Triage Systems (Reorganization and Redistribution)

- Initial symptoms of a COVID-19 infection such as breathlessness, chest pain, or asthenia may mimic the early manifestations of a cardiac disease.
- Also, COVID-19 patients might abruptly develop acute cardiac complications (such as ACS or pulmonary embolism [PE]) and come to the hospital for this reason.
- Patients with possible/probable or confirmed COVID-19 infection should be triaged as COVID-19 infected.

- In particular, critically ill patients for acute CV condition (STEMI patients, out-of-hospital cardiac arrest [OHCA] patients), should quickly access medical or interventional treatment according to the current evidence-based guideline recommendations. Therefore, they should be presumed as SARS-CoV-2 positive, until proven otherwise. Accordingly, HCP should wear adequate PPE, particularly in the triage phase
- Recommendations made by the WHO state that contact precautions (by means of appropriate face masks, eye glasses, hydro repellent lab coats and gloves) are necessary since the very early triage phase.

- A contained number of hospitals equipped with a catheterization laboratory operating 24 hours/7 days should still maintain their hub role for the management of time-dependent acute CVD;
- • Resources and cardiac specialists should be concentrated in the hub centres to guarantee the appropriate acute treatment to all the cardiac patients in need of it;
- • The ambulance networks should be rearranged according to the new hub and spoke organization.

- Hub centres are committed to provide acute reperfusion to all patients requiring an urgent PCI. Patients with STEMI or high-risk NSTEMI should be triaged by the emergency medical services team and timely transported to hub centres, if feasible.
- As a general rule we recommend that the number of catheterization laboratories available for primary PCI should not be reduced during the pandemic, to avoid an increase in door-to-balloon time, to diminish the risk of infection during transfer for both professionals and/or patients, and to unload the health care system.

- The ambulance networks also need to be reorganized in order to bring the patients straight to the COVID-19 referral hospital, skipping the spoke centres from where a secondary transportation could be difficult to arrange and time-consuming.

Emergency department

- A rearrangement of the ED is mandatory to separate suspected COVID-19 patients from patients without SARS-CoV-2 infection;
- • Local protocols to rapidly triage patients with respiratory symptoms should be available as well as facilities where patients wait for the results of COVID-19 screening tests. Patients with mild, stable diseases should be promptly discharged.
- In China for example patients with no geographical or family history of virus infection, fever, respiratory symptoms, fatigue or diarrhoea were considered ‘COVID-19 unlikely’ and their CVD was usually treated with standard protocols

- Patients with mild, stable diseases should be discharged from the ED as soon as possible , with the suggestion to stay at home in quarantine if a COVID-19 infection is suspected or confirmed.
- patients in need of hospital admission for acute CVD with concomitant possible/probable SARS-CoV-2 infection should rapidly undergo testing and be managed as SARS-CoV-2 infected until they have two negative tests within 48 hours.
- Patients in need of hospital admission not suspected of SARS-CoV-2 infection can be managed according to standard of care.

Table 4 Patient risk status[73]

