Resuscitation 123 (2018) 65–70

Contents lists available at ScienceDirect

Resuscitation

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

Clinical paper

Warning symptoms preceding out-of-hospital cardiac arrest: Do patient delays matter?☆

Ziad Nehme[a,b,*], Stephen Bernard[a,c,d], Emily Andrew[a,c], Peter Cameron[c], Janet E. Bray[c], Karen Smith[a,b,c,e]

[a] Department of Research and Evaluation, Ambulance Victoria, Doncaster, Victoria, Australia
[b] Department of Community Emergency Health and Paramedic Practice, Monash University, Prahran, Victoria, Australia
[c] Department of Epidemiology and Preventive Medicine, Monash University, Prahran, Victoria, Australia
[d] Intensive Care Unit, Alfred Hospital, Prahran, Victoria, Australia
[e] Discipline of Emergency Medicine, University of Western Australia, Crawley, Western Australia, Australia

ARTICLE INFO

Article history:
Received 28 September 2017
Received in revised form
27 November 2017
Accepted 14 December 2017

Keywords:
Cardiac arrest
Prodromal symptoms
Patient delay time
Treatment delay
Emergency medical services

ABSTRACT

Background: Although increasing patient delays between symptom onset and activation of emergency medical services (EMS) can lead to poorer outcomes following acute myocardial infarction, its effect in out-of-hospital cardiac arrest (OHCA) populations is unclear.
Methods: Between 1st January 2003 and 31st December 2011, we included adult patients with anginal warning symptoms and subsequent EMS witnessed OHCA of presumed cardiac aetiology from the Victorian Ambulance Cardiac Arrest Registry. Multivariable logistic regression was used to assess the impact of patient delay time (i.e. symptom onset to EMS call time) on survival to hospital discharge.
Results: A total of 1056 EMS witnessed OHCA were screened, of which 515 (48.8%) reported chest pain or anginal equivalent symptoms. The median patient delay time was 25 min (interquartile range [IQR] 9–89 min), and did not differ across survivors and non-survivors. However, patients in lowest quartile of patient delay (≤8 min) also experienced significantly higher rates of non-shockable arrest rhythms and circulatory compromise. A total of 16 baseline and clinical characteristics were tested in a multivariable model of survival to hospital discharge, of which, only six were retained in the final model, including: age, dyspnoea, vomiting, shockable arrest rhythm, systolic blood pressure, and patient delay time. Every 30 min increase in patient delay time was independently associated with a 2.3% (95% CI: 0.4%, 4.1%; p = 0.02) reduction in the odds of survival to hospital discharge. Among patients with ST-segment deviation on the pre-arrest ECG, every 30 min increase in patient delay time was associated with a 3.4% reduction in the odds of survival (OR 0.966, 95% CI: 0.937, 0.996; p = 0.03).
Conclusion: Increasing delays in activating EMS before the onset OHCA may be associated with reduced survival. Future research could explore whether increasing public awareness of the warning symptoms leads to earlier medical contact for OHCA.

© 2017 Elsevier B.V. All rights reserved.

Introduction

Out-of-hospital cardiac arrest (OHCA) is the most common pathophysiological mechanism of death following acute myocardial infarction (AMI) [1]. Patients ignoring or inappropriately responding to prodromal symptoms present a significant challenge for the early treatment of AMI and the prevention of OHCA [2,3]. To date, much of the evidence that has been gathered about the impact of patient delays on clinical outcomes after AMI has involved populations who survive long enough to receive in-hospital treatment [4]. As a result, relatively little is known about the impact of patient delays on survival in OHCA populations [5,6].

Obtaining accurate pre-arrest information from OHCA populations is, however, inherently difficult and often limited to family or bystander accounts [6]. In comparison, emergency medical service (EMS)-witnessed OHCA offer a unique opportunity to collect pre-arrest data which are often lacking in the majority of OHCA events. Several reports involving EMS witnessed OHCA populations have shown that chest pain and anginal warning symptoms are present

☆ A Spanish translated version of the abstract of this article appears as Appendix in the final online version at https://doi.org/10.1016/j.resuscitation.2017.12.019.

