Coronavirus Disease 2019: Where are we and Where are we Going? Intersections Between Coronavirus Disease 2019 and the Heart

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (COVID-19), which has become a pandemic affecting every country in the world. In the province of Bergamo, Italy, more than 2,200 cases of COVID-19 have been reported, which include more than 300 deaths. Most hospitalisations have been at the Papa Giovanni XXIII Hospital. This has imposed a significant burden on our hospital in terms of healthcare personnel, dedicated spaces (including intensive care areas) and time spent by clinicians, who are committed to assisting COVID-19 patients. In this short expert opinion, the authors will focus on new insights related to COVID-19 and the cardiovascular system, and try to investigate the grey areas and uncertainties in this field.

Keywords

Coronavirus disease 2019, cardiovascular system, hospital organisation, personal protection equipment, grey areas

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (COVID-19), which has reached a pandemic level worldwide.[1] Bergamo was the first western town affected by the COVID-19 pandemic and has the sad record of being the city with the highest number of COVID-19 cases and deaths, not only in the Lombardy region but also throughout Italy and the world. The first documented case at Papa Giovanni Hospital in Bergamo was recorded on 23 February 2020. The epidemic was unexpected, violent and prolonged; it was not comparable with any other natural event (such as a tsunami), but was more like trench warfare after a sustained attack.

Although most patients are asymptomatic or have mild symptoms, in up to 15% of infected patients the clinical course of this pathology may be complicated by the onset of a severe form of interstitial pneumonia, which may progress towards acute respiratory distress syndrome (ARDS), multi-organ failure and death.[2–3]

An important, instructive finding gradually emerging from mini autopsies is that damage to the lungs with loss of surfactant is uneven (with serious structural alterations in patches), which is different from typical ARDS where the lung becomes wet and heavy, and is globally damaged. For this reason, lying prone allows more alveoli to be recruited and improves respiratory exchange.

Although lung infection is the predominant pathophysiological scenario, awareness is increasing of the negative impact of the intersection between SARS-CoV-2 infection and the heart on prognosis. This intersection is related to underlying cardiovascular (CV) comorbidities (such as hypertension, diabetes and coronary artery disease) and direct involvement of the heart.[4–6]

Several case series and CV reports are coming out in the literature with the aim of shedding light on the cardiac implications of COVID-19 to make the international cardiology community better prepared worldwide, even in cases of not easily identified manifestations of the viral infection.[7–10]

How Hospitals can Prepare for COVID-19

In the coronavirus era, the organisation of wards and intensive care units in hospitals is of fundamental importance, considering that from one day to the next there could be changes depending on the level of the epidemic.

First of all, during the ascending or the peak phase of the pandemic, patients with acute MI need a clean, fast track from the emergency room to the cath lab to avoid the risk of acquiring a SARS-CoV-2 infection. Every cardiology patient with or without symptoms suspected to have a SARS-CoV-2 infection should be given a swab test for the virus so they can be placed in an appropriate area of the cardiology department.

The cardiology department should be organised into: a SARS-CoV-2-free area; a SARS-CoV-2 area; and a grey area, which hosts patients suspected of having COVID-19 but whose first swab test was negative (given the high incidence of false negatives in nasopharyngeal swabs tests). In this early phase, a significant reduction in the absolute number of acute coronary syndromes and hospitalisation for heart failure (HF) was observed in the entire province of Bergamo.

During the plateau phase, the cardiology department needs to be reorganised to meet the needs of hospitalised patients and those waiting for admission, maintaining a fluidity of beds (patient flow) to optimise the work of all medical staff.

Another important recommendation we have learnt to adopt is to give priority to protecting hospital healthcare staff. A correct, constant use of personal protection equipment (PPE), preferably worn in case of contact with any patient, even if not clearly positive, should always be considered. We doctors should not underestimate the risk that we can unwittingly be a vehicle of infection if we do not adopt the appropriate safety measures using PPE.

It is appropriate to test all medical staff with serological investigations to be aware of possible contagion, and to take the necessary precautions for both personal and professional life. Another suggestion is to enhance and implement telemedicine or telephone calls by nursing staff to manage patients with heart failure or chronic CV disease so they can monitor patients remotely, be aware of clinical events and give therapeutic advice to counteract any deterioration in underlying cardiological conditions.

From a human perspective, on the front line in the hospital, we learnt at our expense that COVID-19 is highly and inexorably contagious. Almost 25% of our colleagues have been infected, which has significant repercussions for the workload of cardiologists who remained healthy or asymptomatic, but positive.

Moreover, the wave of patients who entered our emergency room over a few days dramatically surprised us, filling spaces, organisations and all the comfort zones within the hospital in which we were used to living and sharing. As cardiologists, we therefore had to learn to adapt to a new, more worrying working conditions.

One of the most challenging clinical scenarios we had to face was the recognition of signs and symptoms of HF in patients with COVID-19 pneumonia. In cases of fluid overload and pleural effusion, chest X-rays show pulmonary imbibition, which can be confused with interstitial infiltrates typical of COVID-19, especially if bilateral.

Therefore, it often happened that one pathology masked the other, and we had to deal with cases of re-exacerbations of HF in cardiology patients affected by COVID-19, as if the infectious trigger precipitated the already weak haemodynamic compensation.

As we also are an advanced HF centre, we observed a very high incidence of patients who had had heart transplants hospitalised for acute respiratory syndrome due to COVID-19 pneumonia, and deaths often occurred, especially in patients with longstanding heart transplants.

