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Published in:
Resuscitation

DOI (link to publication from Publisher):
[10.1016/j.resuscitation.2024.110155](https://doi.org/10.1016/j.resuscitation.2024.110155)

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Publication date:
2024

Document Version
Publisher's PDF, also known as Version of record

[Link to publication from Aalborg University](#)

Citation for published version (APA):

Larsen, M. B., Blom-Hanssen, E., Gnesin, F., Kragholm, K. H., Lass Klitgaard, T., Christensen, H. C., Lippert, F., Folke, F., Torp-Pedersen, C., & Ringgren, K. B. (2024). Prodromal complaints and 30-day survival after emergency medical services-witnessed out-of-hospital cardiac arrest. *Resuscitation*, 197, Article 110155. <https://doi.org/10.1016/j.resuscitation.2024.110155>

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Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Prodromal complaints and 30-day survival after emergency medical services-witnessed out-of-hospital cardiac arrest



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Abstract

Background: Out-of-hospital cardiac arrest (OHCA) is a frequent and lethal condition with a yearly incidence of approximately 5000 in Denmark. Thirty-day survival is associated with the patient's prodromal complaints prior to cardiac arrest. This paper examines the odds of 30-day survival dependent on the reported prodromal complaints among OHCA witnesses by the emergency medical services (EMS).

Methods: EMS-witnessed OHCA in the Capital Region of Denmark from 2016-2018 were included. Calls to the emergency number 1-1-2 and the medical helpline for out-of-hours were analyzed according to the Danish Index; data regarding the OHCA was collected from the Danish Cardiac Arrest Registry. We performed multiple logistic regression to calculate the odds ratio (OR) of 30-day survival with adjustment for sex and age.

Results: We identified 311 eligible OHCA of which 79 (25.4%) survived. The most commonly reported complaints were dyspnea ($n = 209$, OR 0.79 [95% CI 0.46: 1.36]) and 'feeling generally unwell' ($n = 185$, OR 1.07 [95% CI 0.63: 1.81]). Chest pain (OR 9.16 [95% CI 5.09:16.9]) and heart palpitations (OR 3.15 [95% CI 1.07:9.46]) had the highest ORs, indicating favorable odds for 30-day survival, while unresponsiveness (OR 0.22 [95% CI 0.11:0.43]) and blue skin or lips (OR 0.30, 95% CI 0.09, 0.81) had the lowest, indicating lesser odds of 30-day survival.

Conclusion: Experiencing chest pain or heart palpitations prior to EMS-witnessed OHCA was associated with higher 30-day survival. Conversely, complaints of unresponsiveness or having blue skin or lips implied reduced odds of 30-day survival.

Keywords: Out-of-hospital cardiac arrest, Emergency medical services, Prodromal complaints, Epidemiology, Public health

Introduction

Out-of-hospital cardiac arrest (OHCA) is a frequent condition with a low survival rate. In Denmark, the yearly incidence is roughly 5000 OHCA.¹ Previous studies of emergency medical services (EMS) witnessed OHCA have shown that the odds of survival is higher in EMS-witnessed OHCA groups (11.2% survived to discharge/30 days post-arrest) compared with unwitnessed (1.3%) or bystander witnessed (5.3%) OHCA.^{2,3}

EMS-witnessed OHCA require contact to emergency services before the arrest occurs, entailing that the patient experiences prodromal symptoms. Such symptoms have previously only been examined sparingly in small and/or selected populations, with some

complaints (i.e. chest-, neck-, and jaw pain) having been demonstrated to have a significant association with the occurrence of an initial shockable rhythm and survival to hospital discharge.⁴⁻⁶ In contrast, abdominal pain, dyspnea, and altered consciousness all reduce the chance of an initial shockable rhythm and survival to discharge.⁴⁻⁶

