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Clinical paper

Outcome after pre-hospital cardiac arrest in accordance with underlying cause

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Abstract

Aim: In terms of treatment options, the underlying cause of out-of-hospital cardiac arrest (OHCA) has an impact on survival. This study aimed to examine the frequencies of different causes of OHCA and their outcomes using data from a national resuscitation registry.

Methods: All pre-hospital cardiopulmonary resuscitations (CPR) documented in the German Resuscitation Registry between 2007 and 2017 were retrospectively investigated with regard to cause of cardiac arrest, return of spontaneous circulation (ROSC), and hospital discharge rate with good neurological outcome. To avoid selection bias, only rescue services with a return rate in the form 'further clinical treatment' of >30% were included, this resulted in a total return rate of 84% of the included data.

Results: In total, 33,772 patients were included. The most common causes of OHCA were cardiac events (62.2%), hypoxia (11.1%) and trauma (3.2%), in 17.2% no or unknown cause were documented. Overall, 44.8% of patients achieved ROSC, 13.1% of patients were discharged alive from hospital and 68.3% of these were in good neurological condition (9.0% of all patients). ROSC rates differed between 8.9% (sudden infant death syndrome) and 64.4% (intracranial bleeding), while discharge rates with good neurological outcome ranged between 0.9% (sepsis) and 14.0% (intoxication).

Conclusion: The most common causes of OHCA are cardiac events and hypoxia. Depending on the underlying cause, outcome after pre-hospital CPR varies widely with a survival rate with good neurological outcome ranging from 0.9 to 14%.

Keywords: Cardiac, Arrest, Out-of-hospital CPR, Outcome

Introduction

Out-of-hospital cardiac arrest (OHCA) is a relevant issue in the care of pre-hospital emergency services. Ten years ago, approximately 275,000 of OHCA cases per year in Europe (estimated population in 2004: 729 million) were assumed,[1] with estimates of current studies suggesting an incidence of 84.0–87.4 cases/100,000 inhabitants per year.[2,3] By extrapolation, this would represent approximately 640,000 OHCA cases each year in Europe (estimated population in 2018: 742 million). Cardio-pulmonary resuscitation (CPR) can be performed by laymen or pre-hospital rescue services at an estimated average of 49 cases/100,000 inhabitants in the European Union.[2] However, despite intensive scientific research and various health promotion campaigns throughout different countries, OHCA survival has barely changed over the last 10 years and still approximates 10%.[2]

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In addition to high-quality performance of CPR as well as early defibrillation (if indicated) as actions of basic life support, advanced cardiac life support includes the identification and treatment of potentially reversible causes.[4] For this purpose, the underlying pathology should be identified and treated as far as possible. For example, the cause of OHCA can be a cardiac event, trauma, metabolic or respiratory disorders, intoxication, stroke (ischaemic or haemorrhagic) or hypothermia. The knowledge of the cause and the associated possibility of therapy could have a relevant and profound influence on the patient's chances of survival.

While there are various prevalence and cross-descriptive studies on cardiac or trauma-associated OHCA and their outcomes,[5] other and less common causes of OHCA have received little attention. Concerning the area of in-hospital resuscitation, Wallmüller et al. compared the frequencies of underlying aetiology in cardiac arrests and demonstrated that this had a relevant impact on the outcome.[6] To date, equivalent detailed investigations for the pre-hospital setting are missing.

The aim of this study was therefore to examine the frequencies of different causes of OHCA and the outcomes depending on the underlying cause, based on a national registry dataset for pre-hospital resuscitation.

Methods

The study was carried out using a retrospective analysis of prospective data from the German Resuscitation Registry (GRR). For this purpose, the data was provided in a completely anonymized form by the GRR, so that conclusions pertaining to individual patients were not possible. The study was approved by the Scientific Advisory Board of the GRR (No. 20170506_HG). Accordingly, the local ethics committee (Ulm University, Germany) did not demand any further ethics vote. The study was carried out in accordance with the requirements of the 2013 Declaration of Helsinki.

Data collection

The GRR is a national registry for recording pre-hospital and in-hospital resuscitations. The GRR is operated by the German Society for Anaesthesiology and Intensive Care Medicine (DGAI) and was inaugurated in 2007. Participation is voluntary for rescue services and hospitals, where data input is entered by the participants via an online database and anonymised by the system afterwards.

