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Original article

## Risk factors of delayed pre-hospital treatment seeking in patients with acute coronary syndrome: A prospective study



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### ABSTRACT

**Objectives:** Despite enormous efforts in public education, treatment seeking time still remains more than optimal in patients with acute coronary syndrome. This prospective study tries to determine the risk factors of pre-hospital delay in patients with acute coronary syndrome.

**Methods:** Descriptive data of 190 patients with diagnosis of acute coronary syndrome attending in 2 tertiary level teaching hospital emergency departments were analyzed to determine risk factors of delayed pre-hospital treatment seeking. Demographic, social and clinical characteristics of patients were obtained and they were asked to fully describe their symptoms and the actions they had done after their symptoms onset.

**Results:** Thirty nine (20.52%) of patients were arrived in emergency department in <1 h of their symptoms onset, 73 (38.43%) were arrived between 1 and 6 h and 78 (41.05%) were arrived in >6 h. Sex, route of transport, scene-to-hospital distance, attributing the symptoms to non-cardiac causes and outpatient physician consultation and cigarette smoking were the risk factors of delayed treatment seeking in our studied patients with acute coronary syndrome. Patients with previous history of ischemic heart disease and Coronary Care Unit admission and patients with underlying diseases like diabetes mellitus, hypertension and hyperlipidemia showed a trend to have more delayed treatment seeking behavior but not with a statistically significant difference. Patients with positive family history of acute coronary syndrome arrived in emergency department earlier than other patients but again with not a statistically significant difference.

**Conclusion:** Most patients with acute coronary syndrome arrived in emergency department in >6 h of their symptoms onset. Sex, route of transport, scene-to-hospital distance, attributing the symptoms to non-cardiac origins, outpatient physician consultation and cigarette smoking were risk factors of delayed treatment seeking in studied patients.

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## 1. Introduction

Despite enormous efforts in public education, pre-hospital treatment seeking time still remains more than optimal in most patients with acute coronary syndrome (ACS).<sup>1–3</sup> Two third of treatment seeking delays in patients with ACS is due to delayed arrival in emergency department (ED). Some studies show that

about 25% of patients with ACS wait more than 6 h before seeking medical care.<sup>4</sup> This is while treatment of ACS should begin within 1 h of symptom onset and every 30 min of delay in seeking medical care can increase the relative risk of 1-year mortality as 7.5% in patients with acute myocardial infarction.<sup>5</sup>

Delayed pre-hospital treatment seeking is a multifaceted problem. Demographic characteristics (like sex, age, race, level of education), behavioral factors (like underestimating the significance of symptoms and the insurance status) and clinical factors (like previous history of ACS, concurrent comorbid disease, experiencing atypical symptoms) have significant role in delayed ED arrival in patients with ACS. Better recognition of these factors can help health system to make more effective interventions and increase the likelihood of on-time treatment seeking in patients with ACS.

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This prospective study evaluates the major risk factors of delayed pre-hospital treatment seeking in patients with ACS in an urban area.

## 2. Methods

### 2.1. Study design and setting

This prospective cross-sectional multi-center study was conducted and September 2013. Study was approved by institutional ethics committee (faculty of medicine, Iran University of Medical Sciences) and was carried out in accordance with Declaration of Helsinki (1989). Informed written consent was obtained from all patients.

### 2.2. Selection of participants

We included  $\geq 18$  year old patients admitted in hospital with diagnosis of acute coronary syndrome (including ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction and unstable angina). Acute myocardial infarction was defined as typical rise and gradual fall or more rapid rise and fall of biochemical markers of myocardial necrosis with at least one value above the 99th percentile of the upper reference limit and with at least one of the following clinical parameters: Ischemic symptoms, electrocardiograph (ECG) changes indicative of ischemia (T wave changes or ST segment elevation or depression), development of pathologic Q waves on the ECG, coronary artery intervention. Unstable angina was defined as the occurrence of one or more angina episodes, at rest, within the preceding 48-hours, corresponding to class III of the Braunwald classification.<sup>6–8</sup> Although sudden cardiac deaths can also be a subtype of ACS they are not included in study population because of difficulties in data gathering. Patients were pain-free, stable and comfort during the interview. They were recruited in study conveniently.

We excluded patients who did not recall the exact time of their symptoms onset or whose exact ED arrival time was not documented; patients who were unable to understand or communicate because of language barrier or mood, memory and cognition disorders (like patients with senile dementia or Alzheimer's disease) or any other reason. Patients who preferred to discontinue their participation (during interview or at any phase of study) were also excluded.