OHCA witnessed by EMS personnel are considered a specific subset of arrests and have not been the subject of similar interest as bystander-witnessed and unwitnessed arrests, probably because most OHCA occur while the patient is alone, or only non-health care professionals are present.¹ The EMS-witnessed OHCA group is distinctly different compared to the other groups with regards to Utstein-style predictors of survival, e.g. bystander cardiopulmonary resuscitation (CPR) and EMS response time.⁷ Those factors are

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<https://doi.org/10.1016/j.resuscitation.2024.110155>

Received 30 December 2023; Received in Revised form 17 February 2024; Accepted 20 February 2024

eliminated in EMS-witnessed cases as EMS personnel is present on scene at the time of arrest and are able to initiate high-quality CPR immediately upon confirming the arrest. Previous research has only had limited focus on the EMS-witnessed OHCA cases, hence, it is not investigated if this subset of patients presents themselves differently regarding prodromal complaints as compared to other OHCA groups. Knowledge of differences in complaints and, possibly, associated risk of death in the EMS-witnessed OHCA patients compared to non-EMS-witnessed OHCA patients is crucial in identifying patients at higher risk of dying, thus requiring immediate assistance. Thus, it is of clinical significance and importance to determine the type of complaints the EMS-witnessed OHCA group presents with prior to their cardiac arrest and the effect of such symptoms on the chance of survival.

Thus, the aim of this study was to examine which chief prodromal complaints were reported by patients with an EMS-witnessed OHCA and their association with 30-day survival rates.

Methods

Study design and participants

This study is a retrospective, observational study of OHCA in Denmark between 2016 and 2018 witnessed by EMS personnel. OHCA in Denmark are defined as cases where resuscitative efforts are initiated outside the hospital setting. Calls to the emergency services or out-of-hours health care services (1-1-2 or 1-8-1-3) within 24 hours of arrest were monitored in the Capital Region of Denmark. Only adults (≥ 18 years) were included.

Setting

The Danish health care system is tax paid and free of charge for all inhabitants in Denmark with inclusion of the prehospital EMS response.⁸ This allows for equal access to medical assistance in case of an emergency across all socioeconomic levels.⁹ Access to the prehospital EMS-unit is facilitated by calling either the emergency number 1-1-2 or the non-emergent medical helpline 1-8-1-3. The medical helpline 1-8-1-3 is staffed by nurses and doctors and is only available out-of-hours. The staff can refer to and schedule appointments at e.g. emergency departments and, if needed, dispatch an ambulance through the Emergency Medical Dispatch Center.^{9,10}

The prehospital EMS-unit consists of three tiers. The first tier includes ambulances staffed by two authorized emergency medical technicians (EMTs).¹¹ The second tier consists of paramedics in rapid response vehicles, and the third tier comprises mobile emergency care units staffed by a physician and an assistant. Furthermore, the national helicopter emergency medical services (HEMS), staffed by a pilot, a physician, and a specially trained paramedic, cover the entire country 24 hours a day.¹²

Data collection and outcome

Data regarding OHCA was collected from the Danish Cardiac Arrest Registry (DCAR).¹³

Chief prodromal complaints were recorded by manual evaluation by a team of researchers¹⁴ of calls to the emergency number 1-1-2 and the medical helpline for out-of-hours 1-8-1-3 assisting with non-emergency calls in the Capital Region of Denmark regarding patients who experienced an OHCA up to 24 hours after the call. Only data from the Capital Region of Denmark was recorded.

The operators handling the call registered only the chief complaint as is standard in the Danish Index¹⁵ even though the patient may have had several complaints. The calls were evaluated using a survey developed specifically for the purpose of categorizing prodromal complaints¹⁴ including specific complaints, identity of the caller, and verbal responses from the dispatcher that led to the dispatch of an ambulance. If the patient called either number more than once, the calls were grouped so that each patient was registered only once, and complaints were pooled. If a patient complained of more than one chief symptom on different calls, the patient would be counted in all relevant complaint groups.

Reported chief prodromal complaints were divided by an assessment of clinical relevance into the groups listed in [Supplemental A](#). Only patients who were breathing at the time of EMS arrival were included.

