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IMPACT OF THE COVID-19 PANDEMIC ON CLINICAL OUTCOMES OF ACS: RETROSPECTIVE ANALYSIS FROM AN ITALIAN CARDIOLOGY NETWORK

*Antonio Oliva [1 #], Lorenzo Belli [2 #], Matteo De Rosa [2 #], Simone Grassi [1 +], Cristian D'Ovidio [3], Marcello Caputo [4], Sante Pierdomenico [2 *], Jacopo Pizzicannella [4 *]*

1. Legal Medicine, Department of Health Surveillance and Bioethics, Università Cattolica del Sacro Cuore, Rome, Italy.
2. Department of Medical, Oral and Biotechnological Sciences, University "Gabriele d'Annunzio", Chieti-Pescara, Chieti, Italy.
3. Legal Medicine, University "Gabriele d'Annunzio", Chieti-Pescara, Chieti, Italy.
4. ASL02 Lanciano-Vasto-Chieti, Ss. Annunziata Hospital, Chieti, Italy.

 # Antonio Oliva, Lorenzo Belli and Matteo De Rosa equally contributed and thus should be considered co-first authors
** Piersante Pierdomenico and Jacopo Pizzicannella are co-senior authors*

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ABSTRACT

Several authors worldwide have reported a significant decrease in hospital admissions for acute coronary syndromes (ACSs) during the most recent months of the COVID-19 outbreak. The causes of this pattern and its impact on patients and hospital management have been studied. We conducted a monocentric, observational, retrospective study aimed at evaluating consecutive patients discharged from our local network with a diagnosis of ACS from the 20th of February 2020 to the 30th of April 2020. 201 patients with ACS were included in the analysis. The number of patients with NSTE (Non-ST elevation)-ACS dropped from 84 (65%) in 2019 to 21 (44.4%) in 2020 (62% reduction, $p < 0.01$), while more patients with a diagnosis of STEMI were admitted in 2020. 38 composite events were observed in 2020, while only 34 patients were free from events. Conversely, in the 2019 ACS group, 37 events were recorded, while 92 patients did not develop any events (RR 1.82; 1.29- 2.6 95% CI; $p< 0.01$). Delay in diagnosis and treatment of patients with ACS has a significant impact on public health costs and sustainability of care, since it is associated with a significant increase in short-term complications and deaths. Public health messaging and proper healthcare services organization should play a crucial role in adjusting the system to the new needs of public health.

1. Introduction

The dramatic and unexpected reorganization of healthcare services due to the COVID-19 pandemic has radically changed the management of inpatients and outpatients affected by cardiovascular disease (CVD) [1]. The European Society of Cardiology (ESC) recently launched an international survey to assess self-reported perceptions of the rate of admission for STEMI in the facilities of healthcare professionals (HPs; both physicians and cardiovascular nurses) who work in cardiology services. As expected, most of the HPs (80%) felt there had been a decrease in STEMI, with the large majority of survey participants reporting a > 40% reduction [2]. Another survey from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) on the COVID-19 impact on interventional cardiology found that 89% of the participants had this opinion [3].

* *Corresponding author*: Simone Grassi, simone.grassi@unicatt.it
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Moreover, other observations of the EAPCI survey related to ACS management were even more striking, including an increase in delays to coronary angiography/ percutaneous coronary intervention (PCI), the choice of fibrinolysis instead of primary PCI for STEMI and an increase in patients presenting with cardiogenic shock or mechanical complications [3]. These findings are supported by several authors worldwide that have reported a significant decrease in hospital admissions for acute coronary syndromes (ACSs) during the most recent months of the COVID-19 pandemic [4-11]. An Australian group found a sudden and sharp four-fold increase in symptom-to-door-time in patients with ACS requiring PCI, with approximately 50% of patients presenting late (>12 h) [12]. Reported patient-related delays in ACS management during this period have been replicated elsewhere [13, 14]. Conversely, De Rosa et al. reported that both patient- and system-related (door to balloon time) delays were significantly increased in the COVID-19 era [6]. Thus, robust and consistent evidence shows that the COVID-19 pandemic has dramatically changed the pattern of ACS admission (ACS patients presenting less often and later) and has promoted a sudden reorganization of both cardiac coronary units (CCUs) and catheterization laboratories, possibly leading to a delay in cardiac interventional procedures. Whether the COVID-19 pandemic consequences have led to a worsening of clinical outcomes of ACS patients admitted to CCUs needs to be further investigated. An initial exploratory analysis, which included a very short period of follow-up, found an increase in the fatality rate and major complications rate in STEMI patients [6]. To prepare for a secondary CVD outbreak following the spread of COVID-19 worldwide, accurate insight into the COVID-19 pandemic impact on CVD management and outcomes is currently mandatory.

