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Review Article

Covid-19 Pandemic: Practical Considerations for Cardiologists

Luigi Biasco[1,2]*, Yvonne Cristoforetti[3], Enrico Cerrato[4], Giuseppe Musumeci[5], Ferdinando Varbella[4], Angelo Di Leo[1], Göran Olivecrona[6], Giovanni Pedrazzini[2,7] and Gaetano Senatore[1]

[1]Division of Cardiology, Azienda Sanitaria Locale TO 4, Ciriè, Italy

[2]Department of Biomedical Sciences, Università della Svizzera Italiana, Lugano, Switzerland

[3]Department of Cardiology, Humanitas Gradenigo, Turin, Italy

[4]Interventional Cardiology Unit, San Luigi Gonzaga University Hospital, Orbassano and Rivoli Infermi Hospital, Rivoli, Italy

[5]Department of Cardiology, Ospedale Mauriziano, Turin, Italy

[6]Department of Cardiology, Lund University Hospital, Sweden

[7]Division of Cardiology, Cardiocentro Ticino, Lugano; Switzerland

***Corresponding Author**: Luigi Biasco, Division of Cardiology, Azienda Sanitaria Locale TO 4, Ciriè, Italy.

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Abstract

The 2019 novel coronavirus disease (COVID-19) is spreading globally and, as of May 25th 2020, 5404512 cases have been certified on a global scale by World Health Organization with 343514 deaths. Health care systems are fighting against time to slow spread of the disease and treat patients. From a cardiological perspective, some initial signals pointing towards significant cardiovascular involvement with myocardial injury and infarction have been reported.

The aim of this report is to give a brief summary on the initial experience of our Italian cardiology network exposed to COVID-19 since late February on how to modify the set-up within the cardiology department in order to maintain evidence based cares while protecting both patients and staff from infection.

Keywords: *COVID-19; Acute Coronary Syndrome; PCI*

Introduction

The current COVID-19 pandemic represents an unforeseen extreme challenge for the society as a whole. While originally identified in the Chinese city of Wuhan, infection has rapidly gain a global spread, hardly striking Europe and Italy in particular.

As for the 25th of May 2020, Italy suffered more than 30000 deaths, being one of the most involved countries after China for extent of infection and the first for fatalities. To date more than 27,000 Italian health care professional tested positive for COVID-19 [1]. In this context, cardiologists are called to an enormous effort in order to maintain the quality and appropriateness of medical and interventional treatments to all patients with acute cardiovascular diseases while impeding further spread of the contagion.

Within a short time frame, the emergence of the novel Coronavirus Disease 2019 (COVID-19) started to severely drain the largest part of health-systems resources and, with such, there is also a severe strain placed on work flows for cardiology patients regarding standardized pathways, diagnostic and therapeutic protocols which are the hallmarks of modern cardiology.

Lack of current evidences supporting treatments in COVID-19 patients, in particular when associated cardiovascular diseases, represents a first challenge for contemporary cardiologists. In addition, absence of definite patient's specific pathways within the cardiology department as well as unprepared facilities, lack of staff training, shortage of personal protective equipment (PPE) and significant risk of professional exposure for health care professional represent additive problems to be taken into consideration [1,2].

Possible concomitant or overlapping manifestations between COVID-19 and acute cardiovascular diseases especially in the setting of acute myocardial infarction (AMI) have to be considered as well.

Thus the aim of this report is to give a brief summary on the initial experience of our Italian cardiology network exposed to COVID-19 and how to modify the set-up within the cardiology department in order to maintain evidence based cares while protecting both patients and staff from infection.

Clinical considerations

No data are yet available connecting COVID-19 infection as a trigger for acute coronary syndromes (ACS) while initial reports show that cardiac involvement is present in the form of myocardial injury [2,3], fulminant myocarditis [4] and potentially as type II Myocardial Infarction (MI) as a consequence of severe hypoxemia.

According to autopsy data reported in the recent Chinese guidelines, cardiomyocytes may be affected showing diffuse degeneration and cellular necrosis with interstitial infiltrate of monocytes, lymphocytes and polymorphonucleates together with dis-epithelization, vasculitis and micro-thrombi highlighting the cardiac and vascular tropism of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [5]. Myocardial injury, evident with a rise in high sensitive cardiac troponin (hs-cTn) I has been reported in 17% of all COVID-19 patients reaching 46% in non-survivors [2], suggesting its possible prognostic role [6].

