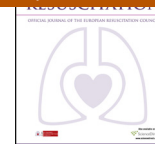




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Clinical Paper

Prodromal symptoms and health care consumption prior to out-of-hospital cardiac arrest in patients without previously known ischaemic heart disease[☆]Henrik Höglund^a, Jan-Håkan Jansson^b, Ann-Sofie Forslund^c, Dan Lundblad^{a,*}^a Department of Public Health and Clinical Medicine, Sunderby Research Unit, Umeå University, Sweden^b Department of Public Health and Clinical Medicine, Skellefteå Research Unit, Umeå University, Sweden^c The Northern Sweden MONICA Myocardial Registry, Department of Research, Norrbotten County Council, Luleå and Department of Health Science, Division of Nursing, Luleå University of Technology, Sweden

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ABSTRACT

Aims: To describe prodromal symptoms and health care consumption prior to an out-of-hospital cardiac arrest (OHCA) in patients without previously known ischaemic heart disease (IHD).**Background:** The most common lethal event of cardiovascular disease is sudden cardiac death, and the majority occur outside hospital. Little is known about prodromal symptoms and health care consumption associated with OHCAs.**Design:** Case-crossover study.**Methods:** Medical records of 403 OHCA cases without previously known IHD, age 25–74 years in the MONICA myocardial registry in Norrbotten County 2000–2008, were reviewed. Presenting symptoms and emergency visits at public primary care facilities and internal medicine clinics in Norrbotten County were analyzed from the week prior to the OHCA and from the same week one year previously, which served as a control week. Unlike most studies we included unwitnessed arrests and those where no cardiopulmonary resuscitation (CPR) was attempted.**Results:** Emergency visits were more common during the week prior to the OHCA than during the control week, both for visits to primary care (29 vs. 6, $p < 0.001$) and to internal medicine clinics (16 vs. 0, $p < 0.001$). Symptoms were more prevalent during the week prior to the OHCA (36.7 vs. 6.7%, $p < 0.001$). The most prevalent symptoms were chest pain (14.6 vs. 0%, $p < 0.001$), gastrointestinal symptoms (7.7 vs. 1.2%, $p < 0.001$) and dyspnoea/peripheral oedema (6.9 vs. 0.2%, $p < 0.001$).**Conclusions:** Patients who suffer an OHCA seek health care and present prodromal symptoms significantly more often the week prior to the event than the same week one year earlier.© 2014 The Authors. Published by Elsevier Ireland Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/3.0/>).

1. Introduction

Cardiovascular disease is the leading cause of death world-wide and is projected to remain so in the future.¹ The most common lethal event of heart disease is sudden cardiac death, and for many victims cardiac arrest is also the first overt manifestation of heart disease.^{2,3} Cardiac arrest occurs most often outside of the hospital setting.² The most common cause of cardiac arrest is ischaemic

heart disease (IHD),^{2,4} although studies have shown that 40–60% of coronary heart disease (CHD) deaths have had no prior history of CHD.^{5–7} Furthermore, the proportion of cardiac arrests occurring without known CHD has increased in northern Sweden between 1989 and 2007.⁷ It is difficult to assess the incidence and survival rates for OHCA because different studies use varying criteria and outcomes. Furthermore, many studies have only included patients who were assessed by emergency medical services.^{8–10} Survival rates at 28 days after the event are below 3% in Northern Sweden when cases in which no CPR was performed were included in the study.⁷

Not much has been published describing symptoms or health care consumption prior to an OHCA in patients without previously known IHD. Many of those who have suffered an OHCA did not have previously known cardiovascular disease,^{3,7,11} and therefore

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they had not been followed regularly by health care providers as are patients with known IHD. There are some studies, which have approached the subject of prodromal symptoms in OHCA cases, and they have shown certain symptoms to be common before a cardiac arrest.^{5,6,12} In those studies different methods were used, and almost all studies included only cases where CPR was attempted, thereby missing many OHCA patients.⁸ Identifying possible characteristics in OHCA patients without previously known IHD is of vital importance to combat a condition that carries such a poor prognosis.^{2,6,7,11,13} Identification of patients at risk is the first step towards possibly finding a way to prevent sudden cardiac arrest. The aim of the present study was to describe prodromal symptoms and health care consumption during the week prior to the OHCA – including unwitnessed events and when no cardiopulmonary resuscitation (CPR) was performed.

