

# Relationship between Mortality Rate of Patients with Acute Chest Pain and Time Trends of Request to Pre-Hospital Emergency Medical Services in Tehran, Iran

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## Abstract

**Background and objectives:** There are rhythmic periods in organisms' body influencing many of their conscious and unconscious activities. In most cases, these rhythms are in coordination with sun exposure time. Over hundreds of cycles and rhythms have been discovered in the human body, which have sophisticated mechanisms to regulate and change. The present study aimed to evaluate the relationship between mortality rate of patients and time trends of request to pre-hospital emergency medical services (PEMS) in Tehran, Iran.

**Material and methods:** In this cohort study with follow-up, 2,094 patients having inclusion criteria were selected among 7,432 requests to the emergency department in Tehran during a six-month period in 2012. The chosen variables were assessed through a researcher-made questionnaire. The relationship between time trends of patient's request and incidence of deaths caused by heart attack and survival of patient was evaluated and interpreted during this period.

**Results:** The findings of our study indicated an almost sinusoid rhythm in 8-hour cycle and an increasing rhythm from morning to night during a four-hour period and a certain elevation in the number of requests during night compared to the daytime. Within the 8-

hour cycle in the study population, the graph had three peaks at early morning, noon and late night. Difference in odds of dying between two genders was significant ( $p$  value = 0.021). Some age ranges showed different patterns of mortality.

**Conclusion:** Acute chest pain in patients appears to have a rhythmic pattern with a maximum incidence at late night and around noon. It seems that the major part of the obtained pattern is different from patterns of other countries.

**Key words:** Acute Chest Pain, Daily Cycle, Time Trends, Pre-hospital Emergency Medical Services

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## Introduction

There are rhythmic periods in organisms' body influencing many of their conscious and unconscious activities. The most common of these rhythms is circadian rhythm that repeats approximately every 24 hours. The circadian rhythm can be used to determine hormone levels, predict the risk of stroke, skin inflammation, body temperature, blood pressure and risk of death caused by cardiovascular events (1-3).

Studying the role of circadian rhythm in the incidence of acute coronary syndrome has risen by Muller et al. for the first time in 1985 [4]. Complementary investigations demonstrated that the most common incidence time of ischemic heart disease occurs in the morning between 6 am and noon 12 pm. The possible mechanism suggested for this rhythm proposes that in the early morning hours after awakening with the onset of physical activities and emotional stress, catecholamine secretion is enhanced which results in elevated blood pressure and heart rate; on the other hand, oxygen supply of cardiac tissue is decreased due to coronary vasoconstriction. Coinciding with the above-mentioned phenomena, platelet adhesion can be increased due to decreased physical activity. Collectively, these parallel and sequential processes cause a systematic approach in repetitions, which can be considered in prediction of the risk of acute coronary syndrome. Evaluation of the time related to the incidence of acute coronary syndrome is important to determine its time pattern based on circadian rhythm. It seems that if a certain process exists in the pattern of circadian cycle, it would be hoped that the incidence of myocardial infarction could be delayed or prevented by modifying this process (5).

Investigating the request pattern of patients with chest pain who call the emergency medical services could act as an approach capable of indicating the time trends of heart attack incidence. Evaluating the factors and backgrounds of cardiovascular diseases incidence plays a key role in the prevention and treatment of these diseases. On the other hand, identification of risk factors such as different incidence times of symptoms including different times of day, month and season of the year can serve as a warning sign for doctors to pay more attention and quickly respond to cardiovascular problems.

This study was designed and conducted to investigate the relationship between mortality of patients with acute chest pain and the incidence time pattern of acute coronary syndromes in Tehran's EMS department, and to determine the request time trends of request for help, to identify additional factors affecting the formation of this time pattern, and to employ the results of this study for choosing strategies of prevention and timely treatment in cardiovascular diseases.

## Materials and Methods

The present cohort study was carried out in a six-month period in 2012 to investigate the factors affecting the short-term mortality of patients with acute chest pain in collaboration with Tehran's EMS department; 3,229 patients with sudden chest pain were examined at different hours of the day.