Cardiac complications including new or worsening heart failure, arrhythmias or myocardial infarction have been also described in patients with COVID-19 associated pneumonia. Acute cardiac injury (rise of hs-cTnI and/or ECG/echocardiographic abnormalities) was reported to occur at a median of 15 days after the onset of symptoms [2].

According to recently published Chinese data, reported mean age of patients hospitalized with COVID-19 ranges from 47 [7] to 56 [1] years with a male predominance (around 60%). In our country cases were slightly older with a mean age of 62 years. Male predominance was also confirmed (54% of cases) [1]. Figure 1 shows mortality rates of Italian COVID-19 patients as for May 25th, 2020. More severe cases occurred in elderly patients or in those with multiple comorbidities [7], thus overlapping the demographic and clinical characteristics of most ACS patients.

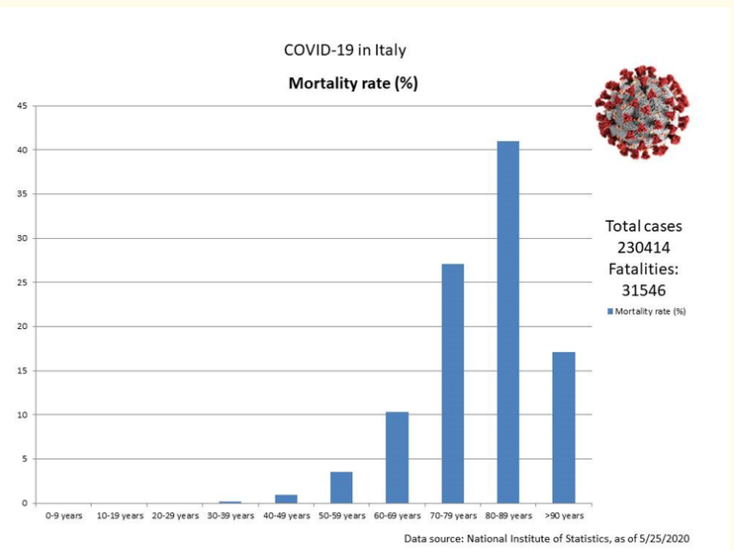

Figure 1: *Mortality rates of COVID-19 in Italy.*

Although the vast majority of patients hospitalised with COVID-19 do have fever at some point during their hospitalisation, this is only present in 43.8% of cases at admittance. This appears only in 36.4% of those requiring mechanical ventilation, admitted to intensive care or with fatal outcome [6]. On the other hand, cough (67.8% - 79%), fatigue (23% - 38.1%), shortness of breath (18.7%), high respiratory rate (29%), hypoxemia and increased hs-cTn, may mimic acute cardiovascular diseases such as ACS, acutely decompensated heart failure or pulmonary embolism [2,3]. No data are currently available on the incidence of associated chest pain as a presenting symptom, nonetheless pulmonary infarctions have been described. Lymphocytopenia (as low as 700 lymphocytes/mm^3 in severe cases) seems to be a marker of infection and outcome in COVID-19 patients and may be used together with increased C reactive protein (CRP) and presence of bilateral pneumonia and multiple mottling and ground-glass opacities as criteria of suspicion in still undetected cases [7].

Treatment of COVID-19 patients is currently mainly based on supportive therapy with fluids, oxygen, ventilation, while some initial experiences are carried out with lopinavir/ritonavir (200 mg/50 mg 2 cp bid max 10 days), chloroquine (500 mg bid for 7 days in patients with body weight > 50 kg) and tocilizumab in severe bilateral pneumonia. Vitamin C and D are also used as supportive treatments. It should be noted that use of the above mentioned pharmas is off label and that several interactions with commonly used cardiac drugs are known. Coadministration of lopinavir/ritonavir or chloroquine with amiodarone and flecainide is not allowed. Apixaban, rivaroxaban clopidogrel, and ticagrelor should not be administered in patients receiving lopinavir/ritonavir while warfarin, dabigatran and edoxaban may have potential interaction and require close monitoring. Aspirin, prasugrel, fractionated and unfractionated heparins, fondaparinux and streptokinase can be safely used in this context. Some other agents routinely used (i.e. lercanidipine, ivabradine, ranolazine, eplerenone) as well statins (simvastatin) should be stopped in case of lopinavir/ritonavir concomitant therapy. A full list of all drugs interaction is available at http://www.covid19-druginteractions.org.

