The National Response to Patients with Acute Coronary Syndrome during the First Wave of the COVID-19 Pandemic in Portugal

A Resposta Portuguesa na Síndrome Coronária Aguda durante a Primeira Onda da Pandemia de COVID-19

ARTIGO ORIGINAL

Helder SANTOS✉[1], Mariana SANTOS[1], Sofia B. PAULA[1], Inês ALMEIDA[2], Samuel ALMEIDA[1], Lurdes ALMEIDA[1], on behalf of the Portuguese Registry of Acute Coronary Syndromes

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ABSTRACT

Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) led to changes in healthcare institutions and medical assistance. Non-SARS-CoV-2 related diseases were indirectly affected by the pandemic. Nonetheless, their treatment remains crucial. Cardiovascular conditions such as acute coronary syndrome (ACS) are common, and it was necessary to adjust medical assistance to these diseases during the pandemic. This study aimed to assess the national impact and healthcare system response during the first wave of the pandemic in patients admitted for ACS.

Material and Methods: Multicenter retrospective study based on the Acute Coronary Syndrome Portuguese National Registry between the 1st January 2016 and the 28th February 2021. Two groups were defined: the previous year to the SARS-CoV-2 pandemic (March, April, May and June 2019) (952 patients) and the first wave of the pandemic (March, April, May and June 2020) (642 patients). Clinical course, time until reperfusion, in-hospital outcomes and follow-up at one year were compared between both periods.

Results: There was a lower incidence of ACS between March and June 2020 compared with the same period in 2019, with a reduction of 32.6%. There were no statistically significant differences between the two periods regarding patient demographic characteristics (except for a higher prevalence of familiar cardiovascular history and chronic obstructive pulmonary disease in 2020 and higher prevalence of diabetes in 2019), clinical features, clinical management, in-hospital major adverse cardiac events, mortality and readmission at one-year follow-up. There was a trend towards longer delays until reperfusion, yet without statistical significance. The patients that developed ACS during the first wave of the SARS-CoV-2 pandemic were less often referred to percutaneous coronary intervention centers ($p = 0.034$) and were more frequently transferred to another hospital ($p < 0.001$).

Conclusion: During the first wave of the SARS-CoV-2 pandemic there was a nationwide reduction in demand of healthcare services due to ACS events. Even though the Portuguese healthcare system was under strain and forced to divert resources and medical assistance towards the pandemic management, it was capable of responding adequately to ACS.

Keywords: Acute Coronary Syndrome; COVID-19; Pandemics; Portugal; SARS-CoV-2

RESUMO

Introdução: O *severe acute respiratory syndrome coronavirus* 2 (SARS-CoV-2) condicionou drásticas alterações nas instituições de saúde e assistência médica. Doenças não relacionadas com SARS-CoV-2 foram indiretamente afetadas pela pandemia, apesar de o seu tratamento se manter fundamental. As doenças cardiovasculares, como a síndrome coronária aguda (SCA), são prevalentes e foi necessário adaptar a assistência a estas doenças durante a pandemia. Este estudo tem como objetivo avaliar o impacto nacional e a resposta das instituições de saúde durante a primeira onda da pandemia em doentes admitidos por SCA.

Material e Métodos: Estudo retrospetivo multicêntrico com dados do Registo Nacional Português de síndrome coronária aguda entre 1 de janeiro de 2016 e 28 de fevereiro de 2021. Foram definidos dois grupos: o ano anterior ao ano da pandemia (março, abril, maio e junho 2019) (952 doentes) e a primeira onda da pandemia (março, abril, maio e junho 2020) (642 doentes). Características clínicas, tempo até à reperfusão, complicações intra-hospitalares e seguimento a um ano foram comparados entre os dois períodos.

