 0.052$) was not associated with a higher survival rate in this small cohort.

Discussion

In the multi-center study presented here, we investigated the impact of lay resuscitation as well as initial ER handling on the outcome of patients with aneurysmal subarachnoid hemorrhage. The key results of our study include: 1) SAH is an important cause of sudden CA 2) with a disproportionate incidence of posterior circulation aneurysms. 3) In case of sudden CA due to SAH lay resuscitation was performed in more than half of the cases, without achieving advantage in outcome. In addition, 4) it was shown that patients who were already co-managed by a neuro-specialist in the ER received the initial CCT scan significantly faster to rule out central nervous system pathology as underlying reason.

Over a 10-year period, we treated a total of 1120 patients with SAH in our neurosurgical departments, of whom 38 patients experienced OHCA, resulting in an incidence of 3.4%. This incidence is also reported in a recent registry study [24]. In this context, it should be mentioned that in our OHCA cohort there was no gender dominance and patients were affected in middle age. This is interesting for two reasons, since in other SAH studies a female gender dominance [25] is described and, on the other hand, in works on cardiovascular disease partly older persons dominate [26].

Regarding the mentioned incidence, it is to be noted that due to the high number of patients dying of CA of unclear etiology in the out-of-hospital setting, the exact incidence is unclear but has been reported in a similar range in other studies [5, 9, 11, 27]. In general, OHCA is identified as a leading cause of death in high-income countries. For this reason, there have been intensive efforts for years to improve the treatment options in the out-of-hospital and hospital setting to enable these patients to survive with best

neurological outcome. The exact etiology of CA in the acute phase of SAH remains unclear [7, 28, 29]. The most common theories are a central dysregulation due to the rapid increase in ICP at aneurysm rupture, which leads to a transient global cerebral ischemia [28]. Fittingly, in our cohort, pulseless electrical activity (PEA) and ventricular fibrillation (VF) are the most commonly described initial cardiac rhythms which confirms the findings of the work of Zachariah et al., who consider non-cardiovertibale cardiac rhythms to be an important clue to an intracranial cause of CA [11, 29, 30]. In this context, we would like to address that ischemia-suspicious changes may be detectable in the ECG after ROSC in SAH patients, which may mimic myocardial infarction. Though it is crucial to involve experienced cardiologists who will consider an intracranial cause in case of discrepancies with coronary vascular territories.

Another interesting and important finding of our study is the disproportionate incidence of posterior circulation aneurysms in patients with OHCA. In comparison, aneurysms of the posterior circulation occurred in only 15% in our overall cohort, which is consistent with data in other studies. Previous studies on this topic report divergent results on aneurysm localization [31, 32]. In our view, this is an abnormality that may well be related to the CA of these patients and could be a possible risk factor for this complication.

Nevertheless, immediate CPR is considered crucial to ensure survival after CA, which is why special attention is paid to lay CPR [13, 17, 20]. Assuming that the "no-flow"-time and thus organ perfusion should be interrupted as shortly as possible, this is considered crucial to increase the chance of primary survival. The current American Heart Assocication (AHA) resuscitation guideline reports a 39% rate of patients receiving lay CPR. In our cohort, immediate lay CPR was performed in 52.6% of patients, which is consistent with these results. Patients without lay CPR had a significantly longer time to initiation of CPR, which is within comparable limits to other studies [12, 13, 20]. Interestingly, this difference does not map in terms of ROSC, which was more likely to occur in professionally resuscitated than in lay resuscitated patients. A possible explanation for this is the presence of optimal equipment (defibrillator, ventilator, etc.) and the existing training of the emergency service personnel. That these points play an important role is repeatedly emphasized in all guidelines and studies on this topic [33, 34], however, no advantage in terms of overall survival could be shown in our study.