### 2.3. Intervention

Patients were interviewed by a single research assistant in 48 h of their hospital admission before discharging home. Patients were asked to fully describe their symptoms and the actions they had done after their symptoms onset. The interviewer completed a questionnaire with 33 items about patients' demographic and socio-economic condition, previous history of ischemic heart disease, Coronary Care Unit (CCU) admission, myocardial infarction; setting and onset of symptoms, treatment seeking behavior, hospital transportation route to, etc.

The questionnaire was designed and tested for reliability and validity after reviewing other studies, consultation with pre-hospital emergency care, cardiology and emergency medicine specialists and the results of an interim analysis of patients-reported causes of pre-hospital delay in Iranian patients with ACS. Final version of questionnaire had a content validity score of 98% and internal consistency of 0.72. Pilot interviews with 15 cases who were not included in final analysis showed that the questionnaire is enough easy-to-use.

Patients were categorized to 3 groups: patients who were admitted in ED in  $< 1$  h of their symptoms onset, patients who were admitted in ED between 1 and 6 h of their symptoms onset and patients who were admitted in ED  $> 6$  h of their symptoms onset. Transportation route was categorized as self-transportation or use of the EMS (initially directed transport by ambulance from home to hospital).

### 2.4. Analysis

Sample size was calculated as 109 according to " $n = t^2 pq / (p^* \delta)^2$ " formula. Descriptive continuous numerical data like age and delay time are presented as minimum, maximum and mean (with standard deviation). Descriptive categorical variables like sex are described as absolute and relative (percentage) frequencies. We used t-test and chi-square test to compare means. P less than 0.05 is considered statistically significant. The internal consistency of the questionnaire was calculated by Cronbach's alpha test. All data analyses were performed with SPSS version 16 (SPSS, Inc., Chicago, IL, USA).

## 3. Results

We enrolled 218 patients in our study. Six patients did not recall the exact time of their symptoms onset. In 8 cases the exact ED arrival time was not documented in patient's file. Twelve patients refused to participate in study. Six patients discontinued their participation in different phases of interview. At last 190 patients were included and analyzed.

Thirty nine (20.52%) patients were arrived in ED in  $< 1$  h of their symptoms onset, 73 (38.43%) were arrived in ED between 1 and 6 h of their symptoms onset and 78 (41.05%) patients were admitted in ED  $> 6$  h of their symptoms onset.

Mean age of patients was 56.50 ( $\pm 10.33$ ) with minimum of 35 and maximum of 78 years old. One hundred and four (55%) of patients were male and 86 (45%) were female. Ninety (47.36%) patients had a positive family history of ischemic heart disease. Nineteen (10.00%) of patients were chronic alcohol drinker and 79 (41.57%) were cigarette smokers. Assessment of past medical history of patients showed that 61 (32.10%) patients had hypertension, 50 (26.31%) had diabetes mellitus, 19 (10.00%) had hyperlipidemia, 65 (34.21%) had ischemic heart disease, 61 (32.10%) had previous CCU admission, 22 (11.57%) had previous myocardial infarction. One hundred and twenty five (66%) patients arrived in ED in day hours and 65 (34) of them arrived at night. One hundred and twenty nine (67.89%) patients were transferred to hospital by EMS and 61 (32.10%) were transferred by other routes. Therapeutic interventions were provided in less than 10 min of ED arrival for 58 (30.5%) patients, between 10 and 20 min of ED arrival for 72 (37.89%) patients and after 30 min of ED arrival for 15 (7.89%) patients.

Ninety (47.37%) patients were located in  $< 30$  km of hospital and 100 (52.63%) cases were located in  $> 30$  km of hospital. One hundred and six (55.78%) patients attributed their symptoms to non-cardiac causes and 79 (41.57%) of them looked for outpatients medical care before admitting in emergency department. Eighty five (44.73%) patients had used sublingual nitroglycerine before their ED arrival. Self-treatment with sublingual nitroglycerine was more common in patients arrived in ED in  $< 1$  h of their symptoms onset, these group of patients responded to nitroglycerine less than other two groups but not with a statistically significant difference (Pvalue = 0.78). Comparison of risk factors is summarized in Tables 1 and 2.