Resultados: Nos meses de 2020 registou-se uma menor incidência de SCA comparando com o mesmo período em 2019, com uma redução de 32,6%. Não se registaram diferenças estatisticamente significativas entre os dois períodos temporais no que diz respeito às características demográficas e clínicas (exceto pela maior prevalência de doença cardiovascular familiar e doença pulmonar obstrutiva crónica em 2020, e maior prevalência de diabetes em 2019), abordagem clínica, complicações intra-hospitalares e mortalidade e readmissão durante o seguimento a um ano. Verificou-se uma tendência para um atraso até à reperfusão, sem significância estatística. Os doentes com SCA durante a pandemia foram menos referenciados para centros com intervenção coronária percutânea ($p = 0,034$) e foram mais frequentemente transferidos para outro hospital ($p < 0,001$).

Conclusão: Durante a primeira onda da pandemia de COVID-19 registou-se uma redução nas hospitalizações por SCA. O sistema nacional de saúde português esteve sob pressão e stresse para prestar assistência durante a pandemia. No entanto foi capaz de fornecer uma resposta adequada aos doentes admitidos por SCA.

Palavras-chave: COVID-19; Pandemia; Portugal; SARS-CoV-2; Síndrome Coronária Aguda

INTRODUCTION

In 2020 the world was confronted with a new pandemic, a highly contagious and deadly virus, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). According to the World Health Organization, over 583 million people were infected and more than 6,4 million deaths were registered,[1] with a mortality rate of approximately 2%.

1. Serviço de Cardiologia. Centro Hospitalar Barreiro-Montijo. Barreiro. Portugal.
2. Serviço de Cardiologia. Hospital de Santa Marta. Centro Hospitalar Universitário Lisboa Central. Lisboa. Portugal.
✉ **Autor correspondente:** Helder Santos. helder33689@gmail.com

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When confronted with the pandemic, all countries were forced to implement several measures to mitigate the impact of the SARS-CoV-2 infection. Portugal started by proposing several individual limitations and social distancing measures. However, it ended up enforcing a national lockdown on the 18th March 2020, where individuals stayed in home confinement except for essential reasons.[2] These measures were essential to contain the pandemic progression and allow the healthcare system to become capable of confronting an unknown and aggressive infection.

The absence of curative or preventive medical treatments at the time caused a significant strain to the healthcare system, by demanding large support from intensive care units and dedicated healthcare professionals. These changes led to a reorganization and restructuring of the resources within the hospitals,[3] the cancelation of non-essential procedures and outpatient clinic appointments to allow the healthcare system to be able to respond to the SARS-CoV-2 infection without neglecting the medical management of prevalent non-SARS-CoV-2 diseases.

The true effect of this pandemic on non-SARS-CoV-2 patients has been difficult to quantify. During the pandemic, physicians raised concerns regarding the reduction of emergency admissions and diagnosis of severe acute conditions, as well as a higher incidence of sudden cardiac arrest.[4] Some of these cases can be a consequence of acute coronary syndrome (ACS) and the delay in its approach and treatment. ACS is a highly prevalent condition that involves a life-saving evidence-based emergent treatment.[5] Worldwide, incidence reports of ACS significantly decreased during the pandemic period.[6-10] A reduction in the diagnosis and treatment of ACS can lead to severe long-term consequences in the Portuguese population. Several explanations were proposed for the reduction of severe acute disease in the emergency department. Some experts postulated that the reduction of ACS incidence was due to the patients' fear of being infected with SARS-CoV-2 in healthcare facilities, an increase in patients' threshold for calling emergency services and a reduction of the capacity of the healthcare system to provide individual attention.[11,12]

Based on previous reports and the overall Portuguese healthcare system support during the SARS-CoV-2 pandemic, our goal was to understand if there were changes in the response of the national healthcare care system to patients with ACS and if the profile of ACS patients during the pandemic period was different from previous years.

