# ACİL SERVİSE BAŞVURAN HASTALARDA AKUT KORONER SENDROMUN DİURNAL VARYASYONUN KORONER ANJİYOGRAFİYE GÖRE DEĞERLENDİRİLMESİ

# **Evaluation of Acute Coronary Syndrome with Coronary Angiography Due To Diurnal Variation in the Patients who Admitted to The Emergency Department**

İbrahim ÇALTEKİN<sup>1</sup>(0000-0002-3973-0655), Şiho HİDAYET<sup>2</sup>(0000-0002-4103-9345), Levent ALBAYRAK<sup>1</sup> (0000-0002-4288-8170), Emre GÖKÇEN<sup>1</sup>(0000-0002-6018-6105), Atakan SAVRUN<sup>3</sup>(0000-0001-7468-4159), Mikail KUŞDOĞAN<sup>1</sup>(0000-0003-4075-8601), Yaşar TURAN<sup>4</sup>(0000-0003-0285-1338)

#### ÖZET

Amaç: Bu çalışmanın amacı, akut miyokard enfarktüslü hastaların diurnal varyasyon gösterip göstermediğini ve etkilenen koroner arter ile bu diurnal varyasyon arasındaki ilişkiyi araştırmaktır.

**Material ve Metodlar:** Ocak-Aralık 2017 tarihleri arasında akut koroner sendrom semptomları ile Yozgat Bozok Üniversitesi Acil Servisine başvuran hastalar retrospektif olarak incelendi. 24 saatlik zaman dilimi içinde diurnal değişimler 6 grupta (00:01-04:00, 04:01-08:00, 08:01-12:00, 12:01-16:00, 16:01-20:00, 20:01-00:00), mevsimsel değişimler 4 grupta (İlkbahar, Yaz, Sonbahar, Kış), haftalık değişimler ise 2 grupta (Hafta içi, Hafta sonu) analiz edilmiştir.

**Bulgular:** Koroner arterlerin gün içindeki diurnal etkilenimleri incelendiğinde istatistiksel olarak anlamlı bir sonuç bulunamadı. Diurnal etkilenimin hafta içi ile hafta sonu değişimleri incelendiğinde ise hafta içi olgularında her üç koroner arter lezyonlarının hafta sonu görülen lezyonlara oranla istatistiksel olarak artmış olduğu saptandı (p<0,05).

**Sonuç:** Çalışmamızın sonucu olarak günlük değişkenlik tespit edilmediyse de, koroner arter hastalığının artmasının, hafta içi günlerde stres ve yoğun iş temposu gibi sosyal nedenlerden etkilendiği açıkça belirlenmiştir.

Anahtar kelimeler: Diurnal ritim; Myocard infartüsü; Acil servis

#### ABSTRACT

**Backround:** The aim of this study is to investigate whether patients with acute myocardial infarction exhibited diurnal variation and the relationship between the affected coronary artery and this diurnal variation. **Material and Methods:** The patients admitted to the emergency department of Yozgat Bozok University with symptoms of acute coranary syndrome between January and December 2017 were retrospectively analyzed. In 24 hour period diurnal changes were analyzed in 6 groups (00:01-04:00, 04:01-08:00, 08:01-12:00, 12:01-16:00, 16:01-20:00, 20:01-00:00), seasonal changes were analyzed in 4 groups (Spring,

Summer, Autumn, Winter), and weekly changes were analyzed in 2 groups (Weekday, Weekend). **Results:** When diurnal effects coronary arteries were examined, no statistically significant results were found. When the changes of diurnal effect were observed at weekdays and weekends, it was found that all three coronary artery lesions were statistically increased at weekdays compared to the lesions seen at weekends (p<0,05).

**Conclusion:** Although daily diurnal variability was not detected as a result of our study, it was clearly determined that the increase in coronary artery disease was affected by social reasons such as stress and intensive work pace during the weekdays.

