

CIRCADIAN VARIATIONS OF UNSTABLE ANGINA AND ACUTE MYOCARDIAL INFARCTION

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Gazi Medical Journal 1998; 9 : 107-111

SUMMARY :

Purpose: The aim of this study was to determine the circadian variations in the time and seasonal onset of acute myocardial infarction (AMI) and unstable angina pectoris (UAP). **Method:** Five - hundred patients with confirmed acute myocardial infarction (n=239) or unstable angina pectoris (n=261) were enrolled in the study. The time of onset of clinical symptoms was learned from patient interviews. **Results:** We observed a circadian variation in the onset of both unstable angina and AMI. Although there were two peaks at the second and third quarter of day for unstable angina pectoris ($p<0.001$), patients with AMI experienced the onset of pain in the third quarters of the day ($p<0.001$). The seasonal distribution of acute coronary syndromes was significantly nonuniform with a peak in autumn ($p<0.05$). **Conclusion:** According to our results, although we observed a different circadian variation in the time onset of both unstable angina and acute myocardial infarction, the autumn peak in the seasonal distribution of acute coronary syndromes was similar to the previous studies.

Key Words : Circadian Rhythms, Coronary Disease.

INTRODUCTION

Several cardiovascular diseases including sudden cardiac death, angina pectoris, and myocardial infarction have been reported to exhibit a circadian variation (1-4). In most studies of acute myocardial infarction (AMI) and angina pectoris the onset of symptoms have been demonstrated to peak either in midmorning or in late afternoon and early evening. Previous studies have shown the relation between onset of symptoms of AMI and awakening (5, 6). Many physiological factors which increase during the early morning hours, such as heart rate, plasma catecholamine levels, plasma cortisol levels, blood viscosity and platelet aggregability and which decrease such as

endogenous fibrinolytic activity, triggers myocardial ischemia during the morning hours (7). In addition, exogenous factors such as physical and mental activities and postural changes upon awakening trigger the morning increase in myocardial ischemia (8). The present study examines the time and the seasonal relation with the onset of AMI and unstable angina pectoris in patients who admitted to the coronary care unit of Gazi University, Faculty of Medicine.

MATERIAL AND METHODS

This retrospective study was based on the data of patients who were admitted to the coronary care unit of Gazi University, Faculty of Medicine with the

diagnosis of AMI or unstable angina pectoris (UAP) between May 1993 to February 1998. Five-hundred patients with confirmed AMI (n=239) or UAP (n=261) were enrolled in the study. The mean age of these patients was 58.26 (11.59); 394 male (79%) with a mean age of 56.81(11.37 and 106 female (21%) with a mean age of 63.65 (10.81). The time of onset of clinical symptoms was learned from the patient interviews. Patients having chest pain (or equivalent) in ischaemic nature or unstable pattern consisting of rest pain, new onset, severe or frequent angina, accelerating angina or clinical symptoms of evolving myocardial infarction, ST segment elevation of 1 mm or more in the extremity leads and of 2 mm or more in the chest leads were included in the study. Exclusion criteria were nonischemic or atypical pain, persistent ST segment elevation.

Data collected from these patients included time onset of pain, risk factors, and the season the patient admitted to the hospital.

Statistical Analysis

In this retrospectively defined analysis, we evaluated the presence of circadian variations in pain onset and seasonal distribution of AMI and UAP. The uniformity of myocardial infarction and unstable anginal onset of pain among all 24 1-hour intervals were tested using the x2 goodness-of-fit test. Based on a previous report of an increased incidence of myocardial infarction during the second quarter of the day, that is, 6:00AM to 12:00 noon x2 goodness-of-fit test was performed to determine differences among four 6-hour intervals

	%	Total/mean
Number of patients		500
Men	79	
Mean age(yr)		58.26±11.59
Men		56.81±11.37
Women		63.65±10.81
History of diabetes	12.8	
History of hypertension	41.2	
History of hyperlipidemia	19.6	
History of familial risk	37.2	
Smoker	59	

Table 1: Patient characteristics.

(12:00 midnight-6:00 AM, 6:00 AM -12:00 noon, 12:00 noon - 6:00 PM, 6:00 PM - 12:00 midnight). Only p values less than 0.05 were considered significant.

Similarly, chi-square statistics were used to test the uniformity of the seasonal onset of AMI and UAP. Only p values less than 0.05 were considered significant.

RESULTS

Clinical characteristics of 500 patients are shown in Table 1. The major risk factors of the patients were as follows: 59% were smoker, 41.2% had a history of hypertension, 37.2% had familial risk factor, 19.6% had hyperlipidemia and 12.8% had a history of diabetes mellitus. The time onset of AMI symptoms and UAP is shown in Fig. 1.

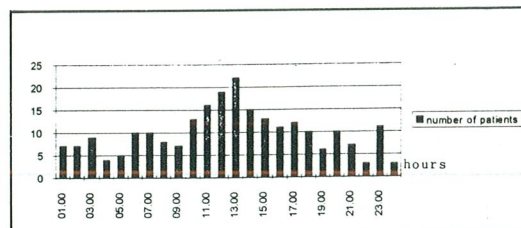
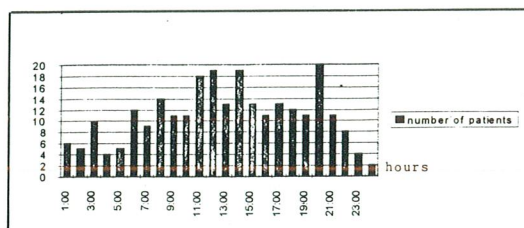


Fig - 1 : Circadian variations of the time onset of UAP (left) and AMI (Right).