MATERIAL AND METHODS

Pro-ACS registry design

The Portuguese Registry of Acute Coronary Syndromes (Pro-ACS– ClinicalTrials.gov NCT 0162329) is a continuous, nationwide, prospective, observational registry launched in 2002. Data is uploaded by participating centers and managed by the Portuguese Society of Cardiology. All ACS patients older than 18 years are eligible for inclusion. ACS episodes are adjudicated according to current guidelines and based on electrocardiogram, myocardial necrosis biomarkers and clinical status.[13] Data collected include patient demographics, baseline characteristics, presenting symptoms, biochemical, electro and echocardiography findings, clinical evolution, medical treatment (background, in-hospital and post-discharge), coronary anatomy, revascularization procedures, and clinical outcomes. Outcome data were collected after hospital discharge and after one-year of follow-up.

Study population

A total of 13 950 validated episodes in the Pro-ACS registry between the 1st January 2016 and the 28th February 2021 were accessed. Considering the seasonality of ACS, we started by comparing the occurrence of ACS between March, April, May and June 2016, 2017, 2018, 2019 and 2020. Then we compared these months in 2020 with the same period in 2019. Finally, we compared the first SARS-CoV-2 wave (between March and June 2020) with the second and third waves (November - December 2020, and January - February 2021).

Each patient might have had more than one episode of ACS. Patients with missing data regarding the ACS type and times until medical care were excluded. ACS episodes were classified according to the Fourth Universal Definition of Myocardial Infarction.[13] Then, patients were categorized in the final diagnosis of ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI) or unstable angina.

Multivessel disease was defined as the presence of two or more coronary artery stenosis (> 50%). Valvular heart disease was defined as severe valvular stenosis or regurgitation or previous valvular intervention. Family history of cardiovascular disease refers to patients with at least one relative that presented a previous cardiac event (including sudden cardiac arrest) before the age of 65. Chronic kidney disease was considered in all the patients with a creatinine level higher than 2 mg/dL or glomerular filtration rate below 30 mL/min/1.73 m^2. Hybrid revascularization was defined as the revascularization technique that combines both percutaneous coronary intervention and coronary artery bypass.

Ethics committee approval

Participation in the registry must be approved by the institutional review board at each institution, the local ethics committee and the Portuguese Data Protection Authority (no. 3140/2010).[14] All ethical requirements in the Helsinki Declaration 2013 were met, not involving any human and/or animal experimentation. Written informed consent for the introduction of patient' data into the registry is available since 2010 and has been applied after approval by the ethics committee of each hospital center.

Statistical analysis

All statistical analyses were performed by a professional statistician within the National Centre for Data Collection in Cardiology (CNCDC), using SPSS software (SPSS Inc., Chicago, IL, USA) for Windows XP (version 20.0).

The groups were characterized according to continuous and categorical variables. Continuous variables being expressed as mean and standard deviation (SD) if normally distributed, or median and interquartile range (IQR) in case of skewed distribution. Comparisons between groups regarding categorical variables were conducted using the chi-square test or Fisher's test. Means of continuous variables were compared using *t* tests whenever possible; otherwise, the Mann-Whitney U test was used to compare the medians. When more than two groups were analyzed together, the chi-square test or the Monte Carlo simulation test for the chi-square statistic was used for categorical variables and analysis of variance or the Kruskal-Wallis test was used for continuous variables. Significance level of 5% was assumed for testing the hypothesis.

RESULTS

Regarding the evaluation of the years before the SARS-CoV-2 pandemic, between March, April, May and June 2016, 2017, 2018, 2019 and 2020, there was a fluctuating incidence of ACS (Fig. 1). Nonetheless, patients admitted with ACS in these periods presented similar baseline demographic, clinical course as well as clinical outcomes. Table 1 in Appendix 1 (https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/18610/Appendix_01.pdf) displays the differences according to the year. Over the years, there was an improvement in STEMI patient referral directly to the catheterization laboratory, as well as an overall reduction in the admission for ACS in centers without percutaneous coronary intervention capacity (PCI).