Independently from any mechanistic link between COVID-19 infection and increased risk of acute cardiovascular events, as is otherwise known for influenza [9], it is estimated that the number of COVID-19 positive subjects will reach 60 - 70% of the western population. Thus, the likelihood of any acute cardiovascular disorder occurring concomitantly in a patient positive for SARS-CoV-2 or with overt COVID-19 is more than concrete with some initial cases already being admitted.

Even in negative patients, contamination might occur during the hospitalization at emergency department, coronary unit or ward. Thus stressing the need to really verify each indication for admission and define site specific protocols to rapidly evaluate, address and treat patients.

Logistical considerations regarding patient's allocation and cath lab

The Italian society of interventional cardiology has recently released a short protocol to advice on how to modify cath-lab organization to face COVID-19 patients with an acute cardiovascular emergency [10].

Due to the current pandemic diffusion, epidemiological criteria are nowadays of little or none utility in defining the pre-test risk of potential COVID-19 patients, at least in Europe and United States. For acute, not-yet hospitalized patients, it is advised to adequately investigate the presence of clinical criteria such as fever, cough, dyspnoea, lab test results as well as taking a history of close contacts with COVID-19 positive subjects in the 14 days prior to admission. Also, in non-suspected cases, body temperature should be measured and surgical mask worn before admission. Rapid SARS-CoV-2 detection test are now available for fast rule in/out with results available within few hours.

It is necessary to organize in-hospital site specific tracks for transport of patients with suspected/confirmed COVID-19 to and from cath-lab facilities to avoid spreading the virus. Fast communication with all the personnel involved has to occur in order to clear the track from unnecessary presence of staff and to avoid potential inadvertent contaminations (such as those occurring in an elevator). As an example, if several elevators are available one could be designated as dedicated to COVID-19 positive or suspected patients.

Whenever possible and facility allows, one of the on-site cath-labs should be dedicated to patients with suspected or confirmed COVID-19. Staff members should carefully ascertain the availability of several personal protection equipments (PPE, table 1) and be trained to use them. Safe areas in close proximity of the cath-lab have to be recognized to allow staff donning (outside), doffing (inside) and adequate disposal of the PPE. During interventional procedures, all required material (e.g. catheters, wires, stents etc.) should readily be available inside the cath-lab to avoid the risk of external contamination. Particular attention has to be given by operators to avoid any nebulization of biological material. An unscrubbed nurse has to be present in a safe place to manage IT devices, allow communication in and out the cath-lab and keep a registry of all personnel involved in the management of a suspect/confirmed COVID-19 case.

Personal protective equipment required in a dedicated COVID-19 cath lab
Surgical masks
N95 or FFP2 and FFP3 respirator
Disposable sterile surgical gown
Disposable shoe covers
Gloves
Protective glasses/ face shields (personal)
Waterproof disposable sterile gown (to be used in case of intubation)

Table 1

A step by step flow chart on how to put on and remove PPE is available in table 2 and 3. Both protocols should be supervised by a buddy maintaining a distance of 2 meters. The buddy should be trained and competent in the use of PPE. A practical demo video, provided by the English national health system is available at https://www.youtube.com/watch?v=kKz_vNGsNhc&feature=youtu.be.

Donning (Put on) protocol
1) Removal of any jewellery and personal item
2) Check PPE integrity
3) Hand hygiene with idro-alcoholic solution.
4) Wear a fit tested FFP2/FFP3 respirator achieving optimal adhesion to face and avoiding any air exhalation from mask contours
5) Wear the cap
6) Wear lead apron
7) Wear shoe covers
8) Wear protective glasses/ face shields (check compatibility with FFP2/FFP3 respirator beforehand)
9) Repeat hand hygiene
10) Wear the first pair of gloves
11) Wear the first sterile surgical gown, a second sterile surgical gown can be considered.
12) Wear the second pair of gloves completely covering the wrists