After ROSC, the next step is expeditious transport to an appropriate hospital for further diagnosis and therapy [15, 35]. Since in most cases a cardiac cause for the CA is assumed, hospitalization with a specialized intensive care unit and the possibility of coronary intervention is usually the goal [15]. In our patient cohort, about half of the patients were treated initially according to this procedure and thus without the presence of a neurologist or neurosurgeon. One measurable factor that is closely related to this and, secondly, plays a critical role in the care of patients with SAH is the time interval from hospital admission to initial CCT scan. In our cohort, this was prolonged 3-fold in patients who were not initially co-managed by a neurologist or neurosurgeon. The consequence from a time delay is a loss of reasonable therapy options, with the consequence that 29% of these patients in our cohort died. If we now focus on the overall outcome, however, we find that there is no statistically significant difference between the patients with initial neurological/neurosurgical care and those without. The same was true

for the type of CPR, whereas a significant impact on survival was seen for a shorter time to ROSC, which is consistent with the results of other studies [12, 13, 36]. The fact that the type of CPR in our cohort had no significant influence on survival could be explained on the one hand by SAH as a severe underlying disease with often negative outcome, but also by the small number of cases in our study. Overall, one-third of our patients survived OHCA and SAH and were discharged from the hospital. Nevertheless, a recent study by Feldstein et al. reported an overall survival of 18% in their cohort, which is significantly lower than our results [23].

The care of ER patients with OHCA is a highly demanding interdisciplinary challenge and requires the treating physicians to be familiar with all relevant differential diagnoses as the cause of OHCA. This goal can be achieved with appropriate treatment paths, continuous training and the adaptation of treatment paths in the event of new scientific findings, such as that an immediate coronary angiography is not necessarily indicated in all patients with OHCA [37].

Overall, we see our data supporting the assumption that SAH is a relevant cause of CA in its acute phase. Even if no survival benefit was shown for lay CPR, it is still a central component in the treatment of OHCA. In this context, it is encouraging that this form of immediate resuscitation was performed in more than half of our cases. Ultimately, in our view, the in-hospital care of these patients offers opportunities for optimization, so we want to raise awareness of SAH as a cause of OHCA.

Conclusion

SAH is a common cause of OHCA in patients. In pre-hospital care, immediate initiation of CPR is critical even if lay CPR has not been shown to have a significant survival benefit in our cohort. In ER teams without neurologist/neurosurgeon, the time to first CCT imaging is significantly prolonged. Even if no positive influence on patient's outcome could be proven in our study, obtaining initial CCT imaging remains an important component of the diagnostic workup in patients with unclear CA.

Declarations

Ethical Approval and Consent to participate

The study was reported to the responsible Ethics Committees (local ethical review board of Hamburg, Germany and Ethics Committee of the Rhineland-Palatinate Medical Association, (WF-010/21)) and was performed in accordance with the ethical standards laid down in the Declaration of Helsinki and its latter amendments. Because the data were anonymized, and the study was retrospective, informed consent was waived.

Human and Animal Ethics

Not applicable

Consent for publication

All participating authors declared their consent to publication in advance of submission.

Availability of supporting data

Not applicable.

Competing interests

The authors have no relevant financial or non-financial interests to disclose.

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Authors' contributions

Tobias Pantel MD*: Conceptualization, Methodology, Writing - Original Draft, *equal contribution

Axel Neulen MD*: Methodology, Validation, Writing - Original Draft, *equal contribution

Marius Mader MD: Formal analysis, Data acquisition

Elena Kurz MD: Data acquisition

Andras Piffko MD: Data acquisition

Verena Fassel: Data acquisition

Manfred Westphal MD: Supervision, Writing - Review & Editing

Florian Ringel MD: Supervision, Writing - Review & Editing

Patrick Czorlich MD[1]: Conceptualization, Supervision, Validation, Writing - Review & Editing

