Cardiovascular disease and Covid 19

Management and treatment

What are the considerations for cardiomyopathy and heart failure in COVID-19?

- *Cardiac dysfunction is moderately common among hospitalized patients with COVID-19 and confers a worse prognosis*

- Both de novo cardiomyopathy and worsening of underlying cardiomyopathy can be observed with COVID-19.

- **Human cardiomyocytes** express the viral entry receptor, **ACE2**, and can be directly infected by SARS-CoV-2. Growth of the virus can cause **contractile dysfunction** and **death of cardiomyocytes.** Autopsy studies have revealed evidence of replicating virus in cardiomyocytes.

‘Continued

- Myocarditis or inflammatory cardiac dysfunction should be considered in patients with COVID-19 who have elevated cardiac biomarkers with worsening hemodynamics and/or arrhythmias.

- **Elevated NT-proBNP, elevated cardiac troponin and a history of preexisting heart failure** are particularly important risk factors for mortality.

- An **ECG should be employed to screen for evidence of ST-T wave changes**.

- The ECG abnormalities in COVID-19 may be due to cytokine storm, hypoxic injury, electrolyte abnormalities, plaque rupture, coronary spasm, microthrombi, or direct endothelial or myocardial injury.

- While sinus tachycardia is the most common abnormality, others include supraventricular tachycardias such as atrial fibrillation or flutter, ventricular arrhythmias such as ventricular tachycardia or fibrillation, various bradycardias, interval and axis changes, and ST segment and T wave changes.

- Several ECG presentations are associated with **poor outcome,** including atrial fibrillation, QT interval prolongation, ST segment and T wave changes, and ventricular tachycardia/fibrillation.

- there is evidence of cardiac dysfunction, consider select views for transthoracic echocardiography to define left ventricular/right ventricular (LV/RV) size and function, wall motion abnormalities, and/or pericardial effusion.

Echocardiography in COVID-19 pandemic

Don't forget PPE !

COVID-induced myocardial damage

Primary cardiac disease (AMI; HF)

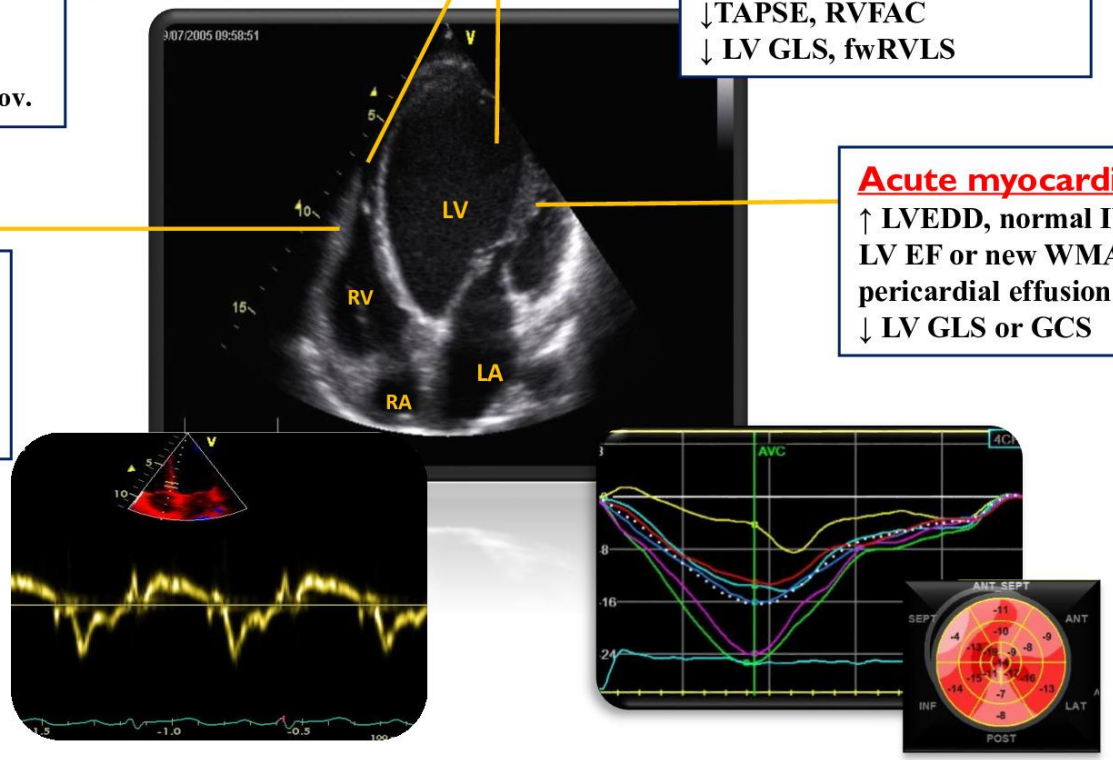
Sepsis
- ↑ E/E'
- ↓ LV GLS (<13%[37])
- ↓ fwRVLS

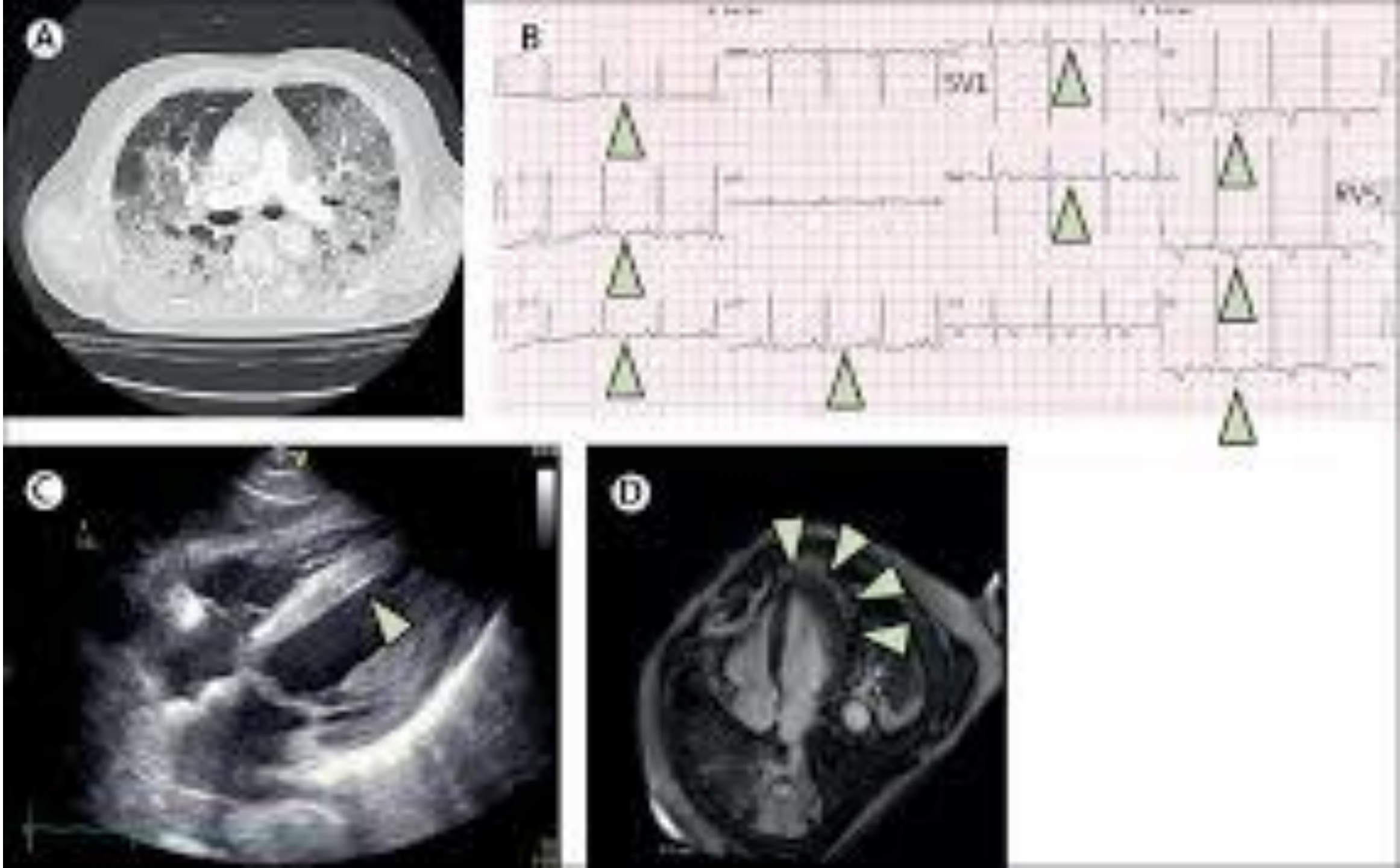
Heart failure
↑ LV EDV, ESV, ↓LVEF
↑ E/E'mit
↑ RV EDD, S.I.,
↓TAPSE, RVFAC
↓ LV GLS, fwRVLS