A total of 952 ACS events were registered during those months in 2019, while the same period in 2020 recorded only 642. This represented a significant reduction of 32.6% in the number of ACS events reported at a national level during the first pandemic wave. On the other hand, the relative proportion of types of ACS remained similar (STEMI 53.7% *vs* 51.6%, $p = 0.406$; NSTEMI 43.6% *vs* 46.1%, $p = 0.322$).

Patients admitted for ACS prior the SARS-CoV-2 pandemic and during the pandemic were similar regarding demographic characteristics, as represented in Table 1. The prevalence of cardiovascular risk factors was similar, except for diabetes mellitus (31.9% *vs* 26.4%, $p = 0.023$). Concerning other comorbidities, only chronic obstructive pulmonary disease revealed a higher prevalence in 2020 (3.5% *vs* 6.3%, $p = 0.019$).

Table 2 illustrates the clinical presentation features in the two periods considered, and no significant differences were found. The pandemic group was more frequently admitted to hospitals without a catheterization laboratory ($p = 0.034$) and, consequently, the rates of transfer to another hospital were higher ($p < 0.001$). Other patterns of hospital admission did not change significantly from 2019 to 2020. Nevertheless, a trend towards a reduction of direct transfers from the pre-hospital emergency medical services to a PCI center ($p = 0.090$) was noticed. Concerning all times for assistance of ACS during the pandemic, there was a trend towards a longer delay in seeking hospital admission despite no significant delays being recorded, transfer delays and longer times until admission and reperfusion were also detected during the pandemic period.

Regarding the clinical management (Table 3) no significant differences were reported between the SARS-CoV-2 year and the previous year. The exception were patients undergoing coronary angiography, which was more frequent during the SARS-CoV-2 period ($p < 0.001$). No differences were observed regarding revascularization strategy, multivessel disease prevalence, intervention performance and

