WHF COVID-19 and Cardiovascular Disease Survey

'SYNOPSIS'

Protocol Version. 1.0 Protocol Date: 16 April 2020

This is the Synopsis for the above titled study. The study is in fact a global registry sponsored by the World Heart Federation, Geneva, Switzerland. The Registry only requires data from the participant and no human samples are required. There is no risk to the participant as there is no study related interventional treatment. No study related phlebotomy will be performed. The patients will receive the relevant Institutions 'gold-standard treatment'.

The Global Principal Investigator at 'The University of Cape Town' is Professor Karen Sliwa, whose role is one of collaboration and coordination only. The Cardiology department at Groote Schuur Hospital may participate as an active site at a later stage.

The novel coronavirus epidemic Coronavirus Disease 2019 (COVID-19) is caused by SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2), which invades cells by attachment to the angiotensin converting enzyme 2 (ACE2) receptor.

COVID-19 is an emerging, rapidly evolving, global pandemic impacting nearly 204 countries and/or regions, and more than 1,341,662 patients worldwide, with more than 75,000 deaths as of April 06, 2020. Available data indicate that COVID-19 is a relatively mild condition in most affected individuals but, in others, it can be very severe and deadly. Progression to pneumonia, acute respiratory distress syndrome (ARDS), multi-organ failure and death occurs, particularly in the elderly and those with key co-morbidities: chronic obstructive pulmonary disease (COPD), cardiovascular disease (CVD), hypertension (HTN) and diabetes mellitus (DM). However, severe disease requiring hospitalization, and even deaths, have been reported in younger adults.

In December 2019, the COVID-19 outbreak started in Wuhan, China. Since then it has spread around the world. On 30 January 2020, the World Health Organization (WHO) declared the outbreak a "public health emergency of international concern".
The spread onto the African continent and other low-income countries is of great concern. Large and densely populated areas and townships with widespread poverty and high migration are the most vulnerable populations for airborne pandemics. Existing epidemics of human immunodeficiency virus (HIV), tuberculosis (TB) and malaria are likely to collide with COVID-19 and may lead to morbidity and mortality patterns different from currently affected "hot spot" countries.
Known risk factors for severe cases of COVID-19, COPD, CVD, HTN, and DM, have a high prevalence in low- and middle-income countries, and these conditions are generally worse controlled in these settings than in high income countries and therefore the potential associated risk might be higher.

Link between Cardiovascular disease and COVID-19

Evidence from previous studies showed that CVD was a common comorbidity in patients with COVID-19 predecessors SARS and MERS. The adverse impact on outcome of CVD comorbidities holds true for COVID-19.

COVID-19 infection sets off an acute inflammatory storm, in fact, the robust inflammatory response is responsible for progressive lung injury. This response may also lead to myocardial injury and impaired cardiac function.

There is concern that COVID-19 is cardiotropic, based on the high prevalence of findings consistent with myocardial injury, disturbances of cardiac function, presence of pericardial effusions in some patients, and absence of obstructive coronary disease in patients with acute myocardial injury and suggestive ECG changes.

Autopsy findings confirm, in some patients, the presence of myocarditis but characterization of the pathophysiology remains incomplete.

Emerging data from the current pandemic shows that COVID-19 interacts with the cardiovascular system on multiple levels. Individuals with underlying chronic CVD are both more susceptible to COVID-19 and more prone to myocardial injury and dysfunction, critical deterioration and death.

Patients with COVID-19 and CVD had a much higher fatality rate (10.5%) with COVID-19 and Hypertension (6.0%), as compared to 0.9% in patients with no reported comorbid conditions.

Arrythmias are present in 17% of patients.

Acute pulmonary infection may destabilize CVD, including heart failure and atherosclerosis, including precipitating acute myocardial infarction, which has been reported in the pandemic. Deterioration of cardiac function would then, in turn, worsen COVID-19 management.

<u>Reasons for the current study</u>

As summarized above, there is emerging evidence that CVD, DM, and HTN are associated with COVID19 and its severity. COVID-19 may be cardiotropic in a subset of patients. Both acute and pre-existing CVD impact outcomes unfavorably.

However, studies so far have been conducted with important limitations (e.g. small numbers, limited geographical representation, lack of data standardization for risk factors and outcomes, limited measurement, lack of appropriate adjustment for important confounders, and missing data).

Considering the high global prevalence of CVD and its risk factors (e.g. hypertension and diabetes) and the suggested link with COVID19 it is urgent to start more robust studies to clarify the many issues early reports have produced.

In order to reach robust conclusions that could inform clinical and policy practices, we will conduct a global study for a better understanding of the cardiovascular conditions that increase the risk of developing severe COVID-19, and a better characterisation of cardiovascular complications in hospitalised patients with COVID-19.

Study Objectives

- To describe cardiovascular outcomes among patients hospitalised with COVID-19;
- To identify cardiovascular risk factors associated with poor in-hospital prognosis among patients with COVID-19.

Methods

Study design

We will conduct a prospective cohort study including consecutive confirmed COVID-19 patients.

Study setting

Participants will be recruited in any hospital where COVID19 patients are hospitalised. We will invite all WHF members from 100+ countries to identify at least two recruiting centres in their respective countries. Each centre should recruit between 50 and 200 consecutive patients. There is no limit in the number of sites to take part.

Study Population

Eligibility criteria

Inclusion Criteria

- All adult (as locally defined) with confirmed COVID-19 infection who are hospitalized are eligible.

Exclusion criteria

- Patients for whom we are unable to obtain informed consent will be excluded.
- Patients who are unlikely to stay in the recruiting centre for 30 days (i.e. likely to be transferred)

Follow up

All patients will be followed up until 30 days, death or discharge whichever occurs first. If patient is discharged prior to 30 days, a phone contact will be made to find out whether patient is alive or dead and if the patient had any re-hospitalization.

Outcomes

- Need of intensive care, need of ventilator,
- death (with cause),
- major adverse cardiovascular events (myocarditis, arrhythmia, heart failure [including left ventricular ejection fraction],
- acute coronary event [type of Myocardial Infarction],
- neurological outcomes,
- pulmonary outcomes

Data collection

This study will be coordinated from the 'Public Health Foundation of India' (PHFI) and the 'Centre for Chronic Disease Control' (CCDC) both in India, and conducted in hospitals in low-, middle- and high-income countries. Data will be collected at each site by local investigators and sent to the coordinating center. Only data outlined on the entry and outcome forms will be collected. Each site will have a research coordinator who will enter in-hospital entry and outcome form via a secure website throughout the entire study period. Hospital-level data will be collected just once when the hospital joins the study.