2. Methods

We conducted a monocentric, observational, retrospective study aimed at evaluating consecutive patients discharged from our local network with a diagnosis of ACS from the 20th of February 2020 to the 30th of April 2020. These data were compared with data from the same time period in 2019. Data were collected through consultation of our informatic system for clinical records, including all cardiac care centers in our local heart network (both CCU Hub hospitals with dedicated cath labs and spoke hospitals located outside the chief town, Chieti). Patients who died before CCU arrival, as well as those discharged from the cardiac surgery department following surgical revascularization, were excluded from the analysis. ACS, STEMI, and NSTE-ACS were defined according to international guidelines [15-17]. Major events were defined as death, life-threatening arrhythmias, mechanical complications (septal or free wall rupture) and acute heart failure (either presence of pulmonary edema or need for inotropic support drugs). The events were considered separately and as composite outcomes. Statistical significance was evaluated using the $\chi 2$ test and Fisher's exact test. All statistical analyses were performed using MedCalc (MedCalc Software, New York, NY, USA).

Ethical approval and consent to participate were not required since the data is completely anonymous with no personal information being collected (General Data Protection Regulation - EU regulation n. 2016/279). Authorization to collect and publish the data from the hospitals of the network was requested and received.

3. Results

A total of 201 patients with ACS were included in the analysis. The clinical characteristics of our population are reported in Table 1. Of interest, all patients with ACS in 2020 were free of Sars-nCoV2 infection, as demonstrated by negative swabs and the absence of any alarming symptoms suggesting viral respiratory infection. Seventy-two ACS cases occurred during the February 20-April 30, 2020 period, while 129 were recorded during the same period in 2019 (44.4% reduction) (Figure 1). We found a significant change in the pattern of admissions to our CCUs according to the class of ACS. In particular, the number of patients with NSTE-ACS dropped from 84 (65%) in 2019 to 21 (44,4%) in 2020 (62% reduction, $p < 0,01$) (Figure 2), while more patients with a diagnosis of STEMI were admitted in 2020.

	2020, n=72	2019, n=129
Age (M±SD)	71.27 (12.6)	70.2 (14.15)
Sex (F), n (%)	19 (26)	36 (27)
Hypertension, n (%)	47 (65)	70 (54)
BMI> 35 kg/m2, n (%)	10 (13.8)	38 (29.4)
Dyslipidemia, n (%)	32 (44)	31 (24)
Diabetes, n (%)	21 (29)	71 (55)
Smoking, n (%)	29 (40)	28 (21.7)
Family history of CVD, n (%)	5 (7)	10 (7)
CKD, n (%)	12 (16)	27 (20)
History of CAD, n (%)	17 (23)	43 (33)
Spoke, n (%)	14 (19.4)	31 (24)
NSTEMI, n (%)	32 (44.4)	84 (65.1)
STEMI, n (%)	40 (55)	45 (34)

Table 1. Clinical characteristics of the patients

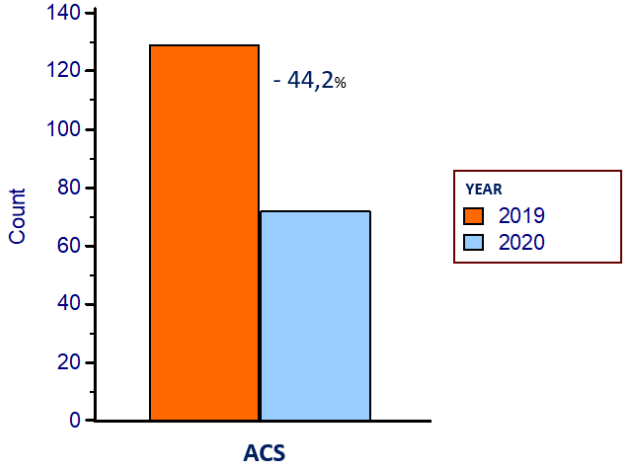

Figure 1. Patients with acute coronary syndromes discharged from our local heart network. The figure reports the number of discharges registered during the 20 February-30 April 2020 period (light blue bar) and during the same period of the previous year for comparison (orange bar).