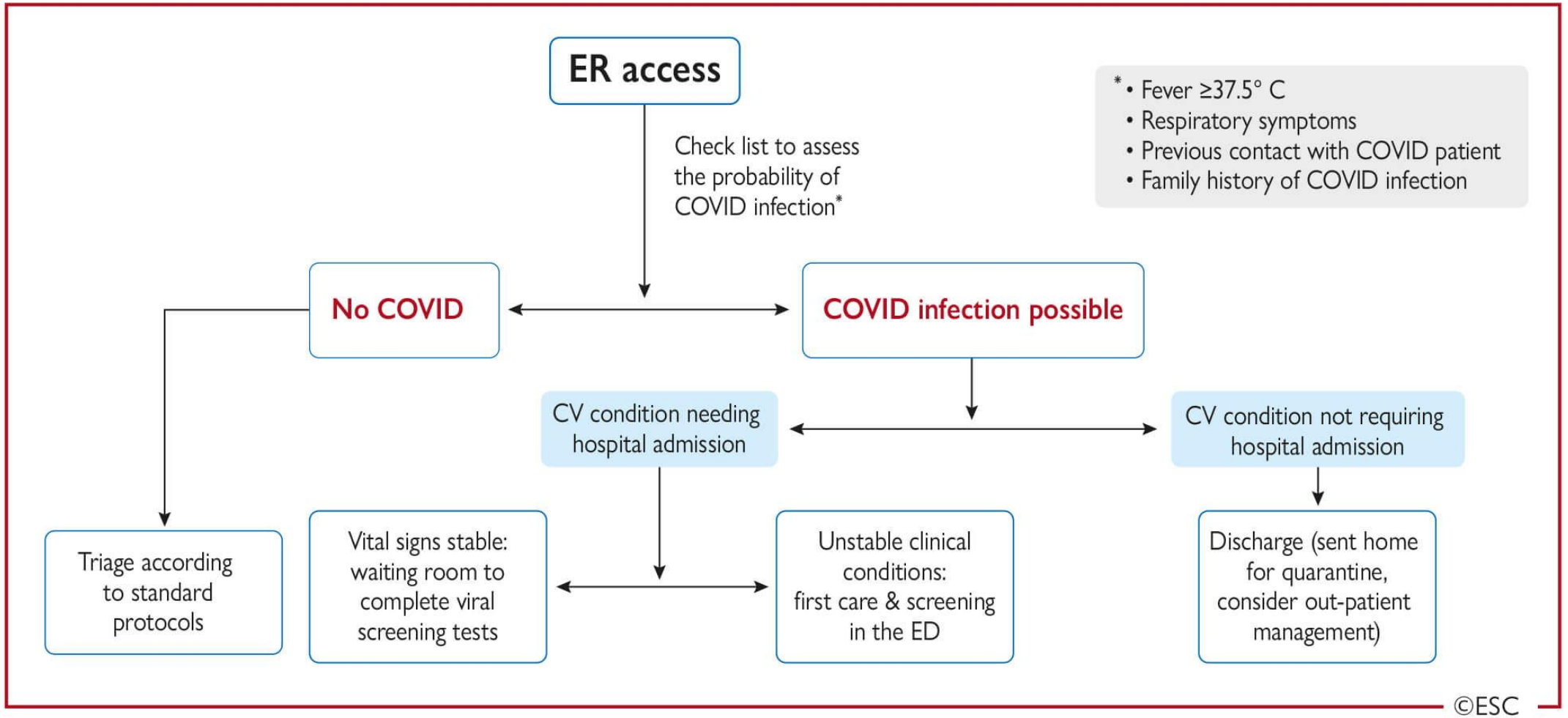
Confirmed case	A person with laboratory confirmation of SARS-CoV-2 infection, irrespective of clinical signs and symptoms.
Probable case	A) A suspected case for whom testing for the SARS-CoV-2 virus is inconclusive, OR B) A suspected case for whom testing could not be performed for any reason.
Suspected case	A) A patient with fever or at least one sign/symptom compatible with SARS-CoV-2 infection AND a history of travel to or residence in a location reporting community transmission of COVID-19 during the 14 days prior to symptom onset, OR B) A patient with fever or at least one sign/symptom compatible with SARS-CoV-2 infection AND having been in contact with a confirmed or probable COVID-19 case in the last 14 days prior to symptom onset, OR C) A patient with severe acute respiratory disease AND requiring hospitalization AND in the absence of an alternative diagnosis that fully explains the clinical presentation.
Negative case	A) A person without COVID-19 symptoms who had contacts with a confirmed or probable COVID-19 case[a] who has a negative SARS-CoV-2 test, OR B) A suspected case with two negative SARS-CoV-2 tests, OR C) COVID-19 patient who recovered from COVID-19 infection who has two negative tests with an interval between the two tests of at least 48 h.