Initially, technicians were investigated on how to record complaint of patients with acute chest pain calling Tehran's EMS. After determining the specified keyword of "heart disease", all recorded audio files of requests were collected. Out of the recorded 7,200 audio files in the six-month study period, 3,229 files met the inclusion criteria; 2,094 of these cases had one-month follow-up information in terms of survival or death, which were found to be suitable to enroll in the study and for collection of data.

Inclusion criteria were men and women over 45 years old with complaint of acute chest pain disseminated in the precordial or substernal regions for 20 minutes (or more) prolonged during the visit by EMS, without any other diagnosis justifying non-cardiac chest pain.

Exclusion criteria included deficiencies in the recorded information, patient's dissatisfaction with treatment in referred center and leaving there with personal consent resulting in uncertainty of illness outcome, death during delivery to the hospital or before arrival of ambulance and outpatient treatment at home.

In order to validate the accuracy of the data, 332 patients with available records in the archives of the hospital out of the 400 patients admitted to three selected hospitals, were studied to compare information extracted from their records with the information recorded by Tehran's EMS. After completing the checklists, the data obtained from the present study was entered into a computer and analyzed by SPSS software. The time of EMS call was calculated using descriptive statistical tests. The differences in studied variables among the different groups were analyzed by t-test and Chi-square in terms of being quantitative or qualitative, and the relationship between the defined factors and the rate of cardiovascular mortality within one week and one month after onset of symptoms was considered significant according to  $P$ -value < 0.05.

## Results

Overall, out of 3,229 eligible cases, 1,617 (50.1%) and 1,612 (49.9%) requests were related to men and women, respectively. Analysis of file-based mortality status demonstrated that 1,135 patients (35.3%) had an uncertain outcome, and mortality rate was 0.9% in the first week and 2.3% in the first month. Considering the uncertain outcomes, survival rate was 64% in the first week and 62.5% in the first month.

The mean age of participants was over 60 years and the mean systolic blood pressure in the first visit was in the border range and diastolic blood pressure was normal (Table 1).

**Table 1: Some quantitative characteristics of patients requesting help from pre-hospital EMS in Tehran, Iran (2012)**

Characteristics of patients	Gender	Mean	Lower limit of 95% confidence interval	Upper limit of 95% confidence interval
Age	Male	62.00	61.23	62.78
	Female	60.76	59.99	61.52
Systolic blood pressure	Male	135.93	134.74	137.12
	Female	135.03	133.90	136.16
Diastolic blood pressure	Male	78.16	77.35	78.96
	Female	77.68	76.92	78.45

**Figure 1: Frequency distribution radar chart for requesting help from pre-hospital EMS during 24 hours of a day in Tehran, Iran (2012)**