**Table 1**  
Comparison of socio-demographic and clinical factors between 3 studied groups of patients.

Variable	<1 h of symptoms onset (n = 39)	1–6 h of symptoms onset (n = 73)	>6 h of symptoms onset (n = 78)	P Value
Age, Mean ( $\pm$ SD)	55.48 ( $\pm$ 9.45)	56.89 ( $\pm$ 10.03)	55.50 ( $\pm$ 9.98)	0.69†
Sex, n (%)				
Male	20 (51.29)	37 (50.68)	41 (52.57)	0.68*
Female	19 (48.71)	36 (49.32)	37 (47.43)	
Positive past medical history, n (%)				
Hypertension	11 (28.20)	24 (32.87)	26 (33.33)	0.89*
Diabetes mellitus	9 (23.07)	19 (26.02)	22 (28.20)	0.28
Hyperlipidemia	3 (7.69)	7 (9.58)	9 (11.53)	0.12
Ischemic heart disease	11 (28.20)	24 (32.87)	30 (38.46)	0.09
CCU admission	11 (28.20)	27 (36.98)	28 (35.89)	0.09
Myocardial infarction	3 (7.69)	6 (8.21)	9 (11.53)	0.32
Positive family history, n (%)	19 (48.71)	37 (50.68)	34 (43.59)	0.06*
Positive social history, n (%)				
Cigarettes	10 (25.64)	37 (50.68)	32 (41.02)	0.04*
Alcohol	4 (10.25)	9 (12.32)	6 (7.69)	0.54
Time of onset, n (%)				
Day	26 (66.67)	49 (67.13)	54 (69.24)	0.87*
Night	13 (33.33)	24 (32.87)	24 (30.76)	
Route of transport, n (%)				
EMS	33(84.62)	61(83.57)	34 (43.59)	0.00*
Others	6 (15.38)	12 (16.43)	44 (56.41)	
Living alone, n (%)	4 (10.25)	3 (4.10)	3 (3.84)	0.48*
Educational level, n (%)				
Undergraduate	9 (23.07)	34 (46.57)	34 (43.59)	0.00*
Graduate	19 (48.71)	24 (32.87)	32 (41.02)	0.00*
Bachelor	9 (23.07)	12 (16.43)	3 (3.84)	0.00*
Master/PhD	2 (5.12)	3 (4.10)	9 (11.53)	0.00*
Knowledge about ACS†† symptoms, n (%)				
Yes	13 (33.33)	24 (32.87)	24 (30.76)	0.56*
No	26 (66.67)	49 (67.13)	54 (69.24)	
Attributing the symptoms to non-cardiac causes, n (%)	15 (38.46)	34 (46.57)	57 (73.07)	0.00*
Stress induced symptoms, n (%)	24 (61.53)	37 (50.68)	32 (41.02)	0.16*
Seeking outpatient medical care before ED** admission, n (%)	4 (10.25)	27 (36.98)	48 (61.53)	0.00*
Nitroglycerin self-administration before ED admission, n (%)	19 (48.71)	32 (43.83)	34 (43.58)	0.56*

†Student's t-test, †† Acute coronary syndrome, \*Chi-Square test, \*\*Emergency department.

**Table 2**  
Comparison of transportation time and disposition between 3 studied groups of patients.

Variable	<1 h of symptoms onset (n = 39)	1–6 h of symptoms onset (n = 73)	>6 h of symptoms onset (n = 78)	P value
Dispatch-to-scene arrival time (minute), Mean ( $\pm$ SD)	9.27 ( $\pm$ 4.28)	10.35 ( $\pm$ 3.85)	9.87 ( $\pm$ 4.35)	0.85†
Scene-to-hospital time (minute), Mean ( $\pm$ SD)	30.89 ( $\pm$ 5.97)	31.79 ( $\pm$ 5.96)	35.45 ( $\pm$ 4.27)	0.78†
Scene to hospital distance (km), n (%)				
<30	25 (64.10)	33 (45.20)	30 (38.46)	0.04†
>30	14 (35.90)	40 (54.79)	48 (61.53)	
Triage-to-treatment time, n (%)				
<10 min	16 (41.02)	22 (30.13)	20 (25.64)	0.45*
10–20 min	12 (30.76)	32 (43.83)	36 (46.15)	0.69*
>30 min	11 (28.20)	19 (26.02)	22 (28.20)	0.75*
On-time therapeutic interventions, n (%)				
Thrombolysis (with streptokinase)	9 (23.07)	9 (12.32)	3 (3.84)	0.01*
Catheterization	1 (2.56)	2 (2.73)	7 (8.97)	0.01*
ED length of stay, n (%)				
<6 h	28 (71.79)	54 (73.97)	70 (89.75)	0.32*
6–12 h	7 (17.95)	16 (21.91)	7 (8.97)	0.45*
>12 h	4 (10.26)	3 (4.10)	1 (1.28)	0.68*
Disposition, n (%)				
CCU admission	19 (48.71)	30 (41.09)	36 (46.15)	0.66*
Discharge from ED	16 (41.02)	24 (32.87)	32 (41.03)	0.68*
Leaving against medical advice	4 (10.25)	16 (21.91)	9 (11.54)	0.75*
Death	0 (0.00)	3 (4.10)	1 (1.28)	0.96*

†Student's t-test, †† Acute coronary syndrome, \*Chi-Square test, \*\*Emergency department.