RV failure in ventilated patients
↑ RV EDD, S.I.,
↓TAPSE, RVFAC, fwRVLS
End-systolic paradoxical IVS mov.

Acute myocarditis
↑ LVEDD, normal IVS
LV EF or new WMA
pericardial effusion
↓ LV GLS or GCS

Acute PE
Pulmonary AcT<60 ms
TRPG < 60ms
«McConnell's sign»
↑ RV EDD, S.I., ↓fwRVLS

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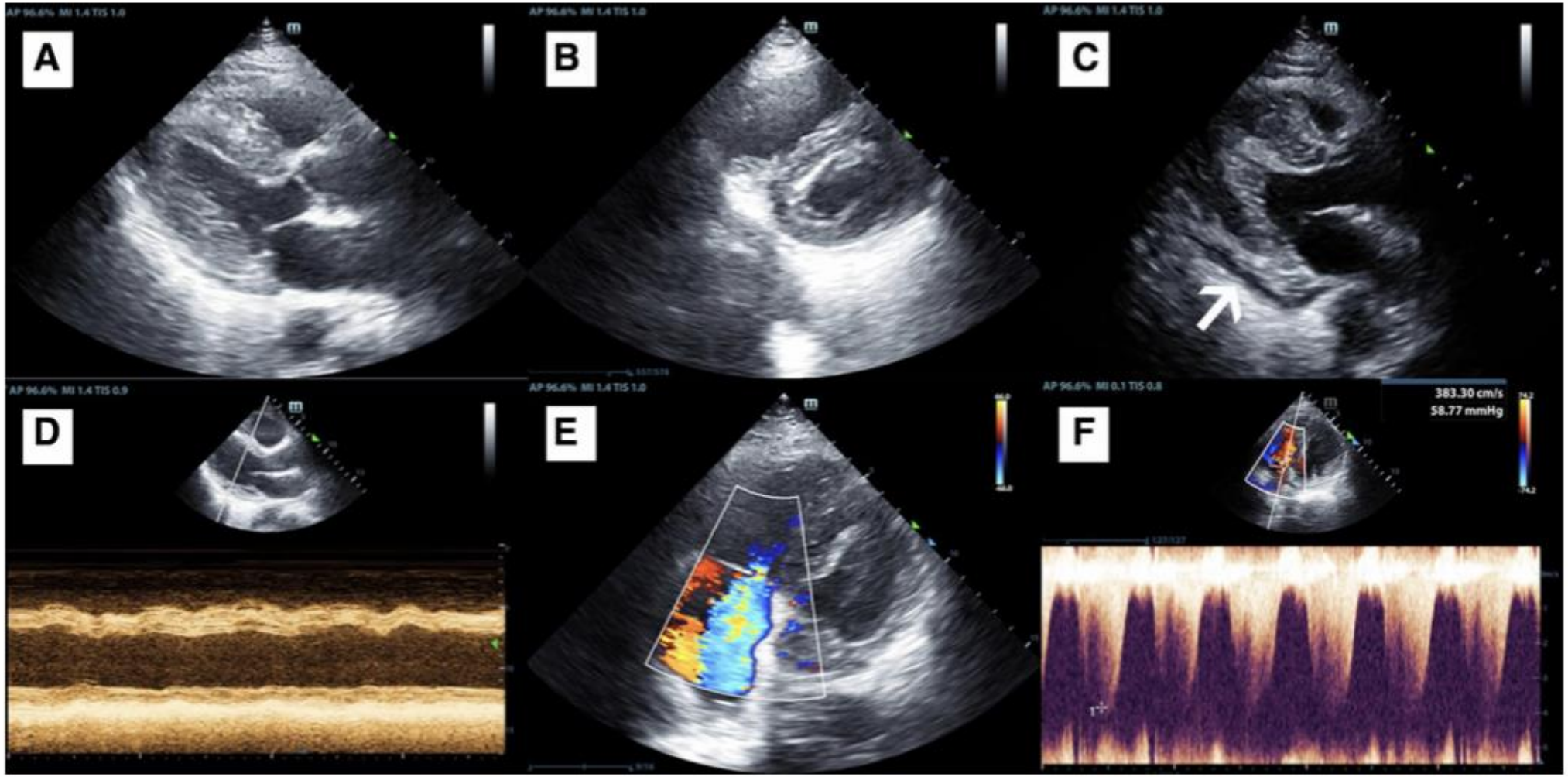
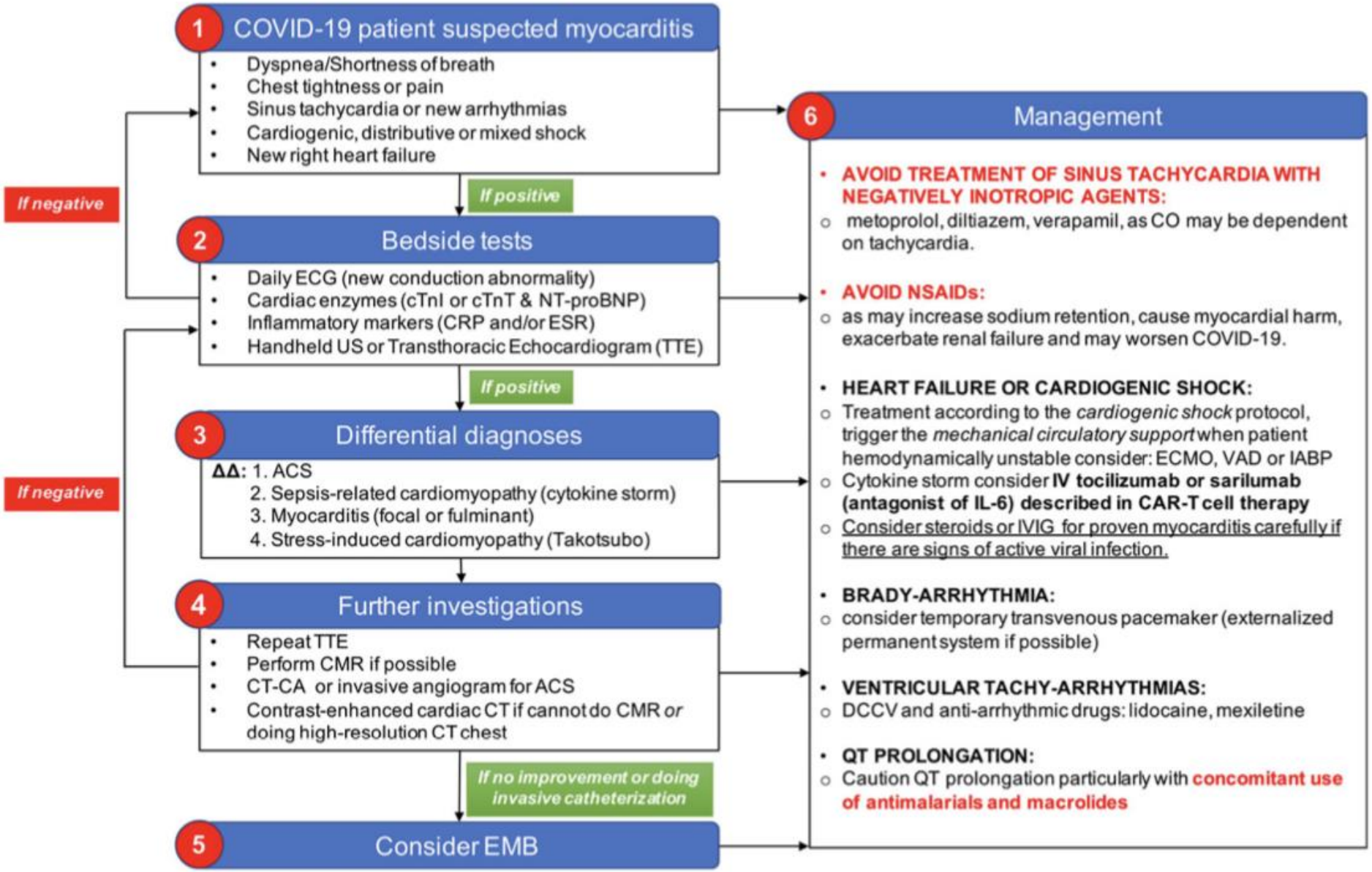