[a]Definition of a contact[73]

A contact is a person who experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms of a probable or confirmed case:

- Face-to-face contact with a probable or confirmed case within 1 meter and for more than 15 minutes;
- Direct physical contact with a probable or confirmed case;
- Direct care of a patient with probable or confirmed SARS-CoV-2 infection without using proper personal protective equipment;
  OR
- Other situations as indicated by local risk assessments.

Figure 8 Algorithm for triaging patients admitted to the Emergency Room (ER) for a suspect acute CV disease



Diagnosis of Cardiovascular Conditions in COVID-19 Patients

- Clinical presentation
- Chest pain and breathlessness is a frequent symptom in COVID-19 infection;
- Chronic and acute coronary syndrome presentations can be associated with respiratory symptoms.

- The symptom of chest pain or tightness is common in patients with active COVID-19 infection. It is usually poorly localized and may be associated with breathlessness due to the underlying pneumonia. Associated profound hypoxaemia together with tachycardia may result in chest pain and electrocardiographic changes suggestive of myocardial ischaemia. Where biomarkers are altered, Type 2 myocardial infarction (MI) may be suggested.
- Patients with ACS do, however, experience the more typical symptoms related to ischaemia.

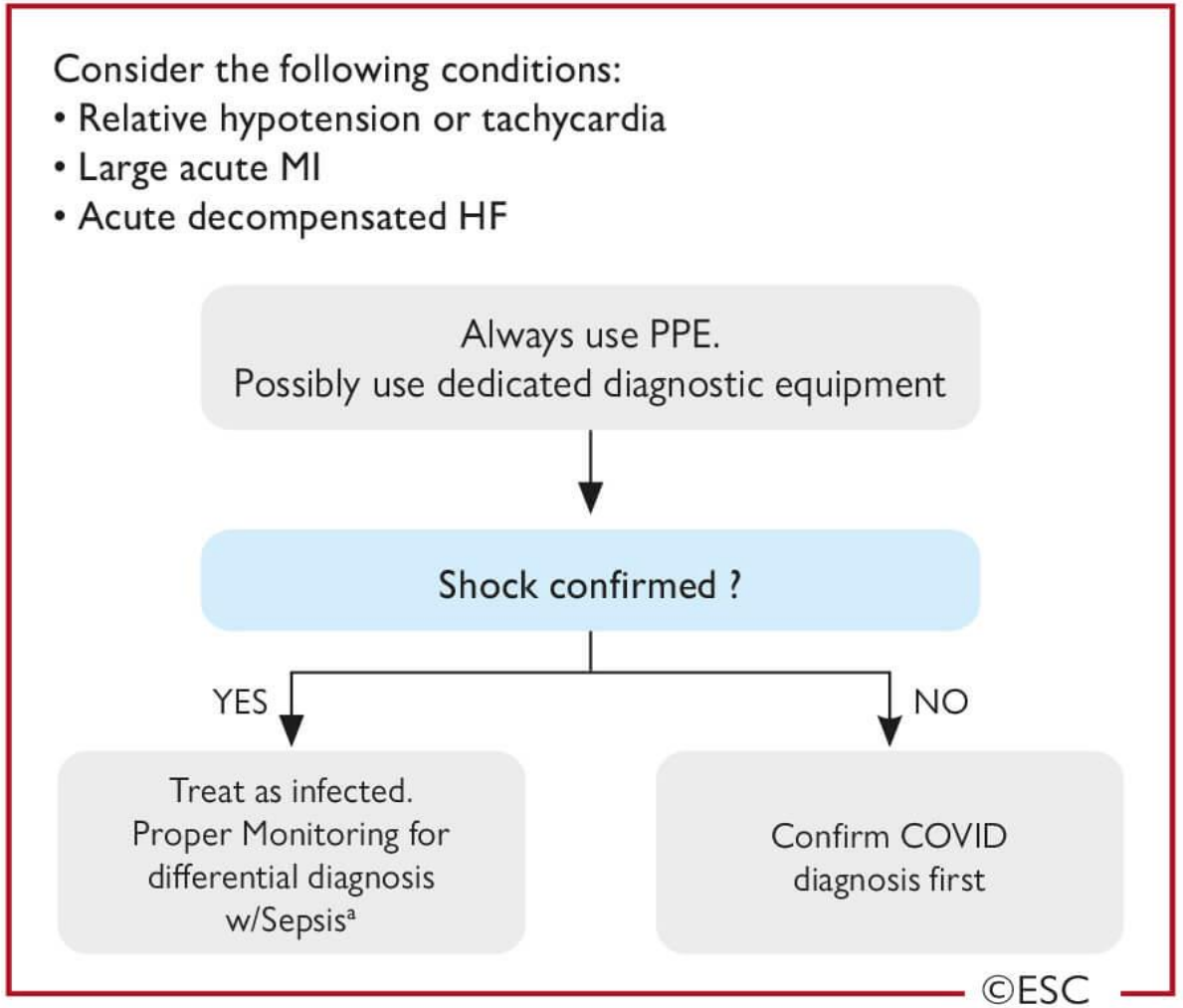
- **Dyspnoea** (shortness of breath) is one of the typical symptoms in COVID-19. Of 1099 adult inpatients and outpatients in China, 18.7% presented with dyspnea.
- Cough is present in 59.4–81.1% of patients with COVID-19, irrespective of disease severity.
- ARDS is characterized by bilateral opacifications on chest imaging (e.g. bilateral ground glass opacifications on CT) and hypoxaemia that cannot be explained by other causes.
- 100 Among 1099 adult inpatients and outpatients in China, ARDS occurred in 3.4%, but in hospitalized patients, the rates are significantly higher (19.6–41.8%). The median time from disease onset to ARDS is 8–12.5 days. The risk of ARDS increases with older age (≥ 65 years old), presence of comorbidities (hypertension, diabetes), neutrophilia, lymphocytopenia, elevated laboratory markers of organ dysfunction (e.g. lactate dehydrogenase [LDH]), inflammation (C reactive protein) and D-dimer.99 Mortality of patients treated for ARDS in COVID-19 is high

