

# Weekly Distribution of Acute Coronary Syndrome. Analysis of the Epi-Cardio Registry.

## *Distribución de la frecuencia de síndrome coronario agudo acorde al día de la semana. Análisis del Registro Epi-Cardio*

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### ABSTRACT

**Background:** Acute coronary syndromes (ACS) seem to have a chronobiological distribution with seasonal, weekly and circadian variations. So far, there is no evidence in the published literature about the weekly distribution of ACS in Argentina; thus, it is unknown whether ACS have a specific pattern and which could be the associated variables.

**Objective:** The aim of this study was to analyze the weekly distribution of ACS and the differences in treatment and clinical outcome.

**Methods:** The distribution of non-ST-segment elevation (NSTE) (n=6,277) and ST-segment elevation (STE) ACS (n=4,237) was retrospectively analyzed according to the day of the week using the 2006-2012 Epi-Cardio registry.

**Results:** The frequency was higher during the first days of the week and descended during the weekend (overall ACS and NSTE-ACS p < 0.001, and STE-ACS p < 0.01), and was not related to either age or sex. In STE-ACS, the indication and the type of reperfusion therapy did not present differences according to the day of the week.

**Conclusions:** The frequency of hospitalization due to ACS is higher within the first weekdays and decreases during the weekend, with no differences in the use of complex resources or in the initial outcome.

**Key words:** Myocardial Infarction, Stress, Acute Coronary Syndrome.

### RESUMEN

**Introducción:** Una particularidad de los síndromes coronarios agudos (SCA) es que su distribución impresiona tener aspectos cronobiológicos, ya que no se mantiene estable a lo largo del año y varía incluso según el día de la semana y la hora del día. No tenemos conocimiento de evidencia publicada acerca de la distribución de los casos de SCA acorde al día de la semana en nuestro país, por lo que se ignora si sigue un patrón determinado y cuáles podrían ser las variables asociadas.

**Objetivo:** Analizar la distribución diaria de los casos de SCA y las eventuales diferencias en el tratamiento y la evolución clínica de los pacientes.

**Material y métodos:** Se estudió el número y la evolución de SCA sin ST elevado (SCA no-STE, n = 6.277) y con ST elevado al ingreso (SCA-STE, n = 4.237) acorde al día de la semana mediante el análisis del registro Epi-Cardio 2006-2012.

**Resultados:** La frecuencia fue mayor en los primeros días de la semana, descendiendo durante el fin de semana (global y SCA no-STE: p < 0,001; SCA-STE: p < 0,01), sin relación con la edad y el sexo. En los SCA-STE, la indicación y el tipo de perfusión no tuvieron diferencias según el día de la semana.

**Conclusiones:** La frecuencia de internaciones por SCA es mayor en los primeros días laborables y menor los fines de semana, sin diferencias en el uso de recursos complejos ni en la evolución inicial.

**Palabras clave:** Infarto del miocardio - Estrés - Síndrome coronario agudo

### Abbreviations

ACS	Acute coronary syndrome	STE-ACS	ST-segment elevation acute coronary syndrome
NSTE-ACS	Non-ST-segment elevation acute coronary syndrome		

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## INTRODUCTION

Since the creation of coronary care units, treatment of acute coronary syndromes (ACS) has evolved, with significant advances and important reduction of morbidity and mortality. (1) The better understanding of cardiovascular risk factors as hypertension, dyslipidemia and smoking habits and their management using complex strategies have reduced the incidence of this condition at early ages prolonging life expectancy. (2) However, there is little information in the literature about several less known aspects of ACS, as triggers of plaque rupture. (3, 4) Acute coronary syndromes seem to have a chronobiological distribution with seasonal, weekly and circadian variations. (5-8) Reasons for this phenomenon have not been well elucidated and the hypotheses explored include variation in hormone secretion, exposure to toxic environmental agents, weather variations and different psychosocial factors. (9)

So far, there is no evidence in the published literature about the weekly distribution of ACS in Argentina; therefore, it is unknown whether ACS have a specific pattern and which could be the associated variables.

The aim of this study was to determine the weekly distribution of ACS in Argentina using the information available in the Epi-Cardio Registry.

