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Morning Brief : Scientific Review

30 April 2020

The purpose of the Morning Brief is to **summarize** and present key information, research articles and other relevant publications pertaining to critical care and COVID-19. We aim to prioritise information, articles and publications released in the preceding 24-48hours.

Stellenbosch University Research Response Team

STELLENBOSCH UNIVERSITY PULMONOLOGY

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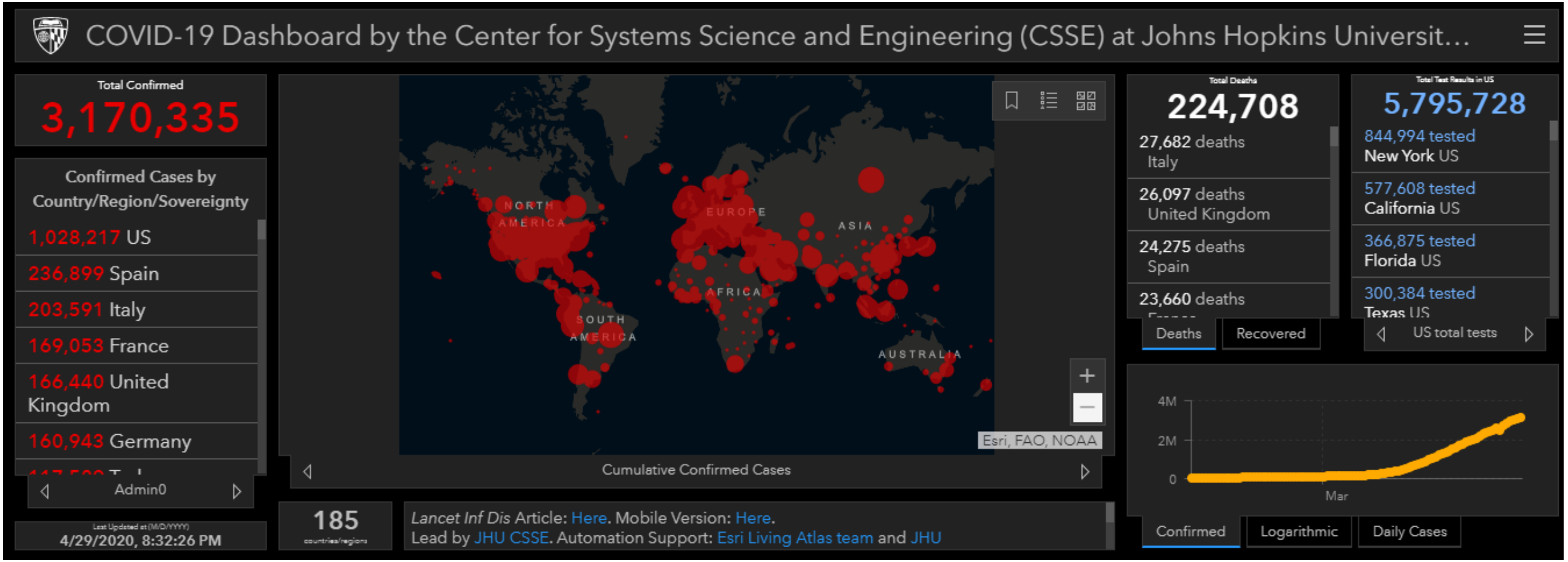
Content of the brief

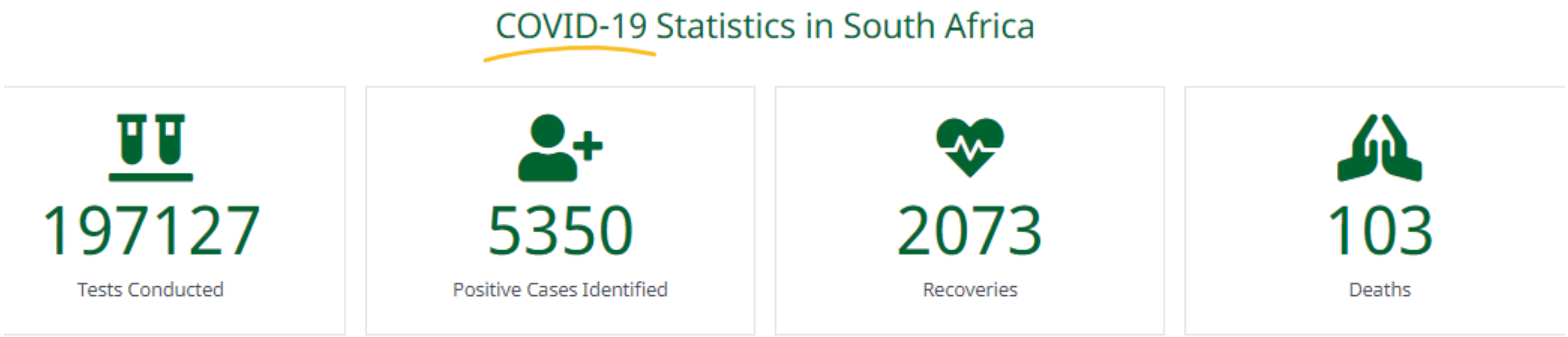
- **Global Statistics**
- **South African Statistics**
- **Topic: COVID-19 and Cardiology**