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Figures

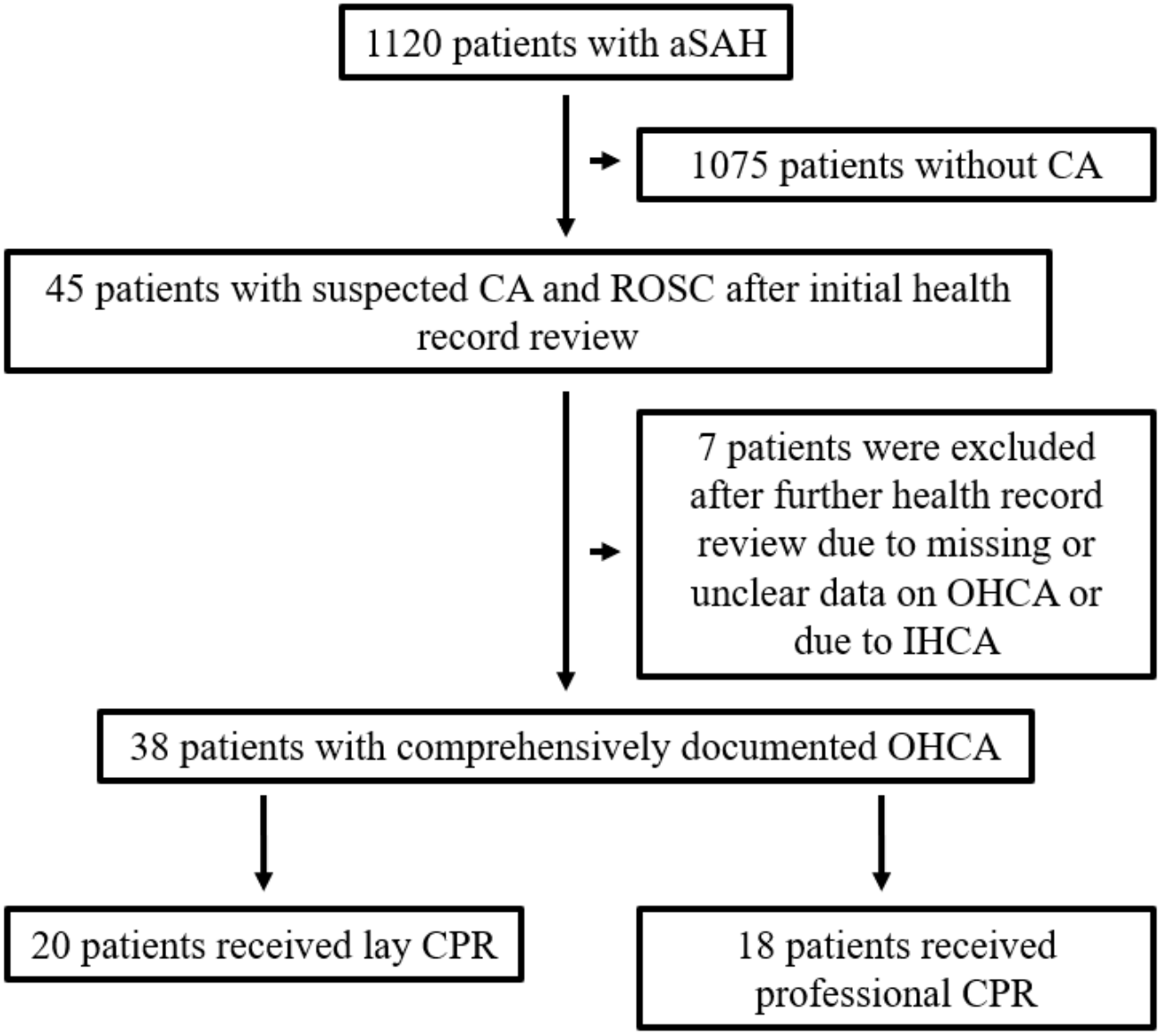

Figure 1

Overview of patient cohort and reasons for exclusion of individual patients. A total of 38 patients with comprehensively documented OHCA were included in the study, 20 of whom were resuscitated by laypersons.