Table 2

Doffing (Put off) protocol
Inside the cath lab
1) Avoid contact between any of the PPE and mucosae, hair or skin.
2) Hand hygiene with outer gloves on (have ready a basin containing alcoholic solution prepared beforehand)
3) Remove surgical gown with smooth movements in order to avoid nebulization (do not press the gown into the trash bin). Avoid to touch the exterior of the gown.
4) Remove the outer glove
5) Hand hygiene with inner gloves (have ready a basin containing alcoholic solution prepared beforehand)
6) Remove glasses, facial shield and dispose/sanitize.
7) Repeat hand hygiene with inner gloves (have ready a basin containing alcoholic solution prepared beforehand)
8) Remove the cap
9) Remove inner gloves.
10) Repeat hand hygiene
11) Leave the cath lab with the FFP2/FFP3 respirator on and promptly close the door.
Outside the cath lab
12) Remove FFP2/FFP3 respirator handling from the posterior side (straps) and dispose.
13) Remove lead coat
14) Hand hygiene

Table 3

Due to the recurrent need of blood gas examinations in COVID-19 patients, arterial vascular access for invasive procedures have to be carefully selected and preserved. In case of doubt about patency of one radial artery or when an arterial line already on site for pressure monitoring and blood sampling, femoral access should be evaluated.

At procedure completion, patient leaves the cath-lab by route of the recognized transport track to a dedicated COVID-19 bed that has to be identified beforehand in an isolation ward and with dedicated latrines. Availability of coronary care/intensive care equipment has to be considered in patient with acute coronary syndromes, this being of particular relevance in cases needing close hemodynamic monitoring. National cardiological societies advice to constitute a single, adequately equipped isolation ward in each hospital, or even COVID-19 dedicated hospitals, rather than isolation rooms spread in different wards [11].

Isolation of the cath-lab has to be ensured by leaving doors opened for the strict necessary (getting on and off the patient). In order to avoid inadvertent contamination and due to the long persistence of viral particles on air and surfaces, it is advised to leave the room for at least 60 minutes after case completion before sanitizing. All personal equipment (facial shields, lead coats and instruments) should be as well sanitized. A recent review of the survival of human coronaviruses on surfaces found a large variability, ranging from 2 hours to 9 days [12] depending on different factors such as type of surface, temperature, relative humidity and specific strain of the virus. The same review also found that effective inactivation could be achieved within 1 minute using common disinfectants, such as 70% ethanol or sodium hypochlorite. World Health Organization issued a technical brief on water, sanitation, hygiene and waste management for the COVID-19 virus available online [13]. When transferred to isolation wards, of all possible protocols of telemedicine including electronic transmission of ECG, lab test results and teleconsultation should be implemented.

Airway and ventilatory support

Suspected or confirmed COVID-19 patients have to wear facial mask if not requiring ventilation at time of catheterization. Conversely, non-invasive ventilation systems have to be avoided given the risk of airborne viral spreading [13]. Patients requiring - or be expected to require -a ventilatory support during percutaneous coronary interventions (PCI), should be better treated with a preventive endotracheal intubation approach in order to minimize cath-lab contamination or staff exposure during PCI [15,16]. Close interaction and team working with supporting anaesthesiologist is thus needed, also in light of evaluating availability of intensive care beds at procedure completion.

Strategies for treatment of ACS in COVID-19 patients

A recent report by Zeng., *et al*. [17] described the protocols from Sichuan Provincial People's Hospital for patients with acute myocardial infarction during COVID-19 epidemics stressing the need to balance indications of current updated therapies, their real clinical benefit in the context of COVID-19 patients and the need to prevent diffusion to patients and medical staff. Some initial considerations have been also recently proposed by the interventional council of the American College of Cardiologists [18]. The basic principles guiding therapeutic choices and their timing is to provide patients currently evidence based therapies in a timely manner while preventing futility and potential contamination of cath-lab and staff. Chinese series show how contagion may occur especially in health care professionals, representing 3.5% of all hospitalized patients [7] while in Italy 9,1% of confirmed cases are health care professionals [8] with obvious impacts on the possibility to maintain efficiency of health-care services with an adequate number trained staff members on the mid-term period.

