Editorial

Myocardial infarction in times of COVID-19

Infartos en tiempos de la COVID-19

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The pandemic triggered by the SARS-CoV-2 coronavirus, the cause of the disease known as COVID-19, is placing considerable and multifactorial stress on health care systems worldwide. The most evident pressure is related to the treatment of the respiratory syndrome directly caused by the SARS-CoV-2 infection. During the most difficult phase of the "first wave" of the pandemic (March-April 2020), a considerable number of Spanish hospitals had to to massively increase their intensive care capacity and adapt a large part of their overall hospital capacity to treat patients with COVID-19. Elective admissions, diagnostic tests, and nonurgent interventions were canceled to devote the vast majority of resources to this high increase in the admission of severe infected patients. Although most of the care programs for urgent conditions unrelated to COVID-19 (eg, acute myocardial infarction [AMI] and stroke) remained active during the crisis, as the weeks passed, health care professionals felt that there had been a dramatic fall in the number of patients attending hospitals for these conditions (or referred by nonhospital emergency services). The general belief was that patients experiencing symptoms compatible with AMI were not attending hospitals due to fear of being exposed to an environment with high risk of SARS-CoV-2 infection. Indeed, the Spanish cardiology community was motivated to undertake a traditional and social media campaign to make the public aware of the need to contact nonhospital emergency services if they experienced any symptoms suggestive of AMI.[1] Another cause of concern was related to the ability of health care systems to provide appropriate care to patients with urgent conditions during the worst phase of the crisis. Due to the stress placed on health care systems, with a saturation of nonhospital emergency services (including their telephone switchboards), in addition to the unavoidable reorganization of hospitals and more complicated patient flow, the worry was that patients with AMI during the pandemic peak would not receive care of the same standards than before the crisis, as well as that the prognoses of these patients would be affected by the situation.

Thanks to the existence of the exceptional Spanish national AMI registry, promoted by the Interventional Cardiology Association of the Spanish Society of Cardiology, we can reliably quantify the incidence of ST-segment elevation AMI (STEMI) treatment during the peak of the pandemic and compare it with that of a similar period from the previous year, as well as study the differences in patient management and short-term prognosis. The results of this comparative analysis have recently been published in *Revista Española de Cardiología* by Rodríguez-Leor et al.[2] The authors performed a comprehensive study of information collected from the 17 Spanish autonomous communities with AMI care networks. The hospitals participating in the (prospective) national registry of AMI in these autonomous communities in 2019 (more than 80 centers) were invited to send data from the worst month of the crisis (March 15 to April 15, 2020). This information was compared with a similar period from 2019 (the entire month of April 2019). The first major result is that the number of patients managed in these specialized networks (which comprise practically all STEMIs) fell significantly: 1305 patients vs 1009 in the 30 days evaluated from 2019 and 2020, respectively. The reperfusion strategy was unaltered, with primary angioplasty the approach chosen in about 95% of patients in both periods. A highly pertinent finding is that the total ischemia time (from symptom onset to reperfusion) was significantly longer (by 15%) in the COVID-19 period. This prolongation was mainly due to a much longer time from symptom onset to first medical contact, given that the average time from first medical contact to reperfusion was identical in the two periods. Another noteworthy finding is that the percentage of patients with STEMI attending hospital on their own initiative fell significantly during the COVID-19 period. No increase was seen in complications during primary angioplasty in the COVID-19 period and there were no differences in TIMI (Thrombolysis in Myocardial Infarction) flow before and after the angioplasty. Notably, the use of mechanical thrombectomy and glycoprotein IIb/IIIa receptor antagonists significantly increased in the COVID-19 period. Polymerase chain reaction (PCR) testing was conducted to diagnose SARS-CoV-2 in 32% of the patients admitted in the pandemic period; 15% showed a positive result. The most impactful outcome of this comparative study is the higher in-hospital mortality of patients admitted with STEMI during the pandemic peak vs the 2019 period (7.5% vs 5%). Due to the design of the registry, no information was collected on the causes of death of these patients, which is why it is difficult to definitively explain the reason for these differences. Although a longer ischemia time is associated with larger AMI, the relationship of this phenomenon with higher acute mortality is unclear.[3] Unfortunately, the registry lacks information on left ventricular ejection fraction, a parameter associated with AMI size and prognosis in STEMI patients.[4]

In another article recently published in *Revista Española de Cardiología*, Solano-López et al.[5] provide complementary information on this topic. Their study concerns patients with AMI (with or

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without ST-segment elevation) admitted in the same period of the pandemic than in the previous work (March 15 to April 15, 2020) to 7 centers that form part of the prospective RECOVID-SCA registry, which includes all consecutive patients in this period. In this case, the authors compared the characteristics and prognoses of patients with positive PCR results for SARS-CoV-2 infection during admission with those with negative PCR results. After the exclusion of 3 patients with a final diagnosis of myocarditis and another 3 with a diagnosis of tako-tsubo syndrome, the study included a total of 187 patients (STEMI, 111; non-ST-segment elevation AMI, 76). PCR was performed in a high percentage of patients (94%), and a positive result was obtained in 18% of those tested. Although the left ventricular ejection fraction was similar in the 2 groups, the patients with COVID-19 were more likely to have severe heart failure at admission (Killip class III-IV). The higher incidence of patients with elevated thrombotic content in the culprit lesion (modified TIMI 4-5) was associated with higher use of mechanical thrombectomy and worse TIMI flow after angioplasty. D-dimer and C-reactive protein levels were significantly higher in patients with proven SARS-CoV-2 infection. The most impactful finding was the significantly higher mortality in patients with diagnosed COVID-19, which was 25% (vs 4% in those negative for SARS-CoV-2 admitted in the same period). Cardiovascular mortality was significantly higher in patients with COVID-19 (15% vs 2%). There were more adverse events in absolute numbers in patients with COVID-19, but the difference was not significant, possibly a result of the lack of statistical power due to the small sample size. In a multivariate analysis, SARS-CoV-2 infection and a GRACE > 140 score were the only independent predictors of mortality.