Global Statistics



Accessed at 21:24 on 29 April 2020
Source: https://coronavirus.jhu.edu/map.html

South African Statistics



Accessed at 21:30 on 29 April 2020
Source: https://sacoronavirus.co.za/

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Text

COVID-19 and Cardiology

ESC Guidance for the Diagnosis and Management of CV Disease during the COVID-19 Pandemic

Last updated on 21 April 2020

Reference

Preamble

- European Society of Cardiology (ESC)
  - guidance document
- Updated on 21 April 2020
- COVID-19 has reached pandemic levels

Introduction

- SARS-CoV-2 not only causes viral pneumonia but has major implications for the CV system
- Patients with cardiovascular (CV) risk factors and established cardiovascular disease (CVD) represent a vulnerable population
- Increased risk of morbidity and mortality.

Cardiovascular complications

- Arterial thrombotic complications)
- Venous thromboembolism (VTE)
- Myocarditis
- A wide range of **arrhythmias**
  - pro-arrhythmic effects of medical treatment targeted at COVID-19 and associated diseases

Impact of Cardiovascular Comorbidities on COVID-19 Infection Outcomes

- CVD risk factors and disease correlate with increasing age
- CV comorbidities are common in patients with COVID-19 infection
- Presence of CVD is associated with increased mortality in COVID-19 infections

Pathophysiology - Mechanism of Disease in Relation with the Cardiovascular System

Key points

- The pathobiology of coronavirus infection involves SARS-CoV-2 binding to the host receptor angiotensin-converting enzyme 2 (ACE2) to mediate entry into cells;
- ACE2, which is expressed in the lungs, heart and vessels, is a key member of the renin angiotensin system (RAS) important in the pathophysiology of CVD;
- CVD associated with COVID-19, likely involves dysregulation of the RAS/ACE2 system due to SARS-CoV-2 infection and due to comorbidities, such as hypertension;
- CVD may be a primary phenomenon in COVID-19, but may be secondary to acute lung injury, which leads to increased cardiac workload, potentially problematic in patients with pre existing HF;
- Cytokine release storm, originating from imbalance of T cell activation with dysregulated release of interleukin (IL)-6, IL-17 and other cytokines, may contribute to CVD in COVID-19. IL-6 targeting is being tested therapeutically;
- Immune system activation along with immunometabolism alterations may result in plaque instability, contributing to development of acute coronary events.

Biomarkers

- The level of Trop I/T and BNP/NT-proBNP concentration correlate with disease severity and mortality
- BNP/NT-proBNP
  - associated with the extent of right ventricular haemodynamic stress

Biomarkers: Trop I

- Mild elevations in cardiac troponin T/I concentrations (e.g. < 2–3 times the ULN)
  - do NOT require work-up or treatment for T1MI, unless strongly suggested by angina chest pain and/or ECG changes
  - explained by the combination of possible pre-existing cardiac disease AND/OR the acute injury related to COVID-19

Figure 10 Temporal changes in high-sensitivity cardiac troponin I concentrations from illness onset in patients hospitalised with COVID-19

Differences between survivors and non-survivors were significant for all time points shown. ULN denotes upper limit of normal (adapted from Zhou et al.[23])