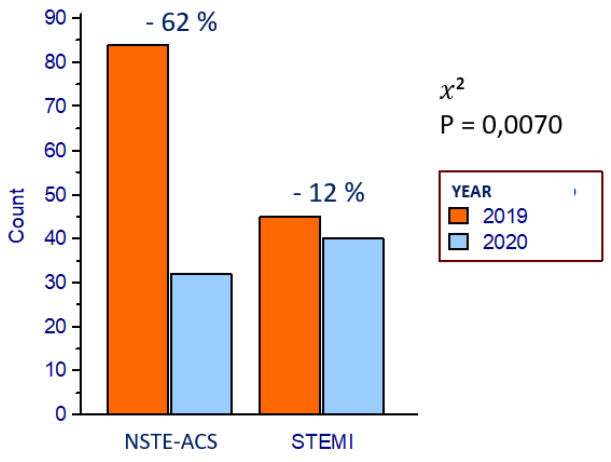

Figure 3. Patients with acute coronary syndromes discharged from our local heart network based on the type of ACS. The figure reports the number of discharges of NSTE-ACS and STEMI registered during the 20 February-30 April 2020 period (light blue bar) and during the same period of the previous year for comparison (orange bar).

Thirty-eight composite events (mortality, life-threatening arrhythmias, mechanical complications and acute heart failure) were observed in 2020, while only 34 patients were free from events. Conversely, in the 2019 ACS group, 37 events were recorded, while 92 patients did not develop any events (RR 1,82; 1,29- 2,6 95% CI; p< 0,01) (Table 2).

We also assessed the relative risk for every single kind of event collected. Arrhythmias and mechanical complications did not differ between the 2019 and 2020 groups, while AHF occurred in 12 (16%) patients in the 2020 group and 9 (6%) in the 2019 group (RR 2,38; 95% CI 1,05- 5,04; p<0,05) (Table 2). Death occurred in 14 (19%) patients in the 2020 group and in 10 (7,7%) patients in the 2019 group (RR 2,5; 95% CI 1,17-5,3; p= 0,01) (Table 2). The same analysis was performed after the exclusion of patients without STEMI. Deaths in the STEMI cohort were significantly different between the 2019 and 2020 groups (2,27% in 2019 vs 25% in 2020; RR 11,2500; 95% CI 1,5058 to 84,0511 p<0,01) (Table 3). Accordingly, both AHF (RR 7,8750; 95% CI 1,0122 to 61,2691; p<0,05) and composite events (RR 2,53 95% CI 1,23-5,17 p < 0,01) occurred more frequently in the 2020 group (Table 3).

Events	2019, n (%)	2020, n (%)	RR	\95% CI	p value
All events	37	38	1.84	1.29-2.6	p<0.01
Death	10 (7.7)	14 (19)	2.5	1.17-5.3	0.017
AHF	9 (6)	12 (16)	2.38	1.05- 5.04	0.036
Arrhythmias	17 (13.1)	10 (13.8)	1.07	0.52-2.22	0.83
Mechanical Complications	1 (0.77)	2 (2.7)	3.58	0.33-38.8	0.29

Number of deaths, AHF, arrhythmias and mechanical complications during the 2019 and 2020 index period are reported. Risk ratios are reported, together with their 95% confidence intervals (95% CI), followed by the P-value.

Table 2. Clinical outcomes in all ACS patients

Events	2019, n (%)	2020, n (%)	RR	95% CI	p value
All events	8	18	2.53	1.23-5.17	<0.01
Death	1 (2.2)	10 (25)	11.25	1.50-84.05	<0.01
AHF	1 (2.2)	7 (17.5)	7.87	1.01- 61.2	0.048

Number of deaths. AHF. arrhythmias and mechanical complications in the STEMI patients during the 2019 and 2020 index period are reported. Risk ratios are reported. together with their 95% confidence intervals (95% CI). followed by the P-value.