Keywords: Diurnal rhytm; Myocardial infarction; Emergency department

<sup>1</sup>1Bozok Üniversitesi Tıp Fakültesi Acil Tıp A.D., Dr. Öğr. Üyesi, Yozgat, Türkiye

<sup>2</sup>Malatya İnönü Üniversitesi Tıp Fakültesi Kardiyoloji A.D., Dr. Öğr. Üyesi, Malatya, Türkiye

<sup>3</sup>Ordu Üniversitesi Tıp Fakültesi Acil Tıp A.D., Dr. Öğr. Üyesi Yozgat, Türkiye

<sup>4</sup>Bozok Üniversitesi Tip Fakültesi Kardiyoloji A.D., Dr. Öğr. Üyesi, Yozgat, Türkiye

İbrəhim ÇALTEKİN, Dr. Öğr. Üyesi Şiho HİDAYET, Dr. Öğr. Üyesi Levent ALBAYRAK, Dr. Öğr. Üyesi Emre GÖKÇEN, Dr. Öğr. Üyesi Atakan SAVRUN, Dr. Öğr. Üyesi Mikail KUŞDOĞAN, Araş. Gör. Yaşar TURAN, Dr. Öğr. Üyesi

#### İletişim:

Dr. Öğr. Üyesi İbrahim ÇALTEKİN, Bozok Üniversitesi Tıp Fakültesi Acil Tıp A.D. Yozgat, Türkiye Yozgat Bozok Üniversitesi Erdoğan Akdağ Yerleşkesi Atatürk Yolu 7. Km 66100 Merkez / YOZGAT Tel: +90530-528 3677 e-mail: drcaltekin@gmail.com

Geliş tarihi/Received: 12.07.2019 Kabul tarihi/Accepted: 24.07.2019 **DOI:** 10.16919/bozoktip.591272

Bozok Tip Derg 2019;9(3):146-150 Bozok Med J 2019;9(3):146-150

# BACKROUND

Atherosclerosis is considered to be a chronic inflammatory disease which is known to develop due to different vascular and extravascular reasons (1). Acute myocardial infarction caused by atherosclerosis is emphasized in recent years when the diurnal variation is observed (2).

Some cardiovascular pathophysiological processes; including acute myocardial infarction, arrhythmia, sudden cardiac death and hemodynamic parameters (blood pressure, heart rate) are affected by the circadian rhythm (3). There is a significant increase in acute myocardial infarction in the first days of the week, seasonal changes, or early hours of the day. (4, 5). However, although it is known that acute coronary syndromes (unstable angina, non-ST elevation myocardial infarction and ST elevation myocardial infarction) frequently show diurnal variation, it cannot be explained by circadian rhythm alone. Pulmonary diseases of the patient, cortisol cycle, hematological properties of blood like fibrinolytic and thrombosis properties are effective with different mechanisms in the development of cardiac events (6).

In this study, we investigated whether patients with acute myocardial infarction exhibited diurnal variation and the relationship between the affected coronary artery and this diurnal variation.

## **METHODS**

Our university hospital is one of the two centers that perform primary percutaneous coronary intervention (PPCI) in Yozgat province. Acute coronary syndrome cases are accepted in the emergency department of our hospital.

In this study, the patients admitted to the emergency department of Yozgat Bozok University with symptoms of acute coranary syndrome between January and December 2017 were retrospectively analyzed. The study population comprised 174 patients who admitted to our emergency department with non-ST elevation myocardial infarction (non-STMI), and ST-elevation myocardial infarction (STMI). The study was approved by the Ethics Committee of Yozgat Bozok University.

All patients with acute coronary syndrome who were admitted to the emergency department by outpatient and emergency responders (112 teams) were included in the study. Age, gender, vital signs, diurnal, seasonal and weekly variations of the patients were examined and evaluated. In 24 hour period diurnal changes were analyzed in 6 groups (00:01-04:00, 04:01-08:00, 08:01-12:00, 12:01-16:00, 16:01-20:00, 20:01-00:00), seasonal changes were analyzed in 4 groups (Spring, Summer, Autumn, Winter), and weekly changes were analyzed in 2 groups (Weekday, Weekend).