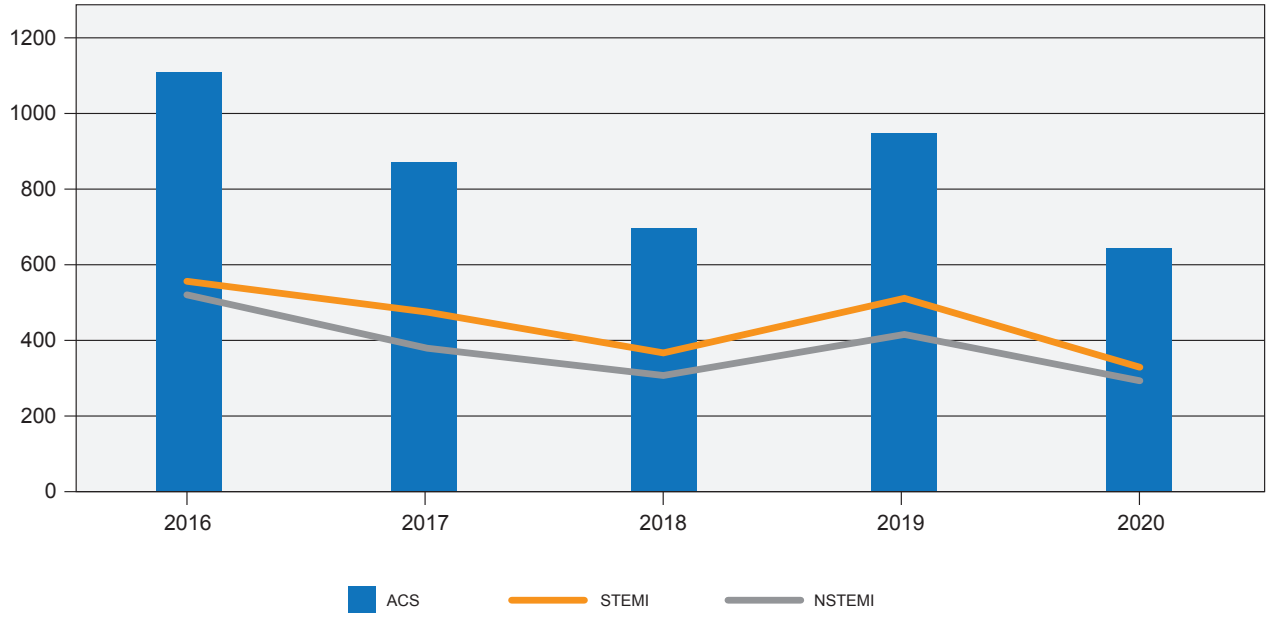

Figure 1 – The incidence of acute coronary syndromes (ACS) in the months of March, April, May and June according to the year
STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction

Table 1 – Demographic characteristics of the patients admitted for acute coronary syndrome according to the year

	2019 (n = 952)	2020 (n = 642)	*p*-value
Age, years	66 ± 13	65 ± 13	0.207
Sex, (male)	708 (74.4%)	499 (77.7%)	0.125
Smoking, n (%)	242 (32.1%)	189 (37.1%)	0.066
Arterial hypertension, n (%)	620 (67.6%)	396 (65.3%)	0.359
Diabetes mellitus, n (%)	277 (31.9%)	160 (26.4%)	0.025
Dyslipidaemia, n (%)	507 (55.3%)	318 (52.6%)	0.296
Familiar cardiovascular history, n (%)	22 (2.4%)	26 (4.5%)	0.023
Angina, n (%)	188 (24.6%)	100 (21.6%)	0.223
Previous ACS, n (%)	132 (16.5%)	87 (18.8%)	0.292
Valvular heart disease, n (%)	18 (2.2%)	13 (2.8%)	0.526
Previous heart failure, n (%)	50 (6.2%)	32 (6.9%)	0.621
Peripheral arterial disease, n (%)	32 (4.0%)	19 (4.1%)	0.907
Chronic kidney disease, n (%)	63 (7.9%)	29 (6.3%)	0.310
Cancer, n (%)	35 (4.4%)	23 (5.0%)	0.601
Chronic obstructive pulmonary disease, n (%)	28 (3.5%)	29 (6.3%)	0.019
Dementia, n (%)	12 (1.5%)	7 (1.5%)	0.970
Previous bleeding, n (%)	16 (2.0%)	8 (1.8%)	0.756

Table 2 – Clinical presentation characteristics of the patients admitted for acute coronary syndrome according to the year

	2019 (n = 952)	2020 (n = 642)	*p*-value
Chest pain, n (%)	695 (92.5%)	462 (94.5%)	0.183
Dyspnoea, n (%)	16 (2.1%)	9 (1.8%)	0.723
Cardiac arrest, n (%)	6 (0.8%)	3 (0.6%)	1.000
Killip-Kimball class > I, n (%)	133 (16.9%)	72 (15.5%)	0.515
ST-elevation myocardial infarction, n (%)	511 (53.7%)	331 (51.6%)	0.406
Non-ST-elevation myocardial infarction, n (%)	415 (43.6%)	296 (46.1%)	0.322
Pre-hospital emergency medical service, n (%)	211 (22.8%)	111 (19.1%)	0.090
Transfer to another hospital, n (%)	143 (15.4%)	152 (26.2%)	< 0.001
Non-percutaneous coronary intervention capable hospital, n (%)	242 (26.6%)	183 (31.7%)	0.034
Time from the onset of symptoms to first medical contact, (min) (median, IQR)	188 (92, 409)	171 (93, 352)	0.362
Time from the first medical contact to hospital admission, (min) (median, IQR)	152 (60, 381)	175 (60, 388)	0.838
Time from the onset of symptoms to reperfusion, (min) (median, IQR)	251 (180, 374)	285 (210, 443)	0.110
Time from the first medical contact to reperfusion, (min) (median, IQR)	105 (60, 168)	106 (57, 171)	0.773
Time from door to reperfusion, (min) (median, IQR)	64 (30, 117)	60 (30, 160)	0.773

min: minutes; IQR: interquartile range

the success rates of all interventions.