A recent European association of percutaneous cardiovascular interventions position statement provided clear guidance for decision making and in hospital pathways of confirmed or suspected COVID-19 patients [19]. The basic principle behind this document is represented by the need to provide all evidence based therapies for confirmed/suspected COVID-19 patients while assuring staff safety. In brief all STEMI patients should be managed as COVID-19 patients, until proven negative. Complete, single procedure, revascularization should be considered in order to shorten hospitalization and avoid re-admissions. Careful risk assessment in NSTEMI patient should guide clinical decision regarding an invasive approach.

Peculiar settings

Patients successfully resuscitated after out of hospital cardiac arrest should be considered as suspected COVID-19 patients and rapidly tested for infection. Due to the known cardiac tropism of SARS-CoV-2 virus, sustained ventricular arrhythmias can represent a possible presentation even without overt pulmonary manifestations (personal communication of one case). In line with current practice, indications for emergent invasive angiography should be reserved for cases with clear evidence of ongoing myocardial ischemia or hemodynamic instability and obviously referral to cath lab should take into consideration the whole clinical picture and the likelihood of a good neurological prognosis.

In outpatient, elective cases requiring a fast-track angiography (e.g. severe aortic stenosis requiring interventions; evidence of diffuse, relevant from a prognostic perspective, myocardial ischemia at non invasive tests) careful history taking by phone call should exclude suggestive symptoms or close contacts with overt COVID-19 cases. In specific cases, pre admission evaluation with nasopharyngeal swab, can direct decision whether or not to proceed. A summary of practical consideration is provided in figure 2.

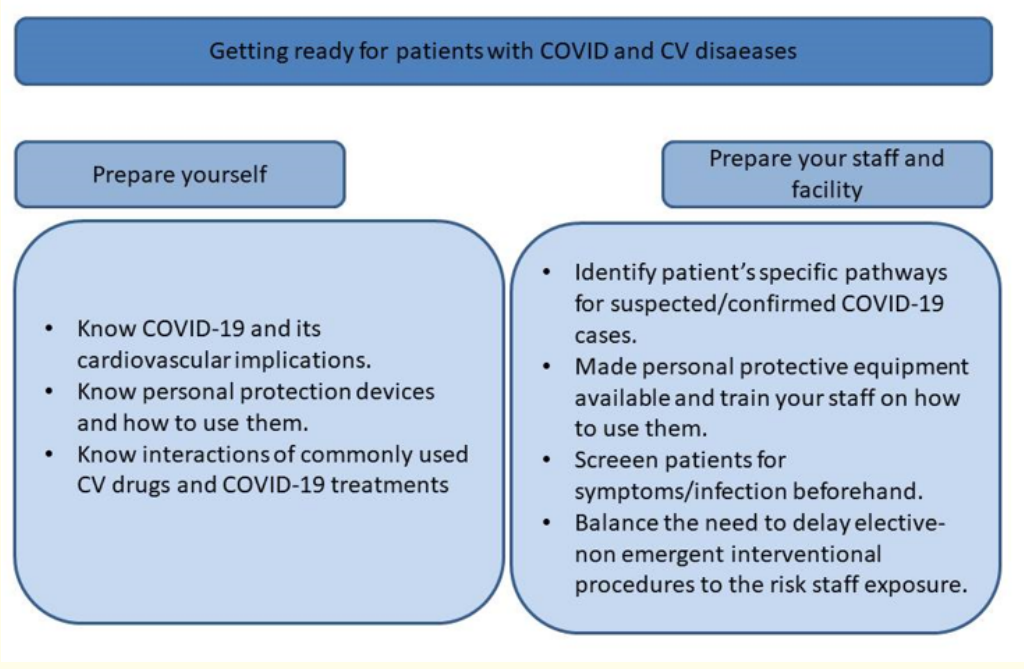

Figure 2: *Summary of practical considerations to develop a COVID-19 pathway for patients with cardiovascular diseases.*

Conclusion

COVID-19 disease causes myocardial damage through different mechanism such as viral mediated myocardial injury, type II myocardial infarction and as a direct effect of systemic inflammation. While not data are still available, it's plausible that viral infection may increase the risk of acute coronary events as well.

In the lack of data and evidences, treatments have to conform to current guidelines for suspected cases while clinical judgment and site specific protocols for the management of confirmed COVID-19 patients with concomitant acute cardiovascular diseases should guide treatment.

Conflict of Interest

No conflict of interest to declare.

Author's Contribution

LB and YC conceived, drafted and edited the manuscript. All other authors critically reviewed the draft.

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