The patients were evaluated according to the results of the angiography, and the pure lesions with acute coronary syndrome were evaluated in 3 anatomical localizations (LAD, RCA, Cx). Patients who were under 18 years of age, who had multiple coronary involvements due to angiography, who had get a diagnosis of unstable angina, who had undergone coronary angiography, who had previously undergone coronary artery disease and who had undergone coronary artery bypass surgery were excluded from our study.

## Statistical analysis

Statistical analyses were completed using the Statistical Package for Social Sciences (SPSS Inc; Chicago, IL, USA) version 20.0 software. Characteristics of the study population were described as means ±SD and standard descriptive statistics were used to analyze the diurnal variation of myocardial infarction. The Chi-square test or Fischer's exact test (when chi-square test assumptions do not hold due to low expected cell counts), where appropriate, was used to compare the proportions in different groups. A value of p<0.05 was accepted as statistically significant.

## RESULTS

A total of 174 patients, 132 (75.9%) male and 42 (24.1%) female were included in the study. Systolic blood pressure (SBP) of the patients was 129.60  $\pm$  17.12, and diastolic blood pressure (DBP) of the patients was 77.33  $\pm$  8.59. When the acute coronary syndromes of patients included in the study were evaluated, 79 (45.4%) were non-STMI and 95 (54.6%) were STMI (table 1).