2. Materials and methods

2.1. Patients

All patients registered from 2000 to 2008 in the northern Sweden MONICA myocardial registry were included based on the following inclusion criteria: 25–74 years of age, resident in Norrbotten county, had an OHCA, and had no history of known or treated chronic IHD prior to the event. OHCA was defined according to WHO MONICA criteria: “If the patient collapsed apparently lifeless, or is found dead outside hospital, or if the first medical record on arrival at hospital shows that the patient was in cardiac arrest on arrival. Cardiac arrest does not have to be witnessed or confirmed by electrocardiographic evidence”.

2.2. Study design

Data concerning design, registration procedure and the validation process for myocardial infarction (MI) diagnosis in the WHO MONICA project have been published elsewhere.¹⁴ The validation includes medical history, clinical symptoms, cardiac biomarkers and electrocardiography (ECG) in the same way for both fatal and non-fatal events. Non-fatal events are validated and registered as definite MI. For fatal events necropsy reports and death certificates are also used, and fatal events are registered as definite MI or possible MI. Based on the original WHO protocol, non-fatal events were defined as being alive at 28 days after the onset of symptoms in relation to the OHCA. In our registry there were 420 patients with OHCA of which 403 cases had sufficient information in their medical records. The 403 cases included 279 with definitive or probable MI aetiology to their OHCA and which were validated using MONICA diagnostic criteria (OHCA-V). In 124 cases, OHCA-V diagnosis criteria could not be fulfilled due to insufficient data.

2.2.1. Emergency care visits

Medical records were checked for any emergency care visits at a public primary care facility and at all internal medicine clinics in Norrbotten County within one week prior to the OHCA and during the same week one year prior to the OHCA, which served as the control week. The purpose of this was to identify differences in health care consumption and to avoid confounding variables, such as differences in life-style and overall health if just an age-matched control would have been used. The number of visits during each of these two weeks was recorded. Emergency visits where the patient himself actively sought health care for any symptom were registered. A visit was defined as any physical visit at a health care facility, and all visits were registered. If a patient visited health care facilities or internal medicine clinics outside the study area this was not registered. Furthermore, the patients did not have

to present with symptoms overtly related to heart disease or the cardiovascular system in general.

2.2.2. Symptom presentation

For each patient, symptoms presented during the week preceding OHCA were also recorded, irrespective of whether or not they were associated with a health care visit. Symptoms were described either by the patient or by health care personnel/relatives/witnesses. The data concerning symptoms in these latter instances was compiled from the notes in the medical records of the patient, which means that they were always indirectly described by the doctor or nurse who wrote the medical record. A typical scenario involved a relative who told the doctor on site that the patient had not been feeling well or that the patient had been in telephone contact with a doctor or nurse and mentioned some symptom. Reports, that were received from friends or acquaintances after the patient had died, that were not associated with a health care visit, were also recorded. Symptoms gathered in the control week one year before OHCA were extracted from medical records from primary care facilities and internal medicine clinics. These records described either a health care visit, a home- or care centre visit or a telephone contact. The symptoms were categorized as: chest pain, palpitations, pre/syncope, dyspnoea/oedema, fatigue, headache, fever/infection, gastrointestinal symptoms, anxiety, other pain, and other symptoms. This selection was based on the most common findings in previous similar studies.^{5,6,12,15} The severity of the symptoms was not assessed. The number of reported symptoms varied from none to all of the above symptoms for each patient. A separate variable was created to record if a patient had at least one of the reported symptoms.