* Corresponding author at: Ziad Nehme Department of Research and Evaluation, Ambulance Victoria, 375 Manningham Road, Doncaster, Victoria 3108, Australia.
E-mail address: ziad.nehme@ambulance.vic.gov.au (Z. Nehme).

https://doi.org/10.1016/j.resuscitation.2017.12.019
0300-9572/© 2017 Elsevier B.V. All rights reserved.

in as many as half of all patients prior to collapse [7,8]. Whether the duration of these warning symptoms hold further prognostic value is unclear.

In this study, we sought to assess the association between delays from symptom-onset to activation of emergency medical services (EMS) and survival to hospital discharge in patients with EMS witnessed OHCA.

Methods

Study design

This was a retrospective observational study of adult (aged ≥16 years) EMS witnessed OHCA of presumed cardiac aetiology between 1st January 2003 and 31st December 2011. We excluded patients who arrested on arrival at hospital and cases with a 'do not resuscitate' directive. As the symptom onset time was infrequently recorded in patients without pain symptoms, we also excluded patients if they did not report chest pain or anginal equivalent symptoms. Ethics approval for this project was granted by the Monash University Human Research Ethics Committee.

Setting

The study setting was Melbourne, Australia, which has a population of 4.1 million people distributed across 9900 square kilometres. The EMS comprises a two-tiered response involving approximately 1500 advanced life support paramedics and 300 intensive care paramedics.

Data sources

The study design, methodology, and definitions used in this report have been described in detail elsewhere [7]. OHCA data were extracted from the Victorian Ambulance Cardiac Arrest Registry (VACAR), a population-based registry of OHCA events attended by EMS in Victoria, Australia [9]. In-field patient care records are captured electronically, the data from which are synchronised wirelessly to a central clinical database. The VACAR identifies potential cardiac arrest events using a database search and manual review of patient care records. Eligible cases are entered into the registry according to international recommendations and definitions [10]. Cardiac arrest aetiology is identified from in-field patient care records, and is presumed to be of cardiac cause in the absence of a known precipitator (e.g. trauma, overdose, drowning etc.). Event survival denotes evidence of sustained return of spontaneous circulation (ROSC) on the treatment record on arrival at the emergency department. Survival to hospital discharge was defined as discharge from acute hospital care. Survival to hospital discharge is verified from hospital medical records in transported cases, and cross-validated against official government death records.

In addition to the Utstein-style descriptors captured by the VACAR, baseline and pre-arrest clinical variables including prodromal symptoms and clinical observations (e.g. systolic blood pressure, respiratory rate, heart rate, and Glasgow coma score), were manually extracted from treatment records by two investigators (ZN and JB) using a standardised electronic case report form. The accuracy of data capture was verified through a random audit of 15% of all manually extracted data. Patient delay time was defined as the time in minutes between symptom onset and call to EMS. Anginal equivalent symptoms were defined as non-traumatic arm, shoulder, neck or jaw pain, with or without chest pain.

Data analysis

The primary outcome measure was survival to hospital discharge. In the included sample, 4 (0.8%) cases had missing survival outcome and 23 (4.5%) cases had missing patient delay time. Categorisation of pre-arrest clinical observations was performed using locally weighted scatterplot smoothing (LOWESS), as described in detail elsewhere [7]. Unadjusted comparisons of baseline and clinical observations were performed for non-survivors and survivors to hospital discharge using the χ^2 test and Wilcoxon rank-sum test, as appropriate. Similarly, we compared baseline and clinical observations of patients across quartiles of patient delay time using the $\chi 2$ test and Kruskal Wallis rank test.

To assess the impact of patient delay time on survival to hospital discharge we constructed a multivariable logistic regression model consisting of patient delay time, in addition to baseline and clinical characteristics. A total of 16 candidate variables which reached significance during unadjusted comparisons ($p < 0.05$) were entered into a stepwise logistic regression model, and variables were backward eliminated at a threshold of $p > 0.10$. We assessed model discrimination performance using the area under the receiver operating characteristic curve (AUC). Effect sizes were reported as odds ratios (OR) and 95% confidence intervals (CI). The effect size for patient delay time was reported as increments of 30 min.

In a subgroup analysis, we re-analysed the parsimonious models separately in patients with and without ST-segment deviation on the pre-arrest electrocardiogram (ECG). As 9.8% (n = 50) of patients had one or more missing variables in our models, we supplemented the primary analysis with a sensitivity analysis consisting of multiple imputation to handle missing data. Twenty imputed datasets were generated, and the final model provided point estimates and confidence intervals which account for the variance within, and between, imputed datasets.

