Journal of the Saudi Heart Association

Volume 32 | Issue 1 Article 4

2020

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Recommended Citation

Rigatelli, Gianluca and Zuin, Marco (2020) "Occurence of left main occlusion on Tuesday: Chronobiology of acute myocardial infarction," *Journal of the Saudi Heart Association*: Vol. 32 : Iss. 1 , Article 4. Available at: https://doi.org/10.37616/2212-5043.1003

ORIGINAL ARTICLE

Occurence of left main occlusion on Tuesday: Chronobiology of acute myocardial infarction due to left main disease

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Abstract

Objectives: **The existence of a "weekend effect" for onset of acute myocardial infarction (AMI) has been suggested in the past, but the relation with the culprit vessel has not been investigated. MI due to left main coronary artery lesion represents a particularly serious life-threatening condition. Our study was aimed to assess the chronobiology of admission to the emergency department for AMI considered to be induced by a left main culprit lesion.**

Methods: **We retrospectively reviewed patients who experienced an AMI due to a left main culprit lesion between January 1, 2008 and January 1, 2018 stratifying them according to the day of admission, on the basis of the symptom onset time; the 30-day cardiovascular mortality was also analyzed on the basis of the time of symptom onset.**

Results: **Out of 1789 patients with AMI, 130 (7.2%, 104 males and 26 females, mean age 74.5 ± 8.1 years) had left main disease as the culprit lesion. Tuesday was significantly over-represented as the admission day ($p < 0.001$ for Tuesday vs. other days; $p = 0.009$ for Tuesday vs. Sunday, respectively). The 30-day cardiovascular survival was not different between patients admitted on Tuesday and those admitted on remaining days (Log-rank, Mantel Cox, $p = 0.43$; Chi-square = 0.611). A significant difference was noted in patients with AMI on Sunday versus remaining days (Log-rank, Mantel-Cox, $p = 0.005$; Chi-square = 7.96). The diameter of the left main artery was larger in patients admitted on Tuesdays than on Sundays ($p < 0.01$).**

Conclusion: **The relation between AMI onset and the day of the week is confirmed by our study, which also suggests that in case of a left main lesion, some delay of the weekend effect might be expected.**

Keywords: Acute myocardial infarction, Chronobiology, Left main

1. Introduction

Over the past years, some chronobiological investigations have demonstrated a higher incidence of the onset of different cardiovascular diseases on the day of the week [1], including acute myocardial infarction (AMI) on Monday [2], suggesting the existence of a "weekend effect" [3]. The clinical presentation of patients with acute left main occlusion or subocclusion is generally characterized to be associated with sudden death or profound cardiogenic shock due to malignant arrhythmias or acute heart failure [4]. A prompt and adequate coronary revascularization remains fundamental to increase the survival of these patients. Short-term mortality and prognosis of AMI caused by a left main occlusion is significantly worse than MI caused by a culprit lesion in other coronary vessels [5,6]. Previous chronobiological investigations have generally studied only the relationship between the AMI and the day of the week, without further subanalysis based on the

Received 23 June 2019; revised 23 October 2019; accepted 24 October 2019.
Available online 17 April 2020

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https://doi.org/10.37616/2212-5043.1003

culprit vessel. Therefore, our study was aimed to assess, for the first time in medical literature, the chronobiology of AMI admission to the emergency department induced by a left main culprit lesion.

2. Methods

2.1. Patient selection

Over the study period, 1789 consecutive patients were admitted and treated in our institution for an AMI with ST-segment elevation (STEMI) between January 1, 2008 and January 1, 2018. Among these, we retrospectively reviewed patients who experienced STEMI due to a left main culprit lesion treated by primary percutaneous coronary intervention (PCI).

2.2. Definitions

Unprotected culprit left main disease was defined as any left main occlusion or subocclusion or stenosis with a diameter of at least of 50% likely to be the culprit lesion and responsible for symptoms.

Angiographic variables were analyzed using quantitative coronary angiography. Lesion location and severity were classified according to the SYNTAX score [7]. The local ethical committee approved the study.