Cardiogenic shock

- In COVID-19 patients with impaired end-organ perfusion at risk of cardiogenic shock (CS) (e.g. large acute myocardial infarction [AMI]), consider also sepsis as possible or mixed aetiology;
- • Myocarditis should be considered as precipitating cause of CS.

- Importantly, key diagnostic testing in patients with suspected CS, including electrocardiogram (ECG), bedside echocardiography, and urgent/emergent coronary angiography, should be integrated into local diagnostic protocols (with dedicated and/or protected equipment whenever possible) to ensure both the best deliverable care and a minimal risk of viral transmission to other patients and health care providers.
- > 7.5% myocardial cells have positive ACE2 receptor expression, the target through which SARS-CoV-2 invades human cells, suggest that myocarditis may complicate COVID-19.

Figure 9 Considerations in patients with suspected (or at risk for) cardiogenic shock and possible COVID-19 infection



[a]consider also myocarditis as potential cause.

Out-of-Hospital Cardiac Arrest, Pulseless Electric Activity, Sudden Cardiac Death, Tachyarrhythmias, Bradyarrhythmias

- In a study of 138 hospitalized patients with COVID-19 in Wuhan;
- arrhythmia was reported in 16.7% of total patients
- 16 of 36 patients admitted to the ICU (44%)
- ventricular tachycardia (VT)/ventricular fibrillation (VF) was reported as a complication of the COVID-19 disease in 11 of 187 patients (5.9%), with a significantly higher incidence in patients with elevated troponin T.
- Hypoxaemia and a systemic hyperinflammation status may lead to new-onset atrial fibrillation (AF)

Hospitalization for Pneumonia and Time Course of Increased Subsequent Risk of Cardiovascular Death

- Pneumonia, influenza and SARS are well known to be associated with a markedly increased short-term risk for subsequent CV events, such as ACS;
- There needs to be a high alertness for CV events, such as ACS and thromboembolic events, in the short-term after pneumonia and a careful risk management approach in individuals with pre-existing CVD.

p][]P

- more common among patients at older age, nursing home resident, and patients with history of HF, coronary disease or hypertension.Moreover, for influenza epidemics it has been demonstrated that there is a consistent rise in autopsy-confirmed coronary deaths. Fatal AMIs have also been observed in the short term after coronavirus associated SARS.
- Moreover, an increased rate of thromboembolic events has been observed in the context of COVID-19 infection.[
- Troponin is a good marker for CV complication prediction

Electrocardiogram

- The same ECG diagnostic criteria for cardiac conditions apply in patients affected by the SARS-CoV-2 infection and in the general population

Biomarkers

- Cardiomyocyte injury, as quantified by cardiac troponin T/I concentrations, and haemodynamic stress, as quantified by B-type natriuretic peptide (BNP) and N-terminal B type natriuretic peptide (NT-proBNP) concentrations, may occur in COVID-19 infections as in other pneumonias. The level of those biomarkers correlate with disease severity and mortality;
- In the absence of typical angina chest pain and/or ischaemic ECG changes, patients with mild elevations (e.g. **< 2–3 times** the upper limit of normal [ULN] do NOT require work-up and/or treatment for Type 1 myocardial infarction [T1MI])

- 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.
- Patients with symptoms and ECG changes suggestive of T1MI should be treated according to ESC-guidelines irrespective of COVID-19 status

- 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. Independently from diagnosis, monitoring of cardiac troponin T/I may help for the purpose of prognostication;
- serial measurements of D-dimers may help physicians in the selection of patients for VTE-imaging and/or the use of higher than prophylactic doses of anticoagulation.

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.[34])