For all analyses, a two-sided significance level of less than 0.05 was considered statistically significant. Statistical analyses were undertaken using Stata Statistical Software 14 (StataCorp, 2015, College Station, TX).

Results

We identified 1379 adult EMS witnessed OHCA of presumed cardiac aetiology, of which 323 were excluded due to missing treatment records (n = 132), do not resuscitate directives (n = 129), or arrests after arrival at hospital (n = 62). The remaining 1056 cases underwent manual screening, of which 515 (48.8%) cases reported a prodromal symptom of chest pain or anginal equivalent (e.g. arm/shoulder pain).

Unadjusted comparisons

Tables 1 and 2 present the baseline and clinical characteristics of included patients, respectively, stratified by survival outcome. When compared to non-survivors, survivors were younger, more often male, and were more likely to experience shockable arrest rhythms ($p < 0.001$ for all comparisons). Non-survivors reported significantly higher rates of dyspnoea, abdominal pain, and vomiting, and more often experienced derangements in vital signs and circulatory compromise.

Patient delay time

The median patient delay time was 25 min (IQR 9–89), and was similar across non-survivors and survivors to hospital discharge (Table 1; 24 vs. 29 min, $p = 0.84$). Also, the median patient delay time did not differ across genders, pre-existing conditions, location of arrest, or arrest rhythm (data not shown). Table 3 compares

Table 1
Comparison of baseline characteristics across non-survivors and survivors to hospital discharge of emergency medical service (EMS) witnessed OHCA.

	Overall n = 515	Non-survivors n = 228	Survivors n = 283	p-value
Age in years, median (IQR)	67 (55, 78)	73 (62, 81)	61 (52, 73)	<0.001
Male gender, n (%)	374 (73.2)	149 (65.4)	225 (79.5)	<0.001
Pre-existing condition, n (%)				
Ischaemic heart disease	205 (40.1)	107 (46.9)	98 (34.6)	0.005
Stroke	33 (6.5)	19 (8.3)	14 (5.0)	0.12
Respiratory disease	49 (9.6)	25 (11.0)	24 (8.5)	0.34
Hypertension	208 (40.7)	100 (43.9)	108 (38.2)	0.19
Diabetes	75 (14.7)	45 (19.7)	30 (10.6)	0.004
Prehospital time intervals in mins, median (IQR)				
Symptom onset to call	25 (9, 89)	24 (6, 143)	29 (10, 69)	0.84
Symptom onset to arrest	61 (37, 123)	57 (37, 155)	65 (37, 111)	0.88
Call to EMS arrival	11 (9, 14)	11 (8, 14)	11 (9, 14)	0.44
EMS arrival to arrest	16 (8, 30)	16 (8, 30)	17 (8, 30)	0.66
Missing	30 (5.9)	20 (8.8)	10 (3.5)	–
Public location, n (%)	75 (14.7)	24 (10.5)	51 (18.0)	0.02
Aged care facility, n (%)	13 (2.5)	10 (4.4)	3 (1.1)	0.02
Arrest rhythm, n (%)				
Shockable	358 (70.1)	89 (39.0)	269 (95.1)	<0.001
Pulseless Electrical Activity	122 (23.9)	115 (50.4)	7 (2.5)	<0.001
Asystole	31 (6.1)	24 (10.5)	7 (2.5)	<0.001
ROSC at any time, n (%)	395 (77.3)	112 (49.1)	283 (100.0)	<0.001
Event survival, n (%)	333 (65.4)	60 (26.3)	273 (97.2)	<0.001
Missing	2 (0.4)	0	2 (0.7)	–
Discharged alive, n (%)	283 (55.4)	0	283 (100.0)	<0.001
Missing	4 (0.8)	–	–	–

IQR denotes interquartile range, ROSC return of spontaneous circulation.
Stated proportions exclude missing data.

Table 2
Comparison of pre-arrest clinical characteristics across non-survivors and survivors to hospital discharge of emergency medical service (EMS) witnessed OHCA.