The primary outcome of this study was to assess the odds of 30-day survival after EMS-witnessed OHCA according to the patients' reported chief prodromal complaints. Data on survival was obtained from the Danish Central Person Registry, in which all inhabitants in Denmark are allotted a unique identifying number that can be linked to DCAR.¹⁶

Statistical analysis

Demographical data are presented using medians and interquartile ranges (IQR), continuous variables and frequencies and percentages for categorical variables. Descriptive data was stratified by the 30-day survival status and compared using the Kruskal Wallis' test for continuous variables and the chi-squared test for categorical variables.

The probability of survival 30 days post OHCA was calculated using logistic regression stratified by complaint groups. The outcome was adjusted for sex and age. The results are presented as the odds ratio (OR) and 95% confidence interval (CI). If a complaint group included fewer than four cases, they were omitted from the analysis or presented as <4 to ensure anonymity as per Statistics Denmark legislation.

Statistical analysis was performed using R version 2022.07.0 with attached packages.^{17–25}

Ethics approval

Registry-based observational studies do not require ethical approval in Denmark. The collection of complaint data was approved by the data responsible institute (Capital Region (Approval number: P-2019191)) and the Danish Patient Safety Authority (Case number: 3-3013-2795/1, reference: EMGW).

Results

A total of 15,674 OHCA occurred during the study period of which 4273 OHCA occurred in the Capital Region of Denmark and were eligible for inclusion. The final sample included 311 OHCA cases of adult patients who suffered an EMS-witnessed OHCA ([Fig. 1](#)).

Characteristics of included patients are shown in [Table 1](#) stratified by complaint group and 30-day survival. Only the most prevalent complaint groups are presented in [Table 1](#), the remaining are presented in [Supplemental B](#). Of the 311 included patients, 79 survived to 30 days post-OHCA (25.4%).

The overall median age was 70 (60;80) years with surviving patients generally being younger (66 [55.5;73.0] years) than non-