During the pandemic, no differences were found concerning re-infarction, heart failure, new onset of atrial fibrillation, cardiogenic shock, mechanical complications, cardiac arrest, stroke, major bleeding and in-hospital all-cause of death (Table 4) between 2019 and 2020. Nonetheless, during the four months of 2020 we noted a higher incidence of atrioventricular block (1.4 *vs* 3.5%, $p = 0.010$) and sustained ventricular tachycardia (0.4 *vs* 1.9%, $p = 0.012$). During these patient's short follow-up period of one year (129 patients with follow-up, 90 in 2019 and 39 in 2020), the pandemic group had a higher incidence of death (10.0 *vs* 20.5%, $p = 0.105$) and readmission for all causes (7.4 *vs* 10.5%, $p = 0.724$) even though without statistical significance.

When comparing the first pandemic peak (March to June 2020) to the second and third peaks in Portugal (November, December 2020 and January, February 2021) no significant differences were found regarding the incidence of ACS, STEMI, all-time components, in-hospital outcomes, in-hospital mortality, readmission for all causes and mortality rates at one-year follow-up [Appendix 1, Table 2 (https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/18610/Appendix_01.pdf)]. Nonetheless a

Table 3 – Clinical management, angiography and revascularization characteristics of the patients admitted for acute coronary syndrome according to the year

	2019 (n = 952)	2020 (n = 642)	*p*-value
Left ventricular ejection function, (%)	50 ± 10	51 ± 10	0.299
Angiography performance, n (%)	573 (60.3%)	494 (77.1%)	< 0.001
Radial access, n (%)	880 (92.5%)	570 (88.9%)	0.093
Multivessel disease, n (%)	328 (34.5%)	247 (38.5%)	0.199
Percutaneous coronary intervention, n (%)	485 (51.2%)	430 (67.3%)	< 0.001
Coronary artery bypass grafting, n (%)	25 (7.6%)	14 (4.3%)	0.074

Table 4 – In-hospital complications of the patients admitted for acute coronary syndrome according to the year

	2019 (n = 952)	2020 (n = 642)	*p*-value
Mortality, n (%)	39 (4.1%)	27 (4.3%)	0.830
Major adverse cardiac events, n (%)	137 (14.4%)	107 (16.8%)	0.244
Reinfarction, n (%)	5 (0.5%)	1 (0.2%)	0.422
Heart failure, n (%)	80 (8.4%)	57 (9.0%)	0.751
Cardiogenic shock, n (%)	26 (2.8%)	14 (2.2%)	0.477
New-onset atrial fibrillation, n (%)	40 (4.2%)	37 (5.8%)	0.173
Mechanical complication, n (%)	2 (0.2%)	0 (0.0%)	0.533
Complete atrioventricular block, n (%)	13 (1.4%)	22 (3.5%)	0.010
Sustained ventricular tachycardia, n (%)	4 (0.4%)	12 (1.9%)	0.012
Cardiac arrest, n (%)	27 (2.9%)	25 (4.0%)	0.321
Stroke, n (%)	6 (0.6%)	4 (0.8%)	0.733
Major haemorrhagic events, n (%)	4 (0.4%)	8 (1.3%)	0.082

higher incidence of diabetes patients and patients admitted in the emergency room in the second and third waves were observed. Moreover, the first wave had a better angiography and percutaneous coronary intervention performance, as well as a higher rates of transfer to another hospital.

DISCUSSION

In this study we found a nationwide reduction of 32.6% in demand of healthcare services due to ACS events during the first wave of SARS-CoV-2 infection. Also, during this period, patients were less often referred to percutaneous coronary intervention centers. Nonetheless, the overall Portuguese healthcare system was capable of responding adequately to ACS during the pandemic.