	Overall n = 515	Non-survivors n = 228	Survivors n = 283	p-value
Accompanying symptoms, n (%)				
Dyspnoea	212 (41.5)	120 (52.6)	92 (32.5)	<0.001
Arm or shoulder pain	149 (29.2)	40 (17.5)	109 (38.5)	<0.001
Neck, jaw or throat pain	45 (8.8)	19 (8.3)	26 (9.2)	0.74
Abdominal pain	24 (4.7)	20 (8.8)	4 (1.4)	<0.001
Back pain	47 (9.2)	24 (10.5)	23 (8.1)	0.35
Dizziness	56 (11.0)	22 (9.7)	34 (12.0)	0.40
Vomiting	65 (12.7)	38 (16.7)	27 (9.5)	0.02
ST-segment deviation on the pre-arrest ECG, n (%)	208 (40.7)	65 (28.5)	143 (50.5)	<0.001
Pulse rate, n (%)				
<60/min	67 (13.8)	35 (16.4)	32 (11.8)	0.14
60–99/min	283 (58.5)	110 (51.6)	173 (63.8)	0.007
>99/min	134 (27.7)	68 (31.9)	66 (24.4)	0.07
Missing	27 (5.3)	15 (6.6)	12 (4.2)	–
Systolic blood pressure, n (%)				
Unrecordable	112 (23.2)	89 (41.2)	23 (8.7)	<0.001
<110 mmHg	107 (22.2)	50 (23.2)	57 (21.4)	0.65
110–139 mmHg	115 (23.9)	45 (20.8)	70 (26.3)	0.16
>139 mmHg	148 (30.7)	32 (14.8)	116 (43.6)	<0.001
Missing	29 (5.7)	12 (5.3)	17 (6.0)	–
Respiratory rate, n (%)				
<13/min	45 (9.0)	29 (12.9)	16 (5.8)	0.006
13–24/min	377 (75.3)	138 (61.3)	239 (86.6)	<0.001
>24/min	79 (15.8)	58 (25.8)	21 (7.6)	<0.001
Missing	10 (2.0)	3 (1.3)	7 (2.5)	–
Glasgow coma score <15, n (%)	118 (23.1)	94 (41.2)	24 (8.5)	<0.001
Missing	2 (0.4)	0	2 (0.7)	–

Stated proportions exclude missing data. ECG denotes electrocardiogram.

the baseline and clinical characteristics of patients by quartiles of patient delay time. Patients in the lowest quartile of patient delay time (≤8 min) experienced the lowest survival rate, but this was accompanied by poorer baseline characteristics including the lowest rate of shockable arrest rhythms and the highest rate of circulatory compromise.

Predictors of survival to hospital discharge

A total of 16 baseline and clinical characteristics were tested in a multivariate logistic regression model, however only 6 variables were retained in the parsimonious model (Table 4). Every 30 min increase in patient delay time was associated with a 2.3% reduction in the odds of survival to hospital discharge (OR 0.977, 95% CI: 0.959, 0.996; p = 0.02). The final model yielded good discrimination properties (AUC 0.89, 95% CI: 0.86, 0.92). The predicted probability of survival to hospital according to patient delay time is shown in Fig. 1. Replacing patient delay time with symptom-onset-to-arrest time yielded similar reductions in survival for every 30 min delay (OR 0.979, 95% CI: 0.961, 0.998; p = 0.03). In the sensitivity analysis involving 20 imputed datasets, the final model yielded similar effect sizes for both patient delay time (OR 0.978, 95% CI: 0.960,

Table 3
Comparison of baseline and pre-arrest characteristics across quartiles of patient delay time.