3. Statistical analysis

A case-crossover design¹⁶ was used where each individual experiencing a health event served as his/her own reference meaning that each individual acted as his/her own control. This study design has been used for other OHCA studies.^{17,18} In our study the week instantaneously preceding the event (OHCA) was the case week during which health care consumption and symptoms were registered and the same week one year before was the control week. Significance tests were performed for differences in health care consumption and for symptoms the week before the OHCA and the week a year earlier. Wilcoxon signed-rank test was used to compare health care consumption. McNemar's test for paired samples was used for symptoms. The Mann–Whitney test was used to compare health care consumption between sexes, and differences in symptoms between sexes were analyzed with the χ^2 -test. For all significance tests, $p < 0.05$ was considered significant. All of the analyses were performed using IBM SPSS Statistics, version 20. Approval for the study was obtained from the Regional Ethical Board.

4. Results

4.1. Characteristics (Table 1)

The final study population comprised 403 patients, and the characteristics of the study population are found in Table 1. There were 75% men and 25% women, and the mean age was 63 years (62 for men, 64 for women), ranging from 30 to 74 years. Of the entire 403 patients only 16 survived beyond 28 days. The cause of OHCA was definitive or probable MI (OHCA-V) in 279 (69.2%). In the remaining 124 cases the diagnosis was not established. Of the total 403 cases, less than half were never attended to by an ambulance team but

Table 1
Characteristics of the studied population with out-of-hospital cardiac arrest (OHCA).

OHCA n (%)	403 (100.0)
OHCA-V n (%)	279 (69.2)
Male n(%)	302 (74.9)
Age, years, mean (SD)	
Men	62.3 (8.7)
Women	64.0 (9.5)
Survival n (%)	16 (4.0)
CPR performed outside hospital n(%)	184 (45.7)
Unwitnessed/unattended OHCA n(%)	187 (46.4)
Necropsy performed n (%)	223 (55.3)

CPR, cardiopulmonary resuscitation; OHCA-V, out-of-hospital cardiac arrest with verified myocardial infarction.

were found dead, and thus less than half received CPR outside hospital after their cardiac arrest.

4.2. Emergency care visits (Fig. 1)

As illustrated in Fig. 1 there was significantly higher emergency health care consumption during the week before the OHCA than during the control week, both for visits at primary care providers and for those at an internal medicine clinic. Thus 39 persons (9.7%) made a health care visit the week before the OHCA, with 23 (5.7%) at a primary care provider, ten (2.5%) at a clinic of internal medicine and six persons (1.5%) at both a primary care provider and a clinic of internal medicine. During the control week six persons (1.5%) had visited a primary care provider and no visits to an internal medicine clinic were recorded. In patients with OHCA-V 22 sought health care at a primary care provider compared to seven in those with

OHCA. At internal medicine clinics 14 persons with OHCA-V had a visit and two persons visited a primary care provider. These were not significant differences in health care consumption ($p=0.410$ and $p=0.107$). Concerning symptoms, the only significant difference between those with OHCA-V and those with OHCA was the prevalence of chest pain the week before OHCA (20.1% for OHCA-V and 2.5% for OHCA).

4.3. Symptoms (Tables 2 and 3)

The week before the OHCA, 36.7% of the 403 cases reported at least one symptom, compared with 6.7% during the control week (Table 2). This included all patients with symptoms whether they had made a health care visit or not. The difference in cases with symptoms between the two weeks was significant ($p<0.001$) and remained so when only symptoms reported by the patient himself/herself the week before OHCA were counted ($p<0.001$).

Table 2
Presentation of symptoms in all 403 patients with out-of-hospital cardiac arrest (OHCA) including witness-reported and patients' self-reported symptoms.