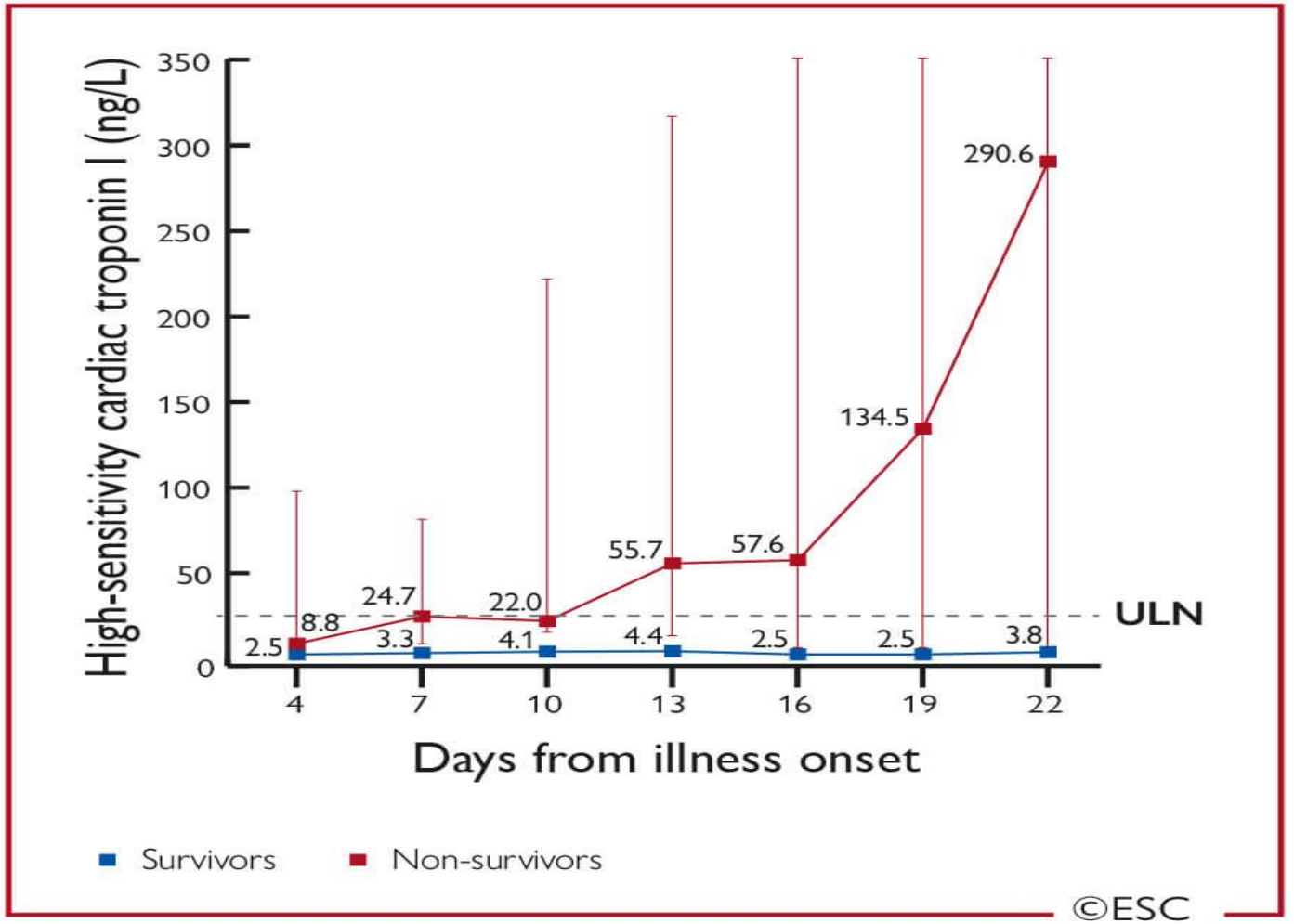