#### 4. Discussion

Behavior of patients experiencing ACS associated symptoms is conflicting in different aspects including interpreting the

symptoms, recognizing the symptoms origin and choosing in-patients/outpatient medical care and on-time calling to EMS.<sup>9,10</sup>

Our study showed that just 20% of patients were arrived in ED in <1 h of their symptoms onset and most of them had a >6 h delay in

their treatment seeking. Our findings are compatible with major studies showing no significant improvement in seeking treatment for ACS symptoms in recent decades. These studies show that 49.5% of ACS patients has a >4 h delay in seeking treatment for their symptoms.<sup>11,12</sup>

Sex, route of transport, scene-to-hospital distance, attributing the symptoms to non-cardiac causes and outpatient physician consultation and cigarette smoking were the risk factors of delayed treatment seeking in our studied patients. Patients with previous history of ischemic heart disease, CCU admission, underlying diseases (like diabetes mellitus, hypertension and hyperlipidemia) showed a trend to have more delayed treatment seeking but not with a statistically significant difference. On opposite, patients with positive family history of ACS arrived in ED earlier than other patients but again with not a statistically significant difference.

Our results about sex, past medical history (especially prior myocardial infarction), family history, social history (cigarette smoking), patient's knowledge about ACS symptoms, attributing symptoms to non-cardiac causes, outpatient physician consultation and location of patients during symptoms onset are similar to some other studies.<sup>13–16</sup> According to our study patients living alone were attended in ED sooner than patients living with family or in institute. Other studies have also shown that family members (especially spouses) often play an inhibitor role and increase the delay time by trying to overwhelm the actual condition and fastest ED arrivals are seen when the patients is accompanied by a coworker or friend.<sup>17–20</sup>

In our study, patients who were located >30 km far from hospital were attended in ED with more delay but not with a statistically significant difference. This shows that the long distance to hospital can potentially postpone the patient's decision to seek medical care but short distance does not necessarily decrease the delays.

Attributing symptoms to non-cardiac causes is another major risk factor in our and other similar studies<sup>21</sup> which shows that despite numerous efforts performed to increase public awareness about heart attack and its symptoms, alarm signs are not optimally identified by most patients. A substantial number of patients who could identify the cardiac origin of their symptoms were the ones who had a positive family history of ACS. Educating people about the importance of calling EMS as soon as possible when experiencing symptoms suspicions to have cardiac origin is as important as educating them about calling EMS as soon as possible because EMS can markedly decrease the scene-to-hospital transfer time even from distant areas but according to some studies only 3% of patients with ACS symptoms directly call EMS and most of them prefer to contact a family member before calling for an ambulance.<sup>21</sup>

Level of education has shown also a relatively complicated effect on patients' decision making times. As according to our study, patients in two ends of educational level spectrum (under graduates and patients with master/PhD) had more delays in treatment seeking after the onset of their symptoms.

Our study showed that occurrence of symptoms during day/night hours had no statistically significant effect on treatment seeking behaviors in patients with ACS, as the mean delay in patients who had experienced their symptoms in day was similar to those experienced their symptoms in night. According to our results, treatment seeking delay had also no significant effect on triage-to-treatment time and ED length of stay. As although 7 from 8 patients who stayed in ED for more than 6 h, have attended in hospital in less than 6 h of their symptom honest but there were no overall correlation between the delay in treatment seeking and ED length of stay.

The final disposition of patients was also independent from delays in pre-hospital treatment seeking. Some patients who had

attended in ED in <1 h of their symptom honest were discharge in less than 6 h and some patients with >6 h delay were admitted in CCU.

#### 4.1. Limitations

We have studied ACS patients attending in a tertiary level university hospital in an urban area, more studies on patients living in rural areas and patients without available access to university hospitals are needed. We found a relationship between educational level and delayed treatment seeking in patients with ACS, but more detailed and qualitative studies are needed to clarify the exact role of this variable on pre-hospital treatment seeking behaviors both in ACS and other diseases. Our delay time categories were considered as <1 h, 1–6 h and >6 h. This is while more precise categorizations will be considered in future studies.

#### 5. Conclusion

Most patients with ACS arrived in ED in >6 h of their symptoms onset. Sex, route of transport, scene-to-hospital distance, attributing the symptoms to non-cardiac causes, outpatient physician consultation and cigarette smoking are some of risk factors of delayed treatment seeking in Iranian population patients with ACS.

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