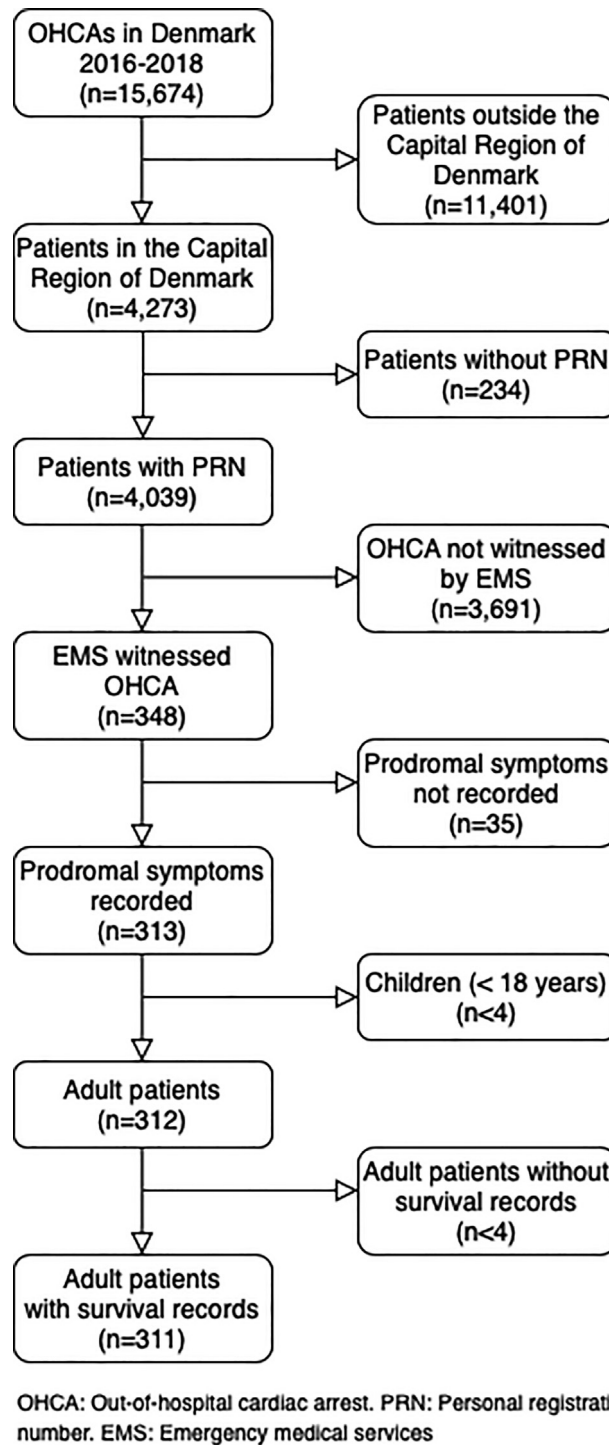


Fig. 1 – Flowchart of inclusion of out-of-hospital cardiac arrest patients in the Capital Region of Denmark between 2016 and 2018. OHCA: Out-of-hospital cardiac arrest. PRN: Personal registration number. EMS: Emergency medical service.

survivors (72 [64;81] years) ($p < 0.001$). The majority (62.4%) of patients were male. When stratified by survival, the proportion of males and females was equally distributed between survivors and non-survivors. The most frequent chief prodromal complaints were dyspnea ($n = 209$), 'feeling generally unwell' ($n = 185$), and unresponsiveness ($n = 114$).

None of the patients initially presenting with swelling, bleeding, or traumatic cardiac arrest survived to 30 days.

Fig. 2 presents the odds ratios (OR) and 95% confidence intervals (CI) of 30-day survival by complaint group adjusted for age and sex (omitting the complaint groups of suicidal behavior, urinary tract symptoms, and symptoms from eyes/ears due to less than four

Table 1 – Descriptive characteristics of included out-of-hospital cardiac arrest patients in the Capital Region of Denmark between 2016 and 2018 divided by complaint groups.

Overall		Non-survivor (n = 232)	Survivor (n = 79)	Total (n = 311)	p-value
Sex, n (%)	Female	93 (40.1)	24 (30.4)	117 (37.6)	0.16
	Male	139 (59.9)	55 (69.6)	194 (62.4)	
Age	Median [IQR]	72 [64, 81]	66 [55.5, 73.0]	70 [60, 80]	<0.001
Dyspnea		Non-survivor (n = 159)	Survivor (n = 50)	Total (n = 209)	p-value
Sex, n (%)	Female	68 (42.8)	17 (34.0)	85 (40.7)	0.35
	Male	91 (57.2)	33 (66.0)	124 (59.3)	
Age	Median [IQR]	71 [64, 80]	64.5 [54.2, 73.8]	70 [61, 80]	0.004
Feeling generally unwell		Non-survivor (n = 138)	Survivor (n = 47)	Total (n = 185)	p-value
Sex, n (%)	Female	59 (42.8)	14 (29.8)	73 (39.5)	0.16
	Male	79 (57.2)	33 (70.2)	112 (60.5)	
Age	Median [IQR]	72 [64, 82]	66 [55.5, 77.0]	70 [60, 82]	0.02
Unresponsive		Non-survivor (n = 102)	Survivor (n = 12)	Total (n = 114)	p-value
Sex, n (%)	Female	49 (48.0)	5 (41.7)	54 (47.4)	0.91
	Male	53 (52.0)	7 (58.3)	60 (52.6)	
Age	Median [IQR]	73 [65.0, 81.8]	61.5 [52.8, 68.2]	71 [63.2, 81.0]	0.004
Chest pain		Non-survivor (n = 35)	Survivor (n = 50)	Total (n = 85)	p-value
Sex, n (%)	Female	8 (22.9)	12 (24.0)	20 (23.5)	1.00
	Male	27 (77.1)	38 (76.0)	65 (76.5)	
Age	Median [IQR]	67 [60.0, 78.5]	64.5 [53.0, 70.8]	66 [55, 73]	0.18
Blue skin or lips		Non-survivor (n < 39)	Survivor (n = 4)	Total (n < 43)	p-value
Sex, n (%)	Female	17 (47.2)	< 4	19 (47.5)	1.00
	Male	19 (52.8)	< 4	21 (52.5)	
Age	Median [IQR]	75.5 [66.8, 80.2]	55.5 [42.8, 62.8]	72.5 [64.8, 80.0]	0.01

IQR: Interquartile range.