Symptoms	The week before OHCA, n (%)	Control week, n (%)	p-Value
Any symptom	148 (36.7)	27 (6.7)	<0.001
Chest pain	59 (14.6)	0 (0.0)	<0.001
Gastrointestinal symptoms	31 (7.7)	5 (1.2)	<0.001
Dyspnoea/peripheral oedema	28 (6.9)	1 (0.2)	<0.001
Fatigue	24 (6.0)	2 (0.5)	<0.001
Fever/infection	17 (4.2)	2 (0.5)	0.001
Pre-/syncope	6 (1.5)	0 (0.0)	0.031
Anxiety	3 (0.7)	2 (0.5)	n.s.
Headache	2 (0.5)	0 (0.0)	n.s.
Palpitations	1 (0.2)	1 (0.2)	n.s.
Other pain	20 (5.0)	8 (2.0)	0.017
Other symptoms	21 (5.2)	10 (2.5)	0.035

n.s., not significant.

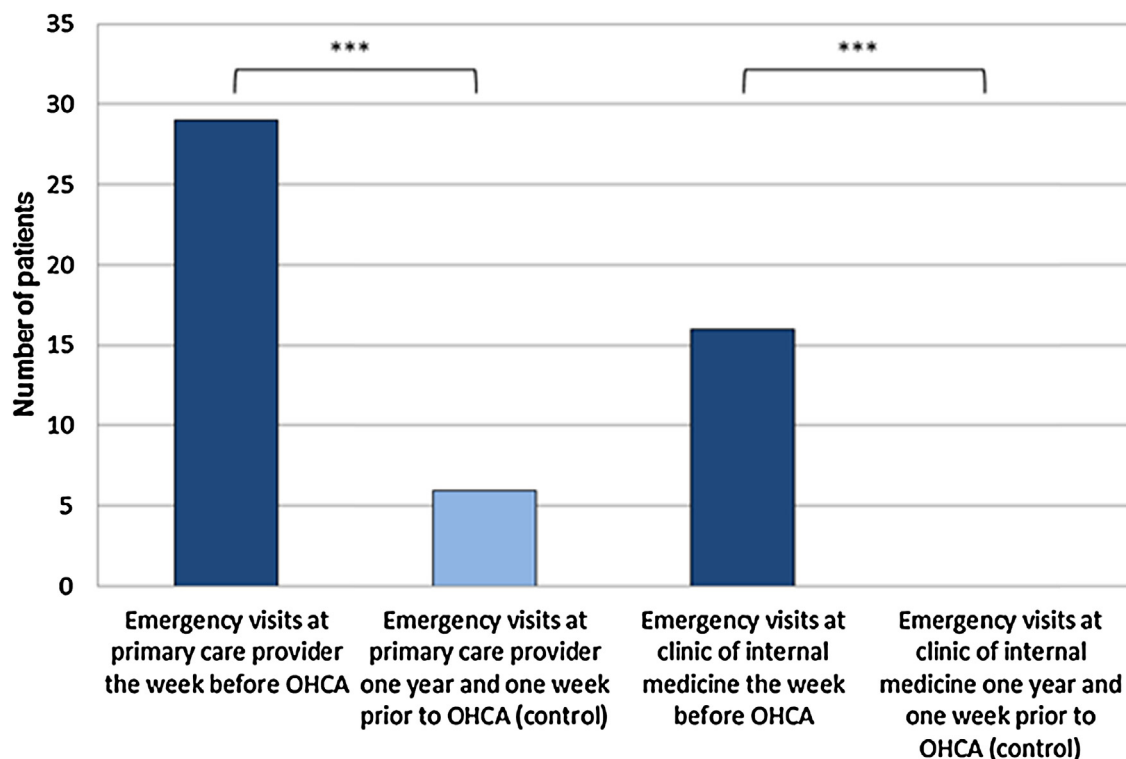


Fig. 1. Number of patients with at least one emergency visit at a primary care provider or an internal medicine clinic the week before the OHCA, compared with the control week. *** $p<0.001$.

