ISSNe: 2182.2883 | ISSNp: 0874.0283
Available: https://doi.org/10.12707/RIV18038

RESEARCH PAPER (ORIGINAL)
ARTIGO DE INVESTIGAÇÃO (ORIGINAL)

Identification of the time of onset of acute myocardial infarction symptomatology

Identificação da hora de início da sintomatologia de enfarte agudo do miocárdio

Identificación de la hora de inicio de la sintomatología del infarto agudo de miocardio

Maria Cristina Mós Bemposta*; Matilde Delmina da Silva Martins**; Norberto Aníbal Pires Da Silva***

Abstract

Background: Acute myocardial infarction is one of the leading causes of death in Portugal and worldwide. Several studies have shown a morning predominance of the onset of symptoms in this pathology.
Objective: Describe the variation in onset of the infarction symptomatology and to analyze the average delay of admission in the emergency service of patients between 2015 and 2016 to a unit in northern Portugal.
Methodology: Retrospective cross-sectional study. Fifty patients were studied, admitted to an emergency department diagnosed with acute myocardial infarction between 2015 and 2016 using clinical records.
Results: The majority of participants were male (52%), with an average age of 79.6 years, presenting with hypertension (72%), dyslipidemia (54%), diabetes (46%), and obesity (20%). Onset time of acute myocardial infarction symptoms was generally between 6 a.m. and 12 p.m. (34%) and on average at 10 a.m.
Conclusion: There was a predominance of symptom onset in the morning period.

Keywords: myocardial infarction; acute coronary syndrome; signs and symptoms

Resumo

Enquadramento: O enfarte agudo do miocárdio é uma das principais causas de morte em Portugal e no mundo. Vários estudos têm evidenciado um predomínio matutino do início dos sintomas nesta patologia.
Objetivo: Descrever a variação da hora de início da sintomatologia de enfarte agudo do miocárdio e analisar a demora média de entrada no serviço de urgência dos doentes admitidos entre 2015 e 2016 numa unidade do norte de Portugal.
Metodologia: Estudo transversal retrospetivo. Realizado em 50 doentes admitidos num serviço de urgência, com o diagnóstico de enfarte agudo do miocárdio, entre 2015 e 2016, recorrendo aos registos clínicos.
Resultados: Os participantes eram maioritariamente do sexo masculino (52%), com idade média de 79,6 anos, apresentavam hipertensão arterial (72%), dislipidémia (54%), diabetes (46%), e obesidade (20%). A hora de início dos sintomas de enfarte agudo do miocárdio ocorreu maioritariamente entre as 6 e as 12 horas (34%) e a média observou-se às 10 horas**.**
Conclusão: Verificou-se um predomínio de início da sintomatologia no período matutino.

Palavras-chave: enfarte agudo do miocárdio; síndrome coronária aguda; sinais e sintomas

Resumen

Marco contextual: El infarto agudo de miocardio es una de las principales causas de muerte en Portugal y en el mundo. Varios estudios han evidenciado un predominio matutino del inicio de los síntomas en esta patología.
Objetivo: Describir la variación de la hora de inicio de la sintomatología del infarto agudo de miocardio y analizar la demora media de entrada en el servicio de urgencias de los pacientes admitidos entre 2015 y 2016 en una unidad del norte de Portugal.
Metodología: Estudio transversal retrospectivo, realizado en 50 pacientes admitidos en un servicio de urgencias, con diagnóstico de infarto agudo de miocardio entre 2015 y 2016, para lo cual se recurrió a los registros clínicos.
Resultados: Los participantes eran mayoritariamente del sexo masculino (52%), con una edad media de 79,6 años, presentaban hipertensión arterial (72%), dislipidemia (54%), diabetes (46%), y obesidad (20%). Los síntomas del infarto agudo de miocardio comenzaron mayoritariamente entre las 6 y las 12 horas (34%), y la media se observó a las 10 horas.
Conclusión: Se verificó un predominio del inicio de la sintomatología en el período matutino.