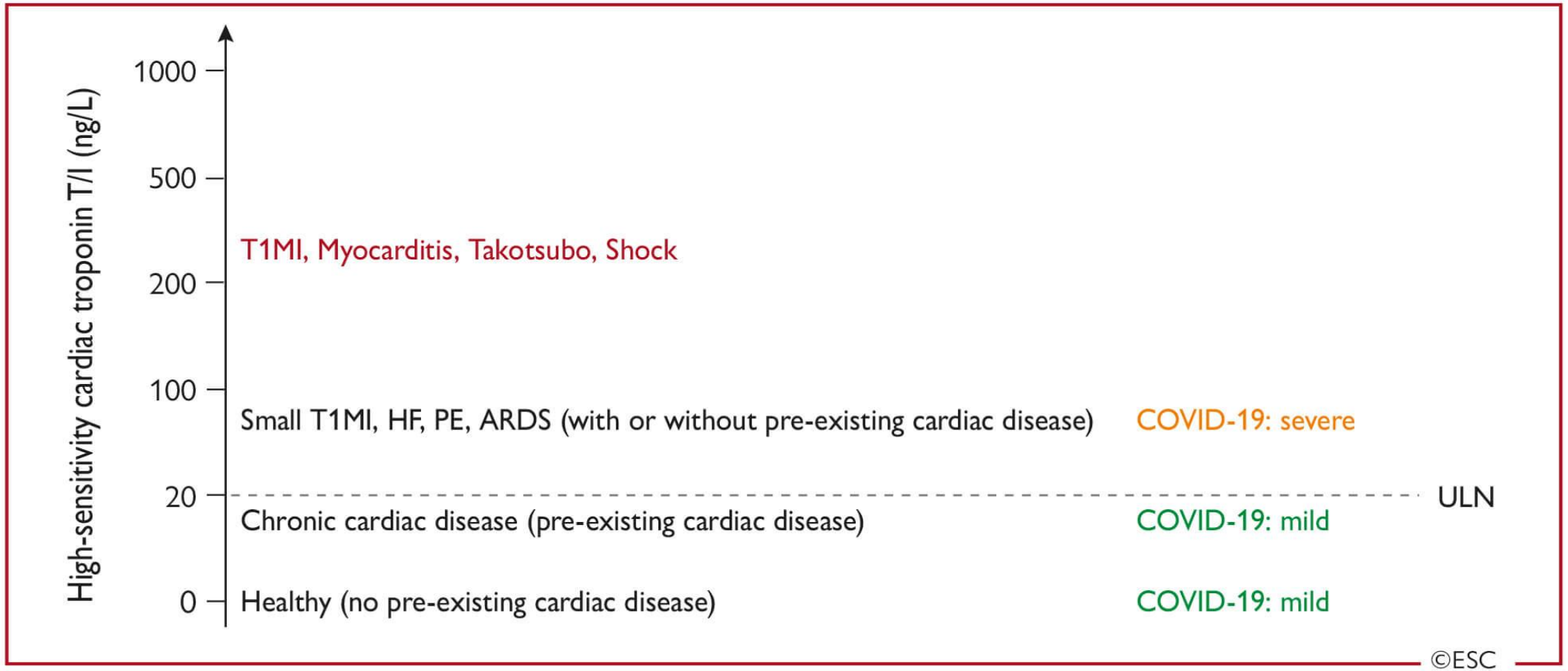