Each rescue service is responsible for entering its data into the register. These data are based on the protocols of the emergency physicians. After entering, they are verified and approved by a central coordinator. There are no general definitions or inclusion criteria for the particular causes, since usually only medical history, actual findings and pre-existing diseases are known and no diagnostic options are available in the pre-hospital setting. Accordingly, in cases where the patient died on the scene, the cause was determined by the attending emergency physician because usually, no autopsy is performed after OHCA in Germany (except presumed death by unnatural causes). In order to be able to act independently as an emergency physician in Germany, it requires after 6 years of study at least a 2–3-year clinical activity in a specialty with emergency medical reference. Often these emergency physicians are specialists or consultants in the fields of internal medicine, surgery or anaesthesia.

In the case of hospital admission, the final and confirmed diagnoses can be reported back to the rescue service and the entered data can be adjusted accordingly. Since the records for further clinical treatment are entered independently of the data records of the prehospital care, this results in a blinding of the outcome to the rescue service.

All data entered into the registry are checked and finally approved by the medical director of each rescue service, at least a specialist or senior physician, before they are reported to the GRR.

At the end of 2017, 128 emergency services were registered for the pre-hospital field, representing a population of approximately 30 million inhabitants.[7] In total, more than 90,000 resuscitations have been documented in the GRR database to the end of 2017.

The GRR dataset consists of the *Primary Care*,*Further Clinical Treatment* and *Long-term Care* modules and is based on the specifications of the Utstein style protocol.[8] Some of the items have been included with more detail for better comparability with and possible integration into the European Registry of Cardiac arrest (EuReCa).[9] This includes the item *(suspected) cause of cardiac arrest*, and the available choices in the GRR are listed in Table 1. An elaborate description of the GRR and a detailed overview of recorded parameters were previously published by Gräsner et al.[10,11] For evaluation in this study, the modules *Primary Care* and *Further Clinical Treatment* were used, which include all necessary information concerning the main endpoints of concern.

Data analysis

All pre-hospital resuscitations from the period 2007–2017 performed by rescue services and documented in the GRR with a complete *Primary Care* dataset were evaluated. In order to mitigate against possible selection bias in terms of survival, only participating rescue services with a return rate >30% for the *Further Clinical Treatment* dataset were included which resulted in a calculated return rate probability >80%. This return rate was considered separately for each service and each year of participation. In preparation for the analyses, data were assigned according to the documented causes as listed in Table 1.

To assess the outcome, the main endpoints were determined as return of spontaneous circulation (ROSC), 30-day survival or discharged alive from hospital and survival with a good neurological outcome at discharge; defined as Cerebral Performance Category (CPC) 1 or 2. For all 3 parameters, outcome of each cause was compared separately with cardiac arrest due to cardiac aetiology as reference group.

Table 1 – Available choices of (suspected) cause of cardiacarrest in the German Resuscitation Registry dataset.

(Suspected) cause of cardiac arrest
- Cardiac
- Trauma
- Drowning
- Hypoxia
- Intoxication
- Intracranial bleeding (incl. subarachnoid bleeding)
- Sudden infant death syndrome
- Exsanguination
- Stroke
- Metabolic
- Sepsis
- Others/unknown

Statistical analysis

Data processing and presentation of the results was conducted using Microsoft Excel 2016 (Microsoft Corp., Redmond, WA, USA), while statistical analysis was performed using IBM SPSS Statistics, version 24 (IBM Corp., Armonk, USA). Analyses of categorical variables were conducted by means of chi-square test. In addition, odds ratios and 95% confidence intervals were calculated. Metric data are expressed as arithmetic mean ± standard deviation. Statistical significance was assumed when $p < 0.05$.

Results

During the period 2007–2017, 77,608 pre-hospital resuscitations were completely documented in the GRR. A total of 33,772 datasets were included in the analyses after exclusion of the rescue services with an insufficient return rate of the *Further Clinical Treatment* module. Excluded cases showed no significant differences to those included in terms of demographic data as well as cardiac arrest characteristics.

The mean age of all included patients was 68.5 years, with 64.8% of patients being male. In total, ROSC was achieved in 44.8% of patients, and 37.6% of the patients were admitted to hospital with ROSC. Furthermore, 13.1% of the patients survived for at least 30 days or were discharged alive from the hospital, with 9.0% having a good neurological outcome (CPC 1 or 2), which represented 68.3% of all discharged patients.