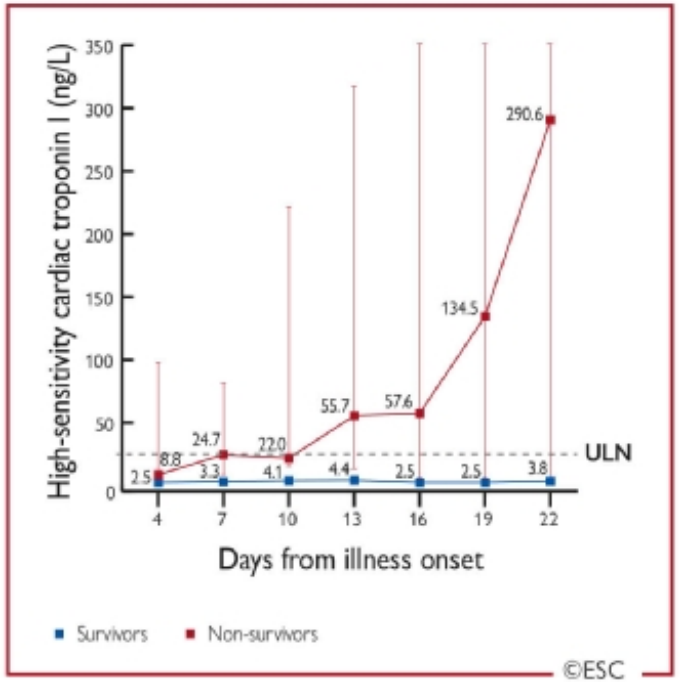
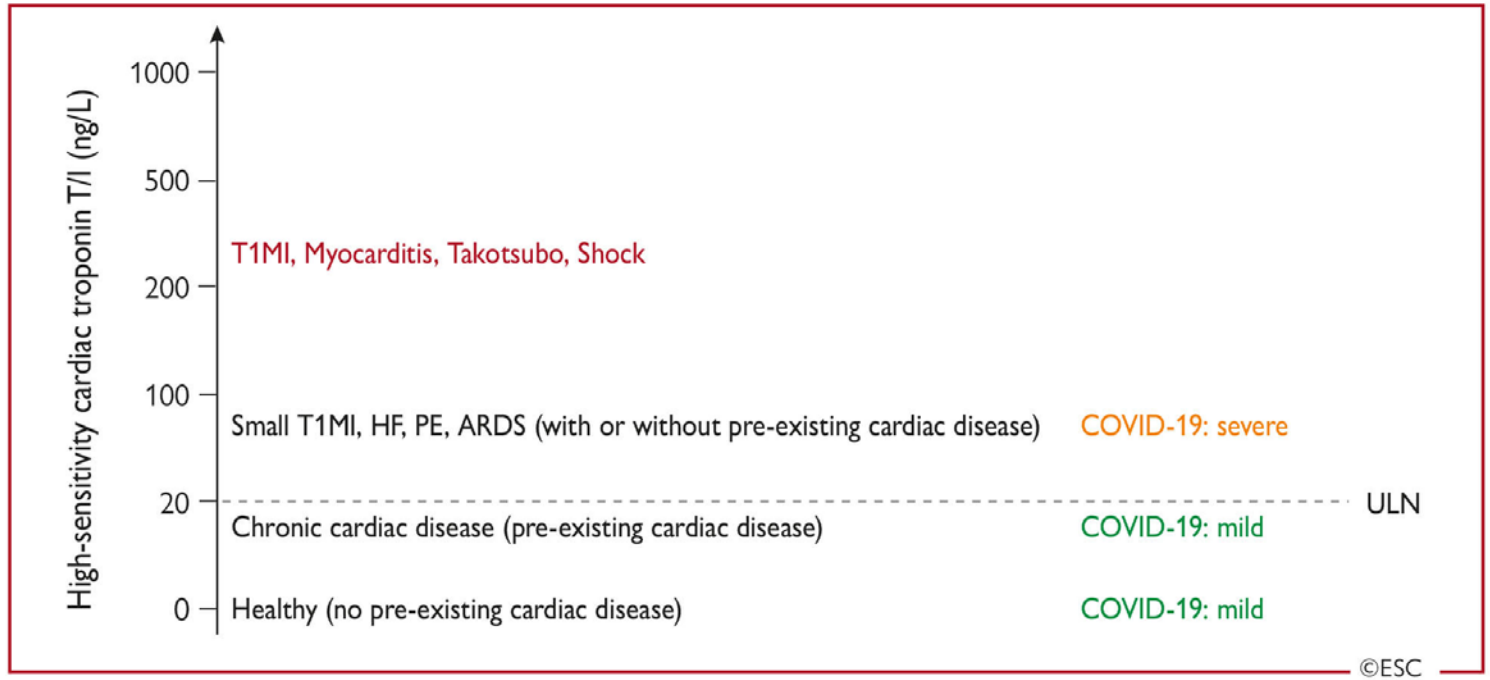


Figure 11 High-sensitivity cardiac troponin (hs-cTn) T/I concentrations should be interpreted as quantitative variables.