Patients were analyzed on the basis of the time of symptom onset in order to investigate the existence of a weekend effect in this subgroup of patients. The 30-day cardiovascular mortality was also analyzed in relation to the day of admission, irrespectively from the global extent of the coronary artery disease.

2.3. Statistical analysis

Continues variables were expressed as mean ± standard deviation and were compared using Student t test if the data had normal distribution, otherwise by Wilcoxon−Mann−Whitney U test. Categorical variables were compared by Pearson's Chi-square test. To estimate the 30-day survival, the Kaplan−Meier method was applied, and the log-rank test was used to evaluate the differences between patients admitted on Sunday or Tuesday. A receiver operating characteristic curve was calculated to identify the optimal SYNTAX score cut-off with respect to 30-day mortality for those patients with the acute cardiovascular event on Tuesday. The multivariate Cox regression analysis was performed to identify independent predictors of 30-day mortality for the same patients. Statistical significance was defined as $p < 0.05$.

Abbreviations

AMI	Acute myocardial infarction
CS	Cardiogenic shock
CVD	Cardiovascular disease
ED	Emergency department
HF	Heart failure
LM	Left Main
PCI	Percutaneous coronary intervention
STEMI	ST-elevation myocardial infarction

Statistical analyses were performed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Population

Over the study period, 7.2% patients (130 out of 1789 with STEMI, 104 males and 26 females, mean age 74.5 ± 8.1 years) were identified to have a left main culprit lesion (Table 1). On admission, systolic blood pressure and heart rate were 81.4 ± 5.8 mmHg and 122.4 ± 3.4 beats per minute, respectively. The mean time between the symptom onset and balloon time was 61.4 ± 32.4 minutes Twenty-two patients (16.9%) had a previous PCI on different vessels. The mean SYNTAX score was 25.2 ± 6.3, whereas intraaortic balloon pump and inotropic supports were needed in 42 (32.3%) and 66 (50.7%) patients, respectively. Arrhythmic complications during the interventional procedure were observed in 40 patients (32.5%); more precisely, ventricular

Table 1. General characteristics and procedural data of the study population.

Characteristics	Mean ± SD or n (%)
Age (y)	74.5 ± 8.1
Male	104 (80)
Systolic blood pressure (mmHg)	81.4 ± 5.8
Heart rate (beats per min)	122.4 ± 3.4
Symptom onset to balloon time (min)	61.4 ± 32.4
Previous percutaneous coronary intervention	22 (16.9)
Shock index	1.5 ± 0.2
SYNTAX score	25.2 ± 6.3
Intraaortic balloon pump	42 (32.3)
Inotropic support	66 (50.7)
Arrhythmic complications during the procedure	
Ventricular fibrillation	15 (11.5)
Ventricular tachycardia	12 (9.2)
Pulseless electrical activity	13 (10)
30-d cardiovascular mortality	5 (7.6)

Data are presented as n (%) or mean ± SD.