Fig. 2 Echocardiographic images of patients with COVID-19. **a** Diffuse thickening of the left-ventricular wall. **b** Right-ventricular enlargement and left-ventricular wall thickening. **c** A small amount of pericardial effusion behind the left-ventricular posterior wall (white arrow). **d** M-mode graph of the left-ventricular basement showed ventricular wall dyskinesia and a decreased left-ventricular ejection fraction. **e** Color Doppler showed moderate-to-severe tricuspid regurgitation. **f** Continuous wave Doppler showed pulmonary hypertension


1 COVID-19 patient suspected myocarditis
• Dyspnea/Shortness of breath
• Chest tightness or pain
• Sinus tachycardia or new arrhythmias
• Cardiogenic, distributive or mixed shock
• New right heart failure
If positive
If negative
2 Bedside tests
• Daily ECG (new conduction abnormality)
• Cardiac enzymes (cTnI or cTnT & NT-proBNP)
• Inflammatory markers (CRP and/or ESR)
• Handheld US or Transthoracic Echocardiogram (TTE)
If positive
If negative
3 Differential diagnoses
ΔΔ: 1. ACS
2. Sepsis-related cardiomyopathy (cytokine storm)
3. Myocarditis (focal or fulminant)
4. Stress-induced cardiomyopathy (Takotsubo)
4 Further investigations
• Repeat TTE
• Perform CMR if possible
• CT-CA or invasive angiogram for ACS
• Contrast-enhanced cardiac CT if cannot do CMR or doing high-resolution CT chest
If no improvement or doing invasive catheterization
5 Consider EMB
6 Management
• AVOID TREATMENT OF SINUS TACHYCARDIA WITH NEGATIVELY INOTROPIC AGENTS:
o metoprolol, diltiazem, verapamil, as CO may be dependent on tachycardia.
• AVOID NSAIDs:
o as may increase sodium retention, cause myocardial harm, exacerbate renal failure and may worsen COVID-19.
• HEART FAILURE OR CARDIOGENIC SHOCK:
o Treatment according to the cardiogenic shock protocol, trigger the mechanical circulatory support when patient hemodynamically unstable consider: ECMO, VAD or IABP
o Cytokine storm consider IV tocilizumab or sarilumab (antagonist of IL-6) described in CAR-T cell therapy
o Consider steroids or IVIG for proven myocarditis carefully if there are signs of active viral infection.
• BRADY-ARRHYTHMIA:
o consider temporary transvenous pacemaker (externalized permanent system if possible)
• VENTRICULAR TACHY-ARRHYTHMIAS:
o DCCV and anti-arrhythmic drugs: lidocaine, mexiletine
• QT PROLONGATION:
o Caution QT prolongation particularly with concomitant use of antimalarials and macrolides

Implications for therapy

- **Nonsteroidal anti-inflammatory** drugs are generally not suggested in patients with myocarditis because they may cause renal impairment and sodium retention, which could further deteriorate acute ventricular dysfunction .

- In patients with fulminant myocarditis, a statement of the AHA recommends implementing the initial management protocol for cardiogenic shock, including administration of inotropes and/or vasopressors and mechanical ventilation . Longer term management may require mechanical circulatory support

High dose of steroids and intravenous immunoglobulins (IVIG)

- use of high-dose steroids in COVID-19 patients has given conflicting results.
- In one retrospective study, there was an improvement of survival but another investigation showed a reduction in viral clearance, increased risk of suprainfection and an increased mortality for all causes

IVIG

- purified IVIG, there is supportive evidence for their use in acute myocarditis .
- They gave encouraging result in a small group of five critical COVID-19 patients without clinically suspected myocarditis but no additional evidence exists in patients with COVID-19 established myocarditis.