The most common documented cause was a cardiac event (62.2%), followed by hypoxia (11.1%) and trauma (3.2%). In 17.2% of the cases, the cause of pre-hospital admission was either unclear or not stated. A detailed overview of demographic data (age, gender) with the distribution of all causes as well as the correspondent Utstein style characteristics "proportion of witnessed cardiac arrest", "initial rhythm shockable", "time interval without CPR" and "proportion of bystander CPR" are shown in Table 2.

Table 2 also demonstrates the outcome after OHCA for each cause separately as well as the odds ratios in relation to cardiac aetiology.

For cardiac arrest due to cardiac cause, ROSC, hospital discharge, and good neurological outcome were better than overall average. For trauma-associated OHCA, all of the aforementioned parameters were significantly worse than cardiac cause, which was the same for exsanguination. While the ROSC rate was higher in hypoxia (54.3%), survival with good neurological outcome was significantly poorer than that of cardiac aetiology at only 6.6%. The best survival, also with good neurological outcome, was found after pre-hospital resuscitation due to intoxication (14.0%), with the worst outcome related to sepsis (0.9%).

Discussion

This study examined pre-hospital resuscitations documented in a national registry over an 11-year period for the underlying causes certified by the emergency physician on scene with simultaneous comparison of the outcome in respect of the cause. In this regard, significant differences were evident depending on the aetiology of OHCA, both for ROSC (8.9–64.4%) as well as for survival with a good neurological outcome (0.9–14.0%). As far as we know, there are no publications concerning this matter in a pre-hospital setting with a comparatively large population.

The study sample in this investigation consists of the rescue services participating in the GRR and currently represents approximately 30 million people in Germany. As participation in the GRR is voluntary, it cannot be assumed that a representative sample is given. However, the demographic data are comparable to other large studies on OHCA, such as EuReCa One (10,682 cases from 27 countries), the study by Hawkes et al. (28,729 patients, United Kingdom), and the study by Hasselqvist-Ax et al. (30,381 cases, Sweden). The survival rate after 30 days in our study was slightly higher than in the aforementioned studies (EuReCa One 10.3%, Hawkes 7.9%, and Hasselqvist-Ax 7.3%).[2,12,13]

The main cause of OHCA in our study was a cardiac event (62.2%). However, if we assigned cases where there was no or an unknown cause to the group of cardiac events,[2,8] this resulted in a percentage of 79.4% of cardiac causes, followed by hypoxia (11.1%) and trauma (3.2%). The best overall survival rate with good neurological outcome after OHCA was noted in patients with intoxication (14.0%), with the worst being associated with sepsis (0.9%). Similar results were found by Wallmüller et al. for in-hospital cardiac arrests.[6]

This study also shows that the outcome after trauma-associated OHCA, with respect to both ROSC rate and 30-day survival, was worse than in cardiac events, as has already been shown in various studies.[5,14] Nonetheless, it seems that survival with good neurological outcome after trauma CPR is possible, and it is therefore important to strive towards optimizing the care of these patients, as has been the case in recent years.[15–17] Considering that approximately 85% of patients with trauma-associated cardiac arrest have life-ending injuries, as described by Kleber et al., a survival rate exceeding 10% can nevertheless still be achieved [18]. However, to achieve this, it is necessary that CPR is adjusted according to the trauma-CPR algorithm recommended for the first time in the guidelines of the European Resuscitation Council 2015, and that early and consequent treatment of the reversible causes such as hypoxia, tension pneumothorax, hypovolaemia, and cardiac tamponade is performed.[4]

Drowning victims in this study tended to have a significantly lower average age, presumably due to a higher proportion of children and adolescents, as has already been described.[19,20] Overall, 12.0% of patients were discharged with good neurological outcome, slightly more than the cardiac aetiology group. Comparable discharge rates after drowning have already been described in previous studies.[21] In addition to hypoxia, hypothermia is a major determinant in the pathophysiology of drowning, especially for neurological outcome.[22] As this was not considered separately in this study, it is not possible to provide statements on the reasons for the aforementioned higher survival rates in this investigation.