Palabras-clave: infarto del miocárdio; síndrome coronario agudo; signos y síntomas

*RN., Nurse, Local Health Unit of the Northeast (ULSNE), 5301-862, Bragança, Portugal [cristina-bemposta@gmail.com]. https://orcid.org/0000-0002-6009-3013. Contribution to the article: literature research; data collection; statistical analysis and treatment; data analysis and discussion; article writing. Address for correspondence: Rua do Erol nº4, 5301-862, Bragança, Portugal.
**Ph.D., Adjunct Professor, Higher School of Health, Polytechnic Institute of Bragança, 5300-121 Bragança, Portugal [matildemartins@ipb.pt]. Health Sciences Research Unit (UICISA). https://orcid.org/0000-0003-2656-5897. Contribution to the article: statistical analysis of data, discussion of results, overall revision of article.
***MSc., Specialist Nurse, Urgent Care, Emergency and Intensive Care Department, Local Health Unit of the Northeast, 5300-587 Bragança, Portugal [norbertosilva@sapo.pt]. https://orcid.org/0000-0002-0689-1567. Contribution to the article: statistical analysis of data, discussion of results, overall revision of article.

Received for publication: 15.06.18
Accepted for publication: 22.10.18

Introduction

Despite the great advances made in cardiology in recent years, worldwide there has been a genuine epidemic of coronary artery diseases, which are the main isolated cause of death (Instituto Nacional de Estatística [INE], 2018). Cardiovascular diseases are the main causes of death in the world, regardless of the country's economic situation. According to the World Health Organization (WHO), cardiovascular diseases were responsible for 17 million deaths in 2011. Of these 17 million, 7 million died of ischemic heart disease and 6.2 million from stroke. Acute myocardial infarction (AMI) is the main representative of ischemic heart diseases (Issa, Oliveira, & Esporatte, 2015; INE, 2018). In 2016, 32,805 people died in Portugal from diseases of the circulatory system (INE, 2018).

The circadian variation in the functioning of the cardiovascular system explains the higher incidence of cardiac cases in the morning, as well as the possible mechanisms involved in this variation throughout the day. In recent years, it was proven that the appearance of acute coronary syndrome (ACS) over the course of the day is not uniform, as there are rhythmic variations (Aroche, Naranjo, Rodriguez, & Llera, 2014; Valero et al., 2016). It has been clearly shown that the start of AMI happens more frequently in the early hours of the morning (Aroche et al., 2014; Dominguez, Navarro, & Alessandrini, 2014).

In the last decade, chronobiology applied to the clinical research of the cardiovascular system and cardiovascular accidents has undergone major development (Castellanos, Granados, & Escobar, 2009; Valero et al., 2016). During the course of the day, the metabolic state of the individual changes and with it the conditions for the cardiovascular functions also vary. According to those authors, the epidemiological studies show that in the first part of the day, the risk of suffering angina pectoris, AMI and stroke is greater. The circadian distribution at the onset of the various cardiovascular pathologies suggests that there are triggering factors for them that display a temporal organization. With this study, we therefore seek to: Describe the variation of the time of the initiation of the symptomatology of acute myocardial infarction and analyze the average delay for admission in the ER of patients admitted between 2015 and 2016 in a unit in northern Portugal.

Background

AMI, more recently called SCA, is the term used to describe the irreversible necrosis of the myocardium, which can result from a sudden reduction or total interruption of the blood supply to a certain area of the myocardium (European Society of Cardiology [ESC], 2017). Chest pain is the main symptom for suspecting SCA. After the suspicion, the electrocardiogram (EKG) has a fundamental role (ESC, 2017).

Based on the EKG, two types of patients must be differentiated: patients with acute chest pain and persistent (more than 20 minutes) ST segment elevation and those patients with acute chest pain, but without persistent ST segment elevation.

The acute coronary syndrome with ST segment elevation generally reflects an acute total coronary occlusion. The majority of these patients develop an AMI with ST segment elevation, the pillar of the treatment being the immediate reperfusion through primary angioplasty or fibrinolytic therapy (ESC, 2017).