Variables         n: 174           Age         62.45±12.3           Male         132 (%75.9)           Female         42 (%24.1)           SBP         129.60±17.12           DPB         77.33±8.59           Weekday         130 (%74.4)           Weekend         44 (%25.3)           Spring         27 (%15.5)           Summer         31 (%17.8)           Autumn         48 (%27.6)           Winter         68 (%39.1)           00:01-04:00         14 (%8)           04:01-08:00         7 (%4)           08:01-12:00         55 (%31.6)           12:01-16:00         51 (%29.3)           16:01-20:00         19 (%10.9)           20:01-00:00         58 (%16.1)           Non-STMI         79 (%45.4)           STMI         95 (%54.6)           LAD         72 (%41.4)           RCA         60 (%34.5)           Cx         42 (%24.1)		
Or         Product           Male         132 (%75.9)           Female         42 (%24.1)           SBP         129.60±17.12           DPB         77.33±8.59           Weekday         130 (%74.4)           Weekend         44 (%25.3)           Spring         27 (%15.5)           Summer         31 (%17.8)           Autumn         48 (%27.6)           Winter         68 (%39.1)           00:01-04:00         14 (%8)           04:01-08:00         7 (%4)           08:01-12:00         55 (%31.6)           12:01-16:00         51 (%29.3)           16:01-20:00         19 (%10.9)           20:01-00:00         58 (%16.1)           Non-STMI         79 (%45.4)           STMI         95 (%54.6)           LAD         72 (%41.4)           RCA         60 (%34.5)	Variables	n: 174
Female       42 (%24.1)         SBP       129.60±17.12         DPB       77.33±8.59         Weekday       130 (%74.4)         Weekend       44 (%25.3)         Spring       27 (%15.5)         Summer       31 (%17.8)         Autumn       48 (%27.6)         Winter       68 (%39.1)         00:01-04:00       14 (%8)         04:01-08:00       7 (%4)         08:01-12:00       55 (%31.6)         12:01-16:00       51 (%29.3)         16:01-20:00       19 (%10.9)         20:01-00:00       58 (%16.1)         Non-STMI       79 (%45.4)         STMI       95 (%54.6)         LAD       72 (%41.4)         RCA       60 (%34.5)	Age	62.45±12.3
SBP         129.60±17.12           DPB         77.33±8.59           Weekday         130 (%74.4)           Weekend         44 (%25.3)           Spring         27 (%15.5)           Summer         31 (%17.8)           Autumn         48 (%27.6)           Winter         68 (%39.1)           00:01-04:00         14 (%8)           04:01-08:00         7 (%4)           08:01-12:00         55 (%31.6)           12:01-16:00         51 (%29.3)           16:01-20:00         19 (%10.9)           20:01-00:00         58 (%16.1)           Non-STMI         79 (%45.4)           STMI         95 (%54.6)           LAD         72 (%41.4)           RCA         60 (%34.5)	Male	132 (%75.9)
DPB         77.33±8.59           Weekday         130 (%74.4)           Weekend         44 (%25.3)           Spring         27 (%15.5)           Summer         31 (%17.8)           Autumn         48 (%27.6)           Winter         68 (%39.1)           00:01-04:00         14 (%8)           04:01-08:00         7 (%4)           08:01-12:00         55 (%31.6)           12:01-16:00         51 (%29.3)           16:01-20:00         19 (%10.9)           20:01-00:00         58 (%16.1)           Non-STMI         79 (%45.4)           STMI         95 (%54.6)           LAD         72 (%41.4)           RCA         60 (%34.5)	Female	42 (%24.1)
Weekday       130 (%74.4)         Weekend       44 (%25.3)         Spring       27 (%15.5)         Summer       31 (%17.8)         Autumn       48 (%27.6)         Winter       68 (%39.1)         00:01-04:00       14 (%8)         04:01-08:00       7 (%4)         08:01-12:00       55 (%31.6)         12:01-16:00       51 (%29.3)         16:01-20:00       19 (%10.9)         20:01-00:00       58 (%16.1)         Non-STMI       79 (%45.4)         STMI       95 (%54.6)         LAD       72 (%41.4)         RCA       60 (%34.5)	SBP	129.60±17.12
Weekend         44 (%25.3)           Spring         27 (%15.5)           Summer         31 (%17.8)           Autumn         48 (%27.6)           Winter         68 (%39.1)           00:01-04:00         14 (%8)           04:01-08:00         7 (%4)           08:01-12:00         55 (%31.6)           12:01-16:00         51 (%29.3)           16:01-20:00         19 (%10.9)           20:01-00:00         58 (%16.1)           Non-STMI         79 (%45.4)           STMI         95 (%54.6)           LAD         72 (%41.4)           RCA         60 (%34.5)	DPB	77.33±8.59
Spring         27 (%15.5)           Summer         31 (%17.8)           Autumn         48 (%27.6)           Winter         68 (%39.1)           00:01-04:00         14 (%8)           04:01-08:00         7 (%4)           08:01-12:00         55 (%31.6)           12:01-16:00         51 (%29.3)           16:01-20:00         19 (%10.9)           20:01-00:00         58 (%16.1)           Non-STMI         79 (%45.4)           STMI         95 (%54.6)           LAD         72 (%41.4)           RCA         60 (%34.5)	Weekday	130 (%74.4)
Summer       31 (%17.8)         Autumn       48 (%27.6)         Winter       68 (%39.1)         00:01-04:00       14 (%8)         04:01-08:00       7 (%4)         08:01-12:00       55 (%31.6)         12:01-16:00       51 (%29.3)         16:01-20:00       19 (%10.9)         20:01-00:00       58 (%16.1)         Non-STMI       79 (%45.4)         STMI       95 (%54.6)         LAD       72 (%41.4)         RCA       60 (%34.5)	Weekend	44 (%25.3)
Autumn       48 (%27.6)         Winter       68 (%39.1)         00:01-04:00       14 (%8)         04:01-08:00       7 (%4)         08:01-12:00       55 (%31.6)         12:01-16:00       51 (%29.3)         16:01-20:00       19 (%10.9)         20:01-00:00       58 (%16.1)         Non-STMI       79 (%45.4)         STMI       95 (%54.6)         LAD       72 (%41.4)         RCA       60 (%34.5)	Spring	27 (%15.5)
Winter         68 (%39.1)           00:01-04:00         14 (%8)           04:01-08:00         7 (%4)           08:01-12:00         55 (%31.6)           12:01-16:00         51 (%29.3)           16:01-20:00         19 (%10.9)           20:01-00:00         58 (%16.1)           Non-STMI         79 (%45.4)           STMI         95 (%54.6)           LAD         72 (%41.4)           RCA         60 (%34.5)	Summer	31 (%17.8)
00:01-04:00       14 (%8)         04:01-08:00       7 (%4)         08:01-12:00       55 (%31.6)         12:01-16:00       51 (%29.3)         16:01-20:00       19 (%10.9)         20:01-00:00       58 (%16.1)         Non-STMI       79 (%45.4)         STMI       95 (%54.6)         LAD       72 (%41.4)         RCA       60 (%34.5)	Autumn	48 (%27.6)
04:01-08:00       7 (%4)         08:01-12:00       55 (%31.6)         12:01-16:00       51 (%29.3)         16:01-20:00       19 (%10.9)         20:01-00:00       58 (%16.1)         Non-STMI       79 (%45.4)         STMI       95 (%54.6)         LAD       72 (%41.4)         RCA       60 (%34.5)	Winter	68 (%39.1)
08:01-12:00         55 (%31.6)           12:01-16:00         51 (%29.3)           16:01-20:00         19 (%10.9)           20:01-00:00         58 (%16.1)           Non-STMI         79 (%45.4)           STMI         95 (%54.6)           LAD         72 (%41.4)           RCA         60 (%34.5)	00:01-04:00	14 (%8)
12:01-16:00       51 (%29.3)         16:01-20:00       19 (%10.9)         20:01-00:00       58 (%16.1)         Non-STMI       79 (%45.4)         STMI       95 (%54.6)         LAD       72 (%41.4)         RCA       60 (%34.5)	04:01-08:00	7 (%4)
16:01-20:00       19 (%10.9)         20:01-00:00       58 (%16.1)         Non-STMI       79 (%45.4)         STMI       95 (%54.6)         LAD       72 (%41.4)         RCA       60 (%34.5)	08:01-12:00	55 (%31.6)
20:01-00:00       58 (%16.1)         Non-STMI       79 (%45.4)         STMI       95 (%54.6)         LAD       72 (%41.4)         RCA       60 (%34.5)	12:01-16:00	51 (%29.3)
Non-STMI         79 (%45.4)           STMI         95 (%54.6)           LAD         72 (%41.4)           RCA         60 (%34.5)	16:01-20:00	19 (%10.9)
STMI         95 (%54.6)           LAD         72 (%41.4)           RCA         60 (%34.5)	20:01-00:00	58 (%16.1)
LAD 72 (%41.4) RCA 60 (%34.5)	Non-STMI	79 (%45.4)
RCA 60 (%34.5)	STMI	95 (%54.6)
	LAD	72 (%41.4)
Cx 42 (%24.1)	RCA	60 (%34.5)
	Сх	42 (%24.1)

