



CORONARY ARTERY DISEASE**Original Studies**

EDITORIAL COMMENT: Expert Article Analysis for:

Percutaneous coronary intervention in patients with COVID-19 and acute coronary syndrome: What if the old normal became the new normal?

Invasive strategy for COVID patients presenting with acute coronary syndrome: The first multicenter Italian experience

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Abstract

Objective: To report our initial experience of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)/acute coronary syndrome (ACS) patients undergoing standard of care invasive management.

Background: The rapid diffusion of the SARS-CoV-2 together with the need for isolation for infected patients might be responsible for a suboptimal treatment for SARS-CoV-2 ACS patients. Recently, the group of Sichuan published a protocol for COVID/ACS infected patients that see the thrombolysis as the gold standard of care.

Methods: We enrolled 31 consecutive patients affected by SARS-COV-2 admitted to our emergencies room for suspected ACS.

Results: All patients underwent urgent coronary angiography and percutaneous coronary intervention (PCI) when required except two patients with severe hypoxemia and unstable hemodynamic condition that were conservatively treated. Twenty-one cases presented diffuse ST-segment depression while in the remaining cases anterior and inferior ST-elevation was present in four and six cases, respectively. PCI was performed in all cases except two that were diagnosed as suspected myocarditis because of the absence of severe coronary disease and three with apical ballooning at ventriculography diagnostic for Tako-Tsubo syndromes. Two patients conservatively treated died. The remaining patients undergoing PCI survived except one that required endotracheal intubation (ETI) and died at Day 6. ETI was required in five more patients while in the remaining cases CPAP was used for respiratory support.

Conclusions: Urgent PCI for ACS is often required in SARS-CoV-2 patients improving the prognosis in all but the most advanced patients. Complete patient history and examination, routine ECG monitoring, echocardiography, and careful evaluation of changes in cardiac enzymes should be part of the regular assessment procedures also in dedicated COVID positive units.

KEYWORDS

acute coronary syndrome, COVID-19, PCI, SARS-CoV-2

1 | INTRODUCTION

In late December 2019, a cluster of pneumonia cases caused by a novel coronavirus (nCoV) occurred in Wuhan, China and has spread rapidly initially throughout China and later in Europe.^{1,2} By April 22, 2020, 2,621,436 confirmed cases have been reported globally, with 182,989 deaths. The infection is now spread in 210 countries, with Italy as the third country with most confirmed cases (187,327).³ The pathogen of this pneumonia was originally called 2019 nCoV and later officially named by the World Health Organization (WHO) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In fact, SARS-CoV-2 targets the respiratory tract and shares many similar clinical symptoms with SARS-CoV and MERS-CoV both coronavirus responsible for 8,422 and 1,600 infections with 916 and 574 deaths, respectively.^{4,5} Common symptoms include fever, dry cough, fatigue, and worsening dyspnea usually associated with a significant increase in biomarkers of myocardial necrosis (a significant increase in high-sensitivity cardiac troponin I—hs-cTnI—levels has been reported in SARS-nCOV-2 patients).⁶⁻⁹ Interstitial pneumonia might rapidly evolve in severe acute respiratory distress syndrome (ARDS) followed by respiratory failure needing invasive ventilation. This rapidly evolving ARDS explains the reason why acute medical treatment in SARS-CoV-2 patients is mainly focused in respiratory care reducing the attention to other active comorbidities often present in the elderly patients showing the worst compromise during these epidemics. In elderly patients, worsening dyspnea can be the only symptom of a concomitant cardiovascular injury. In this article, we report our initial experience of SARS-COV-2/acute coronary syndrome (ACS) NSTEMI/STEMI patients undergoing standard of care invasive management.

2 | METHODS

We prospectively collected data of 31 consecutive patients admitted for worsening dyspnea associated with significant increase in troponin and/or hemodynamic instability. Twelve-leads ECG showed diffuse or regional ST-segment depression in 21 cases; in the remaining, anterior or inferior ST-segment elevation was found in four and six patients, respectively. All patients reported a recent history of fever associated with dry cough and urgent chest X-ray showed signs of interstitial pneumonia and/or patchy edema at various grade of severity. All were initially diagnosed as “suspected for SARS-CoV-2” and confirmed thereafter using the appropriate test.

Patients signed an informed consent for data collection and the study was conducted according to the Declaration of Helsinki.

2.1 | Interventional procedure

Patients not preloaded with oral aspirin and/or clopidogrel received a loading dose of intravenous aspirin (500 mg) followed by Cangrelor

infusion followed by ticagrelor (180 mg) as standard practice. Crushed ticagrelor via a nasogastric tube was used to continue treatment in the intubated patients. Intravenous heparin (70 UI/kg body weight) was administered before the procedure with subsequent boluses aiming at achieving an activated clotting time between 250 and 300 s. No GP IIb/IIIa inhibitors were used. All lesions were treated with stent implantation and high-pressure balloon postdilatation.