In the acute coronary syndrome without ST segment elevation (SCA NSTEMI), the alterations of the EKG may include a transient ST segment elevation, T-wave inversion, flattened T-waves or pseudo normalization of T waves or normal EKG.

The medical history and appropriate physical exam, EKG, myocardial necrosis markers, preferably high-sensitivity troponin, fulfil the conditions to diagnose SCA (ESC, 2017; Valero et al., 2016).

The typical chest pain is the main symptom of SCA, principally the retrosternal sensation of pressure or weight, which irradiates to the left arm (less frequently to both arms or the right arm), neck or jaw, and may be intermittent or persistent. It may be associated with cold sweats, nausea, abdominal pain or lipothymia (ESC, 2017; Marcondes, 2018).

The cyclical variations that occur in the environment (temperature variations, seasons of the year, day – night) mean that all living creatures are exposed to them. So, mankind

had to develop mechanisms of adaptation in order to adjust his physiological processes to the rhythmic, cyclical alterations, adequately preparing these biological rhythms in a timely fashion. The term "circadian" comes from *circa diem* and designates the 24-hour period in which there is an alternation between light and darkness, and on which the entire biological cycle of the human body is based, fundamentally by sunlight (Issa et al., 2015; Novais, 2017).
The accompaniment of this light-dark alternation is done through a *clock* called a *biological clock* that permits the anticipation of cyclical variations in the environment, enabling the individual for all the activities he must perform for sleeping and waking (Novais, 2017).
According to Aroche et al. (2014), the AMI occurs with greater frequency between 6 a.m. and midday. It is known that at these times, blood pressure increases and the heart contracts with greater frequency. Associated with this, there are many variables that increase their activity during the morning, predisposing the appearance of an AMI, such as the increase in cortisol, adrenaline and vasopressin, platelet aggregation, as well as an increased blood viscosity (Miranda & Lima, 2014). Taken together, these variables form an adverse state for the cardiovascular system.

Research Question

What is the circadian variation of the start of the AMI symptomatology in patients admitted in the emergency department of a hospital in northern Portugal, between 2015 and 2016 and what is the average delay of entry in the emergency department?

Methodology

A transversal retrospective study carried out on AMI-diagnosed patients admitted in the medical-surgical emergency department of a hospital in northern Portugal between 2015 and 2016.
The target population of this study was all the patients who were diagnosed with AMI (83), of which 33 were excluded for whom it was not possible to ascertain the time of onset of the symptomatology through the records contained in the clinical file, leaving a sample of 50 patients.
As an instrument of data collection, a grid was set up that includes the information on the patient, age, gender and residence. It also shows the information in regard to the patient's history, specifically the comorbidities: respiratory, endocrine-metabolic, renal, immunological, hematological and cardiovascular. It also contains information on the patient's risk factors, such as arterial hypertension (AH), smoking habits, sedentarism, dyslipidemias, diabetes and obesity, onset of the patient's symptoms and the arrival time at the medical-surgical emergency service (MSED) of the hospital. The data was collected in March 2017.
The data collected was entered into and analyzed by the IBM SPSS Statistics, version 21.0 computer program, using a code number to ensure anonymity and the secrecy of the information.
For the ordinal variations the absolute and relative frequency was determined, and for the continuous variables the average and the standard deviation were calculated. We used the Shapiro-Wilk test to analyze the distribution of the variables, and seeing that the variables did not follow a normal distribution and the sample was small, we chose the nonparametric *U*-Mann-Whitney test for comparing the averages. The level of significance was defined as 5%.
The study had the favorable opinion of the Ethics Committee and authorization from the ULSNE reference no. 005629. The fundamental rights set forth in the Nuremburg Code of Ethics and the Helsinki Declaration were respected.