Extension of table in [Supplemental B](#).

observations). The complaint groups of swelling, bleeding, and trauma all had an OR of 0, since all cases in these groups were fatal and are therefore not included in [Fig. 2](#). Chest pain (OR 9.16 [95% CI 5.03: 16.66]) and heart palpitations (OR 3.15 [1.08: 9.19]) had the largest ORs. The lowest ORs was seen in the complaint groups reporting unresponsiveness (OR 0.22 [95% CI 0.11: 0.44]) and blue skin or lips (OR 0.3 [95% CI 0.1: 0.9]). We found no other significant interaction for any of the other investigated prodromal complaints, including for dyspnea (OR 0.79 [95% CI 0.46: 1.36]) and for the group feeling generally unwell (OR 1.07 [95% CI 0.63: 1.81]).

Discussion

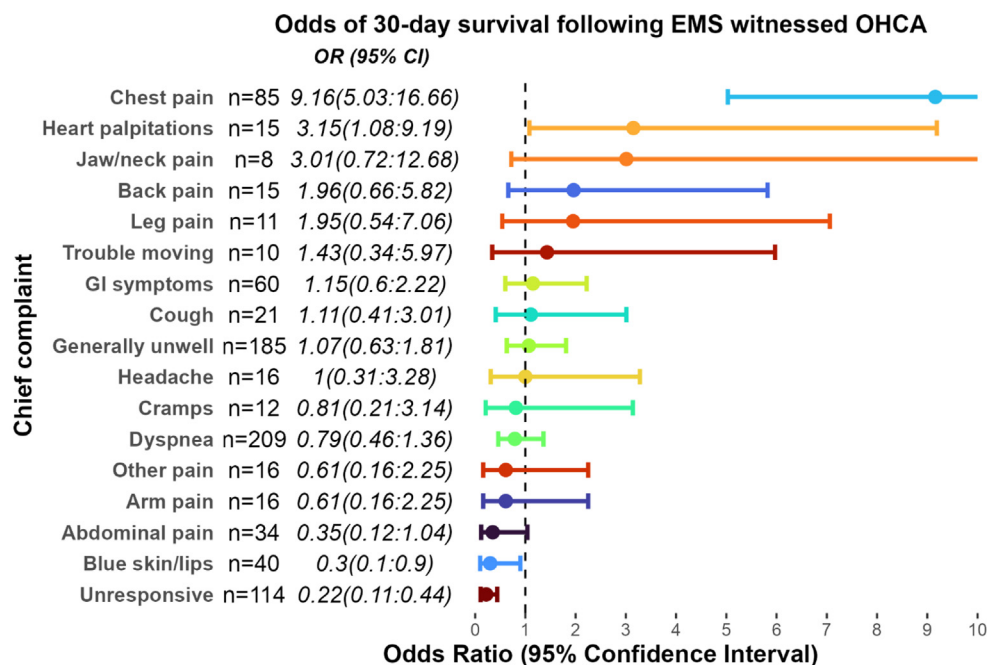
In this observational study, we identified 311 adults from the Capital Region of Denmark who suffered an EMS-witnessed OHCA between 2016 and 2018. We examined which of the chief prodromal complaint presented were associated with increased or decreased 30-day survival. The most commonly reported chief prodromal complaint was dyspnea (n = 209/311). Experiencing chest pain or heart palpitations were associated with a significant increase in the odds of 30-day survival. Conversely, unresponsiveness or blue skin or lips both decreased the odds of 30-day survival. We did not find any other significant association between survival and any other complaint group.