Table 3. Clinical outcomes in STEMI patients

4. Discussion

In many countries, a reduction in admissions due to ACS has been registered [4-11]. Consistent with this evidence, our local heart network recorded a 44% reduction in admissions for all types of ACS. It is still a matter of debate why the incidence of ACS has decreased during the COVID-19 pandemic, and the fear of seeking medical aid in high-risk environments such as hospitals has been proposed as a possible explanation [18, 19]. In our database, we noted a reduction in ACS cases among patients with a personal history of coronary artery disease (CAD) (23% in 2020 vs 33% in 2019). This could be because patients with known previous cardiac episodes avoided going to the hospital because of the advice that people with cardiovascular diseases are at very high risk of developing severe forms of COVID-19. Second, we found a significant change in the pattern of admissions for ACS with a decrease in total ACS cases, guided by a reduction in NSTE-ACS; however, the absolute number of STEMI admissions was temporally unchanged, while the relative number was conversely increased. Patients with NSTE-ACS often complain about milder and nonspecific symptoms and have more comorbidities. These clinical characteristics might have induced them to stay at home, underestimating their symptoms or fearing an increased risk of being infected by COVID-19. Finally, other authors have found a close relationship between the COVID-19 pandemic and the increase in out-of-hospital cardiac arrest (OHCA) [20]. It may be speculated that many patients who died at home as a result of OHCA would have received a diagnosis of ACS, since AMI (acute myocardial infarction) still represents the main cause of out-of-hospital cardiac arrest. Moreover, some authors found that non-COVID-19 mortality may have increased during the COVID-19 pandemic [21]. In accordance with this report, we found an increase in in-hospital mortality (19% in 2020 vs 7,7% in 2019), complication rates (in particular acute heart failure (16% in 2020 vs 6% in 2019)), and in a combined outcome that included in-hospital mortality and mechanic, hemodynamic and arrhythmic complications of AMI (RR 1,82) among ACS cases. Mortality and complication rates in 2019 were consistent with worldwide AMI registries of the last decade. Strikingly, the mortality rate in ACS patients in the first months of 2020, during the COVID-19 pandemic, was comparable to previous findings from the early 1990s, when reperfusion strategies first began to spread worldwide [22, 23]. The worsening of outcomes in the cohort including all ACS during the first months of 2020 was somewhat expected since the pattern of ACS admissions has changed with a larger contribution of very high-risk patients being referred to hospitals for STEMI (55% in 2020 vs 34% in 2019) rather than NSTE-ACS. Thus, we performed the same analysis including only patients with STEMI. Accordingly, both outcomes (in-hospital mortality alone and total events) occurred more frequently in STEMI patients in 2020. STEMI patients in 2020 were not older, and had less frequent previous CAD, diabetes, CKD and obesity; moreover, the burden of classical risk factors was not overrepresented in 2020 when compared to 2019.

The increase in total ischemic time may be the main leading factor since it is consistently reported elsewhere [6, 12, 14, 24]. Primary PCI in STEMI and NSTEMI patients at high risk and, in general, timely angiography and coronary intervention have undoubtedly improved prognosis in ACS patients and are currently recommended by international guidelines [16, 17]. Thus, a major effort of healthcare systems to shortening door-to-balloon time has been pursued over the last few decades. However, patient-related delays remain a primary concern. During a public health emergency, such as the COVID-19 pandemic, these delays become more challenging to predict and are, in general, expected to increase. System-dependent delays represent another important issue to consider. In the COVID-19 era, each patient referred to CCUs or sent to the cath lab for coronary angiography should be considered a possible COVID-19 carrier. Thus, medical societies and heart foundations have published a series of consensus documents to allow a standardized approach to ACS in the COVID-19 era and to protect the hospital environment and healthcare professionals from viral spreading. Ideally, nasopharyngeal and oropharyngeal swabs should be performed on all patients before any procedure, appropriate personal protective equipment (PPE) should be worn by all healthcare workers, and patients with a positive test should be admitted to dedicated COVID-19 Units with the congruous intensity of care according to the clinical status [25-27]. The ANMCO (Italian Association of Hospital Cardiologists) consensus statement, in particular, suggested that after PCI, patients with ACS should be isolated in congruous wards to wait for swab results and then admitted to the COVID-19-free CCU or alternatively to the COVID-19 Unit [28]. According to our experience, we have reorganized our CCU service to create a COVID-CCU in the Hub center (Policlinico "SS. Annunziata" – Chieti) of our local heart network. It was outside but very close to the COVID-19-free-CCU, and it received all patients with acute cardiac syndromes (ACS, acute heart failure, life-threatening arrhythmias) and suspected or confirmed COVID-19. This management would have allowed preservation of the availability of beds in intensive care units (ICUs) for patients demanding invasive mechanical ventilation and guaranteed continuity of cardiac care. Moreover, this model fit well with the organization of facilities at our Hub center. However, after reviewing this two-month experience, we found that many patients requiring acute cardiac care had been unproperly admitted to the COVID-19 CCU. Fear of false negative results of swabs with suboptimal sensitivity, delayed availability of swabs results due to laboratory overload, and an excessive instinct to protect the safe environment of the COVID-19-free CCUs may be possible explanations. This model of management was expected to improve in terms of larger availability of serum assays and faster molecular tests as well as a better recognition and management of COVID-19 patients.