## METHODS

The distribution of non-ST-segment elevation (NSTEMI) and ST-segment elevation (STEMI) ACS cases was retrospectively analyzed according to the day of the week in which the patients were admitted. In-hospital outcome was analyzed in all patients, and the use and type of reperfusion therapy was evaluated in cases of STEMI-ACS. The information was retrieved from the database of the Epi-Cardio registry, a multicenter network of intensive care unit computer-based discharge summaries from 55 centers nationwide, with specific fields for different conditions.

### Statistical Analysis

Qualitative variables were expressed as numbers and percentages and continuous variables as mean and standard deviation. Subgroups were compared using contingency table analysis for discrete variables and the analysis of variance for parametric data for quantitative data. The distribution of cases by weekday was assessed using simple linear regression analysis, and coding day of the week as 1 = Monday and 7 = Sunday.

## RESULTS

The cohort consisted of 10,514 ACS cases, 4,237 of which corresponded to STEMI-ACS. Mean age of the total cohort was 60.6 years and average mortality was 2.8%. The occurrence of ACS was higher on Mondays (16.9%) with a descending trend toward the weekend. The lowest number of ACS occurred on Sundays (10.9%) (Figure 1). The association between the number of hospitalizations and the day of the week was evaluated using simple linear regression analysis and was statistically

significant for the total cohort of ACS ( $p < 0.01$ ;  $R^2$  0.88) as well as for STEMI-ACS ( $p < 0.001$ ;  $R^2$  0.78) and NSTEMI-ACS ( $p < 0.001$ ;  $R^2$  0.85) (Figure 1). When the days of the week were grouped in the pair Monday-Tuesday and compared with the pair Saturday-Sunday, the frequency of STEMI-ACS increased by 29.5% (1,358 vs. 1,048 cases), and that of NSTEMI-ACS by 65% (2,107 vs. 1,248 cases). This difference in the distribution of ACS by weekday was not influenced by age, sex or older age ( $> 65$  years) (Table 1). There were no significant differences in overall in-hospital mortality and in mortality stratified by type of ACS. In the subgroup of STEMI-ACS cases, no differences were observed in the percentage of patients presenting ST-segment elevation in the electrocardiogram (ECG) on admission, in the use of reperfusion treatment or in the type of reperfusion strategy, either thrombolysis or primary percutaneous coronary intervention (Table 1).

## DISCUSSION

Our findings are similar to those reported by previous publications from other countries, with the highest number of ACS occurring on Mondays. The largest registry on this topic was performed by Bodis et al. including more than 90,000 patients admitted to Hungarian hospitals for myocardial infarction over a 5-year period. (10) There was a characteristic weekly distribution of this pathology, with a peak detected on Mondays and a gradually decreasing tendency by the end of the week. A significant reduction in the number of events was observed during holidays compared with workweeks, suggesting an association with occupational stress. Of interest, this seasonal reduction in the frequency of ACS was only seen on Mondays.

The INTERHEART study was a case-control study carried out in 52 countries, evaluating the association between acute myocardial infarction and different cardiovascular risk factors. The odds ratio (OR) for psychosocial stress, including occupational stress, was 2.67, in the third place after dyslipidemia and smoking habits, and was higher than the OR corresponding to hypertension, diabetes and obesity. (11) In another study performed in England including more than 10,000 participants, occupational stress for coronary artery disease had a RR of 1.68. (12) Although as in the study by Bodis et al. we did not measure occupational stress, we can assume that Monday is an equivalent to this factor as it is the first workday. In this way, our results contribute to support a possible association between occupational stress and ACS occurrence.

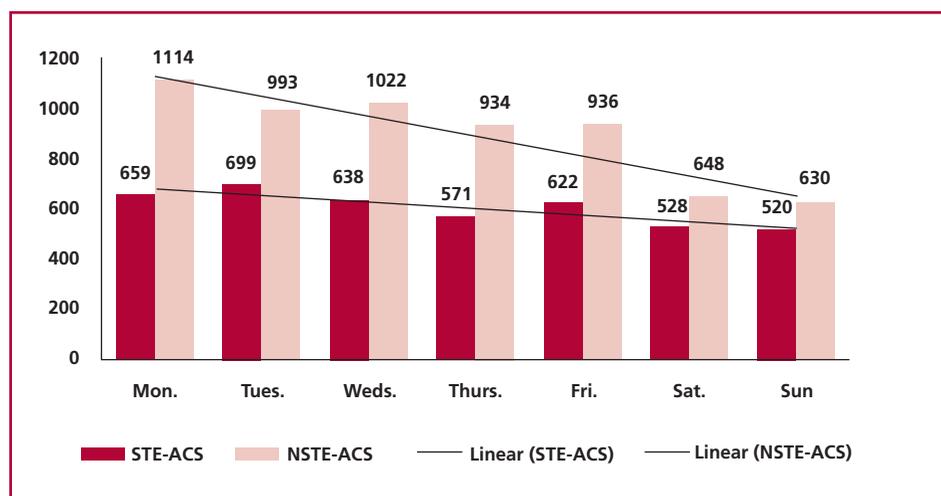
Our study has some limitations. Firstly, the high percentage of ACS hospitalized on Mondays could correspond to patients with symptoms during the weekend seeking late medical care. However, in the subgroup of STEMI-ACS we did not find significant differences in the frequency of ST-segment elevation in the admission ECG or in the use of a reperfusion strategy. Therefore, we may infer that the patients had their first medical contact with the health care system shortly after