	Quartiles of patient delay time				
	≤8 min n = 119	9–24 min n = 124	25–88 min n = 125	≥89 min n = 124	p-value
Age in years, median (IQR)	66 (54, 76)	69 (57, 79)	70 (56, 80)	66 (56, 76)	0.20
Male gender, n (%)	86 (72.3)	97 (78.2)	87 (69.6)	90 (72.6)	0.48
Pre-existing condition, n (%)					
Ischaemic heart disease	48 (40.3)	43 (34.7)	49 (39.2)	58 (46.8)	0.28
Stroke	4 (3.4)	8 (6.5)	8 (6.4)	10 (8.1)	0.49
Respiratory disease	13 (10.9)	8 (6.5)	15 (12.0)	14 (11.3)	0.46
Hypertension	50 (42.0)	41 (33.1)	55 (44.0)	54 (43.6)	0.26
Diabetes	17 (14.3)	17 (13.7)	12 (9.6)	27 (21.8)	0.06
Public location, n (%)	23 (19.3)	17 (13.7)	13 (10.4)	17 (13.7)	0.25
Aged care facility, n (%)	2 (1.7)	5 (4.0)	4 (3.2)	1 (0.8)	0.35
Shockable arrest rhythm, n (%)	73 (61.3)	96 (77.4)	103 (82.4)	77 (62.1)	<0.001
Accompanying symptoms, n (%)					
Dyspnoea	56 (47.1)	51 (41.1)	44 (35.2)	55 (44.4)	0.27
Arm or shoulder pain	27 (22.7)	43 (34.7)	45 (36.0)	34 (27.4)	0.08
Neck, jaw or throat pain	9 (7.6)	5 (4.0)	14 (11.2)	16 (12.9)	0.07
Abdominal pain	3 (2.5)	5 (4.0)	8 (6.4)	7 (5.7)	0.48
Back pain	12 (10.1)	9 (7.3)	15 (12.0)	11 (8.9)	0.63
Dizziness	16 (13.5)	12 (9.7)	18 (14.4)	11 (8.9)	0.44
Vomiting	20 (16.8)	16 (12.9)	18 (14.4)	11 (8.9)	0.32
ST-segment deviation on the pre-arrest ECG, n (%)	47 (39.5)	57 (46.0)	52 (41.6)	48 (38.7)	0.66
Pulse rate, n (%)					
<60/min	21 (19.3)	15 (12.6)	14 (11.6)	12 (10.3)	0.20
60–99/min	59 (54.1)	76 (63.9)	76 (62.8)	66 (56.4)	0.35
>99/min	29 (26.6)	28 (23.5)	31 (25.6)	39 (33.3)	0.36
Systolic blood pressure, n (%)					
Unrecordable	41 (37.3)	19 (16.1)	21 (17.8)	23 (19.5)	<0.001
<110 mmHg	17 (15.5)	33 (28.0)	25 (21.2)	26 (22.0)	0.15
110–139 mmHg	24 (21.8)	31 (26.3)	23 (19.5)	33 (28.0)	0.40
>139 mmHg	28 (25.5)	35 (29.7)	49 (41.5)	36 (30.5)	0.06
Respiratory rate, n (%)					
<13/min	13 (11.2)	9 (7.5)	10 (8.1)	9 (6.6)	0.60
13–24/min	82 (70.7)	94 (78.3)	101 (81.5)	89 (73.0)	0.19
>24/min	21 (18.1)	17 (14.2)	13 (10.5)	25 (20.5)	0.15
Glasgow coma score <15, n (%)	37 (21.4)	22 (17.9)	21 (16.8)	29 (23.4)	0.03
ROSC at any time, n (%)	88 (74.0)	99 (79.8)	105 (84.0)	95 (76.6)	0.25
Event survival, n (%)	67 (56.3)	87 (70.2)	96 (78.1)	78 (62.9)	0.002
Discharged alive, n (%)	56 (47.5)	76 (62.3)	86 (68.8)	59 (47.6)	0.001

IQR denotes interquartile range, ROSC return of spontaneous circulation, ECG electrocardiogram.
Stated proportions exclude missing data.

Table 4
Multivariable logistic regression of survival to hospital discharge.

	Overall population (n = 461)		Sub-group with ST segment deviation on the pre-arrest ECG (n = 198)		Sub-group without ST segment deviation on the pre-arrest ECG (n = 263)	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age, per year increase	0.96 (0.94, 0.98)	<0.001	0.95 (0.92, 0.99)	0.006	0.96 (0.94, 0.98)	0.002
Arrest rhythm						
Non-shockable	Reference		Reference		Reference	
Shockable	18.21 (9.27, 35.78)	<0.001	27.12 (5.52, 133.14)	<0.001	16.42 (7.51, 35.88)	<0.001
Dyspnoea	0.61 (0.36, 1.04)	0.07	0.45 (0.19, 1.06)	0.07	0.69 (0.34, 1.39)	0.30
Vomiting	0.42 (0.20, 0.87)	0.02	0.55 (0.18, 1.62)	0.28	0.36 (0.12, 1.04)	0.06
Systolic blood pressure						
Unrecordable	0.38 (0.17, 0.82)	0.01	0.67 (0.18, 2.42)	0.54	0.31 (0.11, 0.89)	0.03
<110 mmHg	1.28 (0.63, 2.58)	0.49	0.99 (0.36, 2.77)	0.99	1.49 (0.55, 4.07)	0.44
110–139 mmHg	Reference		Reference		Reference	
>139 mmHg	3.04 (1.52, 6.08)	0.002	4.28 (1.35, 13.61)	0.01	2.57 (1.00, 6.56)	0.05
Patient delay time, per 30 min increase	0.977 (0.959, 0.996)	0.02	0.966 (0.937, 0.996)	0.03	0.984 (0.960, 1.008)	0.20

ECG denotes electrocardiogram. Sample size indicative of all patients included with no missing data.