- The immunomodulatory effects of IVIG are multifactorial, because they showed not only anti-viral effects, but also antiinflammatory effects by suppressing inflammatory cytokine

Antiviral agents

- Different anti-viral agents were expected to be effective in patients hospitalized with COVID-19: **remdesivir, hydroxychloroquine, lopinavir/ritonavir, and interferon beta1a**.

- Unfortunately, all these drugs had little or no effect on overall mortality, initiation of ventilation, and duration of hospital stay

- Due to concerns for myocarditis-related **ventricular arrhythmias** that may occur in the setting of ongoing inflammation, it is recommended that **athletic patients** **avoid** competition for **three to six months** after the initial diagnosis of COVID-19-related myocarditis.

- Return to competition can be considered after that time if LVEF and cardiac/inflammatory biomarkers have normalized and no concerning finding are seen on maximal exercise treadmill testing and ambulatory ECG monitoring

What are thrombosis risk and management considerations in COVID-19?

- Thromboembolism is a frequent complication for patients hospitalized with COVID-19.
- VTE incidence was higher among patients admitted to the intensive care unit (ICU; 27.9%) than the general medical wards (7.1%)
- Patients hospitalized with COVID-19 are also at risk for **arterial thrombosis**.
- In an analysis of 1,114 patients with COVID-19 (hospitalized and non-hospitalized), the **30-day event rates for major cardiovascular events were 8.3%**, including **catheter- or device-related arterial thrombosis** (1.0% overall, 6.5% in ICU), **myocardial infarction** (1.3% overall, 7.7% in ICU), and **stroke** (0.1% overall).

- Routine use of VTE prophylaxis is strongly recommended for all patients hospitalized with COVID-19.
- For most patients, use of standard doses of low- molecular-weight heparin (e.g., enoxaparin 40 mg once daily) or unfractionated heparin (e.g., 5,000 units three times daily) is recommended by most society guidelines and guidance documents.
- For patients with critical illness in moderate or intensive care units, consideration can be made for intensifying the prophylactic regimen (e.g., enoxaparin 30-40 mg twice daily, unfractionated heparin 7,500 units three times daily).

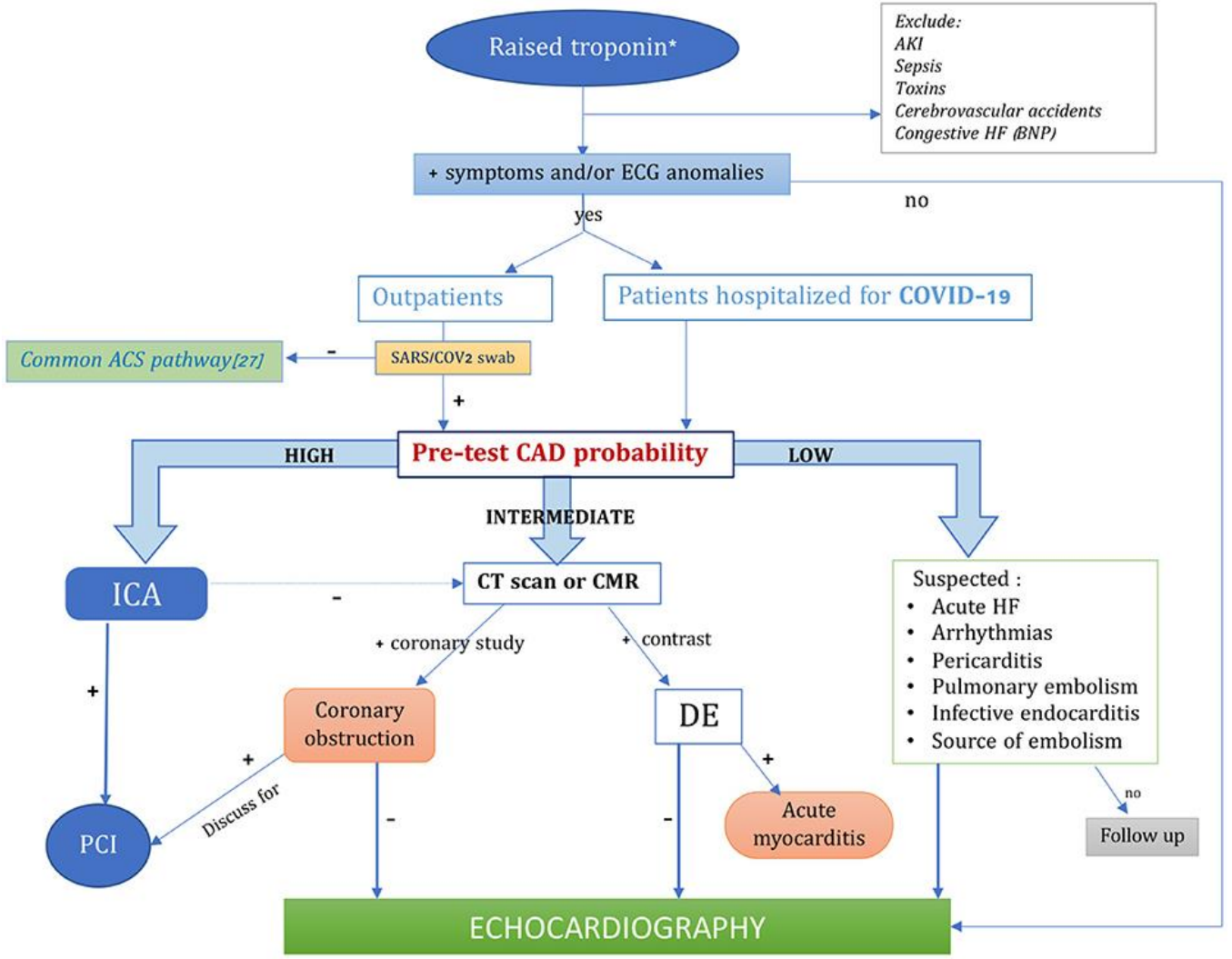
- VTE prophylaxis is generally not recommended for patients with COVID-19 who are not hospitalized. The role of antiplatelet therapy (e.g., daily aspirin) is unknown at this time.

Different etiologies and hypothesized mechanism of COVID-induced myocardial injury.