Results

Of the 50 patients that participated in the study, 52% were male and the age group with the highest frequency was that from 80 to 89 years (38%), the average (X) age being 79.6 years, with a standard deviation (*SD*) of ± 11.6 years. Most of the patients were from the municipality of Bragança (54%) and the rural area (70%; Table 1).

Table 1
Distribution of the participants by sex, age and origin (n = 50)

		Nº	%
Sex	Male	26	52%
	Female	24	48%
Age (years)	<70	7	14%
	70 - 79	17	34%
	80 - 89	19	38%
	>90	7	14%
Municipality	Vimioso	7	14%
	Bragança	27	54%
	Vinhais	8	16%
	Miranda do Douro	2	4%
	Mogadouro	5	10%
	Freixo de Espada à Cinta	1	2%
Residence	Urban	15	30%
	Rural	35	70%

[a]X = 79.6 years; *DP* = ± 11.6 years.

The predominant cardiovascular risk factors were AH in 72% of the patients, dyslipidemia in 54% of the patients, diabetes in 46% of the patients and obesity in 20% of the patients. In relation to the comorbidities of the patients studied, cardiovascular problems (60%), endocrine/metabolic problems, especially diabetes (52%), and respiratory problems (16%; Table 2) were prevalent.

Table 2
Distribution of the participants by cardiovascular risk factors and comorbidities (n = 50)

Cardiovascular risk factors		*Nº*	%
Arterial hypertension	Yes	36	72%
	No	14	28%
Smoking habits			
Non-smoker		45	90%
Smoker	Up to 20	1	2%
	> 21 - 40	3	6%
	> 40	1	2%
Dyslipidemias	Yes	27	54%
	No	23	46%
Diabetes	Yes	23	46%
	No	27	54%
Obesity	Yes	10	20%
	No	40	80%
Comorbidities		*N*	%
Respiratory problems	Yes	8	16
	No	42	84
Endocrine/metabolic	Yes	26	52
	No	24	48
Renal problems	Yes	9	18
	No	41	82

Hematological problems	Yes	6	12
	No	44	88
Cardiovascular problems	Yes	30	60
	No	20	40

A very significant prevalence of the onset of AMI symptoms was noted in the morning, that is, 64% (32) of the patients in this study experienced the start of symptomatology between midnight and midday. In only 36% (18) of patients did the symptomatology begin in the afternoon hours, that is, between midday and midnight. The mean hour of the start of symptoms in the patients of this study was 10:01 a.m., with a standard deviation of 6 hours and 35 minutes. In regard to the hour of entry in the Emergency Service (ES), 34% of the patients entered this service between 6 a.m. and midday; 22% between midday and 6 p.m., 26% between 6 p.m. and midnight, and 18% in the period between midnight and 6 a.m. The mean hour of entry in the ES was 12:26 p.m.. Of the 50 patients studied, 38% entered the ES up to 2 hours following the start of the symptoms, 32% entered between 2 and 4 hours after the start, and the remaining patients (30%) 4 hours or later after the symptomatology began. The minimum difference recorded between the start of symptoms and the entry in the ES was 48 minutes and the maximum 23 hours and 46 minutes. On average, the patients in this study took 4 hours and 22 minutes after the start of the symptomatology to enter the ES (Table 3).

Table 3

Distribution of the participants by time of start of symptoms, time of entry in the emergency service, and the time elapsed between the time of start of symptoms and the time of entry in the ES (n = 50)

		Nº	%	Average/standard deviation (min)
Time of start of symptoms	[12 - 6 a.m.[	15	30%	*X* = 10:01 *SD* = ± 6:35
	[6 a.m. 12 p.m.[	17	34%	
	[12 – 6 p.m.[	9	18%	
	[6 p.m. – 12 a.m.[	9	18%	
Time of entry in ES	[12 - 6 a.m.[	9	18%	*X* = 12:26 *SD* = ± 6:25
	[6 a.m. 12 p.m.[	17	34%	
	[12 - 6 p.m.[	11	22%	
	[6 p.m. - 12 a.m.[	13	26%	
Time elapsed between time of start of symptoms and entry in ES (h)	[0 - 2[	19	38%	*X* = 4:22 *SD* = ± 4:05
	[2 - 4[	16	32%	
	> 4	15	30%	

Note. X = Average; *SD* = Standard Deviation.