0.996; p = 0.02) and symptom-onset-to-arrest time (OR 0.980, 95% CI: 0.962, 0.999; p = 0.04).

For the subgroup analyses, every 30 min increase in patient delay time was associated with a 3.4% reduction in the odds of survival among patients with ST-segment deviation on the pre-arrest ECG (OR 0.966, 95% CI: 0.937, 0.996; p = 0.03). In patients without ST-segment deviation on the pre-arrest ECG, the association between patient delay time and survival was not significant (OR 0.984, 95% CI: 0.960, 1.008; p = 0.20). The findings were not altered in a sensitivity analysis using multiple imputation to handle missing data.

Discussion

Our findings suggest that delays in activating EMS after the onset of prodromal symptoms may be associated with poorer sur-

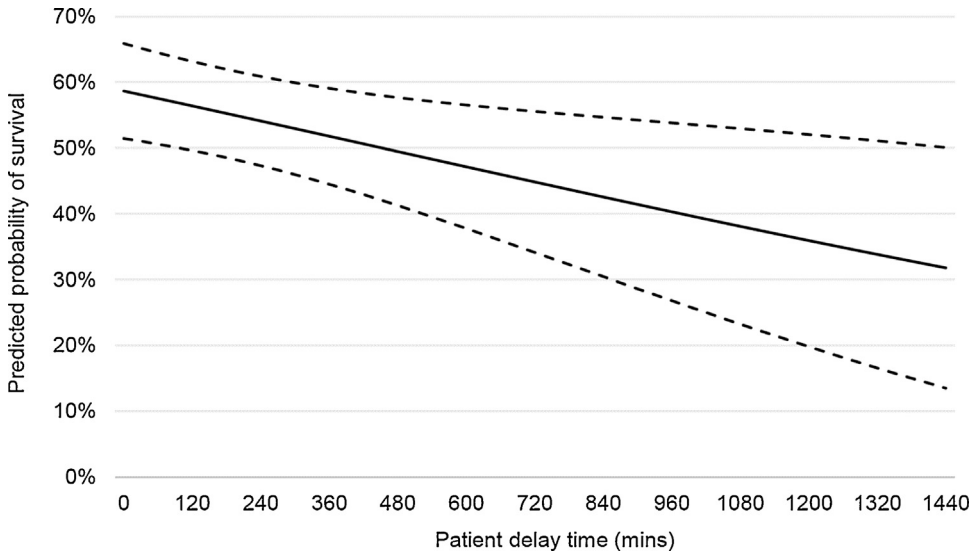

Fig. 1. Predicted probability (with 95% confidence intervals) of survival to hospital discharge according to patient delay time.

vival outcomes in EMS witnessed OHCA populations. The effect size appears to be modest, indicating a 2.3% reduction in the odds of survival to hospital discharge for every 30 min delay in EMS activation after the onset of chest pain symptoms. In addition, among patients with evidence of ST-segment deviation on the pre-arrest ECG, there was a 3.4% reduction in the odds of survival for every 30 min delay in EMS activation.

In our study, the median patient delay time of 25 min differs from two earlier studies [6,11]. A study from Germany reported a median chest pain duration time of 120 min (IQR: 20, 630) in 88 patients with OHCA of presumed cardiac aetiology [11]. In contrast, a more recent study from Japan involving 644 witnessed OHCA of presumed cardiac aetiology reported that one in five patients described chest pain for a median duration of 3 min prior to their arrest [6]. The definition of patient delay time used in our study does not account for the interval between the EMS call and arrest, which would extend the total symptom duration time before arrest to 61 min (IQR: 37, 123). This would suggest that one half of our population had experienced chest pain warning symptoms for at least one hour, while one quarter experienced symptoms for over 2 h before arrest.

