Circadian and weekly variation and the influence of environmental variables in acute myocardial infarction

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Abstract

Objectives The aim of our study was to investigate the circadian and weekly variation and assess the influence of environmental variables on the occurrence of acute myocardial infarction (AMI).

Methods Our study population consisted of 2983 consecutive patients admitted with AMI between January 2006 and May 2008. Data were abstracted from hospital records and partially from an electronic database. In patients with a known time of onset of AMI, circadian variation was analysed. In all patients, weekly variation of onset of AMI was analysed. Information on daily mean temperature, sunny hours, rainy hours, maximal humidity and mean atmospheric pressure was obtained from the KNMI database and the influence of these environmental variables on the incidence of AMI was analysed.

Results and conclusion Incidence of AMI shows a circadian pattern with an increase in occurrence during daylight. AMI occurs equally on each day of the week and no relation was found between environmental variables and the occurrence of AMI.

Keywords Acute myocardial infarction · Circadian variation · Daily variation · Environmental variables

Introduction

According to the literature, the time of onset of acute myocardial infarction (AMI) has a circadian pattern, which has been described in a number of studies during the past decades. Most of these studies show an early morning peak [1–5]; i.e. a peak in onset during the dark-to-light transition period, although a secondary peak in the evening has also been reported [4, 6]. Diabetics seem to lack a specific risk in the morning and have a more uniform day distribution [7], whereas no difference was found in various subsets of patients defined with respect to gender, age and previous myocardial infarction [4, 5]. A circadian rhythm could not be detected either in patients receiving beta-adrenergic blocking agents [3].

Besides a circadian pattern, a weekly variation in time of onset of AMI has been suggested with an increased risk on Monday, presumably associated with stress [8]. Other possible external triggers that have been mentioned are physical exertion, sexual activity, mental stress and extreme emotional stress as seen in war situations [5, 9, 10]. Seasonal variation has also been reported, showing an increase in AMI during the winter months compared with the other seasons [11, 12].

Only a few studies have investigated the relationships between meteorological variables and the incidence of AMI [12, 13]. Previous data suggest a potential harmful effect of low temperatures on the occurrence of cardiovascular events. Conflicting results are reported concerning maximal ambient humidity, with most research showing a relationship between high humidity and the occurrence of coronary heart disease [12].

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The aim of our study is first to investigate the presence and characteristics of circadian variations in the onset of AMI in a large single-centre population in the Netherlands. A second aim is to assess the possible effects of environmental variables on the occurrence of AMI. Identification of specific triggers for the onset of AMI might be helpful for improving preventive strategies and to adjust logistics in hospitals during possible vulnerable periods.

Methods

Data source

We retrospectively analysed data from all STEMI patients who underwent primary PCI at the Catharina Hospital in Eindhoven between January 2006 and May 2008. During that period, 907 patients were participating in a randomised trial and data on baseline characteristics and time of onset were abstracted from the electronic database of that trial. Of the other patients, data were collected by reviewing hospital charts. Time of onset was noted in the hospital charts according to the oral information the treating physician received from the patient. Environmental data were obtained from the Dutch Meteorological Institute (KNMI). The studied variables were: hour of the day, day of the week, 24-hour mean temperature (degrees Celsius), daily sunshine (hours), daily rain (hours and mm), maximal relative humidity (percent) and 24-hour mean atmospheric pressure (hPa).

Data analysis

The time of day of AMI onset was analysed in patients with a known time of onset and was divided into one-hour intervals during 24 h and in four 6-hour intervals: 00.00–06.00 h; 06.00–12.00 h; 12.00–18.00 h; 18.00–24.00 h. Furthermore, the incidence of onset during daylight was compared with incidence at night. The definition of day/night was calculated according to the different sunrise and sunset times during the study period. For analysing weekly variations, all patients presenting during the considered period were included. Chi-squared goodness-of-fit tests were performed to test for uniformity of the distribution of onset of symptoms and risk ratios were calculated for each individual day of the week.

All the environmental variables were binned into categories (Table 1). The number of AMIs per day was hypothesised to be independent of environmental variables. Deviation from the presumed uniform distribution was assessed by chi-squared tests. A p-value <0.05 was considered significant. Relative risk for a particular variable was expressed as a ratio to the risk associated with the presumed uniform distribution. To assess seasonal variation, seasons

Table 1 Environmental variables and daily distribution of AMI in the considered period