Figure 11 High-sensitivity cardiac troponin (hs-cTn) T/I concentrations should be interpreted as quantitative variables.
In non-critically-ill patients with COVID-19, mild elevations (e.g. up to 3-times the ULN) elevations are in general well explained by the combination of possible prior cardiac disease 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.



- As quantitative markers of haemodynamic stress and HF, the concentrations of BNP/NT-proBNP in a patient with COVID-19 should be seen as the combination of the presence/extent of pre-existing cardiac disease AND/OR the acute haemodynamic stress related to COVID-19.
- D-dimers are generated by cleavage of fibrin monomers by prothrombin and indicate the presence of thrombin formation or reflect an unspecific acute phase response from infection or inflammation. D Dimers also may indicate the presence of disseminated intravascular coagulation associated with shock.

Which Biomarkers Should be Measured and When?

- Detailed clinical assessment including chest pain characteristics, assessment of COVID-19 severity, hs-cTn T/I measurement at 3 hours, and cardiac imaging including echocardiography are the key elements for the identification of MI in this heterogeneous subgroup.
- Similarly, BNP/NT-proBNP should be measured whenever on clinical grounds HF is suspected.
- as most critically-ill patients have substantial elevations in BNP/NT-proBNP, most likely due to the near-universal presence of haemodynamic stress and HF in these patients

Non invasive imaging

- Do not perform routine cardiac imaging in patients with suspected or confirmed COVID-19;
- Prevent contamination from patients to other patients, to imagers and imaging equipment;
- Perform imaging studies in patients with suspected or confirmed COVID-19 only if the management is likely to be impacted by imaging results;
- Re-evaluate which imaging technique is best for your patients both in terms of diagnostic yield and infectious risk for the environment;
- The imaging protocols should be kept as short as possible.

Transthoracic and Transesophageal Echocardiography

- Avoid performing transthoracic, transesophageal and stress echocardiograms in patients in which test results are unlikely to change the management strategy;
- TEE carries increased risks of spread of COVID-19 due to exposure of HCP to aerosolization of large viral load and should not be performed if an alternative imaging modality is available;
- In COVID-19 infected patients, the echocardiogram should be performed focusing solely on the acquisition of images needed to answer the clinical question in order to reduce patient contact with the machine and the HCP performing the test;
- POCUS, focused cardiac ultrasound study (FoCUS) and critical care echocardiography performed at bedside are effective options to screen for CV complications of COVID-19 infection.