When we note the difference in averages between the time of start of symptoms and the time of entry in the ES, we see that no statistically significant differences were recorded ($p > 0.05$) for all the variables except for dyslipidemia ($p = 0.04$). However, we can see that those that took the most time to come to the ES were the diabetic patients and smokers, the dyslipidemic and obese patients the least amount of time (Table 4).

Table 4

Distribution of participants by time elapsed between the time of onset of symptoms and the time of entry in the ES, according to sex, age, residential environment, and cardiovascular risk factors (n = 50)

		Time elapsed between time of start of symptoms and entry in the ES		PV
		Average	Standard deviation	
Sex	Male	3:47	4:24	0.171
	Female	5:00	5:20	
Age	> 70	2:27	1:44	0.698
	70-79	6:26	7:29	
	80-89	3:47	2:31	
	> 90	2:50	1:13	
Residential environment	Rural	4:12	4:39	0.743
	Urban	4:44	5:28	
Hypertension	Yes	4:33	5:14	0.820
	No	3:54	3:51	
Dyslipidemias	Yes	3:29	4:11	0.040*
	No	5:23	5:27	
Diabetes	Yes	5:24	6:03	0.280
	No	3:29	3:26	
Obesity	Yes	3:39	4:24	0.459
	No	4:33	5:00	
Smoking habits	Yes	1:39	0:26	0.055
	No	4:40	4:40	

Note. PV = Probative Value. *significant at 5%.

The mortality rate of the patients studied was 34%, of which 35.3% died in the first week following the occurrence of the AMI, 17.6% in the 6 months following the episode, and 23.5% died more than 1 year after suffering the AMI. On average, the patients who survived went to the ES 1 hour and 20 minutes sooner than those who died. The patients who died had an average delay of 5 hours and 15 minutes between the onset of symptoms and their entry in the ES, while for those who survived, the delay was under 4 hours: 3 hours and 54 minutes.

Discussion

During the execution of this work, we came up against difficulties and limitations related to the small sample and the paucity of scientific papers published on this theme, so that the discussion essentially focuses on the interpretation of the data collected.

The sample in this study was made up principally of patients 80 to 89 years old, the average age being 79.6 years, men, and living in their own home. The average age was higher than that in the studies consulted, such as that of Aroche et al. (2014) in which the average age was 69.9 years and of Iquise (2017), which had an average age of 63.4 years. These differences in the average age may be related to the aging of the population in the region where our study was carried out. This region, according to the data of PORDATA (2015), has an aging index higher than the national average, 200 elderly people for every 100 young people. According to the 2011 census, the age group over 65 in this district was higher than the national average (19%). Various studies have shown advanced age to be a risk factor for this pathology (Aroche et al., 2014; Lotufo, 2008; Bourbon, Miranda, Vicente, & Rato, 2016).

In all the studies consulted, there was a predominance of males, which is a non-modifiable cardiovascular risk factor (Lotufo, 2008). Men have a greater risk of developing cardiovascular diseases than do women in any age group (Aroche et al. 2014; Lotufo, 2008), and this

risk increases with aging (Bourbon et al., 2016). AH, dyslipidemia, diabetes and obesity were the most common risk factors in our sample. In full 21st century, AH continues to be the most prevalent cardiovascular risk factor in the world for cardiovascular pathology and thromboembolic phenomena (Iquise, 2017; Lotufo, 2008; Macedo & Ferreira, 2015; Bourbon et al., 2016). AH and diabetes are currently considered the most important cardiovascular risk factors, and when found together in the same patient, they self-enable their deleterious vascular effects, particularly affecting the renal, cerebral and cardiac systems. A large percentage of the population presents AH and diabetes simultaneously, about 50% of patients with high blood pressure present dyslipidemia (Macedo & Ferreira, 2015). These results corroborate the pioneer study, Framingham Heart Study, which was started in 1948 with the objective of identifying the epidemiology and risk factors of cardiovascular diseases, cited by Lotufo, 2008, and the INTERHEART study, an international, standardized, case-control study projected as a first step towards evaluating the importance of risk factors for cardiac diseases around the world, cited by Yusuf, Hawken, and Lisheng (2014).