In non-critically-ill patients with COVID-19, mild elevations (e.g. up to 3-times the ULN) elevations are in general well explained by the combination of possible prior cardiac disease AND the acute cardiomyocyte injury related to COVID-19. Even higher concentrations indicate the presence of specific acute cardiac disease such as T1MI, myocarditis, or takotsubo syndrome.

ULN denotes upper limit of normal and is assay-specific, HF denotes heart failure, PE denotes pulmonary embolism, ARDS denotes acquired respiratory distress syndrome, T1MI indicates type 1 myocardial infarction.



Biomarkers

- Marked elevations in cardiac troponin T/I concentrations (e.g. > 5 times the ULN)
  - may indicate the presence of shock as part of COVID-19, severe respiratory failure, tachycardia, systemic hypoxaemia, myocarditis, Takotsubo syndrome or T1MI triggered by COVID-19.
- In the absence of symptoms or ECG changes suggestive of T1MI, echocardiography should be considered in order to diagnose the underlying cause.

Biomarkers

- **In patients with COVID-19, as in patients with other pneumonias, it is suggested to measure cardiac troponin T/I concentrations only if the diagnosis of T1MI is being considered on clinical grounds, or in new onset LV dysfunction.**

Biomarkers

- D-Dimers can be increased in a third of patients with COVID-19
- Monitoring of D-Dimer concentrations might help to anticipate deteriorating cases but could also cause confusion regarding the presence of acute PE.
- D-dimer should only be determined in case of clinically suspected PE
- Other markers of coagulation activation could be monitored for the purpose of prognostication

The Science Underlying COVID-19:

Implications for the Cardiovascular System

Running Title: *Liu et al.; Science & COVID-19*

Peter P. Liu, MD[1,2]; Alice Blet, MD, PhD[1,3,4]; David Smyth, PhD[1,2]; Hongliang Li, MD, PhD[5,6,7]

[1]University of Ottawa Heart Institute and University of Ottawa, Ottawa, Ontario, Canada;

[2]Departments of Medicine and Cellular & Molecular Medicine, University of Ottawa, Canada;

- Patients with pre-existing cardiovascular conditions represent large proportions of patients with symptomatic infection, and experience disproportionately worse outcomes at between 5-10 fold increase in mortality

Table 1. Death rate to date of patients with COVID-19 infection and specific pre-existing conditions (WHO Data)

PRE-EXISTING CONDITION	DEATH RATE
Cardiovascular disease	**10.5%**
Diabetes	**7.3%**
Chronic respiratory disease	**6.3%**
Hypertension	**6.0%**
Cancer	**5.6%**
no pre-existing conditions	**0.9%**

Clinical Spectrum of Cardiovascular Involvement in COVID-19

- Between 8-28% of patients with COVID-19 infections will manifest troponin release early in the course of the disease
- A similar proportion of patients also manifest elevations of natriuretic peptides
- Troponin and BNP, together with the presence of underlying cardiovascular diseases or cardiovascular risk factors, are highly prognostic of requirement for
  - ICU admission,
  - ventilation and
  - death