- In COVID-19 infected patients, echocardiography should focus solely on the acquisition of images needed to answer the clinical question in order to reduce patient contact with the machine and HCP.

- It should not be forgotten that the risk of infection remains in the reading rooms and therefore the material used should be also frequently sanitized.

Computed tomography

- CV CT should be performed in hospitalized patients only with indications in which imaging results will likely impact management;
- CCTA may be the preferred non-invasive imaging modality to diagnose CAD since it reduces the time of exposure of patients and personnel;
- Cardiac CT may be preferred to TEE in order to rule-out left atrial appendage (LAA) and intracardiac thrombus prior to cardioversion;
- In patients with respiratory distress, chest CT is recommended to evaluate imaging features typical of COVID-19;
- Check renal function when contrast is indicated.

- evaluation of symptomatic suspected CAD, acute symptomatic heart valve dysfunction, left ventricular assist device (LVAD) dysfunction, PE, urgent structural intervention.
- Cardiac CT is preferred to TEE to rule out the presence of intracardiac thrombus. In patients with acute chest pain and suspected obstructive CAD, CCTA is the preferred non-invasive imaging modality since it is accurate, fast and minimizes the exposure of patients.

Nuclear imaging

- Nuclear cardiology should be performed only in specific indications and when no other imaging modalities can be performed;
- The shortest duration of scan time and exposure should be used;
- Standard dose imaging with rapid protocols of data acquisition are recommended.;
- Attenuation corrected imaging should be considered;
- Positron emission tomography (PET) minimizes the acquisition times.

- The use of PET-CT can be limited to patients with suspected endocarditis of prosthetic valves or intracardiac devices when other imaging modalities are inconclusive or to avoid the performance of a TEE which is associated with larger risk of spreading.
- Single photon emission computed tomography (SPECT) or PET may also be used for diagnosing ischaemia in patients with suspected obstructive CAD when CCTA is not appropriate or available.

Cardiac Magnetic Resonance

- The risks of contamination during a CMR scan is probably similar to a CT scan, but lower than during an echocardiographic study. Only clinically urgent CMR scans should be accepted.
- One indication for an acute CMR might be suspicion of acute myocarditis, which has been reported in patients with COVID-19. Typical symptoms might be elevated troponins, ventricular dysfunction and/or severe arrhythmias that cannot be explained by other diagnostics and imaging methods.

Exercise testing

- Performance of exercise testing (either conventional, Echo or nuclear) has major limitations in the COVID-19 era.
- During exercise the patient increases breath rate and the amount of aerosol or droplets production, even if wearing a surgical mask (that could strongly affect his/her exercise capacity). This problem is further increased since rooms of outpatient clinics are rarely large and well aerated.
- Performance of exercise testing is discouraged in COVID-19 suspect or positive patients and, in general, in every patient in COVID-19 epidemic or potentially epidemic areas. Alternative diagnostic methods for CAD not requiring exercise should be used as an alternative to exercise testing whenever possible.

- In COVID-19-infected patients with clinical presentation compatible with CVD, three main entities should be considered:
- Patients with COVID-19 infection can present cardiac events, that can be favoured by the infection or unrelated. Those include ACS (STEMI and NSTEMI), acute HF, arrythmias, thoromboembolic events, CS, and cardiac arrests. Those syndroms require a quick diagnosis and management, and should not be overlooked due to the presence of COVID-19 infection;
- Infection-related cardiac injury can also lead to a clinical presentation suggestive of cardiac event, and should also be considered as a differential diagnosis.
- Patients with COVID-19 infection can present with symptoms mimicking CV events, including chest pain, dyspnoea, and shock, even in the absence of cardiac injury.