Table 3

Symptoms in patients with any emergency visit the week before the OHCA, reported by the patient himself/herself.

Symptoms	The week before OHCA (n = 39), n(%)	Control week (n = 39), n(%)	p-Value
Chest pain	15 (38.5)	0 (0.0)	<0.001
Gastrointestinal symptoms	12 (30.8)	3 (7.7)	0.012
Dyspnoea/peripheral oedema	5 (12.8)	0 (0.0)	n.s.
Fatigue	9 (23.1)	1 (2.6)	0.008
Fever/infection	12 (30.8)	0 (0.0)	<0.001
Pre-/syncope	2 (5.1)	0 (0.0)	n.s.
Anxiety	1 (2.6)	0 (0.0)	n.s.
Headache	1 (2.6)	0 (0.0)	n.s.
Palpitations	1 (2.6)	1 (2.6)	n.s.
Other pain	11 (28.2)	2 (5.1)	0.004
Other symptoms	8 (20.5)	4 (10.3)	n.s.

n.s., not significant.

Symptoms during the week before the OHCA were reported by the patient himself/herself in 47.3% of the cases and by a relative or witness in the rest.

Table 2 shows each symptom compared individually between the week before the OHCA and the control week; there were significantly more reports of chest pain, dyspnoea/peripheral oedema, fatigue, gastrointestinal symptoms, fever/infection, other symptoms, other pain, and pre-syncope/syncope during the week prior to the OHCA than during the control week. There were no differences for palpitations, headache and anxiety. Of the 403 OHCA-patients 39 had an emergency visit the week before the OHCA and the most prevalent symptoms, compared with the control week, were chest pain, fever/infection, fatigue, gastrointestinal symptoms and other pain (Table 3). An ECG recording was performed in 18 of the 39 OHCA patients (46.1%). Twelve of these were admitted to hospital with an MI, ten died of an OHCA a few days after discharge from hospital and two survived an OHCA after discharge from hospital. In three patients ECG were considered normal and the patients returned home and died within a week. For the remaining three patients, the ECG recordings were not accessible. Two were interpreted as ST-elevation MI (STEMI), one died one day after discharge, one survived an OHCA after discharge. The third patient had a NSTEMI and survived an OHCA after discharge. Out of 15 persons who sought health care with chest pain, an ECG was performed in 13 (86.7%).

Symptoms were described either by the patient or health care personnel/relatives/witnesses the week before OHCA in 35% of the men and 41% of the women. This difference was not statistically significant. Gastrointestinal symptoms were more common in women (13%) than in men (6%) ($p = 0.024$). Dyspnoea and/or peripheral oedema were slightly more common in women ($p = 0.072$). Neither frequency of ECG registration nor health care consumption differed between the sexes.

5. Discussion

The results of this study suggest that people during the week prior to an OHCA do indeed seek health care and present symptoms more frequently than during an average week of their lives. Identifying individuals with CHD before the OHCA event is a prerequisite to prevent it. There are studies approaching this subject, and some have shown certain symptoms to be common before a cardiac arrest.^{5,6,12} However, the studies differ in the methods used, and almost all include only cases where CPR was attempted, thereby missing many OHCA patients, according to our study, and one other – about 50%.⁸ Also, some have studied sudden cardiac death while others have studied OHCA which, at least partially, may explain

diverging results. To the best of our knowledge, the only studies that have included cases where no CPR was attempted are the ones by Norris¹⁵ and de Vreede-Swagemakers et al.⁵ The study by Norris describes 1290 cases in the UK where symptoms were registered from records by general practitioners and necropsy reports. Only cases where the cause of death was ischaemic heart disease were considered, and no control population was used. The most common specific symptoms found were chest pain and breathlessness. The Dutch study by de Vreede-Swagemakers, et al. included 515 cases and registered symptoms by interviewing witnesses after the OHCA; they found chest pain and nausea/malaise to be common prodromes. A history of cardiac disease was known in 54% in that population.