symptom onset. Neither were there significant differences in in-hospital mortality, suggesting that the time window from symptom onset to reperfusion was similar throughout the entire week (Table 1). Conversely, the exaggerated tendency toward lower occurrence of NSTEMI-ACS during the weekend could be partially attributed to delays in the first medical contact, and the information available cannot rule out this possibility.

Secondly, we did not consider appropriate to perform a comparative analysis of the frequency of ACS during workweeks and holidays because our study was not a national public registry as it happened with the study by Bodis et al., since the participation in the Epi-Cardio registry is voluntary and, thus, does not include all the myocardial infarctions occurring nationwide. In this way, the possible reduction observed during holidays could not be true as it does not consider the flow

of tourists increasing the incidence of ACS in tourist centers.

Finally, when the category “elderly” (>65 years), which includes a greater proportion of retirees was separately analyzed, the distribution of ACS cases was similar to the one observed for the rest of subjects (higher frequency of occurrence on Mondays). This is opposed to the hypothesis that occupational stress triggers plaque rupture. Moreover, a similar pattern was observed in the Hungarian study and in a meta-analysis of studies reporting the frequency and temporal distribution of myocardial infarction and sudden death. (10, 13) This finding could indicate that occupational stress does not explain entirely the higher risk of ACS on Mondays and suggests the presence of chronological aspects that still have to be more thoroughly studied. (14)



**Fig. 1.** Acute coronary syndrome distribution according to the day of the week in which the patients sought medical care. Numbers indicate ACS cases by day of hospitalization. Linear regression analysis for STE-ACS:  $y = -27.786x + 716.29$ ,  $R^2 = 0.7829$  and for NSTEMI-ACS:  $y = -79.571x + 1215$ ,  $R^2 = 0.8519$ .

**Table 1.** Distribution of clinical variables analyzed by day of ACS occurrence

	Mon.	Tues.	Weds.	Thurs.	Fri.	Sat.	Sun.	p
Mean age, years	60.5	60.8	60.9	60.1	60.5	60.7	60.7	NS
Male sex, %	77.8	74.1	74.7	76.6	77.2	75.9	76.8	NS
Age >65 years. %	33.2	33.8	35.4	32.0	32.3	33.3	31.2	NS
Mortality, %	2.6	2.7	2.6	3.1	3.5	2.9	2.5	NS
STE-ACS								
ST at admission, %	81.5	82.1	80.7	80.9	79.3	77.3	81.5	NS
Reperfusion, %	63.9	63.3	59.6	64.9	61.7	64.6	63.4	NS
Percutaneous coronary intervention	36.9	40.7	38.4	41.9	37.6	36.1	40.6	NS
Thrombolysis	27.3	24.3	20.1	25.1	25.5	29.6	24.8	NS
Mortality, %	4.6	4.9	3.8	4.2	6.4	4.5	4.2	NS
NSTEMI-ACS								
Mortality, %	1.4	1.1	1.9	2.5	1.6	1.5	1.1	NS

## CONCLUSIONS

The retrospective analysis of more than 10,000 ACS cases in our country shows a distinctive weekly distribution during workdays (particularly on Mondays) and a gradual reduction toward the weekend. This finding suggests a possible association between occupational stress and plaque rupture while it opens the door to a chronobiological exploration of ACS in order to establish the underlying mechanisms related with psychosocial, genetic and environmental aspects which may act as triggers of the event.

## Conflicts of interest

None declared

(See authors' conflict of interest forms in the web/ Supplementary Material).

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