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ORIGINAL ARTICLE

Influence of Circadian Rhythms and Seasonal and Annual Variations on Acute Myocardial Infarction Incidence

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Abstract

Background/Aim: Acute myocardial infarction (AMI) is a consequence of complete coronary artery occlusion. There is a considerable seasonal variation in the incidence of AMI. The aim of the study was to establish a circadian and seasonal pattern of AMI.

Methods: A retrospective observational study was conducted, using the database of the Institute of Emergency Medical Service of the City of Novi Sad. The study included 982 patients, both male and female, diagnosed with AMI (I.21 - ICD-10 code) in the period between 15 March 2018 and 14 March 2022. Data were classified according to the time of the day, days of the week, quarters and months. Data were analysed by using descriptive statistical methods, Mann- Whitney U test, Chi-squared test and Fisher's exact test.

Results: AMI most frequently occurred between 6 am and 2 pm (389; 39.6 %). A statistically significant incidence of AMI was calculated for the periods between 6 am and 2 pm ($\chi^2 = 39.69$; $p < 0.001$) and between 2 pm and 10 pm ($\chi^2 = 28.06$; $p < 0.001$). Most cases of AMI were noted on Monday (153; 15.6 %) and in January (93; 9.5 %). The highest incidence of AMI was in the period between 15 March 2021 and 14 March 2022 (304; 31.0 %), while the lowest incidence was noted between 15 March 2019 and 14 March 2020 (190; 19.3 %).

Conclusion: Circadian, seasonal and annual rhythm may have a significant impact on the incidence of AMI. This fact can have an important role in the prevention, timely recognition and adequate treatment of acute coronary disease.

Key words: Acute myocardial infarction; Circadian rhythm; Seasonal variations; Annual variations.

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Introduction

Acute myocardial infarction (AMI) is a consequence of complete coronary artery occlusion and a leading cause of death worldwide. In the last decades, there is growing evidence of circadian rhythms and their influence on the pathogenesis of cardiovascular diseases.[1-3] Biological rhythms are cyclical and represent a periodical and predictable component of biological rhythmic patterns. Depending on cycle length, these oscillations can be circadian, related to biological processes that occur regularly at 24-hour intervals (its name is derived from the Latin *circa*, meaning around, and *dies* – day); *circaseptan* (7-day interval); *circamensual* (approximately 28-day interval) or *circannual* (one-year interval).[3]

In humans, biological rhythms are evidenced in many organic processes. The effects of circadian rhythm on heart frequency and systolic and diastolic blood pressure are well documented. The

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maximal diuresis is between 1 pm and 10 pm. The vital capacity of the lungs reaches its peak between 8 am and 3 pm. In addition to the circadian rhythms, there are seasonal variations of the physiological parameters as well. The highest values of arterial blood pressure are recorded in winter.[3]

Many studies have investigated the impact of circadian rhythms and seasonal variations on the pathogenesis of some diseases. Studying the effects of biological rhythms on the human organism could help in the identification of the risk factors, prevention and treatment of these diseases. So far, most articles from the literature have been dealing with its effects on vascular disorders.[2]

Aim of the study was to analyse the influence of circadian rhythms and seasonal variation on the incidence of AMI and establish a circadian and seasonal pattern of AMI.

Methods

A retrospective observational study was conducted, using the database of the Institute of Emergency Medical Service of the City of Novi Sad, collecting prehospital records of 982 patients, both male and female, diagnosed with AMI (I.21 - ICD-10 code) in the period between 15 March 2018 and 14 March 2022. Analysed data were classified into the 8-hour periods (6 am-2 pm; 2 pm-10 pm; 10 pm-6 am), days of the week, quarters and months. Data were analysed by using descriptive statistical methods, the Mann-Whitney U test, Chi-squared test and Fisher's exact test.