SBP (sistolic blood pressure), DPB (diastolic blood pres)sure), Non-STMI (non-ST elevated myocardial infarction), STMI (ST elevated myocardial infarction), LAD (left anterior descending), RCA (right coronary artery), Cx (circumflex artery)

 Table 2. Diurnal variation of coronary arteries

	00:01- 04:00	04:01- 08:00	08:01- 12:00	12:01- 16:00	16:01- 20:00	20:01- 24:00	р
LAD	5 (6,9%)	3 (4,2%)	24 (33,3%)	17 (23,6%)	8 (11,1%)	15 (20,8%)	0,640
RCA	7 (11,7%)	3 (5,0%)	19 (31,7%)	17 (28,3%)	5 (8,3%)	9 (15,0%)	0,796
Сх	2 (4,8%)	1 (2,4%)	12 (28,6%)	17 (40,5%)	6 (14,3%)	4 (9,5%)	0,338

LAD (left anterior descending), RCA (right coronary artery), Cx (circumflex artery)

The patients were classified as LAD (left anterior descending) 72 (41.4%), RCA (right coronary artery) 60 (34.5%) and Cx (Circumflex artery) 42 (24.1%) according to the affected coronary artery (tablo 1). When diurnal effects of these coronary arteries were examined, no statistically significant results were found. When examined respectively; p=0,640 for LAD, p=0,796 for RCA and p=0,338 for Cx (table 2).