Type of myocardial injury	Possible mechanism	Clinical consequences	Available evidence
Type 1 myocardial infarction	*Systemic inflammatory response syndrome*: ↑risk of plaque rupture and thrombus formation **Cytokine storm** due to imbalanced TH1/TH2 response ⇒**DIC** [*71.4% non-survivors vs. 0.6% survivors* (8)]: MOF	STEMI or NSTEMI (9) **Thrombosis** of coronary epi- and subepicardial arteries ⇒focal myocardial necrosis and dysfunction (10)	Bangalore et al. (11) Xhuan et al. (12) Tang et al. (8) Sugiura et al. (10)
Type 2 myocardial infarction	**Myocardial oxygen imbalance** (↑demand for sepsis state, not satisfiable for COVID-19 induced hypoxaemia and vasoconstriction)	Severe myocardial ischaemia, ++ in patients with underlying CAD	Li et al. (5) Shi et al. (13) Guo et al. (14)
Venous thromboembolism	Hypercoagulable status + active inflammation + propensity for DIC + prolonged immobilization + oxidative stress + endothelial dysfunction + increased platelet reactivity + mechanical ventilation + liver dysfunction + central venous catheters + nutritional deficit	↑D-dimer *(>1μg/mL on admission ⇒↑ in-hospital death)*, FDP, fibrinogen Pulmonary embolism or deep venous thrombosis *[22.7% non-ICU and 27% in ICU patients* (15)]	Tang et al. (10) Han et al. (15) Klok et al. (16)
Acute myocarditis	*Indirect mechanism:* innate immunity activation ⇒inflammatory cascade and exaggerated cytokine release *Direct mechanism*: ACE2 receptor (used by SARS-CoV2 for binding, overexpressed in diseased hearts)	STEMI-like presentation with myocardial degenerative changes and necrosis	Zhou et al. (17) Yao et al. (18) Beri et al. (19) Tavazzi et al. (20) Hu et al. (21) Zeng et al. (22) Sala et al. (23)
Stress cardiomyopathy	Infective +/- emotional trigger ⇒catecholamine induced myocardial stunning or macro- and micro-vascular spasm	Tako-tsubo syndrome	Moderato et al. (24) Meyer et al. (25) Chadha et al. (26)

ACE2, angiotensin-converting enzyme-2; CAD, coronary artery disease; DIC, disseminated intravascular coagulation; ICU, intensive care unit; MOF, multi-organ failure; NSTEMI, non ST-elevation myocardial infarction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; STEMI, ST-elevation myocardial infarction; TH1, T-helper lymphocytes 1; TH2, T-helper lymphocytes 2; VTE, venous thromboembolism.
+, plus; ++, above all; ↑, higher.

Algorithm for the diagnosis of COVID-induced acute myocardial injury



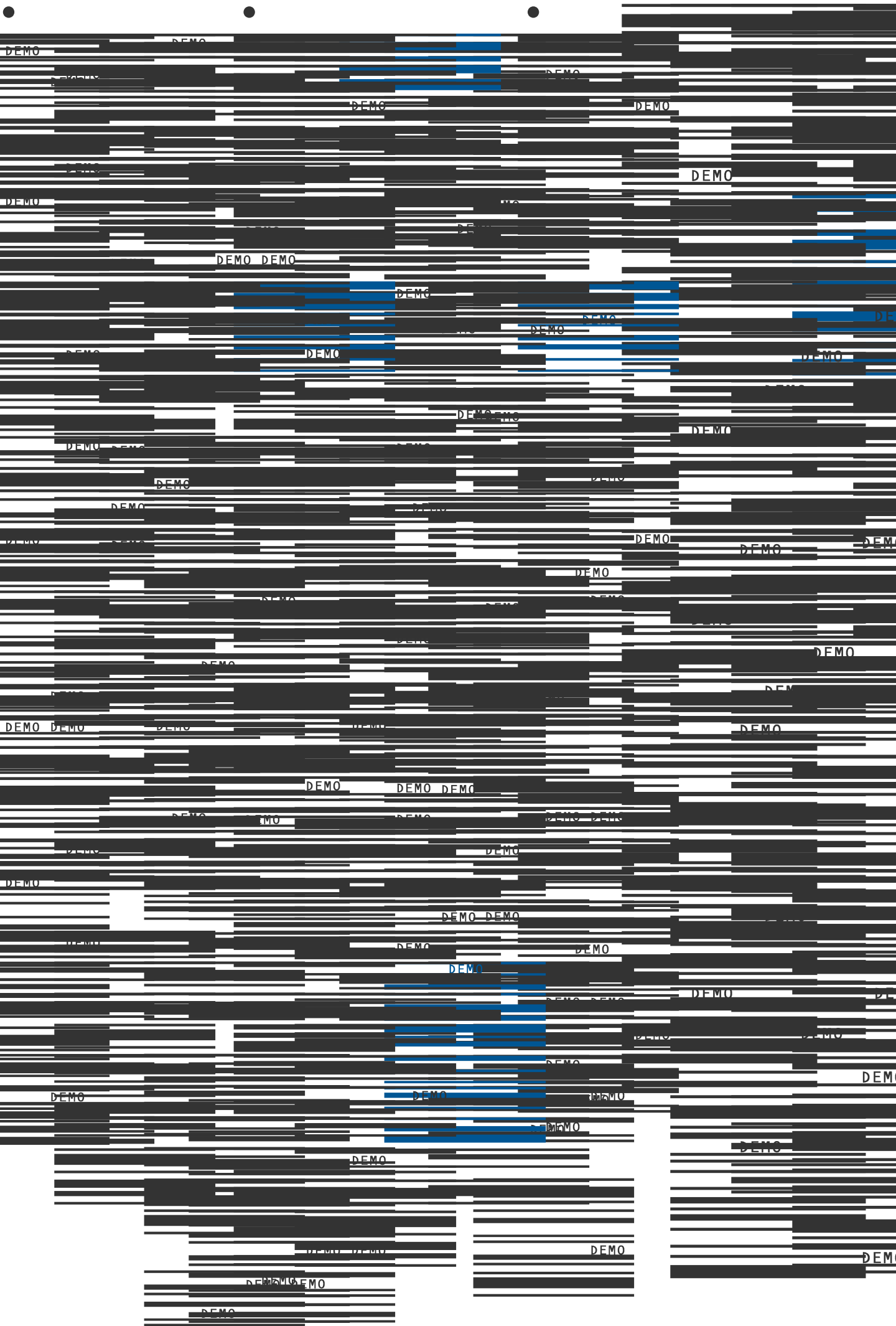
NSTEMI management an approach based on individual risk is recommended

- *very high risk NSTEMI* patients should follow a similar management of STEMI;
- • *high risk NSTEMI* patients should follow medical treatment while waiting for SARS-CoV2 test results and planning an early invasive therapy, possibly <24 h; in case of positive test, the patients should undergo ICA in a COVID-19 hospital;
- • *low risk NSTEMI* could be firstly evaluated non-invasively, in order to exclude alternative etiology to type 1 MI, using coronary CT, if possible; if low risk is confirmed, they should follow conservative strategy.

summarizes the criteria for risk stratification of NSTEMI patients

Very high risk	High risk	Low risk
- Hemodynamic instability - Cardiogenic shock - Recurrent/refractory chest pain despite medical treatment - Life-threatening arrhythmias - Mechanical complications of myocardial infarction - Acute HF related to NSTEMI - ST-segment depression > 1 mm in 6 leads + ST-segment elevation in aVr and/or V1	- NSTEMI diagnosis already established - Symptomatic/ asymptomatic - dynamic new (or presumably new) contiguous ST-T segment changes - Resuscitated cardiac arrest without ST-segment elevation or cardiogenic shock - GRACE risk score > 140	No recurrence of symptoms and none of the *very high* or *high-risk* criteria. Also includes patients with: - History of revascularization - Early post-infarction angina - LVEF<40% or congestive HF - GRACE risk score 109–140 - Diabetes mellitus Ruled out based on troponin levels