Patients suffering cardiac arrest due to intoxication were younger than the mean, the arrest was less often witnessed and the initial rhythm was rarely shockable. However, these patients regained more often ROSC and had an above-average survival (19.9%), also with good neurological outcome (14.0%). Comparable results were shown in prior studies like Salcido et al.[23]

The lowest ROSC rate in all groups was observed in infants with sudden infant death syndrome (SIDS), which was only 8.9%. The reason for this is probably due to the long therapy-free interval, since SIDS usually occurs during sleep, is thus unobserved and less amenable to intervention. The discharge rate was correspondingly low (3.6%) but cases with a good neurological outcome are nevertheless possible. Similar results were obtained by Fink et al. in several regions of the USA and Canada (ROSC: 6.5%, discharge rate 3.2%).[24]

Table 2 – Demographic data, baseline characteristics and outcome of patients with prehospital cardiac arrest according to suspected cause of cardiac arrest. Outcome data shown in relatives and odds ratio with 95% confidence interval (compared to cardiac aetiology, bold numbers).

(Suspected) cause of cardiac arrest	Total cases	Gender: male	Mean age [years]	Witnessed cardiac arrest	Bystander CPR	Mean time to begin of CPR [min]	Initial rhythm shockable (VF/VT)	ROSC	Survival to discharge	Survival with CPC 1/2
All causes	33,772 (100%)	64.8 %	68.5 ± 17.0	53.7%	29.2%	6.3	24.6%	44.8%	13.1%	9.0%
Cardiac	20,990 (62.2%)	67.7%	70.7 ± 14.3	58.4%	31.1%	6.2	33.8%	47.8%	15.6%	11.2%
								1.0	**1.0**	**1.0**
Trauma	1095 (3.2%)	75.3%	52.8 ± 22.3	54.7%	23.7%	7.7	6.0%	30.1%*	4.4%*	2.1%*
								0.47 (0.41–0.54)	**0.24 (0.18–0.32)**	**0.17 (0.11–0.26)**
Drowning	167 (0.5%)	66.5%	47.1 ± 29.0	28.7%	47.3%	9.0	6.6%	46.1%	18.0%	12.0%
								0.93 (0.69–1.27)	**1.21 (0.81–1.80)**	**1.08 (0.67–1.72)**
Hypoxia	3741 (11.1%)	56.1%	66.7 ± 20.2	56.2%	28.3%	6.0	5.1%	54.3%*	12.5%*	6.6%*
								1.30 (1.21-1.39)	**0.75 (0.68-0.84)**	**0.56 (0.49-0.64)**
Intoxication	478 (1.4%)	72.0%	43.3 ± 15.8	28.9%	31.2%	7.5	8.4%	50.2%	19.9%*	14.0%
								1.10 (0.92–1.32)	**1.34 (1.06–1.68)**	**1.29 (0.99–1.68)**
ICB	298 (0.9%)	48.3%	69.2 ± 15.9	57.7%	25.5%	5.8	11.7%	64.4%*	12.8%	8.4%
								1.98 (1.56-2.51)	**0.76 (0.54-1.08)**	**0.73 (0.48-1.10)**
SIDS	56 (0.2%)	51.8%	1.4 ± 7.3	12.5%	39.3%	17.0	0.0%	8.9%*	3.6%*	3.6%
								0.11 (0.04–0.27)	**0.20 (0.05–0.84)**	**0.29 (0.07–1.21)**
Exsanguination	561 (1.7%)	63.5%	64.8 ± 17.5	43.9%	12.5%	6.2	5.5%	23.1%*	1.6%*	1.1%*
								0.37 (0.30-0.45)	**0.08 (0.04-0.16)**	**0.09 (0.03-0.19)**
Stroke	109 (0.3%)	48.6%	71.7 ± 15.8	62.4%	21.1%	5.3	12.8%	49.5%	12.8%	8.3%
								1.07 (0.74–1.56)	**0.75 (0.42–1.34)**	**0.71 (0.36–1.41)**
Metabolic	340 (1.0%)	57.9%	66.7 ± 16.8	47.4%	20.0%	5.1	12.9%	47.6%	10.0%*	6.8%*
								0.99 (0.80-1.23)	**0.61 (0.43-0.88)**	**0.57 (0.38-0.88)**
Sepsis	113 (0.3%)	57.5%	67.8 ± 18.6	56.6%	25.7%	4.7	4.4%	48.7%	5.3%*	0.9%*
								1.04 (0.72–1.50)	**0.31 (0.14–0.71)**	**0.07 (0.01–0.51)**
Others/unknown	5814 (17.2%)	60.0%	68.7 ± 17.4	38.9%	25.6%	7.1	13.3%	30.9%*	7.0%*	4.3%*
								0.49 (0.46–0.52)	**0.40 (0.36–0.45)**	**0.35 (0.31–0.41)**

ICB: intracranial bleeding, SIDS: sudden infant death syndrome, CPR: cardiopulmonary resuscitation, VF: ventricular fibrillation, VT: ventricular tachycardia, ROSC: return of spontaneous circulation, CPC: cerebral performance category.