When the changes of diurnal effect were observed at weekdays and weekends, it was found that all three coronary artery lesions were statistically increased at weekdays compared to the lesions seen at weekends (p<0,05)(table 3) (figüre 1).

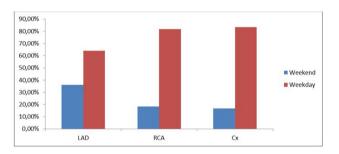


Figure 1. Distribution of coronary lesions according to weekday and weekend However, when the seasonal changes of these lesions were examined, no statistically significant result was found (p=0.747) (tablo 3).

**Table 3.** Seasonal and weekly diurnal variation of coronary arteries

Özellikler	LAD N:72	RCA N: 60	Cx N: 42	р	
Weekend	26 (36,1%)	11 (18,3%)	7 (16,7%)	0.022	
Weekday	46 (63,9%)	49 (81,7%)	35 (83,3%)	0.022	
Spring	13 (18.1%)	6 (10.0%)	8 (19.0%)		
Summer	14 (19.4%)	11 (18.3%)	6 (14.3%)	0.747	
Autumn	19 (26.4)	16 (26.7%)	13 (31.0%)	0.747	
Winter	26 (36.1)	27 (45.0%)	15 (35.7%)		

LAD (left anterior descending), RCA (right coronary artery), Cx (circumflex artery)

At the same time, there was also no statistically significant result of diurnal changes in acute coronary syndromes (non-STMI, STMI) (p=0,882)(table 4).

# DISCUSSION

It is known that acute myocardial infarction is one of the most important causes of death and causes wide clinical situations ranging from silent ischemia to sudden cardiac death (7). There are some studies showing diurnal variation even in patients developing cardiac arrest for various reasons including obstructive sleep apnea syndrome (8, 9).

Some studies have reported a significant increase in acute myocardial infarction in the early hours of the day (10) and this is the result of circulating changes in the hormonal, catecholaminergic system, coagulation mechanisms, blood pressure, and heart rate (11).

However, it was also reported that some inflammatory mediators have been shown to play a role in the pathogenesis of acute coronary syndromes and these mediators increased in the morning (1, 12). While diurnal variation was analyzed during the day, 24 hour period was examined in 12 equal parts in some studies (2), and in 4 equal parts in some studies (10). In our study, results were analyzed in 6 equal parts. It was reported that there was a peak in the early first hours of the day and a second peak in the cases after the second half of the day. (12-14). However, in our study, no significant results were found when all three coronary artery lesion development was examined according to six groups of 24 hours.

It was determined that the frequency of acute coronary syndromes increased during the first day of the week. Sayer et al., stated that there was a significant increase in the admission of the patients especially in the first days of the week and emphasized that all of the clinics like silent angina, non-STMI, STMI, and variant angina can be seen in this period (4). In accordance with the literature, in our study, it was determined that there were a statistically significant increase in acute coronary syndromes in all three coronary arteries (LAD, RCA, Cx) lesions during the weekdays.

In addition to the studies indicating that the diurnal changes of acute coronary syndromes (15), additional pathologies in these patients have been shown to have an effect on this diurnal variation (6). In our study, coronary anatomy was considered in many aspects, statistically, there was no statistical significance in the diurnal variation during the day and seasonally, however, a significant increase in the incidence of acute coronary syndromes were observed in the winter period.