HF, heart failure, NSTEMI; LVEF, left ventricular ejection fraction; non-ST-elevation myocardial infarction.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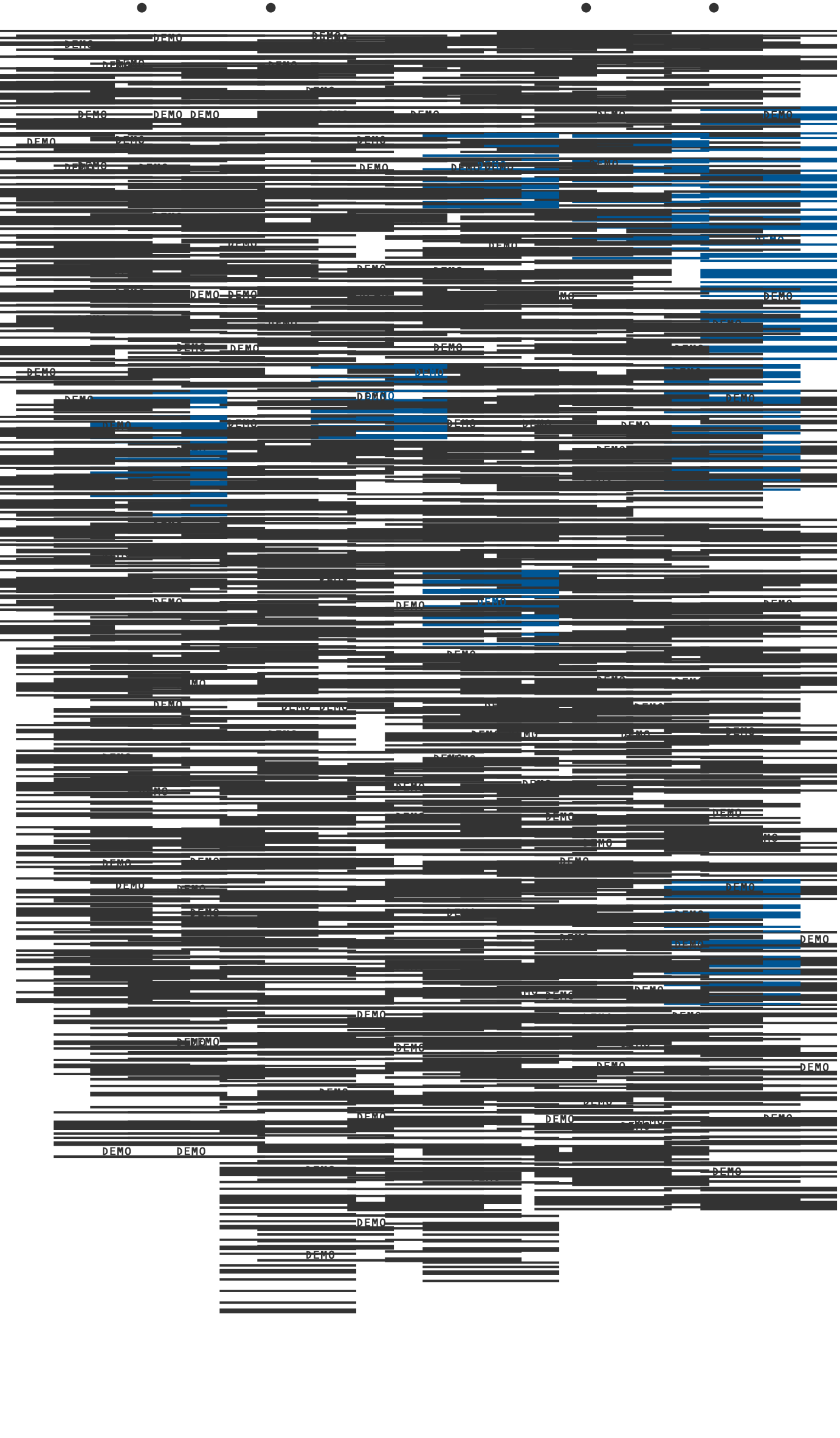
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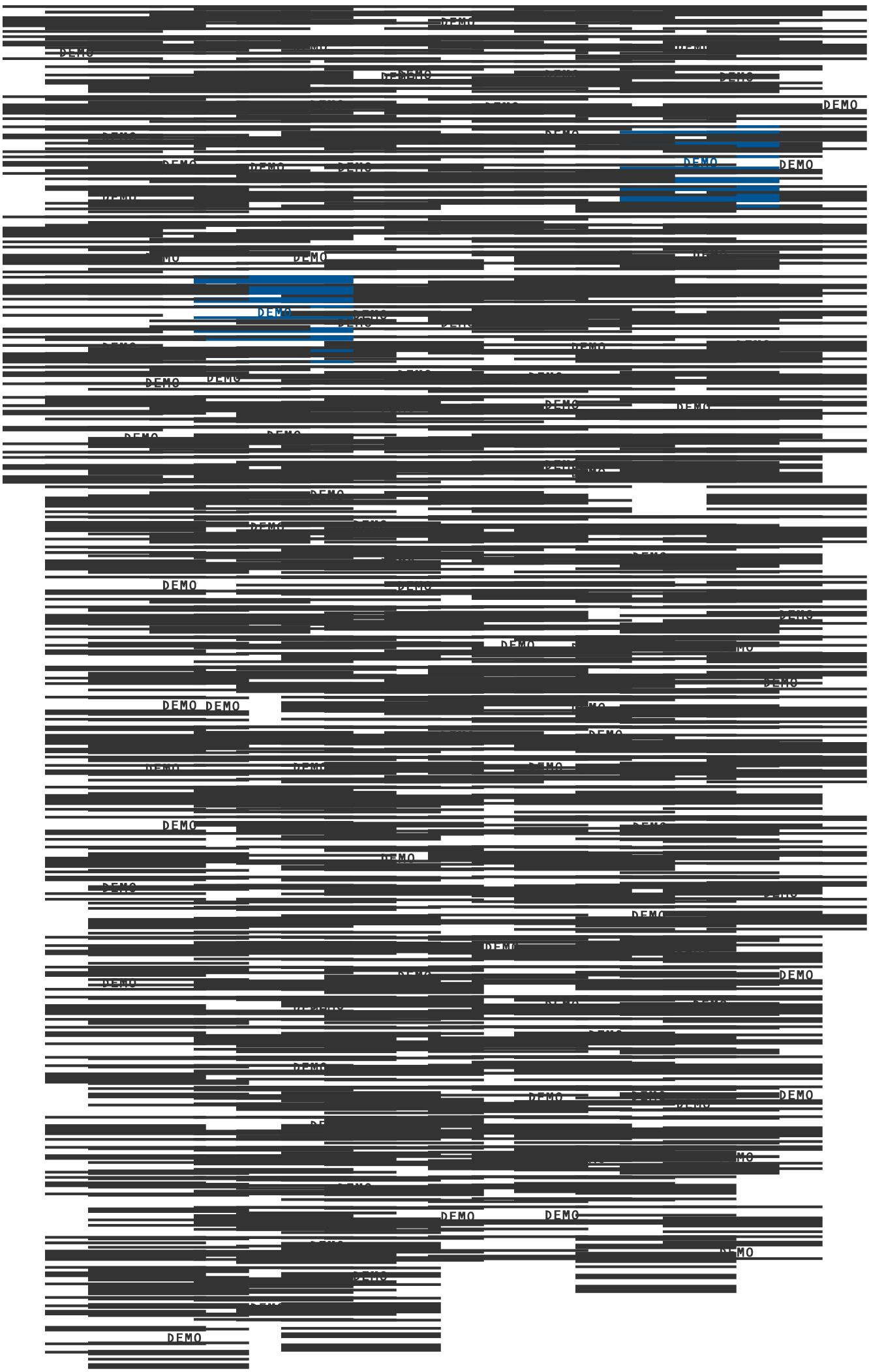
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Multi-disciplinary collaboration of systems for the management of STEMI diagnosed at non-PCI capable locations.