1. All these findings have substantial implications for healthcare service management and public health. It is unclear when the pandemic will end and thus how long the reorganization of healthcare services will be necessary. If these rigorous measures, which are undoubtedly critical for controlling the COVID-19 pandemic, may unintentionally affect established integrated care systems, they should be investigated in a timely manner.

2. From a medico-legal point of view, it is important to consider that cardiology is not one of the most exposed medical specialties to medical malpractice claims [29-31], but COVID-19-related mortality mainly concerns elderly and comorbid patients (who typically suffer from cardiologic conditions); thus, new liability profiles linked to this field are emerging [32-34].

3. In particular, home-to-hospital delays, misdiagnosis of cardiologic symptoms such as dyspnea, and reductions in hospitalizations and in operative interventions can lead to the worsening of health conditions (or death) and then expose healthcare institutions and professionals to avoidable malpractice claims, further complicating the issue of the economic sustainability of the pandemic [35].

4. However, the main issue linked to a decrease in admissions for ACS is economic. Costs of services not directly linked to COVID-19 management/treatment have been cut [36, 37]. Heart failure hospitalizations and the related costs, which amount to 550 million euros/year in Italy, are expected to increase as a consequence of delayed or missed ACS patient referral to hospitals. Missed diagnosis and inadequate treatment could severely impact these costs due to the increased risk of short- and long-term complications (the so-called "post–COVID-19 cardiac syndrome") and thus the increased length of hospitalization and direct health costs [38].

5. Healthcare systems should invest in a proper economic organization and in proper public health messaging: patients at risk should be educated on the importance of preserving primary (e.g., regular physical activity, diet) and secondary (e.g., seeking immediate medical attention in the presence of red flags) prevention interventions during the pandemic. At the same time, patient education efforts should aim at raising awareness of the increased health risks for those with past cardiac accidents or relevant health conditions and at avoiding being overcome by the fear of high-risk environments such as emergency rooms and hospitals.

5. Conclusions

Strong evidence supports the finding that the COVID-19 pandemic has led to a reduction in hospitalizations for myocardial infarction, as well as to an increase in its mortality and complication rate. Underlying mechanisms are still unknown, but both patient- and system-related issues might be involved. As stated by Ciro Indolfi, president elected of Italian Society of Cardiology (SIC): "Cardiology went back 20 years during the COVID-19 period". It is of paramount importance to understand this trend so that established evidence-based measures can be put in place, even during the COVID-19 pandemic, to avoid a subsequent cardiovascular pandemic that would lead to unnecessary death, disability and costs. Public health decision-makers and hospital managers must organize cardiology services to isolate inpatients and outpatients from infected cases and to permit regular access to CCUs. A quick solution to allow organization of the COVID-CCUs, to decrease ICU overload and to guarantee the best clinical practice in ACS patient management is desirable. Moreover, Heart Team professionals should improve protocols for management of ACS complications in COVID-19 patients, whose incidence is rapidly increasing again, following the delayed or missed clinical presentation of ACS patients.

Abbreviations

ACS: acute coronary syndrome; NSTE: Non-ST elevation; CVD: cardiovascular disease; European Society of Cardiology: ESC; HP: healthcare professional; EAPCI: European Association of Percutaneous Cardiovascular Interventions; PCI: percutaneous coronary intervention; CCU: cardiac coronary unit; CAD: coronary artery disease; AMI: acute myocardial infarction; ICU: intensive care unit; ANMCO: Italian Association of Hospital Cardiologists.

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