As we also found, another sensitive issue concerns the management of patient with ST-elevation MI (STEMI) with pulmonary impairment. In our series of almost 50 patients admitted to the cath lab for acute coronary syndrome (both STEMI and non-STEMI), an age above 75 years, hypertension and diabetes were more frequently observed in COVID-19 compared to control patients. In-hospital mortality was more than 40% in patients with COVID-19 and 0% in the control group. Of note, patients who died presented with severe hypoxic respiratory failure, frequently combined with a reduced ejection fraction of the left ventricle (unpublished data).

Cardiovascular Involvement: Several Doubts and Few Certainties

COVID-19 causes not only pulmonary involvement with respiratory failure mainly due to bilateral interstitial pneumonia, but also systemic multi-organ involvement with a strong inflammatory response mediated by cytokines and interleukins.[11,12] An important issue related to the CV impact of COVID-19 is the development of myocardial injury in infected patients, as reported in two Chinese studies by Shi et al. and Guo et al.[13,14] Elevated troponin levels were detected in a cohort of hospitalised COVID-19 subjects; specifically, the higher the troponin levels, the higher the in-hospital mortality. Of note, the highest mortality rate was found in patients with a history of CV disease, as if a pathological cardiac substrate contributed to a poorer prognosis.

Other recent observations corroborate this hypothesis, suggesting that patients with underlying CV comorbidities are most likely to experience complications from COVID-19, including death. At the cardiac level, few cases of myocarditis due to direct cardiac damage have recently been reported, and coronavirus has been found in histological slides of myocytes from infected patients, highlighting a marked cardiac tropism.[7–9]

As mentioned above, an intense network of cytokines and chemokines are activated during COVID-19 infection, causing both vascular and myocardial inflammation, the latter probably due to a viral direct damage of the myocardium.

Recently, Tavazzi et al. described a case of an acute cardiac injury directly linked to myocardial localisation of COVID-19, with an endomyocardial biopsy demonstrating viral particles, suggesting either a viraemic phase or macrophage migration from the lung.[15] In this regard, a remarkable aspect to be investigated and clarified in the near future is the prevalence of myocarditis. Several reports show that patients at greater risk of developing acute myocarditis triggered by COVID-19 already have increased troponin values at first contact in the emergency room.[7,16] Therefore, proper identification of those patients would be important to diagnose myocarditis, even in an atypical clinical scenario.

Other cardiac effects of COVID-19 are related to ischaemic cardiac injury secondary to hypoxia, thrombosis of the microvascular vessels and MI due to thrombosis of the epicardial coronary artery. The role of not only troponins but also other cardiac biomarkers in confirmed cases of COVID-19 are uncertainties that needed to be addressed.

In a retrospective analysis involving 799 patients with COVID-19 in Wuhan, concentrations of cardiac troponin I, N-terminal pro-brain natriuretic peptide and D-dimer were markedly higher in deceased patients than in recovered ones.[17] Cardiac biomarker elevation seems to be a prominent feature in COVID-19 associated with worse outcomes.[13,18]

Surprisingly, the mortality risk associated with elevated circulating biomarkers of acute cardiac injury was more significant than age, diabetes, chronic pulmonary disease or history of CV disease.[12] In all this, the fact that comorbidities play a key role in the clinical evolution of COVID-19 patients and affect prognosis has been demonstrated and deserves attention.[19] In particular, elderly people with CV comorbidities, included hypertension and a history of coronary artery disease, have a greater risk of a having a more severe clinical picture and a fatal outcome.[20]

A well-discussed grey area for cardiologists is concern regarding the potential of an increased risk related to medications that act on the renin-angiotensin-aldosterone system in patients with COVID-19. Recently, Reynolds at al. examined the relationship between previous treatment with angiotensin-converting-enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs), beta-blockers, calcium-channel blockers or thiazide diuretics and the likelihood of a positive or negative result of the swab test for COVID-19 among 12,594 patients. No association between any single medication class or an increased likelihood of a positive test was observed, nor were any medications associated with a substantial increase in the risk of severe illness in patients who tested positive.[21]

Similarly, Mancia et al. observed that, among a population of 6,272 positive patients in Lombardy, there was no evidence that ACE inhibitors or ARBs affected the risks of COVID-19.[22]

An important grey area for cardiologists is making a correct differential diagnosis between HF and pneumonia, since the symptoms often overlap. While it is true that in the acute phase of the pandemic many HF patients avoided the emergency room because they were afraid of being infected by COVID-19 in the hospital (with a consequent reduction of HF hospitalisations), it is also true that many complicated cases are now being observed. It is therefore inevitable that, in the near future, we will have to address this difficult issue, and try to acquire the knowledge and tools to categorise a patient properly as soon as possible.

Interesting pathophysiological issues concern the right ventricle in regard to pressure overload due to pulmonary embolism, which is increasingly being documented in COVID-19 patients. This is probably due to an impaired coagulation drive with activation of fibrinolysis processes, and fluid overload because of a pulmonary shunt.

In the end, from our perspective, COVID-19 has changed how our work is organised and the approach to clinical practice, leading us to study a new, unknown disease, with many grey areas and more doubts than certainties.[23] We, therefore, propose some reflections that around three questions.

- There is a clear intersection between the SARS-CoV-2 infection and the heart. How much will cardiac injury or pulmonary embolism due to COVID-19 affect the natural history of patients with chronic HF following the acute phase of the infection?
- We all are facing a new disease and there are several doubts around it. Will the attitude of cardiologists, who have always been trained to work using the evidence-based medicine, have to be changed?
- In a short time, international literature has provided a large number of articles related to COVID-19 and clinicians learn rapidly from each other. Is it more scientifically correct to think of waiting for robust data before drawing conclusions about the CV impact of COVID-19? ■

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