Although it could be inferred from our findings that delays in activating EMS after the onset of prodromal symptoms could influence survival from OHCA, the pathophysiological basis for our findings remain unclear. In patients with ST-elevation myocardial infarction (STEMI), total ischaemic time prior to initiation of reperfusion therapy is strongly correlated with myocardial infarct size and mortality [12]. As the cause of arrest in our population is most likely to be the result of an AMI [13], it is plausible that increasing delays to definitive care would also be associated with an increased risk of in-hospital mortality after OHCA. Indeed, high-risk STEMI patients, such as those with cardiogenic shock, experience a sharp increase in early mortality with increasing delays to reperfusion [14].

Although the effect size for patient delay time appears to be modest in our study, its true impact on survival from OHCA would be influenced by a range of factors that are unmeasured. For instance, inclusion of a broader population of OHCA patients, such as those without prodromal symptoms or 'sudden' collapse, could diminish the effect of patient delay time in our models. In addition, patient delay is only one component of the total ischaemic duration, and this could weaken its association with patient outcomes [12]. Furthermore, causes of arrest other than AMI may be less sensitive to patient delay time, and this could also diminish its effect in our models. This may explain why we did not observe an association between patient delay time and survival in patients without ST-segment deviation on the pre-arrest ECG.

Nevertheless, it is also intuitive that increasing delays in accessing EMS after the onset of prodromal could lead to poorer survival outcomes among OHCA patients. A recent study from Portland, Oregon (Unites States), showed that approximately one half of sudden cardiac arrest patients experienced warning symptoms in the four weeks prior to the arrest, but fewer than one in five activated EMS in response to symptoms [15]. When compared to patients who did not activate EMS, patients who activated EMS observed a five-fold improvement in the odds of survival to hospital discharge (OR 4.82, CI: 2.23, 10.43). Importantly, the association between EMS activation and survival was independent of baseline and arrest confounders, and this could indicate that EMS activation is a surrogate for shorter patient delay time.

Future research could explore whether increasing public awareness of the warning symptoms leads to earlier medical contact for OHCA. In Australia, a recent heart attack public awareness campaign was associated with significant increase in EMS use for chest pain complaints in the community [16], and led to a substantial reduction in the incidence of OHCA between 2009 and 2013 [17]. Early activation of EMS after the onset of prodromal symptoms could also lead to an increase the proportion of arrests witnessed by EMS personnel [15], which would in-turn yield better survival outcomes [18–20].

Limitations

This study has several limitations. First, our study is retrospective in design and was conducted in a select population of EMS witnessed OHCA patients. As such, the validity of our findings in a broader population of OHCA patients is unclear, and requires further investigation. As the symptom-onset time was infrequently recorded in patients without chest pain, we could not investigate the influence of symptom duration among all EMS witnessed arrests. Due to missing treatment records, we were also unable to collect information from 132 EMS witnessed OHCA cases during the study period. Although our study collected and adjusted for a large number of pre-arrest data, it is also possible that patient delay time may be confounded by other factors not measured in our study. Indeed, we could not adjust for hospital-based factors which would

also have an effect on survival. Finally, despite the performance of our models, the effect size of our covariates had wide confidence intervals and larger prospective studies are needed to confirm our findings.

Conclusion

In patients attended by EMS with chest pain and subsequent OHCA, increasing delays from symptom onset to activation of EMS were associated with poorer survival. Although the pathophysiological basis for this association remains speculative, it is likely that patient delays represent a surrogate for total ischaemic duration which could influence survival outcomes in OHCA populations. Our study supports the need for ongoing public health initiatives which aim to reduce patient delays to accessing care after the onset of prodromal symptoms.

Conflicts of interest

None declared.

Sources of funding

JB is funded by a Heart Foundation Fellowship (#101171).