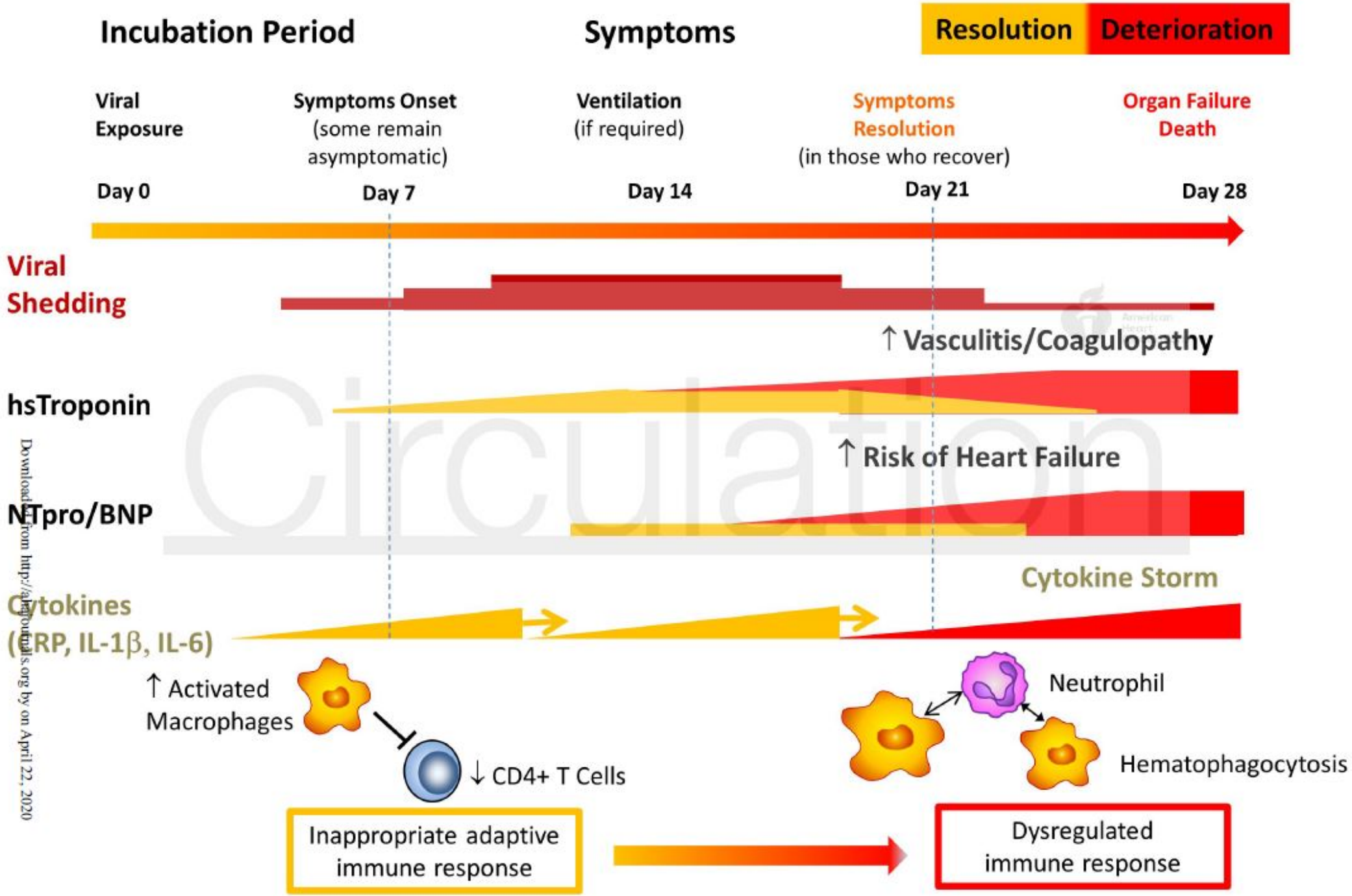
- In addition to increased propensity and worse outcomes for COVID-19 in patients with pre-existing cardiovascular diseases
- Patients with new COVID-19 infections can also develop cardiovascular complications, such as
  - heart failure,
  - myocarditis,
  - pericarditis,
  - vasculitis,
  - and cardiac arrhythmias

Pathobiology

- Whether SARS-CoV-2 can directly proliferate in the heart is unknown.
- There are very few pathology studies on COVID-19 patients.
- HOWEVER, previous analysis of human hearts in patients who died from SARS demonstrated that 7 of 20 (35%) hearts harbored virus in the myocardium.
- Direct viral entry into the myocardium and blood vessels.
- Observed cardiac damage is due to
  - ?viral injury, or
  - ?due to an immunological response impacting the myocardium and related structures, such as the pericardium and conduction system.

Oversimplification of pathogenesis

- The virus uses the ACE2 receptor for internalization, aided by (transmembrane protease serine 2)TMPRSS2 protease
- Virus-induced ACE2 down regulation may attenuate its function, diminish its anti-inflammatory role, and heightened angiotensin II effects in predisposed patients.
- The ensuing Inflammation in the vascular system can result in diffuse microangiopathy with thrombosis.
- Inflammation in the myocardium can result in myocarditis, heart failure, cardiac arrhythmias, acute coronary syndrome, rapid deterioration and sudden death.



Treatment

- Aggressive support based on early prognostic indicators with expectant management can potentially improve recovery
- Appropriate treatment for heart failure, arrhythmias, acute coronary syndrome and thrombosis remain important