These two articles published in *Revista Española de Cardiología* provide highly valuable information that helps us to describe the events occurring during the most severe weeks of the pandemic. On the one hand, the data show how our AMI care system has passed the stress test of an extreme situation related to the unprecedented spread of this disease. On the other hand, the results reveal the direct impact of the SARS-CoV-2 infection on the pathophysiology of AMI and its prognosis. The article by Rodríguez-Leor et al. shows that, in the worst part of the first wave of the pandemic, there was a significant reduction—up to 30%—in the number of patients treated for AMI in our health care system. This outcome has been seen in other countries[6–9] and thus appears to be global. The most plausible explanation is that patients chose to stay at home with symptoms that previously would have motivated emergency service contact or hospital attendance. This hypothesis is supported by the significant increase in out-of-hospital cardiac arrest in Italy.[10] However, in the article by Rodríguez-Leor et al.,[2] the incidences of cardiogenic shock at admission, need for orotracheal intubation, and mechanical complications were not different between patients admitted during the COVID-19 period and those from the previous year, which fails to support the theory that many patients experienced AMI at home and only contacted the emergency services when the symptoms were very severe (when the AMI was advanced). An alternative (and complementary) explanation would be that the massive confinement of the population lowered physical activity and, above all, drastically reduced pollution, which is a known trigger of AMI.[11]

A worrying datum in the work by Rodríguez-Leor et al. is the longer time between symptom onset and first medical contact. The prolongation of this time has also been seen in other countries.[12] The most plausible initial interpretation is that patients delayed more in contacting the nonhospital emergency services due to fear of COVID-19. An alternative (or complementary) interpretation is that the nonhospital emergency services suffered a delay to their response times due to the saturation of the entire system. Unfortunately, the registry used as the basis for this study does

not record the time of the patient's call to the emergency services. Very probably, both circumstances together explain the prolongation of up to half an hour in the time from symptom onset to first medical contact.

The work by Rodríguez-Leor et al. shows that the reperfusion strategy was unaffected during the peak of the pandemic, with primary angioplasty chosen for the overwhelming majority of patients (95%). At the start of the COVID-19 crisis, it was suggested that fibrinolysis might be worth considering due to, for example, the difficulty in moving patients. Indeed, a study from China reported a significant increase in fibrinolysis frequency.[13] The Spanish STEMI registry shows that the system has continued to use the strategy of choice (primary angioplasty), despite the logistic complications, a fact that we must highlight. In addition, the association of COVID-19 with a hypercoagulable state[14,15] means that fibrinolysis might be less effective and more risky than in situations without COVID-19. Indeed, the work by Solano-López et al.[5] revealed that patients with STEMI and SARS-CoV-2 infection have a higher level of D-dimer than STEMI patients without infection, which indicates an aggravated prothrombotic state. Along this line, in the RECOVID-SCA registry, the proportion of patients with high thrombus burden in culprit lesions of AMI was much higher among those infected with SARS-CoV-2.[5] Moreover, a significant increase was seen in the use of mechanical thrombectomy. Other series have obtained similar findings. Choudry et al.[16] recently reported that patients with STEMI and active SARS-CoV-2 infection have a higher incidence of lesions with high thrombus burden (TIMI 4-5), higher incidence of multivessel thrombosis, higher incidence of the use of glycoprotein IIb/IIIa antagonists and thrombectomy, worse coronary perfusion (TIMI scale) after angioplasty, and a need for higher heparin doses to achieve therapeutic activated clotting times. A salient finding of the work was the significantly higher incidence of acute stent thrombosis in patients with STEMI and SARS-CoV-2 infection.[16] Unfortunately, Solano-López et al.[5] did not report the rate of acute stent thrombosis.

The article by Solano-López et al.[5] did report an alarming datum indicating significantly increased in-hospital mortality in patients with STEMI and SARS-CoV-2 infection vs patients admitted in the same period without PCR evidence of infection. Other series[16] have shown a numerical (but not always significant) increase in mortality in patients with STEMI and active infection. It is important to unravel if this elevated mortality is due to cardiovascular complications associated with, for example, an aggravation in the prothrombotic state or to the respiratory process typical to COVID-19. In this regard, the series by Solano-López et al.[5] determined that the main cause of death that could explain this difference is acute respiratory distress syndrome.

These two articles recently published in *Revista Española de Cardiología* report data obtained from the peak of the pandemic, when the health care systems were in a critical situation and the lethality rate of the SARS-CoV-2 infection was very high. Accordingly, the findings are not necessarily applicable to the current circumstances. However, in the event of a return to an extreme health care situation, the results reported in these studies should be educational and help to ensure that we are better prepared and have better evidence supporting the optimal strategies and that we are ready to use all therapeutic tools available in the context of AMI with a very intense procoagulant state.

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CONFLICTS OF INTEREST

The author has no conflict of interest to declare.

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