Variables ^a	Days	# AMI	# AMI observed/day	P
Mean temperature (°C)				1.00
<0	33	107	3.24	
0–5	138	510	3.70	
5–25	450	1591	3.53	
15–25	229	750	3.28	
>25	8	25	3.13	
Sunny hours (h)				0.98
0–5	499	1761	3.53	
5–10	257	906	3.53	
>10	102	316	3.10	
Rainy hours (h)				0.98
<5	757	2649	3.5	
5–10	81	260	3.2	
>10	20	74	3.7	
Maximal humidity (%)				1.00
<80	37	111	3.00	
80–90	105	362	3.45	
90–95	272	940	3.46	
95–98	277	964	3.48	
>98	167	606	3.63	
Mean pressure (hPa)				1.00
<1000	53	196	3.70	
1000–1010	176	616	3.50	
1010–1020	331	1124	3.40	
1020–1030	234	811	3.47	
1030–1040	58	213	3.67	
>1040	6	23	3.83	

^a Values are per 24 h

were defined as follows: winter (21 December to 19 March), spring (20 March to 20 June), summer (21 June to 22 September) and fall (23 September to 20 December). The length of the seasons was adjusted to 91 days because of the varying lengths of each season.

Statistical analyses were performed using SPSS version 19.0. Continuous data were expressed as mean $\pm$ SD, and categorical data as a percentage.

Results

A total of 2983 patients with AMI were admitted during the study period. The mean age of all patients was 62.0 years (SD $\pm$ 12.5) and 73 % were male. Reliable information about time of onset was available in 2003 patients. No other differences in baseline characteristics were present between these patients and those without knowledge of time of onset, except for a higher rate of (ex) smokers in the group with a known time of onset.

Time of onset of pain

The frequency of symptom onset by 1- and 6-hour intervals and during daylight versus night is shown in Fig. 1. The incidence of onset of AMI was highest during the daytime between 09.00 and 16.00 h. Baseline characteristics of patients with onset symptoms during the daylight versus night-time are shown in Table 2. The occurrence of AMI was equally distributed for each day of the week (Fig. 2; Table 3).

Environmental variables

Table 4 shows how the environmental variables are distributed during the period from January 2006 to May 2008. The Netherlands has a mild climate, generally with mean daily temperatures between 5 and 15 degrees Celsius. On colder days (between 0 and 5 degrees Celsius), the average daily number of AMIs was slightly higher than on warmer days, but this difference was not significant. Also comparison of occurrence of AMI in the four different seasons showed an equal distribution (Fig. 2.) No relationship was found between the incidence of AMI and the number of rainy hours a day, maximal humidity and mean pressure.

Discussion

Our study shows an increased incidence of onset of AMI during daylight in a large study population. Furthermore, the occurrence of AMI showed no weekly variation. No significant influence of environmental variables was found.

Circadian variation and day of the week variation

Our finding of a higher incidence of onset of AMI during daylight is in contrast with the results of almost all previous reports on this subject, suggesting an early morning peak [1, 3–5, 7]. The occurrence of an early morning peak with an increased incidence of onset of AMI between 06.00 and 12.00 h is also mentioned in textbooks on cardiology [14]. The following possible underlying mechanisms have been proposed: a morning increase in sympathetic tone leading to increases in blood pressure, heart rate, coronary tone and myocardial contractility; a morning increase in blood viscosity, coagulability and platelet aggregability; and increased morning levels of serum cortisol and plasma catecholamines leading to sympathetic over-activity resulting in increased myocardial demand. However, based upon our study results, these hypotheses should be considered conjectural. Only one earlier study in STEMI patients, by Henriques et al., also found a circadian variation in onset of AMI similar to our results, but that study was primarily

Fig. 1 Circadian pattern of pain onset in patients with an acute myocardial infarction by 1-hour intervals (a), 6-hour intervals (b) and in daylight versus night-time (c) ($n=2003$)

Table 2 Demographic, clinical and angiographic characteristics according to time of treatment

		Daylight		Night	
		<i>n</i> =1204		<i>n</i> =799	
Age, years	2003	61.4±12.2		61.1±12.2	
Gender					
Male	1462	871	59.6 %	591	40.4 %
Female	541	333	61.6 %	208	38.4 %
Diabetes					
Yes	202	118	58.4 %	84	41.6 %
No	1569	948	60.4 %	621	39.6 %
Unknown	232	138	59.5 %	94	40.5 %
Hypertension					
Yes	580	367	63.3 %	213	36.7 %
No	1197	704	58.8 %	493	41.2 %
Unknown	226	133	58.8 %	93	41.2 %
Hyperlipidaemia					
Yes	449	265	59.0 %	184	41.0 %
No	1301	787	60.5 %	514	39.5 %
Unknown	253	152	60.1 %	101	39.9 %
History of cardiovascular disease					
Yes	385	218	56.6 %	167	43.4 %
No	1432	876	61.2 %	556	38.8 %
Unknown	186	110	59.1 %	76	40.9 %
Smoking					
Yes	907	555	61.2 %	352	38.8 %
No	637	384	60.3 %	253	39.7 %
Unknown	459	265	57.7 %	194	42.3 %
Family history					
Yes	775	440	56.8 %	335	43.2 %
No	735	482	65.6 %	253	34.4 %
Unknown	493	282	57.2 %	211	42.8 %
Culprit					
LAD	781	462	59.2 %	319	40.8 %
RCA	822	524	63.7 %	298	36.3 %
CX	339	184	54.3 %	155	55.7 %
Graft	24	13	54.2 %	11	45.8 %
1, 2 or 3 vessel disease					
1	1027	627	61.1 %	400	38.9 %
2	580	334	57.6 %	246	42.4 %
3	353	214	60.6 %	139	39.4 %

LAD left anterior descending artery, *RCA* right coronary artery, *CX* circumflex artery

designed to investigate the impact of circadian variation on the practice of primary angioplasty. They found better outcomes and procedural success rates in patients treated during duty hours compared with patients treated during off-hours [15].