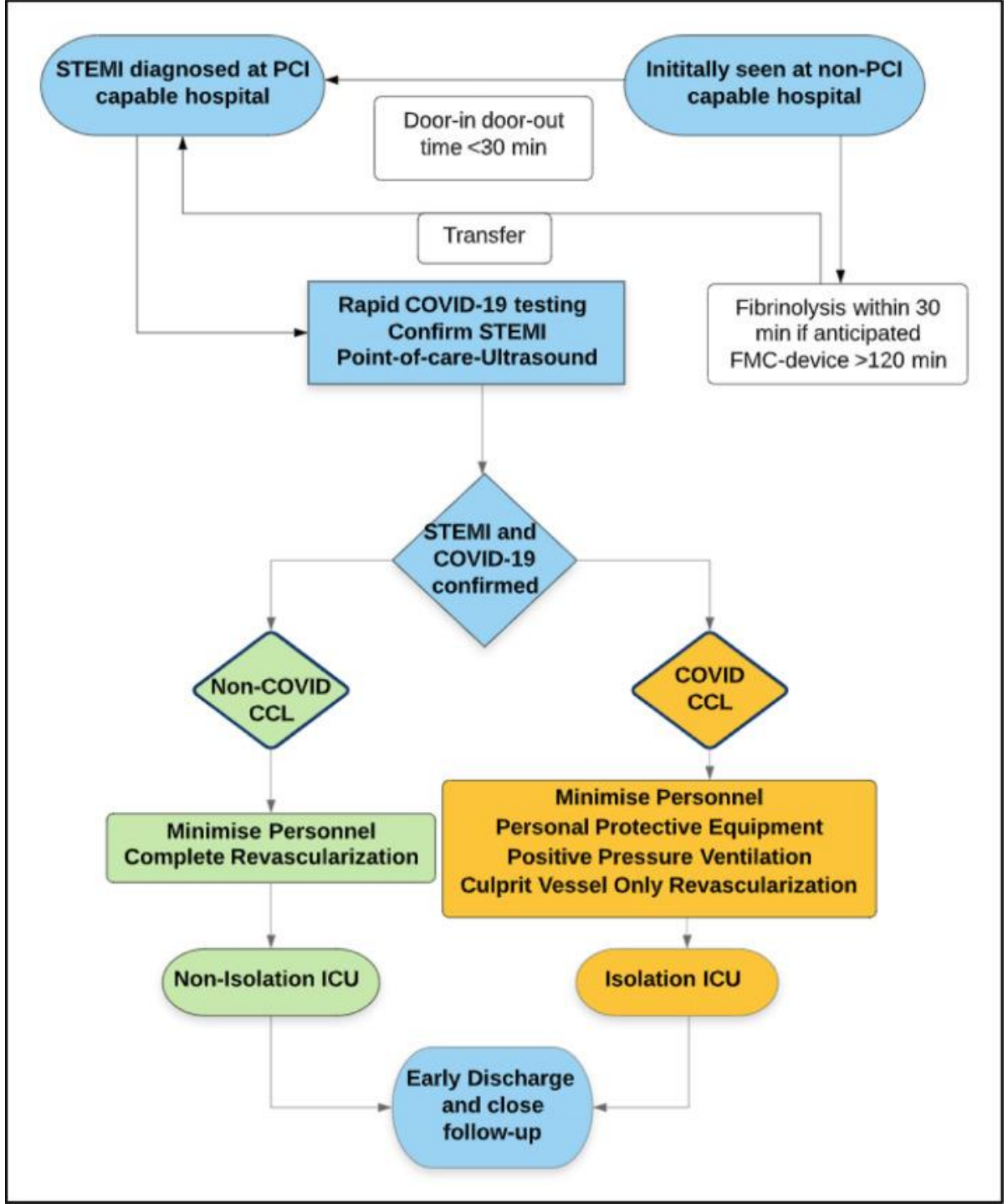
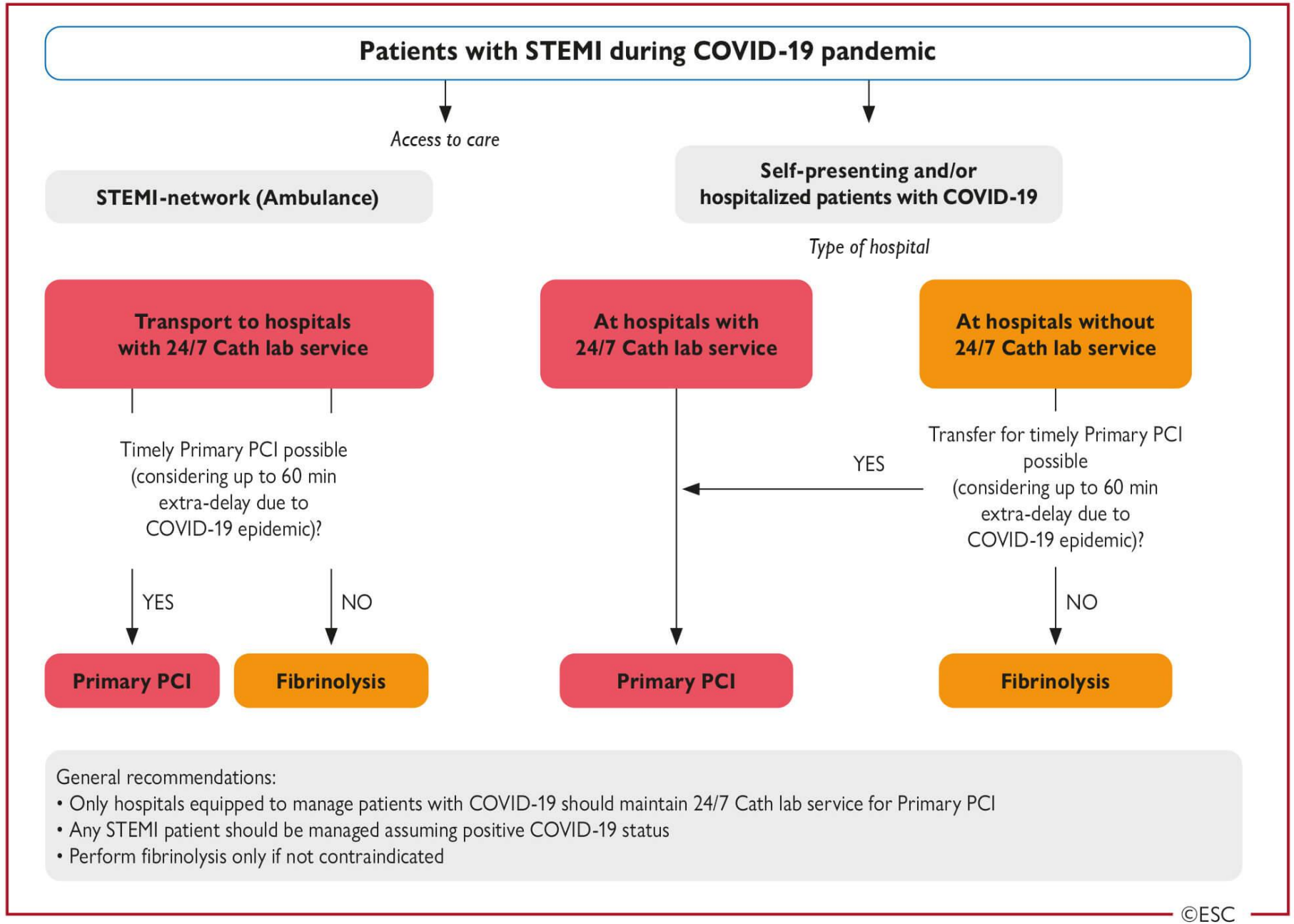