Table 4. Diurnal variation of acute coronary syndrome

	Diurnal Period						
	00:01-04:00	04:01-08:00	08:01-12:00	12:01-16:00	16:01-20:00	20:01-24:00	р
STMI	8 (57,1%)	4(57,1%)	29 (52,7%)	25 (49,0%)	12 (63,2%)	17 (60,7%)	
							0,882
non-STMI	6 (42,9%)	3 (42,9%)	26 (47,3%)	26 (51,0%)	7 (36,8%)	11 (39,3%)	

Non-STMI (non-ST elevated myocardial infarction), STMI (ST elevated myocardial infarction), LAD (left anterior descending), RCA (right coronary artery), Cx (circumflex artery)

#### CONCLUSION

There are many studies that show the diurnal, weekly and seasonal variations of acute coronary syndromes, however, there were no studies determining the effect of coronary anatomy and retained coronary arteries on this diurnal change. Although daily diurnal variability was not detected as a result of our study, it was clearly determined that the increase in coronary artery disease was affected by social reasons such as stress and intensive work pace during the weekdays.

#### REFERENCES

**1.** Dominguez-Rodriguez A, Abreu-Gonzalez P, Kaski JC. Inflammatory systemic biomarkers in setting acute coronary syndromes--effects of the diurnal variation. Current drug targets. 2009;10(10):1001-8.

**2.** Bae MH, Ryu HM, Lee JH, Lee JH, Kwon YS, Lee SH, et al. The impact of circadian variation on 12-month mortality in patients with acute myocardial infarction. Korean circulation journal. 2010;40(12):616-24.

**3.** Suarez-Barrientos A, Lopez-Romero P, Vivas D, Castro-Ferreira F, Nunez-Gil I, Franco E, et al. Circadian variations of infarct size in acute myocardial infarction. Heart (British Cardiac Society). 2011;97(12):970-6.

**4.** Sayer JW, Wilkinson P, Ranjadayalan K, Ray S, Marchant B, Timmis AD. Attenuation or absence of circadian and seasonal rhythms of acute myocardial infarction. Heart (British Cardiac Society). 1997;77(4):325-9.

**5.** Reiter R, Swingen C, Moore L, Henry TD, Traverse JH. Circadian dependence of infarct size and left ventricular function after ST elevation myocardial infarction. Circulation research. 2012;110(1):105-10.

**6.** Durgan DJ, Young ME. The cardiomyocyte circadian clock: emerging roles in health and disease. Circulation research. 2010;106(4):647-58.

**7.** Leiza JR, de Llano JM, Messa JB, Lopez CA, Fernandez JA. New insights into the circadian rhythm of acute myocardial infarction in subgroups. Chronobiology international. 2007;24(1):129-41.

**8.** Jones-Crawford JL, Parish DC, Smith BE, Dane FC. Resuscitation in the hospital: circadian variation of cardiopulmonary arrest. The American journal of medicine. 2007;120(2):158-64.

**9.** Gami AS, Howard DE, Olson EJ, Somers VK. Day-night pattern of sudden death in obstructive sleep apnea. The New England journal of medicine. 2005;352(12):1206-14.

**10.** Seneviratna A, Lim GH, Devi A, Carvalho LP, Chua T, Koh TH, et al. Circadian Dependence of Infarct Size and Acute Heart Failure in ST Elevation Myocardial Infarction. PloS one. 2015;10(6):e0128526.

**11.** Celik M, Celik T, Iyisoy A, Yuksel UC, Bugan B, Demirkol S, et al. Circadian variation of acute st segment elevation myocardial infarction by anatomic location in a Turkish cohort. Medical science monitor : international medical journal of experimental and clinical research. 2011;17(4):Cr210-5.

12. D'Negri CE, Nicola-Siri L, Vigo DE, Girotti LA, Cardinali DP. Circa-

dian analysis of myocardial infarction incidence in an Argentine and Uruguayan population. BMC cardiovascular disorders. 2006;6:1. **13.** Li J, Hua Q, Pi L, Tan J, Li B. Circadian variation on the onset of acute ST segment elevation myocardial infarction in diabetic subjects. Journal of cardiovascular disease research. 2010;1(1):23-6. **14.** Kanth R, Ittaman S, Rezkalla S. Circadian patterns of ST elevation myocardial infarction in the new millennium. Clinical medicine & research. 2013;11(2):66-72.

**15.** Virag JA, Lust RM. Circadian influences on myocardial infarction. Frontiers in physiology. 2014;5:422.