The predominant comorbidities in our study were cardiovascular problems, and of these, congestive heart failure, prior AMI and atrial fibrillation stood out. A significant number of participants (14%) presented three or more cardiovascular problems simultaneously. Endocrine-metabolic dysfunctions, specifically diabetes, were found in a high proportion, followed by renal, respiratory and hematological dysfunctions, data corroborated by the studies of Dominguez et al. (2014) and Iquise (2017).

The start of symptomatology was more prevalent in the morning, between 6 a.m. and midday. This fact may be related to the increase in sympathetic activity in the morning. The interaction between the catecholamines and the platelet aggregation affects the atherosclerotic plaque, as well as variations related to the hemodynamic responses, including blood pressure, blood flow, heart rate, fibrinogen concentration, and blood clotting factors, as observed in other studies (Castellanos et al., 2009; Miranda & Lima, 2014; Valero et al., 2016).

Aroche et al. (2014) and Dominguez et al. (2014) also concluded in their studies that AMI has a morning incidence, with a tendency to a marked increase from the start of the symptoms in the early hours of the morning, progressively growing weaker during the night, which gives it a circadian rhythm. Morning stress at the start of the day (planning and organizing the family tasks and travel to work) causes hyperactivation of the central nervous system, with the increased release of catecholamines and higher levels of BP and HR, favoring the occurrence of AMI (Marcondes, 2018).

The patients had an average delay of 4 hours and 22 minutes between the onset of the symptoms and admission in the ES. It is known that the time elapsed between the start of symptoms and the reestablishment of blood flow to the myocardium is crucial in the prognosis (Iquise, 2017). When the treatment is carried out in the first 6 hours, the results are better, seeing that after 12 hours it has no effect on the reduction of mortality (ESC, 2017). The current ESC guidelines recommend primary angioplasty as the strategy of choice for the treatment of AMI with ST-segment elevation (ESC, 2017). The increase in time between the entry of the patient in the hospital and the start of revascularization treatment through fibrinolysis affects the clinical results (ESC, 2017; Miranda & Lima, 2014). Despite not having observed statistically significant differences, it was found that the survival rate is higher in patients seeking the ES sooner after the start of the AMI symptomatology, which is in line with the literature consulted (ESC, 2017; Iquise, 2017; Valero et al., 2016), because the sooner the treatment of AMI is started, the greater the probability of survival. Hence, in this study, the patients that survived sought out the ES, on average, 1 hour and 20 minutes sooner than those that died. Those who died had an average delay between the start of the symptoms and the entry in the ES of 5 hours and 15 minutes, while that of the survivors was under 4 hours: 3 hours and 54 minutes. The mortality rate was 34%, lower rates (22%) being recorded in the study of Rengifo and Oliva (2013), and 15.6% in the study by Aroche et al. (2014), which may be related to the mean age in this study being higher and to the distance of access to the nearest ES. Although there is no statistically significant difference in the time elapsed between the start