Figure 13 Management of patients with STEMI during COVID-19 pandemic



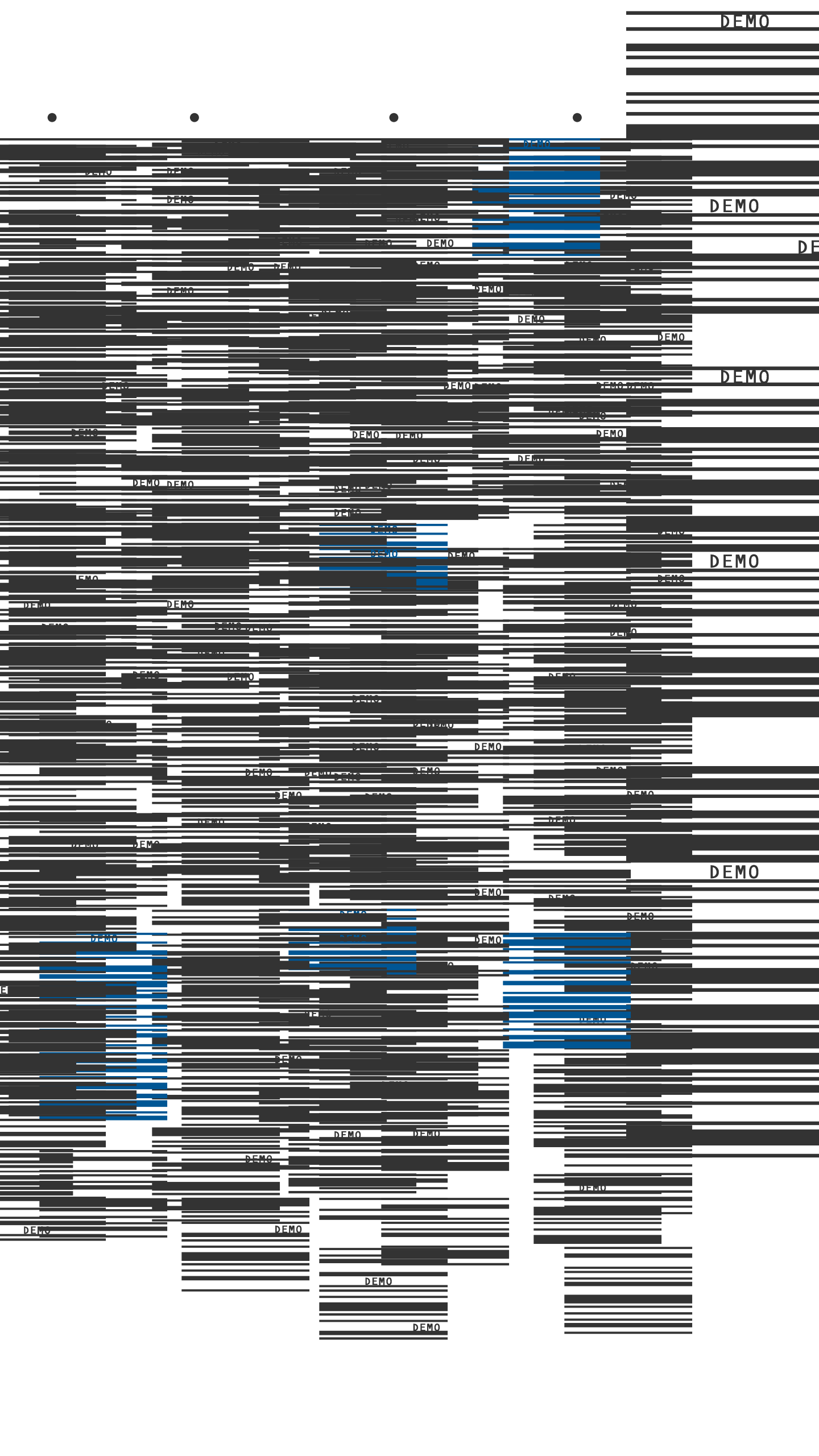

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Table 13 Management of chronic coronary syndromes during COVID-19 pandemic

- Continuation of medications in CCS patients is recommended during COVID-19 pandemic
- Follow-up of CCS patients via tele-health is recommended
- Revascularization of CCS patients must be postponed in low to intermediate risk patients
- Postponing of non-invasive testing of CCS patients should be considered during COVID-19 pandemic
- CT angiography should be preferred to non-invasive functional testing during COVID-19 pandemic
- Screening for SARS-CoV-2 infection should be considered before cardiac surgery with nasopharyngeal swab and CT scan
- Revascularization of high-risk[a] CCS patients may be considered during COVID-19 pandemic
- PCI may be considered over CABG in selected patients during COVID-19 pandemic[b]
- Identification of COVID-19-free hospitals may be considered as "Hub" for cardiac surgery
- Invasive management of CCS in SARS-CoV-2 positive patients should be deferred until the patient has recovered whenever possible.

[a]Patients with high-risk symptoms and/or coronary anatomy and/or large ischaemia as assessed by Heart team.
[b]To shorten hospital stay and keep ICU beds available for patients with COVID-19.


THANK
YOU