The presumed existence of an early morning peak is based on studies reporting the same 6-hour time intervals

Fig. 2 Weekly (a) and seasonal (b) distribution of acute myocardial infarction (*n*=2396)

as in our study. These 6-hour time intervals have been reported repeatedly and seem to be chosen randomly, just taken for granted and repeated by every following author. When looking at the four different bins, a higher incidence of AMI could be presumed between 06.00 and 12.00 h. However, when split into 24 h (Fig. 1), the presumed peak diminishes and the range with a higher occurrence of onset of AMI broadens from 09.00 h to at least 16.00 h. Comparing daylight versus night-time further strengthens the finding of a higher occurrence of AMI during the day. Thus,

Table 3 Relative risks for different timing of onset symptoms

	# AMI observed	RR
Day/night		
Daylight	1204	1.20
Night	799	0.80
Day of the week		
Sunday	439	1.03
Monday	423	0.99
Tuesday	375	0.88
Wednesday	441	1.03
Thursday	420	0.99
Friday	486	1.14
Saturday	399	0.94
Seasons		
Spring	634	1.06
Summer	568	0.95
Fall	631	1.05
Winter	563	0.94

findings strongly depend on the methods used to show differences during daytime and the results of such analyses (including ours) must be interpreted carefully.

In contrast to other studies, we found no evening peak [4, 6]. Neither did we find a weekly pattern in occurrence of AMI in our study. Previous studies on the weekly distribution of AMI showed conflicting results. A Monday peak was reported in some papers [8, 16], suggesting the stress of returning to work may induce a heart attack. Since the mean age was 62 years in our study, it can be presumed that a great deal of our study population was already retired and therefore did not experience any work-related stress. Furthermore, the distribution of AMI during the week was not different between patients above 60 years of age compared with younger patients in our study (Fig. 3).

Environmental variables

We found no influence of environmental variables on the time of onset of AMI, in contrast to some other studies showing an increase of AMI in the winter months [11, 12,

Table 4 Median values of the meteorological variables in the considered period

Variables	Median	Minimal	Maximal
Mean temperature (°C)	10.3	−4,4	28.5
Sunny hours (h)	4.6	0	15.4
Rainy hours (h)	1.75	0	21.8
Maximal humidity (%)	96	47	100
Mean pressure (o.1 hPa)	10,162	9819	10,441

Fig. 3 Weekly distribution of acute myocardial infarction according to age over (a) and under (b) 60 years ($n=2982$)

17]. Furthermore, many studies indicate that low temperature alone or large intraday temperature differences increase the rate of AMI [18, 19]. This potentially harmful effect of cold on the occurrence of AMI was suggested to result from increased sympathetic nervous activity in cold conditions. The mild climate in the Netherlands with less extreme temperature changes can be the reason we could not confirm these results.

The MONICA project, a 10-year survey amongst 257,000 patients with myocardial infarction and coronary deaths, found a V-shaped relationship for atmospheric pressure and the rate of events [18]. Our study found no relationship between AMI and atmospheric pressure at all, which is in line with other studies performed in parts of Europe with a comparable climate to that in the Netherlands [12]. Furthermore, one study suggested that the amount of rain and wind speed is associated with a reduction in the occurrence of winter mortality, explained by a reduction of outdoor excursions when it is raining and thereby preventing outdoor cold stress. We did not find any relationship between the amount of rain and the rate of AMI.

Limitations

Our study has several limitations. First, the exact time of onset of symptoms is sometimes hard to determine because the information is subjective and was not always reported. Other retrospective studies used the enzyme-estimated (CK-MB) onset of infarction, with a presumed 4-hour lag-time between onset of symptoms and the rise of enzymes. Second, measured temperatures and pressures in a specified area may not accurately represent the actual individual exposure to those variables. Third, the lack of influence of environmental variables on the occurrence of AMI could be explained by the mild climate in the Netherlands and therefore cannot be extrapolated to regions with more extreme differences in temperature.

Conclusions

In contrast to previous studies, the present study shows an increased incidence of AMI during daylight without influence of the day of the week. There was no early morning peak, as often believed. Furthermore, the occurrence rate of AMI was not influenced by environmental variables in the Netherlands.

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