The SARS-CoV-2 pandemic caused significant strain to the healthcare system all around the world. Yet, most of the studies during this period argued that the SARS-CoV-2 impact was only modest and did not overload the healthcare system.[15] However, this impact can also play a role on the decline of ACS incidence. Some patients did avoid accessing the healthcare system by fear of getting infected, and the strict measures applied by national authorities may have contributed to a reduction in the number of emergency admissions[16] and, as a consequence, a reduction in hospital admissions due to non-related SARS-CoV-2 diseases, notably ACS.[9,17,18] A different explanation for the reduction of ACS during the pandemic argues that different factors like a decline in atmospheric pollution, a reduction in physical activity and other radical adjustments due to the lockdown were capable of influencing the atherosclerotic plaques and promote its stabilization.[19] The present analysis is not capable of considering the factors presented in the last hypothesis.

Portugal was no different from most countries, as a decrease in emergency admissions and an increase of the overall mortality rate during the first SARS-CoV-2 wave was found. Nonetheless, this increase in the mortality rates was possibly not entirely related with the SARS-CoV-2 infection,[20] thus strengthening the importance of establishing efficient health policies to manage non-related SARS-CoV-2 disease. In this national database, we reported a lower nationwide incidence of ACS admissions. However, the pandemic ACS patients did not present major differences regarding their characteristics, management and prognosis in comparison with the same period in the previous year.

National and international publications corroborate our findings of a substantial reduction in the incidence of ACS[4,21-23] in 2020. Moreover, the pandemic led to a reduction in hospitalizations due to coronary artery disease, cardiac diagnostic procedures, PCI and structural interventions worldwide.[23] Many Portuguese centers described the impact of the pandemic on their healthcare assistance, namely its impact on STEMI patients.[24,25] Moreover, different authors reported a more substantial reduction in the incidence of

NSTEMI over STEMI.[10,26] Our data reported an overall reduction of ACS events, with an absolute decrease of all types of ACS at a national level, although the proportions of the ACS subtypes remained the same. The demographic characteristics of patients were similar and coronary artery disease had the same severity between the two periods, which is in agreement with previous reports from various Portuguese regions.[24,27] Nonetheless, without mortality data from the non-SARS-CoV-2 patients, we still do not know if there was a real reduction in ACS incidence or just a reduction of ACS admissions secondary to decreased demand for medical assistance.

The pressure in the healthcare system was so overwhelming in some regions of the world that these regions had to adjust the reperfusion strategy in ACS, and implemented fibrinolysis protocols over percutaneous coronary intervention as the first measure in case of STEMI patients.[28] This was not the case in Portugal since no differences in reperfusion strategies were found in the national database or other national series.[24,25,27] Also, no differences were reported concerning the clinical presentation and management of the ACS between the two periods.

Our results demonstrated the absence of delays regarding all times to medical assistance and reperfusion in the pandemic context, which is in line with several series of Portuguese healthcare institutions, although a trend towards a delay during the pandemic was observed.[24,25,27] Other countries reported different outcomes, given some countries were able to maintain the times from the onset of symptoms until reperfusion[29,30] while others presented a delay.[22] Therefore, in Portugal, the overall provision of medical assistance and reperfusion did not seem to have been influenced by the SARS-CoV-2 pandemic, probably because the Portuguese healthcare system did not collapse[31] during the first wave of the pandemic.