* $p < 0.05$.

Despite high ROSC rates after hypoxia-related OHCA (54.3%), only 6.6% of the patients survived with good neurological outcome, and nearly half of all survivors experienced severe neurological impairment. Orban et al. described a similar conclusion in a French multicentre study where a good neurological outcome after hypoxia-related OHCA was significantly lower compared with cardiac events (19% vs. 42%). However, only patients who were admitted to a hospital and treated with mild therapeutic hypothermia were included in that study. Accordingly, the proportion of patients who were discharged alive with a good neurological outcome was significantly higher than in this study.[25] These results are also consistent with various studies that examined outcome after attempted suicide through hanging as one possible cause of hypoxia.[26-28]

Surprisingly, neurological outcome after OHCA due to stroke (intracranial haemorrhage, apoplexy) in this study was only slightly worse than that of the total population, although this would be expected due to the cause. A possible explanation for this could be that primary brain damage alone is less crucial in the pathogenesis of cardiac arrest, compared with a closed airway and consequent hypoxic cardiac arrest. However, no research regarding this has been published to date.

Limitations

When evaluating the results of this study, the documentation of the resuscitation data performed by pre-hospital emergency physicians must be taken into account. In patients who died on scene only the suspected cause could be documented because, with few exceptions (presumed death by unnatural cause), in Germany usually no autopsy is performed. Therefore, the underlying cause is not always determined with certainty. Also, for patients who were admitted to hospital, clinical diagnoses were not always available to confirm the pre-hospital suspected cause.

In Germany, an emergency physician is consulted for every patient with OHCA. Therefore, all documented causes of this study are doctor's diagnoses. For this purpose, in cases in which the patient died on the scene, the suspected cause was tried to detect by taking the medical history, medical findings as well as pre-existing illnesses of the patient into account. This diagnosis (at its best) was then documented in the resuscitation registry.

In addition, the discrimination between causes like trauma and bleeding or, in case of suspected stroke, the differentiation between intracranial bleeding and ischaemic apoplexy may often be difficult at a pre-hospital level, which could influence the results of the subgroups. Kürkciyan et al. were able to show that many resuscitations could correctly identify the associated underlying cause with the aid of medical history and typical symptoms,[29] but this was shown 20 years ago in a slightly different setting. They compared suspected causes of OHCA in the emergency room with clinically confirmed causes. To our best knowledge, no recent studies regarding the comparison of pre-hospital suspected and in-hospital confirmed causes exist. Accordingly, it remains unclear how accurate the causes documented in the GRR are. Recently, Chen et al. published a new algorithm to classify arrest aetiology with a more detailed cause description (especially with regard to cardiac causes).[30] Though, this algorithm can only be used in patients who are admitted to hospital alive because several diagnostic steps are necessary. For cardiac arrest patients who die on scene, it is not applicable.

Because of missing *Further Clinical Treatment* datasets, slightly more than half of the documented pre-hospital resuscitations had to be excluded on the level of the participating EMS systems. Although the excluded cases did not differ significantly from those included in terms of demographic and arrest characteristics, potential for a possible exclusion bias has to be kept in mind.

As another limitation of this study, it should be noted that the analyses of the survival rates in this study, apart from the underlying cause, do not take into account any further influencing factors, such as therapy-free interval, lay resuscitation, or defibrillation. Conclusions on causalities or the probability of survival of the individual patient are therefore not possible. However, since this was not part of the aims of this predominantly descriptive study, the objectives, description of the causes of the OHCA and their outcomes, are not affected.

Conclusion

The most common causes of OHCA are cardiac events and hypoxia. Survival rates vary widely depending on the underlying cause, with good neurologic outcome at hospital discharge ranging between 0.9–14.0%. Accordingly, the aetiology of pre-hospital cardiac arrest should be included in the considerations and decisions of emergency medical services during their treatment, especially with regard to potentially reversible causes.

Conflict of interest

All authors declare they have no conflict of interest.

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