Results

AMI most frequently occurred between 6 am and 2 pm (389 patients; 39.6 %). There was a statistically significant difference for the periods between 6 am and 2 pm ($\chi^2 = 39.69$; $p < 0.001$) and between 2 pm and 10 pm ($\chi^2 = 28.06$; $p < 0.001$) in relation to the period between 10 pm and 6 am. No statistically significant difference was found for the periods between 6 am and 2 pm and 2 pm and 6 pm ($\chi^2 = 1.05$; $p = 0.31$) (Table 1).

Table 1: Distribution of acute myocardial infarction (AMI) according to the part of a day

8-hour period	N	%
6 am-2 pm	389	39.6
2 pm-10 am	361	36.8
10 pm-6 am	232	23.6
Total	**982**	**100.0**

N: number of patients; %: percentage of total number of patients;

According to the EMS Call Centre, AMI was most frequently diagnosed on Monday (153 patients; 15.6 %) (Table 2). However, no statistically significant difference was found between the days of the week ($\chi^2 = 11.43$; $p = 0.07$).

Table 2: Daily distribution of acute myocardial infarction (AMI)

Days	N	%
Monday	153	15.6
Tuesday	145	14.8
Wednesday	152	15.5
Thursday	145	14.8
Friday	152	15.5
Saturday	111	11.2
Sunday	124	12.6
Total	**982**	**100.0**

N: number of patients; %: percentage of total number of patients;

AMI was most frequently recorded in January (93 patients; 9.5 %) (Table 3). However, no statistically significant difference was found between the months ($\chi^2 = 7.64$; $p = 0.75$).

Table 3: Monthly distribution of acute myocardial infarction (AMI)

Month	N	%
January	93	9.5
February	64	6.5
March	85	8.7
April	84	8.6
May	79	8.0
June	75	7.6
July	83	8.5
August	80	8.1
September	82	8.4
October	92	9.3
November	84	8.6
December	81	8.2
Total	**982**	**100.0**

N: number of patients; %: percentage of total number of patients;

AMI occurred most frequently in the fourth quarter of a year (257 patients; 26.3 %). Nevertheless, no statistically significant difference was found between the quarters ($\chi^2 = 0.82$; $p = 0.85$).

Table 4: Yearly distribution of acute myocardial infarction (AMI)

12-month period	N	%
15/03/2018 - 14/03/2019	235	23.9
15/03/2019 - 14/03/2020	190	19.3
15/03/2020 – 14/03/2021	253	25.8
15/03/2021 – 14/03/2022	304	31.0
Total	**982**	**100.0**

N: number of patients; %: percentage of total number of patients;

Most cases of AMI were recorded in the period between March 2021 and March 2022 (304 patients; 31.0 %), while its lowest frequency was between March 2019 and March 2020 (190 patients; 19.3 %). In this period, a statistically significant lower incidence of AMI was noted, compared to the periods between March 2018 and March 2019 (χ^2 = 4.77; p = 0.03), between March 2020 and March 2021 (χ^2 = 8.96; p = 0.003) and between March 2021 and March 2022 (χ^2 = 26.31; p < 0.001). In addition to this, the incidence of AMI significantly increased in the period between March 2021 and March 2022, compared to the periods between March 2018 and March 2019 (χ^2 = 8.83; p = 0.003) and between March 2020 and March 2021 (χ^2 = 4.67; p = 0.03) (Table 4).

Discussion

Circadian rhythms and seasonal variations affect many physiological processes in the organism. Their effect on the pathogenesis of AMI has been researched for decades. Presented study shows a higher incidence of AMI during the winter months, with the peak in January and during the morning hours (between 6 am and 2 pm). The USA study also points to the significant seasonal variations in the incidence of AMI, with 53 % more cases in the winter months than in the summer months. The winter peak was also reported in studies from Greece, Great Britain and most European countries. Besides, these studies show that the highest incidence of AMI was on Monday, in the morning hours.[3-8]