A significant number of patients was not directly referred to a hospital with PCI capacity which favors the system delay and overload, since it implies a logistic effort to transfer the patient, and forcing healthcare professionals to adopt protective measures during the transfer and during PCI, with both healthcare institutions needing to have a dedicated area to receive these patients, thus extending the time until the reperfusion. This was an issue our database did not explore, but nonetheless was mentioned by other colleagues in one Portuguese region.[25]

Prognosis, in-hospital mortality and in-hospital complications were more prevalent in the pandemic group, but without statistically significant differences. Other authors reported similar findings,[17,25,27] which suggest that Portugal's public health measures were able to maintain primary care services for ACS patients. Even so, some authors from Portuguese healthcare institutions presented different results, with a higher incidence of mechanical ACS complications and in-hospital mortality.[24] Nonetheless, if we consider the reduction in the number of documented ACS events nationwide, it's possible that the prognosis of the patients properly identified as ACS during the pandemic is the same as the patients in the previous years. If we consider that the reduction of ACS events may be due to patients avoiding healthcare systems, the overall prognosis of ACS may be worse than perceived, given that eventually patients without proper assistance during the acute event may develop heart failure and other late complications. These complications, which would probably be avoided or attenuated by diagnosis and prompt treatment, may result in higher costs, either for both the healthcare systems (monetary costs) and for patients (poorer quality of life, higher morbidity and mortality).

In the first pandemic wave, the Portuguese healthcare system was capable of responding without the entire system collapsing, given that the incidence of SARS-CoV-2 infection was lower than in other countries. With the second and third waves, a reorganization of the emergency and of other departments was required to be able to respond to the overload of SARS-CoV-2 patients. New circuits and more healthcare professionals were recruited to carry out different assignments from their everyday practice to support their colleagues, something that further compromised the ability to provide care to patients with non-related SARS-CoV-2 diseases.

Health authorities were crucial in the prompt and efficient ACS response. Since the first SARS-CoV-2 pandemic wave, health authorities developed campaigns to ensure the safety of the healthcare institutions in managing other diseases and that medical assistance to ACS was safe and with a low risk of infection.[24] This may explain why the response to ACS care during the second and third waves was similar to the first wave. Although those waves were worse in terms of number of infections and overload of resources, the in-hospital outcomes were similar to those of the first wave. A reduction of the overall number of ACS events was also recorded in these waves compared to numbers prior to the pandemic.

This study described the nationwide management of ACS during the first three pandemic SARS-CoV-2 waves in Portugal. It showed that the healthcare system was able to provide high-quality cardiovascular care to the population. Nonetheless, continuous cardiovascular educational programs are crucial in order to maintain this level of care, since it's possible that in coming years an increasing number of patients might attend the emergency department as a consequence of ACS that was not treated during the SARS-CoV-2 pandemic. Moreover, this experience could be beneficial to establish new protocols and as preparation in case of future pandemics.

Limitations

There are several limitations to be considered in the study design and interpretation.

This was an observational and non-randomized study, which can have associated confounders that can influence the outcomes. Some of the patients could have misclassified characteristics or incomplete records. The analysis of differences between patients with and without the combined

endpoint was performed with univariable, non-adjusted models without correction of multiple inferential tests. Acute morbidity and mortality could have been underestimated since the pre-hospital care was not considered, and we did not have data from these patients. If we had had access to all the autopsies in these periods, we would also be able to further understand if the excess of unexplained mortality was related to undetected ACS or not.

Other complications, namely non-cardiovascular complications, could have interfered with the patient's prognosis, but were not considered in the registry. Even considering the high number of patients in the registry, only a few patients had a documented follow-up after the hospitalization.

This study did not evaluate the potential relationship between the presence of SARS-CoV-2 infection and a concomitant occurrence of ACS.

CONCLUSION

During the first wave of the SARS-CoV-2 pandemic waves there was a reduction in the incidence of ACS, including STEMI and NSTEMI. The Portuguese system was able to provide adequate assistance to patients with ACS. Further research is needed to understand the causes that were associated with the reduction in the number of ACS admissions during the first wave of SARS-CoV-2 pandemic and the long-term repercussion of the pandemic on cardiovascular health.

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AUTHOR CONTRIBUTIONS

HS: Writing of the manuscript.

MS, SBP: Statistical analysis, revision of the manuscript.

IA, SA, LA: Critical review.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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