of AMI symptomatology and the time of entry in the ES with the socio-demographic variables, it was found that the male patients enter the ES sooner after the start of AMI symptoms than the female patients (3 hours 47 minutes *vs* 5 hours) confirming the study by Saraiva (2015), men take longer to identify the symptoms, but when they do identify them, they seek health care more rapidly (Munõz, Nogueira, & Filho, 2014; Nascimento, Pupe, & Cavalcanti, 2016). The age group under 70 years is the one that takes less time to seek the ES after the start of the symptomatology, while the 70 to 79 year old age group takes the most time, which may be related to the speed of transmission of the nervous system slowing with age, which implies that the motor functions are slower and not as well controlled, the reflexes are slower, walking is slower, and reactional capacities are less efficient (Nascimento et al., 2016). In the study by Munõz et al. (2014) pain in the elderly has significantly lower values than in the young, the elderly present a lower sensitivity to pain. There is a statistically significant difference in the time elapsed between the start of AMI symptomatology and the time of entry in the ES, with the variable dyslipidemia. These patients are probably more alert to the possibility of suffering an AMI, seeing that dyslipidemia is one of the most prevalent cardiovascular risk factors. It was found that diabetic patients take the longest amount of time to seek the ES after the start of AMI symptoms, and dyslipidemia patients take the least amount of time (5 hours and 24 minutes *vs* 3 hours and 29 minutes). Diabetic neuropathy encompasses a group of alterations related to the structural and functional involvement of the sensory nerve fibers, producing a lower perception of pain in diabetic patients (Nascimento et al., 2016). The time elapsed between the start of the AMI symptomatology and the time of entry in the ES for patients with comorbidities is greater than for those patients without comorbidities, which may be due to the patients with comorbidities interpreting the AMI symptoms as a worsening of a chronic disease, slowing down their turning to the ES, as opposed to those who do not have comorbidities more quickly realizing the nature of the symptomatology and going to the ES more rapidly (Munõz et al., 2014; Nascimento et al., 2016).

Conclusion

From this study, it was concluded that the onset of AMI symptomatology was in the morning, particularly in the period between 6 a.m. and midday. The predominant cardiovascular risk factors were AH, diabetes, dyslipidemia, obesity and smoking. On average, patients took 4 hours and 22 minutes between the start of AMI symptomatology and entry in the ES, with a statistically significant difference being recorded for the variable dyslipidemia.
It is suggested that the population of this region be made aware of this fact that the incidence of AMI is greater in the morning, and of the crucial importance of seeking immediate health care. Also, other studies with larger samples in other institutions should be carried out, which will enable comparisons to be made between regions, with inferences for the general population.

References

Aroche, R., Naranjo, A. A., Rodriguez, A. Y., & Llera, R. E. (2014). Factores de riesgo cardiovascular en el ritmo circadiano del infarto agudo de miocardio. *Revista de la Federacion Argentina de Cardiologia*, *43*(1), 32-37. Retrieved from http://www.fac.org.ar/1/revista/14v43n1/art_orig/arorig04/aroche.pdf

Bourbon, M., Miranda, N., Vicente, A. M., & Rato, Q. (2016). *Sabe como prevenir? Doenças cardiovasculares.* Retrieved from https://www.sns.gov.pt/wp-content/uploads/2016/03/DoencasCardiovasculares.pdf

Castellanos, M. A., Granados, A. R., & Escobar, C. (2009). De la frecuencia cardiaca al infarto. Cronobiología del sistema cardiovascular. *Revista de la Faculdad de Medicina, 52(3)*, 117-121.

Dominguez, A. A., Navarro, A. R., & Alessandrini, G. A. (2014). Diferencias del ritmo circadiano de los síndromes coronarios agudos según variación del segmento ST del eletrocardiograma. *Revista Avances Cardiologia, 34(4)*, 286-294.

European Society Of Cardiology. (2017). Esc guidelines for the management of acute myocardial infarction in patients presenting with st-segment elevation: The task force for the management of acute myocardial infarction in patients presenting with st-segment elevation of the european society of cardiology (ESC). European Heart Journal, *39*(2), 119-177. doi:10.1093/eurheart/ehv320

Iquise, C. (2017). Características clínico-epidemiológicas en pacientes diagnosticados com infarto agudo de miocardio según género en el hospital de emergências José Casimiro Ulloa durante el período 2014-2015 (Ph.D Thesis). Universidad Ricardo Palma. Retrieved from http://cybertesis.urp.edu.pe/bitstream/urp/883/1/Iquise%20Contreras%20Eddy%20Guillermo_2017.pdf