2.2 | Data collection and follow-up

Angiographic results and in-hospital outcome were prospectively collected and entered into a dedicated interventional cardiology database. Clinical events were evaluated postprocedure, during hospitalization and after discharge by a telephone interview.

3 | RESULTS

From February 20 to April 15, 2020, 31 SARS-CoV-2 patients admitted in our hospitals developed clinical and biochemical signs suggesting ACS STEMI/NSTEMI/TTS. Patients and lesion/procedural characteristics are shown in Table 1. The average age was 72.3 ± 9 years with a prevalence of male sex (77.4%) and high prevalence of risk factors (hypertension 71%, diabetes 38.7%, current smoking 35.5%, dyslipidemia 58%). In 11 patients, a history of coronary artery disease (CAD) was present, with previous percutaneous coronary intervention/coronary artery bypass graft (PCI/CABG) in nine and six, respectively (four patients received both CABG and PCI). All patients presented to hospital because of dyspnea and fever and the suspicion of an ACS was raised only when the patients were already admitted to the dedicated COVID ward or intensive therapy unit because of sudden chest pain and/or ECG signs of ACS NSTEMI/STEMI, with confirmatory hs-cTnI increase and echocardiographic

TABLE 1 Clinical and procedural characteristics

Age	72.3 ± 9 years
Sex	M 77.4%, F 22.6%
LVEF	36.8 ± 11%
LVEF <40%	48.4%
ETI	19.3%
STEMI	32.2%
NSTEMI	51.6%
TTS	9.7%
Myocarditis	6.5%
Death	9.7%
Follow-up	26.3 ± 10 days

Abbreviations: ETI, endotracheal intubation; LVEF, left ventricular ejection fraction; TTS, Tako-Tsubo syndrome.

regional LV wall motion abnormalities. All patients underwent urgent angiography except two patients with severe hypoxemia and unstable hemodynamics that were conservatively treated. Coronary angiography/PCI was routinely performed with standard techniques via femoral (one case) or radial approach (28 cases) using six French guiding catheters. Evidence of acute coronary occlusion with thrombus or subocclusive lesions with plaque rupture was present in 8 out of 10 STEMI patients who underwent wire crossing 43 ± 12 min after diagnosis. In five patients (two anterior STEMI, the others with diffuse ST-segment depression), no coronary disease was detected on angiography. Three of them presented clear apical ballooning on ventriculography/echocardiography (ECG) and were diagnosed as Tako-Tsubo syndromes (TTS) while the remaining two patients were diagnosed as probable myocarditis. Cardiac MRI could not be performed because of difficulties to apply this test in these highly infectious patients. Coronary angiography showed multivessel disease in 12 patients. A discrete severe lesion responsible for ischemia was detectable in all cases but one. The complexity of the lesions treated was confirmed by the need for the use of a guide extension in seven cases and more than two stents in 12 cases. In one case in cardiogenic shock, severe subocclusive three-vessel disease was associated with severe aortic stenosis and required complete coronary revascularization and subsequent urgent aortic balloon valvuloplasty. In all the remaining cases, PCI was limited to the most severe culprit lesion with completion of treatment of the nonculprit vessels/lesions delayed after recovery from the acute viral infection. Our case series comes from the initial experience of five different hospitals. Four of the hospitals have two or more catheterization laboratories so that one could be exclusively reserved to COVID-ACS or suspected COVID-ACS patients, with a separate path and holding area. Two of these catheterization laboratories also benefited from a negative pressure system. In the remaining two hospitals no differentiation was possible but still in all of them personal protection equipment including respirator masks, goggles, fully impermeable gowns, and shoe covers were worn by all the staff allowed into the room following a standard-assisted procedure. All laboratories were sterilized as appropriate. Up to now, none of the Cath Lab personnel developed COVID-19 infection, and all of them have been tested with at least one or more RT-PCR assay of a nasal swab and /or search of specific IgM/IgG antibodies in blood.

3.1 | Clinical outcome

All patients were moved immediately after angiography/PCI to isolation beds in COVID intensive care unit (ICU), and then transferred to dedicated COVID wards as soon as possible. In all patients received dual antiplatelet therapy with Ticagrelor/Aspirin except four that received Clopidogrel/Aspirin. No major bleeding complications were reported. Two patients conservatively treated died at Days 1 and 3. The remaining patients undergoing PCI survived except one that required endotracheal intubation (ETI) and died at Day 6. ETI was required in five more patients while in the remaining cases noninvasive ventilation with cPAP was used for respiratory support for few days following PCI. At a mean follow-up of 26.3 ± 10.1 days (range 4–58 days) all the remaining patients are in

good clinical condition and most have been discharged at home except three that are still hospitalized.