References

[1]. Myerburg RJ, Junttila MJ. Sudden cardiac death caused by coronary heart disease. Circulation 2012;125:1043–52.
[2]. Nolan J, Soar J, Eikeland H. The chain of survival. Resuscitation 2006;71:270–1.
[3]. Moser DK, Kimble LP, Alberts MJ, Alonzo A, Croft JB, Dracup K, et al. Reducing delay in seeking treatment by patients with acute coronary syndrome and stroke: a scientific statement from the American Heart Association Council on cardiovascular nursing and stroke council. Circulation 2006;114:168–82.
[4]. Austin PC, Mamdani MM, Van Walraven C, Tu JV. Quantifying the impact of survivor treatment bias in observational studies. J Eval Clin Pract 2006;12:601–12.
[5]. Norris RM, Wong PS, Dixon G, Morris N, Penny WJ, El Gaylani N, et al. Effect of time from onset to coming under care on fatality of patients with acute myocardial infarction: effect of resuscitation and thrombolytic treatment. Heart 1998;80:114–20.
[6]. Nishiyama C, Iwami T, Kawamura T, Kitamura T, Tanigawa K, Sakai T, et al. Prodromal symptoms of out-of-hospital cardiac arrests: a report from a large-scale population-based cohort study. Resuscitation 2013;84:558–63.
[7]. Nehme Z, Andrew E, Bray JE, Cameron P, Bernard S, Meredith IT, et al. The significance of pre-arrest factors in out-of-hospital cardiac arrests witnessed by emergency medical services: a report from the Victorian Ambulance Cardiac Arrest Registry. Resuscitation 2015;88:35–42.
[8]. De Maio VJ, Stiell IG, Wells GA, Spaite DW. Cardiac arrest witnessed by emergency medical services personnel: descriptive epidemiology, prodromal symptoms, and predictors of survival. Ann Emerg Med 2000;35:138–46.
[9]. Nehme Z, Bernard S, Cameron P, Bray JE, Meredith IT, Lijovic M, et al. Using a cardiac arrest registry to measure the quality of emergency medical service care: decade of findings from the Victorian Ambulance Cardiac Arrest Registry. Circ Cardiovasc Qual Outcomes 2015;8:56–66.
[10]. Perkins GD, Jacobs IG, Nadkarni VM, Berg RA, Bhanji F, Biarent D, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update of the utstein resuscitation registry templates for out-of-hospital cardiac arrest: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian and New Zealand Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia); and the American Heart Association Emergency Cardiovascular Care Committee and the council on cardiopulmonary, critical care, perioperative and resuscitation. Resuscitation 2015;96:328–40.
[11]. Muller D, Agrawal R, Arntz HR. How sudden is sudden cardiac death. Circulation 2006;114:1146–50.
[12]. Denktas AE, Anderson HV, McCarthy J, Smalling RW. Total ischemic time: the correct focus of attention for optimal ST-segment elevation myocardial infarction care. JACC: Cardiovas Interventions 2011;4:599–604.
[13]. de Vreede-Swagemakers JJ, Gorgels AP, Dubois-Arbouw WI, Dalstra J, Daemen MJ, van Ree JW, et al. Circumstances and causes of out-of-hospital cardiac arrest in sudden death survivors. Heart 1998;79:356–61.
[14]. Cannon CP, Gibson CM, Lambrew CT, Shoultz DA, Levy D, French WJ, et al. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. JAMA 2000;283:2941–7.
[15]. Marijon E, Uy-Evanado A, Dumas F, Karam N, Reinier K, Teodorescu C, et al. Warning symptoms are associated with survival from sudden cardiac arrest warning symptoms and sudden cardiac arrest. Ann Intern Med 2015;164:23–9.
[16]. Nehme Z, Cameron PA, Akram M, Patsamanis H, Bray JE, Meredith IT, et al. Effect of a mass media campaign on ambulance use for chest pain. Med J Aust 2017;206:30–5.
[17]. Nehme Z, Andrew E, Bernard S, Patsamanis H, Cameron P, Bray JE, et al. Impact of a public awareness campaign on out-of-hospital cardiac arrest, incidence, and mortality rates. Eur Heart J 2016;38:1666–73.
[18]. Nehme Z, Andrew E, Bernard S, Smith K. Comparison of out-of-hospital cardiac arrest occurring before and after paramedic arrival: epidemiology, survival to hospital discharge and 12-month functional recovery. Resuscitation 2015;89:50–7.
[19]. Hostler D, Thomas EG, Emerson SS, Christenson J, Stiell IG, Rittenberger JC, et al. Increased survival after EMS witnessed cardiac arrest: observations from the resuscitation outcomes consortium (ROC) epistry-cardiac arrest. Resuscitation 2010;81:826–30.
[20]. Hollenberg J, Herlitz J, Lindqvist J, Riva G, Bohm K, Rosenqvist M, et al. Improved survival after out-of-hospital cardiac arrest is associated with an increase in proportion of emergency crew–witnessed cases and bystander cardiopulmonary resuscitation. Circulation 2008;118:389–96.