The data in this study has been subject of investigation previously.^{14,26} Both included all OHCA, not limited to only EMS-witnessed OHCA. The aims were to characterize prodromal complaints related to time before OHCA²⁶ and to identify prodromal

symptoms and compare patient- and OHCA characteristics in regards to when EMS was first contacted (<24 hours before OHCA, or during OHCA event).¹⁴ This study focuses on the association between prodromal complaints and 30-day survival rate after EMS-witnessed OHCA.

Dyspnea has previously been reported as the most commonly reported prodromal symptom prior to EMS-witnessed OHCA,^{4,5} as was the case in our study. However, chest pain has also been reported as the most commonly reported prodromal symptom.^{4-6,27} In non-EMS-witnessed populations, chest pain is often reported as the most common prodromal symptom as well,^{28,29} although dyspnea has been identified as the most common prodrome as well.³⁰ If an actual difference in the most common prodromal symptoms is present cannot be definitely concluded based on current research. Any possible differences might be associated to which complaints are most likely to trigger a fast EMS dispatch, or it might be because of small study populations.

Patients with chest pain or heart palpitations prior to OHCA presented with higher odds of survival in accordance with previous studies.^{5,6,27} It has been proposed that prodromal complaints are a result of deterioration of preexisting conditions, signifying that chest pain might be due to cardiac ischemia and respiratory complaints due to e.g. congestive heart failure or pulmonary conditions.¹⁵ If the underlying condition ultimately resulting in OHCA is acute myocardial infarction (AMI), the odds of survival is higher.²⁷ This is supported by Lee et al. as they found the odds of survival higher in patients with cardiac complaints if the arrest was of cardiac etiology.⁵ Nishiyama et al. reported that the 30-day survival and favorable neurological outcome were higher in OHCA of cardiac origin, however, fewer



EMS: Emergency medical services. OHCA: Out-of-hospital cardiac arrest. OR: Odds ratio. CI: Confidence interval.
GI: Gastro-intestinal.

Fig. 2 – Forest plot of odds ratio calculated by performing a linear regression analysis on 30-day survival for each complaint group in out-of-hospital cardiac arrest patients in the Capital Region of Denmark between 2016 and 2018 adjusted for sex and age. Odds ratio <1 is indicative of reduced odds of 30-day survival and odds ratio >1 higher odds of 30-day survival. EMS: Emergency medical services. OHCA: Out-of-hospital cardiac arrest. OR: Odds ratio. CI: Confidence interval. GI: Gastro-intestinal.

patients with OHCA of cardiac origin achieved return of spontaneous circulation and survival to hospital admission than OHCA of non-cardiac origin. We were unable to account for etiology in this study, but our findings do support the aforementioned notion. Nehme et al.⁶ also reported that the odds of the initial arrest rhythm being shockable is more strongly associated with survival in patients presenting with chest pain before OHCA.

Additionally, Lee et al. reported that patients experiencing cardiogenic OHCA had good neurological outcomes if complaining of cardiac symptoms prior to OHCA, and patients suffering noncardiogenic OHCA had better outcomes if experiencing prodromal respiratory symptoms.⁵

Unresponsiveness and blue skin or lips can both indicate hypotension or shock.³¹ Nehme et al. has described that a systolic blood pressure <110 mmHg or unmeasurably low is associated with lower odds of survival.⁶ While unresponsiveness and blue skin or lips can be observed in cases of AMI, they are not typical complaints of such and might be indicators of another underlying condition, thus resulting in reduced odds of survival.^{27,32}