4 | DISCUSSION

Hypoxemia, increased respiratory workload, tachycardia, and hypertension may develop while the patient is maintained in spontaneous or noninvasive-assisted ventilation. Intubation may improve hypoxemia but general anesthesia causes hypotension, arrhythmias, and the need of inotropic support, triggering a vicious circle with worsening myocardial ischemia in the presence of severe coexistent CAD. This is the most likely explanation in NSTEMI, the most frequent ACS observed in SARS-nCoV-2 patients. STEMI patients were rarer. Anxiety, interruption of preexisting medication, and the general pro-inflammatory effect of the acute infection may explain the development of plaque rupture in patients with existing diffuse coronary disease. Interestingly, the relatively high rate of TTS encountered (3 out of 31) might be explained by the fact that these patients were elderly with a possible clear stress trigger. According with previous report of SARS-CoV and MERS-CoV^{4,5} we reported two cases of suspected myocarditis because of normal coronary angiography; unfortunately, the cardiac MRI has still not confirmed the diagnosis. The need for isolation in dedicated COVID-positive units or hospitals may limit access to examinations such as ECG and increased myocardial enzymes can be dismissed as a consequence of widespread viral organ involvement.^{10,11} Even when there is a clear diagnosis, there might be reluctance to apply in these patients the aggressive approach recommended in current Guidelines. In the recently published protocols from Sichuan Provincial People's Hospital, the authors suggest performing thrombolysis in most of the ACS STEMI/NSTEMI syndromes¹² certainly a suboptimal treatment in the urgent/primary PCI era. Furthermore, a recent statement from the American College of Cardiology's Interventional Council and the Society of Cardiovascular Angiography and Intervention suggests that fibrinolysis can be considered as an option for the relatively stable STEMI patient with active COVID-19.¹³ These findings might partially explain the high mortality rate in ICU admitted SARS-nCoV-2 patients compare with non-ICU ones.^{6,14}

In our experience, we maintained the same proactive attitude recommended by Guidelines and standard in our hospitals. Despite a slight delay due to extra precautions during transportation and the preparation of the operators with appropriate individual protection means (surgical mask, double gloves, glasses, fully disposable complete sterile gowns, and caps), the average time from diagnosis to reperfusion for STEMI patients was 43 ± 12 min, within recommended standards. A standard approach was also followed for the angioplasty, avoiding immediate multivessel treatment in the presence of a likely culprit for ischemia also in NSTEMI patients, in order to facilitate patients' tolerance in terms of respiratory distress (only one emergency intubation was required) and renal dysfunction. There was only one cardiac death in the group treated with PCI (a man with previous CABG and three-vessel disease associated with severe aortic stenosis), an incidence consistent with the good outcome of urgent PCI in ACS, while both patients treated conservatively without any

angiographic examinations died. Despite this, we still support the avoidance of futile procedures in patients with too advanced respiratory failure and multiorgan compromise. Withdrawal of PCI, however, should not be caused by an overflow of extremely ill patients straining the hospital facilities or by an excessive fear of spreading infection among the hospital staff, unlikely for these relatively short procedures when performed by well-protected staff. We believe that the rapid application of revascularization techniques consistently proven to be beneficial and life-saving in multiple controlled trials and large registries helped to avoid more deaths. Elderly patients with unstable hemodynamics subject to the stress of severe respiratory distress and intubation are unlikely to be particularly prone to the deleterious effects of ischemia. Pharmacological treatment is unlikely to offer a similar advantage and thrombolysis is less efficacious than primary PCI in STEMI patients and not indicated in NSTEMI patients. With a small sample size of 10 STEMI patients and no comparison group it is impossible to prove that outcome was better with PCI than with thrombolysis. We prove, however, that angioplasty can be delivered rapidly without endangering hospital staff. With a number of COVID patients exponentially growing and spreading outside the countries initially affected, confidence in using the proactive attitude suggested by current guidelines is likely to save more lives also in this challenging scenario.

5 | LIMITATIONS

Myocarditis may induce ST segment changes and enzyme rise in SARS-COV-2 patients. In this series, no consistent use of cardiac MRI was used to exclude the typical mid-wall patchy late gadolinium enhancement typical of myocarditis.

Our patients are relatively old, with several cardiovascular risk factors and high rates of previous PCI and/or CABG. Both symptoms of dyspnea and chest oppression and rise in troponin might be part of the COVID infection itself and the increased respiratory workload and tachycardia could have caused ischemia because of preexisting critical CAD. Still the rapid normalization of ECG changes, the pattern of the enzymatic curve after PCI with rapid rise and fall, the dissociation from other biomarkers of worsening inflammation and multiorgan failure and the rapid clinical and hemodynamic improvement in most cases suggest that a true ACS was the main operative mechanism of cardiac impairment.

6 | CONCLUSIONS

Urgent PCI for ACS is often required in SARS-CoV-2 patients and a policy of timely rapid PCI irrespective of the acute respiratory illness may improve prognosis in all but the most advanced patients. Complete patient history and examination, routine ECG monitoring, careful evaluation of changes in cardiac enzymes, and echocardiographic examinations with urgent cardiological consultations when needed should be part of the regular assessment procedures also in dedicated COVID positive units.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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