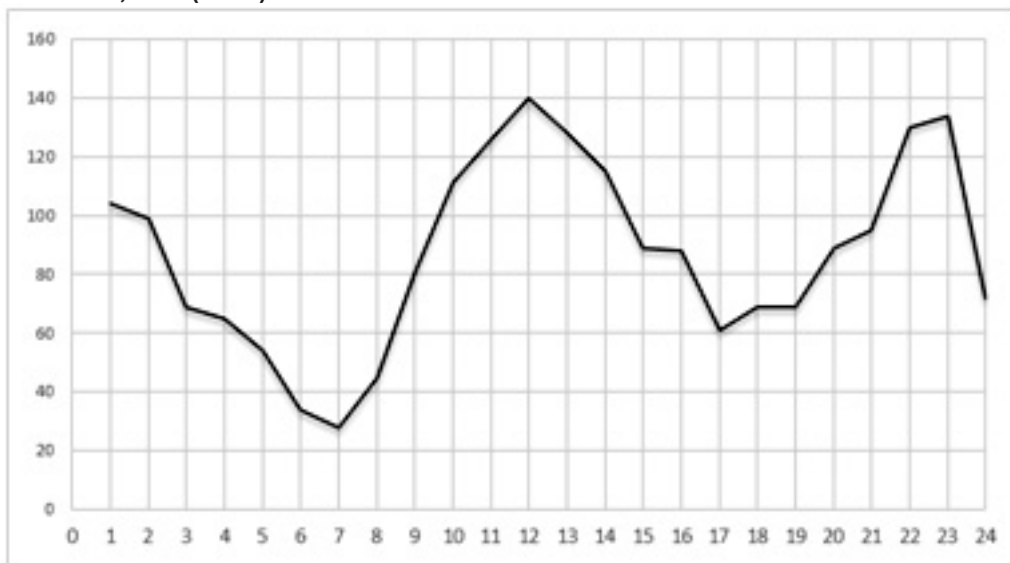


Figure 1 represents the 24-hour request pattern in 3,229 cases recorded with the primary complaint of chest pain. According to this figure, the highest requests for help are related to between 10 am to 2 pm, the second at 10 pm to 12 pm and the third at 1 am to 4 am. By dividing 24 hours into day (0:00 am-6:00 am) and night (6:01 am to 24:00 pm), the highest requests for help are related to day with 79.7%. By dividing 24 hours into four periods (with six-hour intervals), the highest requests for help were seen at 18:00 pm- 24:00 pm with 30.8%; the requests in the second place were found at 12:00 pm -18:00 pm with 27.8%. In dividing the 24 hours into six periods (with four-hour intervals), the number of requests was increased at late night (20:00 pm to 24:00 pm) with 20.6% and at noon (12:00 pm to 16:00 pm) with 20.1%. The highest mortality rate among the population in the first week of follow-up was in the age range of 80-84 years and then over 85 years. Totally, the highest number of deaths was observed respectively in 12:00 pm to 14:00 pm, 1:00 am to 2:00 am, 18:00 pm to 21:00 pm and 9:00 am to 10:00 am.

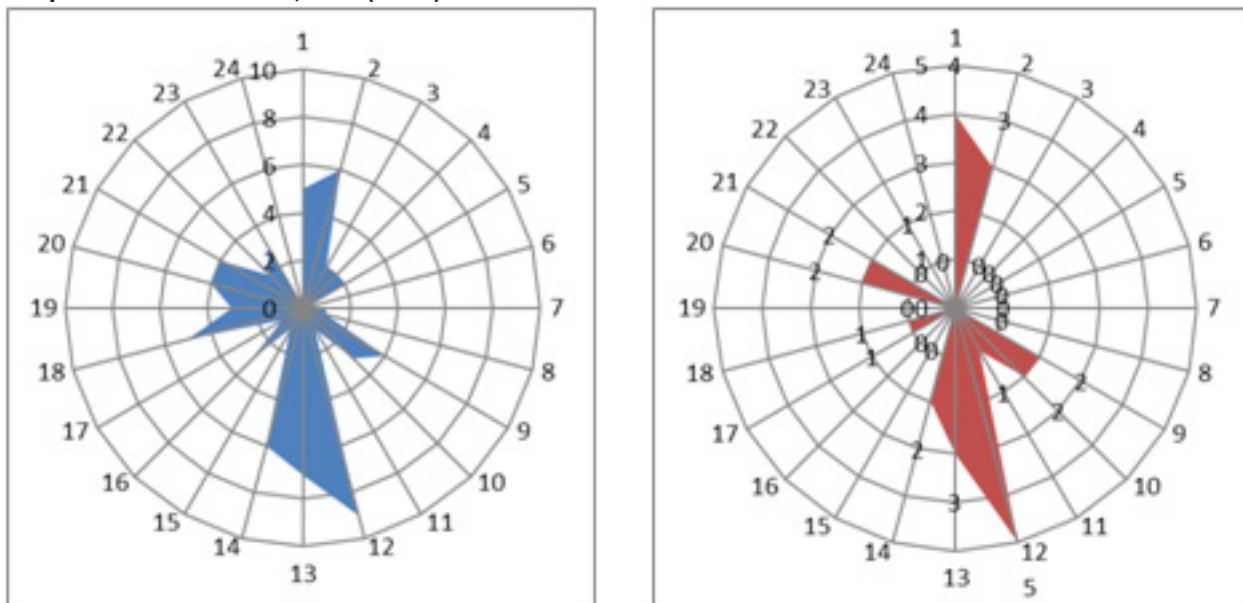
According to detailed reviews and studying the patients at an early stage of follow-up, the most EMS calls by dividing 24 hours into two periods were related to the nighttime; the request pattern in the first week and the first month in 24 hours is comparable (Figure 2). In the same group, most of the requests, by dividing 24 hours into four periods (with six-hour intervals) were associated with late night (18:00 pm to 24:00 pm) with 30.8%, and the second place was related to early afternoon (12:00 pm to 18:00 pm) with 27.8%. By dividing 24 hours into six periods (with four-hour intervals), the most requests for help were in late night (20:00 pm to 24:00 pm) with 20.6% in first place, shortly before noon (8:00 am to 12:00 pm) with 21.8% in at second place, and in the early hours of the afternoon (12:00 pm to 16:00 pm) with 20.1% in third place (Table 2).