The incidence of myocardial infarction assessed by onset of clinical symptoms exhibited a circadian variation with two peak periods during the second and the third quarter of the day (6:00 AM - 12:00 noon and 12:00 noon to 6:00 PM; Table 2 p<0.001). When we looked at the statistical analysis between these two groups the third quarter of the day makes the statistically significant peak in the incidence of myocardial infarction during the 24-hour circadian variations ($\chi^2=0.68$, p<0.05).

The incidence of UAP exhibited a circadian variation with two peaks during the second and the third quarter of the day (06:00 AM-12:00 noon and 12:00 noon-6:00 PM; Table 2 p<0.001). There was no statistically significant difference between these two peaks.

distribution was significantly nonuniform with a peak in autumn (p<0.05). While the seasonal distribution of AMI was having a peak during summer (Fig. 3A), UAP had a peak during winter (Fig. 3B). These peaks were statistically significant for two groups.

DISCUSSION

We observed a circadian variation in the onset of both unstable angina and AMI. Although there were two peaks at the second and the third quarter of the day for UAP, patients with AMI experience the onset of pain in the third quarter of the day. Our observations are not similar to those in previous studies. In most studies, the onset of AMI and UAP has been shown to occur with a peak in mid-morning and a secondary peak in late afternoon and

	Time of day			
	12:00midnight- 6:00AM	6:00AM- 12:00noon	12:00noon- 6:00PM	6:00PM- 12:00midnight
AMI patients(n)	43	73	83*	40
(%)	18	30.5	34.7*	16.7
UAP patients(n)	42	82**	81**	56
(%)	16.1	31.4**	31**	21.5

* p<0.001 compared with other times of the day

**p<0.001 compared with other times of the day but there are no statistically significant differences between the two of them.

Table 2 : Circadian Variations in the Incidence of AMI and UAP.

The seasonal distribution of AMI and UAP (acute coronary syndromes) is shown in Fig. 2. The

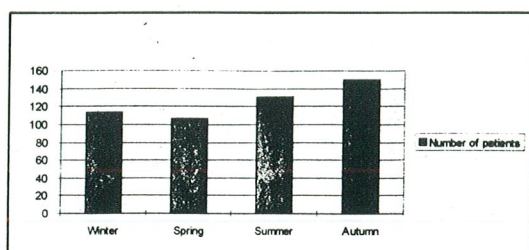


Fig - 2 : Seasonal distribution of AMI and UAP (Acute coronary syndromes).

early evening. Previous studies have shown that many factors such as blood pressure, heart rate, increased sympathetic tone, platelets, endogenous fibrinolytic activity, high plasma cortisol and epinephrine levels effect circadian variation in patients with UAP and AMI (7). It has been shown that various episodes may exist due to different mechanisms in the same individual (9). Willich et al. determined the time onset of AMI in all patients (n=1741) of the ISAM (Intravenous Streptokinase In Acute Myocardial Infarction) Study. The incidence of myocardial infarction was markedly increased between 6:00 AM and 12:00 noon in different subgroups. On the other hand, patients receiving β -adrenergic blockers before their infarction did not have an increased morning incidence of myocardial infarction. This subgroup experienced increasing incidence of myocardial infarction during the daytime until 6:00 PM (10). In a recent report, Goldberg et al. studied the relation

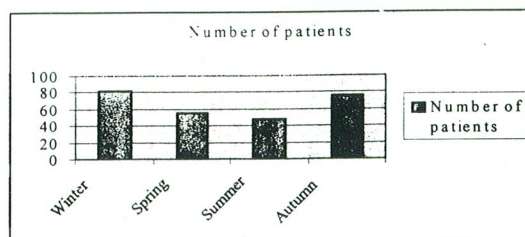
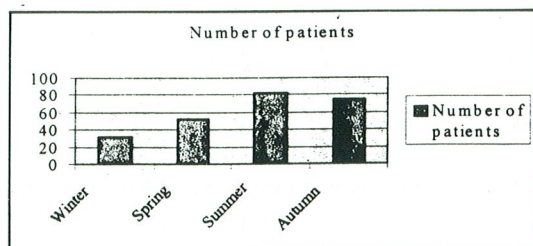


Fig - 3 : Seasonal distribution of acute AMI (Left) and UAP (Right).

between awakening and time onset of initial symptoms of AMI. They observed a 5-fold increase in the frequency of the onset of symptoms of AMI in the first hour after awakening (5). Peters et al also reported the time of onset of AMI and its relation with time of awakening. Their findings were similar to those in previous studies except a secondary peak 11 to 12 hour after awakening (11). In a recent study which used the database from the Holter Registry of the Cardiac Arrhythmia Suppression Trial (CAST) (n=22516) the analysis of seasonal data revealed nonuniform distribution with a peak in winter and autumn (12).

In conclusion, as our study was a retrospective study, all patients with acute ischemic symptoms at the time of presentation were included. Previous cardiac functions, previous therapy, waking-up time habits, and/or cultural differences may effect the late onset of peak values of AMI and UAP. Also there may be cultural differences between the studied populations of AMI and UAP, such as waking-up time habits, meal schedules, or activity patterns.

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