In a Japanese population of 1466 OHCA victims where CPR was attempted, prodromal symptoms were studied by interviewing witnesses and/or emergency medical service personnel.¹² That study had the limitation that only symptoms directly before the OHCA were included; potential symptoms in the days or weeks before the OHCA were not included. Furthermore, interviewing witnesses after the event may introduce a recall bias. A German study of 406 cases of OHCA where CPR was attempted considered only symptoms within 24 h prior to the cardiac arrest.⁶ Dyspnoea and chest pain were the most frequent complaints prior to the OHCA.

A Canadian study included 100 survivors of cardiac arrest who afterwards underwent systematic clinical evaluation without evident cardiac disease. The proportion with cardiac symptoms in this group was compared with the proportion with cardiac symptoms in a control population made up of relatives of the OHCA patients. In the OHCA group, episodes of chest pain prior to the event were more common, but several symptoms were equally common in the control and OHCA groups.¹⁹ The limitations in that study were the small number, the highly selected population with all cases being survivors of OHCA, and all free from cardiac disease. Other studies have also shown that prodromal symptoms are common in OHCA,^{5,6,12,15} and some studies have only studied subpopulations such as young people with OHCA.^{20,21} Depending on the studied population, symptoms differ somewhat, the most frequent symptoms being chest pain, dyspnoea, syncope and nausea.

A large Danish study has shown that most people who suffer an OHCA have been in contact with a health care provider at some point during the year before as well as within 30 days before the event.²² This may be at least partially due to the fact that these patients seek healthcare at a significantly higher rate because of previously known cardiovascular disease. The study used an age-matched control population, and therefore did not consider the contribution of differences in cardiovascular health between the two groups. IHD was known in 20.8% of the OHCA cases in that study. The corresponding figure in the control population was not presented. Presumably it was much lower because those subjects were considered to be healthy controls. The studied time interval before OHCA was also much longer than in our study, which makes it difficult to compare the results.

5.1. Strengths and limitations

One of the strengths of our study was that it included unwitnessed OHCA and cases where no cardiopulmonary resuscitation was attempted. As almost every second OHCA event was unwitnessed in our study, the majority of the OHCA cases are probably missed in studies where only cases with CPR attempt are included. Another strength with our study was the crossover design where the cases were their own controls. Thus, we avoided differences in comorbidity and health-care consumption patterns that may

be a problem when using an age-matched control group. Another factor to consider is that using the patients as their own controls ensures that a difference in health care consumption does not simply reflect differences in travel distance or convenience in seeking care. Drawbacks in our study were that the included population was relatively small and contained a rather small number of women. This was probably caused by the fact that the MONICA study only includes patients up to the age of 74 years, and women are usually older than men when they suffer a cardiac arrest.^{2,23} With our study design there is a risk for recall bias as symptoms the week before OHCA may be more likely to be remembered by relatives compared to symptoms a year earlier.

5.2. Implications

Today, the number of OHCA survivors is increasing, but it is still very small. Hence, the high number of deceased is a huge challenge. For those who die without prodromal symptoms in a first MI, only better primary prevention can affect the outcome. However, a major problem is that many patients had experienced symptoms but had not sought medical care as described after the event by bystanders. Although chest pain is a symptom that can be related to CHD, 60% had other symptoms, and these were often nonspecific and may have been considered unimportant. Thus, it is reasonable to assume that better public education would only have a limited impact to help the person to realize that a symptom may be serious and that he/she should seek medical care. For those who seek medical care, especially with chest pain, a thorough medical examination, more frequent ECG registrations, and a stress test such as a tread mill test, may help to identify patients at risk for OHCA. However, the problem with risk stratification for cardiac arrest still remains as many suffering OHCA have no obvious risk factors.²⁴

6. Conclusions

In conclusion, patients who suffer an OHCA seek health care and present prodromal symptoms significantly more often the week prior to the event than the same week one year earlier.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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