Except from the above-mentioned complaints, no statistically significant associations between prodromal complaints and 30-day survival were identified. This could be due to the small sample size which is also reflected in the large confidence intervals. However, the groups of dyspnea and feeling generally unwell were not shown to be significantly associated with odds of survival despite being the two largest groups (dyspnea $n = 209$, feeling generally unwell $n = 185$). This suggests that the two complaint groups may not be associated with the odds of survival. Additionally, the investigated group of patients is most likely highly diverse in terms of comorbidities

and etiology of cardiac arrest, with several different conditions that may lead to dyspnea or to feeling generally unwell, thus obscuring the direct linkage to survival.^{33,34}

Nehme et al. showed that delays in activating EMS prior to EMS-witnessed OHCA modestly reduced odds of survival,⁴ and Nishiyama et al. supports this, reporting that early activation of EMS improves both survival and neurological outcome.³⁰ This is important as the subjective evaluation of urgency and risk of severe disease or death might differ depending on the age or comorbidities of the patient as well as the experienced symptoms.^{28,26} Thus, if patients have no known history of e.g. heart disease or experience atypical symptoms, they might delay contacting EMS. This could in turn affect the odds of 30-day survival in specific complaint groups.

In addition to delaying activation of EMS, some complaints could potentially trigger different approaches and/or algorithms, e.g. basic life support vs. the Airway, Breathing, Circulation, Disability, Exposure (ABCDE)-approach, when EMS arrives which might, in turn, increase survival rates. Potentially, the ability to more easily and with more accuracy identify patients in risk of OHCA and the initiation of the proper EMS response, approach, and treatment could avert the cardiac arrest which (presumably) reduces mortality. However, the validity of this assumption is difficult to research.

Limitations

This study is observational and conducted in a limited population, thus, the results may not be transferable to a broader group of patients other than those with EMS-witnessed OHCA in Denmark. However, patient characteristics in our study, e.g. male to female

ratio and median age, correspond well to other reports.^{2–4,6,27} Furthermore, the observational nature of the study only allows uncovering associations, and no causal relations can be proven.

Residual confounding, such as patients' individual burden of disease prior to OHCA, could also influence our results. Such factors should be included in future studies, e.g. by comparing the disease burden in EMS-witnessed groups and non-EMS-witnessed groups. Additionally, the sample size hindered adjusting each group of complaints for the others in the logistic regression analysis. This issue is also reflected by large confidence intervals in the analysis.

When analyzing the calls to extract the prodromal complaints, novel complaints were registered in free-text fields. The inter-rater reliability was not evaluated. Thus, possible differences in symptom detection and categorization are unknown. However, such novel symptoms appeared in a minority of calls, and we assume that novel complaints were not registered differently than pre-defined complaints which had high agreement scores when tested before data collection.¹⁴

Conclusion

In cases of EMS-witnessed out of hospital cardiac arrest, patients complaining of chest pain or heart palpitations when contacting the EMS-services had significantly higher odds of surviving 30 days post cardiac arrest. Conversely, unresponsive patients and patients presenting with blue skin or lips had significantly decreased odds of survival. Additional studies with larger sample sizes are warranted to ratify these results and, hopefully, assist in allocation of EMS resources to the patients with the most immediate need.

Submission declaration

This manuscript has not been published previously and is not under consideration for publication elsewhere. If accepted, it will not be published elsewhere without written consent.

It has been approved by all authors.

Data statement

Data unavailable to access due to confidentiality.

CRedit authorship contribution statement

Mia Bang Larsen: Writing – original draft, Visualization, Software, Project administration, Methodology, Formal analysis, Conceptualization. **Emil Blom-Hanssen:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Filip Gnesin:** Writing – review & editing, Software, Methodology, Formal analysis, Conceptualization. **Kristian Hay Kragholm:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Thomas Lass Klitgaard:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Helle Collatz Christensen:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Freddy Lippert:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Fredrik Folke:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Christian Torp-**

Pedersen: Writing – review & editing, Visualization, Supervision, Software, Project administration, Methodology, Formal analysis, Conceptualization. **Kristian Bundgaard Ringgren:** Writing – review & editing, Visualization, Supervision, Software, Project administration, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.resuscitation.2024.110155>.

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