Based on one-hour division of 24 hours, the highest number of requests for help was respectively at 12:00 pm, and then at 23:00 pm and 24:00 pm. Most of the requests (66.3%) were found in the age range of less than 65 years (Figure 2).

**Table 2: Relationship between mortality rates during four-hour periods a day (in the first week and first month) of the patients requesting help from pre-hospital EMS in Tehran, Iran (2012)**

Periods	At the end of the first week			At the end of the first month	
	Total	Survival	Dead	Survival	Dead
0:00 am to 4:00 am	337(100)	330(97.90)	7(2.1)	322(95.5)	15(4.5)
4:00 am to 8:00 am	161(100)	161(100)	0(0.0)	157(97.5)	4(2.5)
8:00 am to 12:00 pm	457(100)	447(97.8)	10(2.2)	440(96.3)	17(3.7)
12:00 pm to 4:00 pm	420(100)	415(98.8)	5(1.2)	403(96)	17(4)
4:00 pm to 8:00 pm	288(100)	284(68.6)	4(1.4)	275(95.5)	13(4.5)
8:00 pm to 24:00 pm	431(100)	428(99.3)	3(0.7)	422(97.9)	9(2.1)
Total	2094(100)	2065(98.6)	29(1.4)	2019(96.4)	75(3.6)

The obtained statistics on mortality were different in terms of gender and age of the patients. Most deaths caused by heart attack in the first week occurred in people older than 65 years, which has statistically significant difference ( $P$  value = 0.000). In the first month, the highest cases of cardiac death were in the patients older than 65 years and that has statistically significant difference ( $P$  value = 0.000). In the present study, significant difference was observed in mortality rate within one week and one month between women and men; so that it was 2% in men and 0.8% in women during one-week follow-up, and was 4.4% in men and 2.7% in women during one-month follow-up. The odds of dying were significantly different in two genders ( $P$  value = 0.021). The odds of dying specific for heart disease was elevated with increasing the rank of age range, which was predictable and represented the effect of symptoms and increased early mortality in these age ranges (Table 3).

**Figure 2: Frequency distribution of mortality in studied population based on one-hour periods during 24 hours of a day, (blue diagram in the first month and red diagram in the first week after requesting help from pre-hospital EMS in Tehran, Iran (2012))****Table 3: Frequency distribution of mortality in the first week after requesting help from pre-hospital EMS relative to population in Tehran, Iran (2012)**