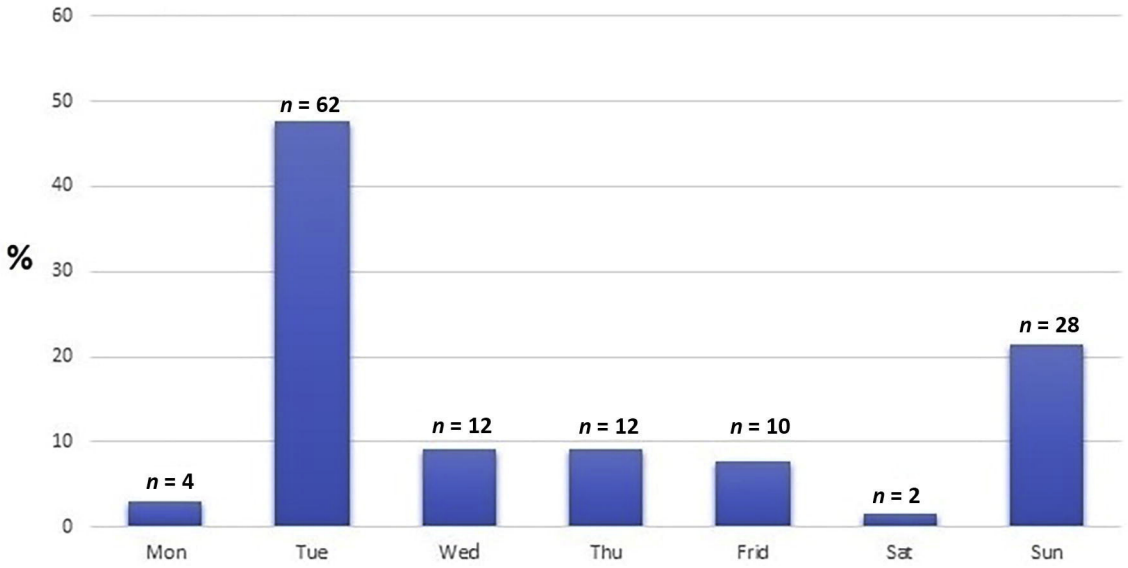

Fig. 1. Histogram bars representation of acute myocardial infarction occurrence divided by the day of the week.

fibrillation, ventricular tachycardia, and pulseless electrical activity were detected and treated in 15 (11.5%), 12 (9.2%), and 13 (10.0%) patients, respectively. Acute success was achieved in 100% cases, and no patients died perioperatively.

Ostial left main culprit lesion was found in 69 out of 130 patients (53%), whereas a left main body and a distal bifurcation culprit lesion was present in 20 (15.3%) and 41 patients (31.5%), respectively. Single stent implantation was performed in 73 patients (56.1%), whereas a double stent implantation was performed in 57 patients (43.8%): Culotte in 18 (31.5%), Nano-Crush in 26 (45.6%) and T-stenting in 13 (22.8%). The 30-day cardiovascular mortality was 7.6% ($n = 5$).

3.2. Left main chronobiology and prognosis

The distribution of treated patients according to the day of admission is shown in Fig. 1. Tuesday was

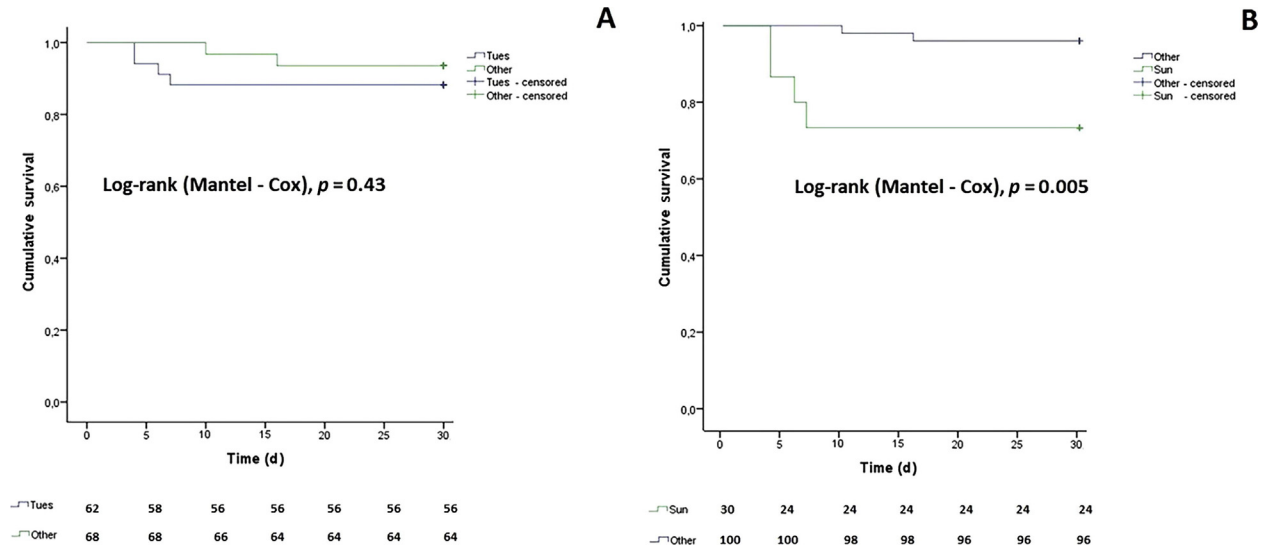

Fig. 2. (A) Cumulative survival analysis between the events occurred on Tuesday versus the other day of the week. (B) Cumulative survival analysis demonstrating a difference in 30-day cardiovascular mortality for those events occurred on Sunday versus the other days of the week.