Instituto Nacional de Estatística. (2018). *Boletim mensal de estatística*. Retrieved from https://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ine_publicacoes&-PUBLICACOESpub_boui=339312655&PUBLICACOESmodo=2

Issa, A. F., Oliveira, G. M., & Esporatte, R. (2015). *Manual de atualização e conduta Síndrome Coronariana Aguda*. Retrieved from https://socerj.org.br/wp-content/uploads/2015/11/manual-de-conduta.pdf

Lotufo, P. A. (2008). O escore de risco de Framingham para doenças cardiovasculares. *Revista Medicina, 87*(4), 232-7. Retrieved from http://www.revistas.usp.br/revistadc/article/viewFile/59084/62070

Macedo, M. E. & Ferreira, R. C. (2015). A hipertensão arterial nos cuidados de saúde primários, em Portugal: Contributo para o conhecimento epidemiológico da população em 2013. *Revista Factores de RISCO, 36,* 47-56.

Marcondes, M. S. (2018). Apresentação clínica do infarto agudo do miocárdio. *Revista Uniplac, 6*(1). Retrieved from http://revista.uniplac.net/ojs/index.php/uniplac/article/view/3674/0

Miranda, M. R., & Lima, L. M. (2014). Marcadores bioquímicos do infarto agudo do miocárdio. *Revista Médica de Minas Gerais, 24*(1), 98-105.

Munõz, R. L., Nogueira, G., F., & Filho, E. N. (2014). Percepção de dor em idosos e adultos e jovens: Diversidade semiológica em avaliação multidimensional da experiência dolorosa. *Revista Brasileira de Medicina, 71*(9), 287-293. Retrieved from http://www.moreira-jr.com.br/revistas.asp?fase=r003&id_materia=5928

Nascimento, O. J., Pupe, C. C., & Cavalcanti, E. B. (2016). Neuropatia diabética. *Revista Dor, 17*(Sup. 1), 46-51. *d*oi:10.5935/1806-0013.20160047.

Novais, V. (2017). Nobel da Medicina para os mecanismos que regulam o relógio biológico. *Observador*. Retrieved from https://observador.pt/2017/10/02/nobel-medicina-2017

PORDATA. (2015). Base de dados de Portugal Contemporâneo. Retrieved from http://www.pordata.pt/

Rengifo, P. G., & Oliva, C. R. (2013). Características clínicas, morbilidad y mortalidad de los pacientes con síndrome coronario agudo y elevación del segmento ST en la derivada aVR. *Revista de la Sociedad Peruana de Medicina Interna, 26(4),* 177-183.

Saraiva, F. (2015). Caraterização do doente com enfarte agudo do miocárdio. *Egitania Sciencia*, 163-177. Retrieved from http://bdigital.ipg.pt/dspace/bitstream/10314/3321/1/8_163-178CARATERIZA%C3%87%C3%83O%20DO%20DOENTE%20COM%20ENFARTE%20AGUDO%20DO%20MIOC%C3%81RDIO.pdf

Valero, M. C., Leiza, J. R., Encarnación, D. B., Montesinos, J. B., Ortiz, A. F., Barrientos, A. S., …. Ibáñez, B. (2016). Variabilidad circadiana de la efectividad de la técnica de reperfusión y del pronóstico del infarto de miocardio com elevación del ST tratado mediante angioplastia primaria. *Emergencias, 28*, 327-332.

Yusuf, S. D., Hawken, S. & Lisheng, L. B. (2014). Efeito de fatores de risco potencialmente modificáveis associados ao infarto do miocárdio em 52 países (estudo INTERHEART): Estudo caso-controle. Retrieved from https://secure.jbs.elsevierhealth.com/action/showLogin?code=lancetsite&pii=S0140-6736%2804%2917018-9&redirectUri=%2Fjournals%2Flancet%2Farticle%2FPIIS0140-6736%2804%2917018-9%2Ffulltext%3Fcode%3Dlancet