The role of circadian rhythms and seasonal variations in the pathogenesis of AMI has never been completely elucidated. Many studies established a correlation between increased sympathetic activity and ischaemic events in patients with existing cardiovascular diseases. Sympathetic tonicity is increased in low ambient temperatures and early morning hours, leading to arterial blood pressure elevation, increased heart rate and higher viscosity of blood. In patients with cardiovascular diseases, the higher concentration of catecholamines with increased myocardial oxygen demand and elevated vascular resistance result in hypertension and symptoms of acute coronary disease.[3-5] Compared to this, studies based on the surgical registers of appendectomy revealed no seasonal variations in the number of cases and no significant decrease in the incidence of appendicitis during the summer. Taking into consideration the higher incidence of AMI on cold days, regardless of the season, it is reasonably presumed that climate conditions may have a part in the pathogenesis of AMI.[5]

Although presented study found no statistically significant difference between the days of the week, AIM most frequently occurred on Mondays. This is consistent with the results of other studies from the literature. Many authors relate the age of patients and their employment status to the prevalence of particular days of a week in the pathogenesis of AMI. This study included patients over 18 and most of them were older than 65 and retired, so adaptation to the stress in the working environment can be excluded from the pathogenesis. German studies found no significant difference in the sex of the patients.[4, 9, 10]

In the previous studies, AIM was most common in the early morning hours, with the peak at 9 am. Presented study also showed the highest incidence of AIM in the hours between 6 am and 2 pm, with a statistically significant difference for the periods between 6 am and 2 pm and between 2 pm and 10 pm compared to the period between 10 pm and 6 am. In the early morning hours, sympathetic tonicity is increased and there are higher concentrations of catecholamines and cortisol in the blood. Combined with higher blood viscosity and platelet agglutination, this can result in arterial plaque rupture and the development of thrombosis. Some of the earlier studies reported a lower morning peak of the incidence of AIM in smokers. This can be explained by the decreased sensibility of catecholamine receptors due to prolonged stimulation. The heart rate in smokers is constantly increasing. It was also shown that medications for tachycardia and hypertension may have a role in the prevention of AMI. The morning peak in the incidence of AIM is flattened in the population of patients taking beta-blockers and aspirin. This study did not analyse the therapy of patients due to incomplete data in database.[10-13]

In the period between March 2021 and March 2022, there were significantly more patients with AIM than in the periods' of March 2018 –March 2019 and March 2020 – March 2021. On the other hand, the lowest incidence of AIM was in the period between March 2019 and March 2020, which was statistically significant. A similar phenomenon, with a reduction of the incidence of AMI in the pre-pandemic period and its steady increase during the pandemic, was observed in the studies conducted in Great Britain, New York, Italy and worldwide. Such a dynamic can be ascribed both to the outbreak of the COVID-19 pandemic with the overload of healthcare systems and to the reluctancy of patients (sometimes with high-risk medical conditions) to go for regular check-ups due to the fear of acquiring infection in the hospital, which resulted in an initial lower number of cases with AMI. A study in Italy reported a lower incidence of patients presenting with STEMI, compared to non-STEMI, while in the studies from Austria and the USA, no significant difference was found between the two types of AMI. Symptoms of STEMI are more pronounced and hard to ignore. Presented study did not analyse the type of AMI. With additional data, it could be possible to identify factors that could lead to the increased incidence of AMI, with the ultimate goal of a timely diagnostic and early recognition, as well as the education of the population, especially the elderly, about the signs and symptoms of AMI.[14-16]

Limitations of the study

This study did not analyse age- and sex-specific differences, comorbidities and chronic therapy. These characteristics could be considered in future studies to identify the subgroups at higher risk.

Conclusion

This study showed the influence and significance of circadian rhythms and seasonal variations on the incidence of AMI. A higher incidence was observed in the winter months, especially in January, in the early morning hours. These facts can play a significant role in the prevention, early recognition and treatment of cardiovascular diseases.

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Conflict of interest

None.

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