significantly over-represented compared with the hospital admission on other days ($p < 0.001$ for Tuesday vs. other days; $p = 0.009$ for Tuesday vs. Sunday, respectively). Moreover, about one out of four patients experienced the acute cardiovascular event on Sunday. The 30-day cardiovascular survival was not different between patients admitted on Tuesday and those admitted on remaining days (Log-rank, Mantel Cox, $p = 0.43$; Chi-square = 0.611; Fig. 2A). Conversely, a significant difference in the 30-day cardiovascular survival was noted in patients who experienced AMI on Sunday versus remaining days (Log-rank, Mantel-Cox, $p = 0.005$; Chi-square = 7.96; Fig. 2B). Intriguingly, the diameter of the left main calculated on quantitative coronary angiography was larger in patients admitted on Tuesdays than on Sundays (AMI occurrence: 4.5 ± 0.7 mm vs. 3.4 ± 0.8 mm, respectively; $p < 0.01$). A receiver operating characteristic curve analysis demonstrated that the optimal cut-off for SYNTAX score with respect to 30-day cardiovascular mortality for those patients experiencing the event on Tuesday was SYNTAX score ≥ 20 [area under curve = 0.81, 95% confidence interval (CI) = 0.74–0.87, $p = 0.001$]. Multivariate Cox-regression analysis demonstrated that a SYNTAX score ≥ 20 [hazard ratio (HR) = 2.08, 95% CI = 1.18–3.16, $p = 0.01$] was an independent predictor of 30-day cardiovascular mortality for patients who experienced the event on Tuesday independently from previous PCI (HR = 1.76, 95% CI = 1.05–2.18, $p = 0.002$), door-to-balloon time (HR = 1.94, 95% CI = 1.43–2.58, $p = 0.001$), and shock index ≥ 1 at admission (HR = 1.19, 95% CI = 1.13–1.32, $p = 0.03$).

4. Discussion

Our brief study suggests that as per other medical conditions [2,5], including leukemia, chronic obstructive pulmonary disease, and some cardiovascular diseases, such as stroke and pulmonary embolism, some differences in the onset and mortality after interventions exist during the week. AMI generally has been found to occur more often after the weekend, especially on Monday, when higher stress, causing an increased release of stress hormones and catecholamines, is expected. However, Tuesday resulted unexpectedly to be the preferred day for left main lesion destabilization and subsequent plaque rupture in our analysis.

Among all the different anatomical and clinical features involved in this time correlation, the diameter of the left main, which usually is expected to be 1.5 mm or 2 mm larger than left anterior descending and left circumflex coronary arteries, might be the main determinant [8]. Indeed, "larger the vessel, longer the time" for which a large thrombus can produce symptoms after the weekend. This hypothesis seems to be confirmed by our data: the mean left main size in STEMI occurring on Tuesday was 1 mm more than that on Sunday. The SYNTAX score in such patients has been confirmed to have a correlation with the chronobiology of left main occlusion and 30-day cardiovascular mortality, suggesting that the diameter of left main might play a major role in the shift of the weekend effect from Monday to Tuesday.

4.1. Study limitation

Our brief investigation has some limitations including the relatively small number of patients enrolled, the monocentric and retrospective design of the study, and the potential impact on outcomes of different stent strategy, optimization techniques, and stent composition [9]. Moreover, the exclusion of patients immediately referred to bypass surgery or not treated with PCI could represent a bias. Nevertheless, our study represents the first attempt in literature to describe the chronobiology of such serious life-threatening conditions.

5. Conclusion

Although our study needs to be confirmed by larger studies, our research seems to confirm a relation between STEMI onset and the day of the week raising the hypothesis that in larger vessels, such as the left main, some delay of the weekend effect might be expected.

Conflict of interest

The authors declare no conflict of interest.

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