Myocardial injury in COVID-19 patients and heart transplantations in times of the pandemic

Coronavirus Disease 2019 (COVID-19) and Cardiovascular Disease

LITERATURE - CLERKIN KJ, FRIED JA, RAIKHELKAR J ET AL., - CIRCULATION. 2020. DOI: 10.1161/CIRCULATIONAHA.120.046941

The review article by Clerkin *et al.* in *Circulation* describes the clinical presentation of COVID-19 patients and shows prevalence rates of CVD in patients with COVID-19. Moreover, this article draws attention towards reports of COVID-19 patients with myocardial injury, and of patients who underwent heart transplantation and were subsequently infected with SARS-CoV-2, the virus causing COVID-19. Finally, an overview of treatments that are currently under investigation is given.

COVID-19 in patients with CVD

CVD is a prevalent comorbidity among patients with COVID-19. In a cohort of 191 patients, any comorbidity was present in 48% of COVID-19 patients (67% of non-survivors), hypertension in 30% (48% of non-survivors), diabetes mellitus (DM) in 19% (31% of non-survivors) and CVD in 8% (13% of non-survivors) [1]. A cohort of 138 hospitalized COVID-19 patients shows similar rates: 46% for any comorbidity, hypertension in 31%, CVD in 15% and DM in 10%. Rates were higher in patients requiring ICU care [2]. In an outpatients and inpatient cohort of 1,099 COVID-19 patients, 24% had any comorbidity, 15% had hypertension, 7.4% with DM, and 2.5% with coronary heart disease. Again, rates were considerably higher in those requiring intubation or in non-survivors [3]. The reason why CVD is a prevalent comorbidity in COVID-19 patients remains currently unclear.

Continued use of ACEi and ARB in COVID-19 patients

SARS-CoV-2 infection is caused by binding to the human angiotensin-converting enzyme 2 (ACE2), which is highly expressed in the lungs and heart [4-6]. The use of ACEi and ARB

are common in patients with CV disorders. At this time,
the ESC and HFSA/ACC/AHA have recommended continued use of ACEi, ARB, or other RAAS antagonists, as speculation of unsafety of these drugs in relation to COVID-19 is not evidence-based.

Myocardial injury in COVID-19 patients

In a cohort of 138 hospitalized COVID-19 patients, cardiac injury (defined as elevated high sensitivity Troponin I [hs-cTnI] or new ECG or echocardiographic abnormalities) was present in 7.2% of patients (22% of patients requiring ICU care) [2]. Furthermore, a report of the National Health Commission (NHC) of China described that elevated troponin levels and cardiac arrest during hospitalization was prevalent in almost 12% of patients without known CVD [7].

Early reports indicate that there are two patterns of myocardial injury with COVID-19. A retrospective cohort study in 191 patients hospitalized in Wuhan, China showed that hs-cTnI was above the 99th percentile upper reference limit in 46% of non-survivors, and in only 1% of survivors. At day 4 after symptom onset, median hs-cTnI levels were 8.8 pg/mL in non-survivors vs. 2.5 pg/mL in survivors. Median hs-cTnI did not change significantly among survivors in the following days (2.5-4.4 pg/mL). In contrast, in non-survivors the median hs-cTnI increased over time (24.7 pg/mL on day 7, 55.7 pg/mL on day 13, 134.5 pg/mL on day 19, and 290.6 pg/mL on day 22). Similar patterns were seen in D-dimer, ferritin, IL-6, and lactate dehydrogenase levels [1]. This may also point to the possibility of a cytokine storm or secondary hemophagocytic lymphohistiocytosis instead of an isolated myocardial injury. Other case studies of patients with cardiac symptoms suggest a different pattern of potential viral myocarditis or stress cardiomyopathy [8,9]. Mechanisms that could explain the cardiac involvement in COVID-19 remain unclear at this time and are under investigation.

Heart transplantations in times of COVID-19

A survey of 87 heart transplant recipients showed no higher risk of infection with SARS-CoV-2 if routine preventive measures were used [10]. A recent case study reported about the clinical courses of two heart transplant recipients who got infected with SARS-CoV-2. Both patients had fevers and had laboratory results and CT scans that were similar to non-

immunosuppressed individuals with COVID-19. One patient had relatively mild symptoms, while the other required hospitalization and supplemental oxygen. Both patients were treated with antibiotics and antivirals. The more ill patient was also treated with methylprednisolone and IVIG and required cessation of immunosuppression. Both patients survived [11].

Current recommendations from major societies are to continue heart transplantation without changes in immunosuppression if the recipient has not tested positive for SARS-CoV-2 and has not had exposure to or symptoms of COVID-19 in the last 2-4 weeks. Recommendations further include avoidance of donors with known or suspected COVID-19. If a donor had COVID-19, they should be COVID-19 free (as confirmed by PCR) for at least 14 days [12-13].

Treatments under investigation

Preventive measures are currently the best strategy against COVID-19. Several investigational therapies that use clinically approved drugs targeting SARS-CoV-2 cell invasion and replications are under investigation. Examples of drugs currently studied in the context of COVID-19 include recombinant human ACE (APN01), the serine protease inhibitor camostat mesylate, remdesevir, cloroquine, hydroxychloroquine, the combination protease inhibitor lopinavir/ritonavir, antiviral medications oseltamivir and arbitol, favipiravir, and IL-6 receptor antagonists tocilizumab and sarilumab.