Age group	Cardiac death in the first week				Cardiac death in the first month			
	Alive	Deceased	Population	Rate	Alive	Deceased	Population	Rate
45-49	(100) 467	(0) 0	536009	0.087	(100) 467	(0) 0	536009	0
50-54	(99.7) 339	(0.3) 1	459349	0.074	(99.7) 339	(0.3) 1	459349	0.002
55-59	(100) 225	(0) 0	352510	0.064	(98.7) 222	(1.3) 3	352510	0.008
60-64	(98.9) 267	(1.1) 3	247074	0.109	(96.7) 261	(3.3) 9	247074	0.036
65-69	(98.7) 148	(1.3) 2	181695	0.083	(93.3) 140	(6.7) 10	181695	0.055
70-74	(98.2) 218	(1.8) 4	137243	0.161	(94.6) 209	(5.4) 12	137243	0.087
75-79	(95.1) 154	(4.9) 8	101477	0.159	(88.3) 143	(11.7) 19	101477	0.187
80-84	(99.4) 161	(0.6) 1	61527	0.016	(97.5) 158	(2.5) 4	61527	0.065
+85	(89.7) 87	(10.3) 10	52801	0.189	(82.5) 80	(17.5) 17	52801	0.321
Total	(98.6) 2065	(1.4) 29	2129685	0.013	(96.4) 2019	(3.6) 75	2129685	0.035

## Discussion

In a study conducted on a Berlin medical service between 1987 and 1988, incidence time of respiratory distress symptoms, chest pain or loss of consciousness in patients with heart failure were studied based on age and gender. This study demonstrated that circadian variations in incidence of cardiopulmonary emergencies have maximum level between 6:00 am and 12:00 pm; this finding is inconsistent with the results of the present study. The remarkable point in this study that is somewhat consistent with the findings of our study is observing an increasing peak in patients with chest pain and respiratory disease in the evening or late daytime. The results of this study also indicated a higher mortality rate below 65 years old in the afternoon, and higher mortality rate in patients with age of 65 years in the morning. These ratios had no association with patient complaints and gender (7).

In a study conducted on 2,231 patients with acute myocardial infarction, the onset of acute chest pain was investigated during 12-hour and 6-hour periods. The results showed that the majority of symptoms occur between 10:00 am and 10:00 pm. The results of the present study are almost in line with this study (8).

There are several reports on the circadian pattern of myocardial infarction in diabetic patients. In research on 3,882 patients at 64 medical centers of the USA between August 1989 and September 1996, the patients with and without diabetes were studied and compared. This study revealed that increase in the incidence of acute myocardial infarction was in the early morning hours in both groups. In the present study, the most requests in patients with diabetes were related to noon between 10:00 am to 14:00 pm (9).

Mueller et al. (1985) investigated circadian cycle in myocardial infarction in the USA for the first time. A sharp rise in the numbers of pain onset was observed in the early hours of the morning (6:00 am). In 703 patients, the first increase in CK-MB level was considered as the onset time of myocardial infarction. Given that maximum cases of myocardial infarction in early morning hours were about three times more than late night, the increase in CK-MB level confirmed the impact of circadian rhythm (4). The results of this study are inconsistent with our findings.

In another study by Kinjo et al. (2001) in Japan entitled "effect of circadian rhythm variation on the incidence of acute myocardial infarction", the researchers examined the role of circadian rhythm changes in acute coronary syndrome within 6 periods of 4 hours a day, starting from 8:00 am. The highest incidence of the disease was observed in two periods of 8:00 am-12:00 pm (in the morning) and 20:00 pm-24:00 pm (at night). Assessments of subgroups demonstrated that the highest incidence in the early morning period included women over 65 years old. In addition, the highest incidence in the night period involved men less than 65 years old, employees and those who had a habit of smoking and alcohol consumption. Finally, the

researchers concluded that the risk of myocardial infarction in smoking and alcoholic young men is higher in the early hours of morning (10), which is less consistent with the results of our study in terms of the incidence time pattern of chest pain. The periodicity of the cycle of myocardial infarction incidence is in line with the results of the present study.

## Conclusion

The results of this study emphasize a certain circadian pattern in the patients with acute chest pain. Most of the requests were related to the nighttime and then around noon. In addition, the mortality of the age ranges in the morning and evening showed a different pattern in comparison with other studies. It made findings of this study different from other studies, indicating further attention to conduct better-organized studies.

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