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Considerations for Management of Acute Coronary Syndromes During the SARS-CoV-2 (COVID-19) Pandemic

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Accumulating evidence suggests that influenza and influenza-like illnesses can act as a trigger for acute myocardial infarction.\textsuperscript{1-4} In this document, we suggest recommendations as to how to triage patients diagnosed with acute coronary syndromes (ACSs) and provide with algorithms of how to manage the patients and decide the appropriate treatment options in the era of COVID-19 pandemic. We also address the inpatient logistics and discharge to follow-up considerations for the function of already established ACS network during the pandemic. © 2020 Elsevier Inc. All rights reserved. (Am J Cardiol 2020;131:115–119)

Accumulating evidence suggests that influenza and influenza-like illnesses can act as a trigger for acute myocardial infarction.\textsuperscript{1-4} In this document, we suggest recommendations as to how to triage patients diagnosed with acute coronary syndromes (ACSs) and provide with algorithms of how to manage the patients and decide the appropriate treatment options in the era of COVID-19 pandemic. We also address the inpatient logistics and discharge to follow-up considerations for the function of already established ACS network during the pandemic.

Definitions

To minimize the misunderstanding in COVID-19 case definitions between healthcare workers we recommend adopting the World Health Organization guidelines on case definitions as following:

- **Confirmed case (COVID-19 +)** — a patient with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms.
- **Suspected case (COVID-19 +/-)** — a patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath), OR a patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath), AND for whom first testing for the COVID-19 virus is inconclusive or negative — being the result of the test reported by the laboratory, AND in the absence of an alternative diagnosis that fully explains the clinical presentation AND/OR a patient belongs to the risk group (Table 1).
- **Contact case (COVID-19 C)** — a patient with no clinical signs and symptoms AND having been in face-to-face/direct contact or direct care for the patient without proper personal protective equipment (PPE) with a confirmed COVID-19 case AND being in self-isolation.
- **Nonsuspected case (COVID-19 NS)** — a patient is not suspected for COVID-19 disease.

Logistics Management

The triage of patients is recommended on the basis of COVID-19 probability, being described as confirmed, suspected, contact or nonsuspected cases for COVID-19 disease. All the patients must be fitted with disposable face masks once they enter the hospital.

Confirmed COVID-19 cases according to the severity of patients’ condition and the need for services should be admitted to either a COVID ward or COVID CCU/ICU. All confirmed COVID-19 cases can be treated with no isolation in the same rooms. COVID ward or COVID CCU/ICU are considered infectious zones.

Suspected COVID-19 cases according to the severity of patients’ condition and the need for services should be admitted to either a COVID ward or COVID CCU/ICU. Suspected cases ideally must be treated in single rooms (isolated) and have a separate restroom.

Contact COVID-19 cases according to the severity of patients’ condition and the need for services should be admitted to either a Cardiology ward or CCU/ICU. Contact cases must be treated in single rooms (isolated) and have a separate restroom. Cardiology ward or CCU/ICU are considered as noninfectious zones.

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Donning and doffing sequences (Table 2). All staff members care workers is the appropriate usage of PPE and proper Personal Protective Equipment (PPE).

Ventilation equipment with the most commonly used balloon and stent sizes, wires, catheters and other equipment. It should contain COVID dedicated lead aprons, conventional equipment with the most commonly used balloon and stent sizes, wires, catheters and other equipment. Ventilation systems in dedicated COVID laboratories should ideally be converted to negative pressure systems. This conversion would offer optimal protection to personnel working in adjacent areas. However, if temporary conversion to negative pressure room is performed, cross contamination of other rooms may occur. Cleaning procedures before and after the cases must be strictly followed according to the institutional policies. Intense cleaning of lead aprons should be added to the protocols. Cardiac procedures for all other cases should be performed per usual protocols with standard equipment in non-COVID dedicated catheterization laboratories.

Personal Protective Equipment

The vital aspect in stopping the virus spread in healthcare workers is the appropriate usage of PPE and proper donning and doffing sequences (Table 2). All staff members providing healthcare for patients with confirmed or suspected COVID-19 cases must be equipped with FFP2/FFP3 (N95) respirators, goggles and/or face shields, long sleeved gowns, tall disposable shoe covers, extra gloves. Personnel who provide care for the contact COVID-19 cases should at least wear disposable face masks, disposable gowns, head covers and gloves. It is also recommended during the pandemic that even noncontact patients who are hospitalized be fitted with disposable face masks given a potential rapid change in the epidemiologic situation.

Patient Selection

All patients with COVID-19 confirmed or suspected disease, presenting with ACS can be divided into 3 main categories as described below to achieve a simplified workflow. Despite these unprecedented times providers should not overlook ACS guidelines, but may choose to modify the recommended approach in situations with confirmed or suspected COVID-19 disease to reduce possible staff contamination and to provide further discussion of the risks and benefits for all personnel involved in these cases.

- Patients diagnosed with non-ST elevation ACSs (unstable angina or NSTEMI) without high-risk features for ongoing myocardial ischemia (Table 3).

If these patients present to the emergency department, they should be admitted to the ward and zone described above based on COVID-19 disease probability. Medical treatment for ACS needs to be initiated without any delay. Upon first medical contact in the emergency

### Table 1
Groups at high risk for severe illness (adopted from Centers of Disease Control and Prevention CDC)

| Category                                                                 | Details                                                                 |
|--------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Age ≥65 years                                                             | - BMI ≥40 kg/m²                                                             |
| - Chronic lung disease and/or moderate to severe asthma                  | - Residing in a nursing home or long-term care facility                 |
| - Heart failure (class II-IV NYHA)                                       | - Poorly controlled HIV                                                    |
| - Diabetes Mellitus                                                      | - Smoker                                                                 |
| - Malignancy (last cancer treatment within last 2 years)                 | - Chronic kidney disease undergoing dialysis                             |
| - Liver disease                                                          | - Prior bone marrow or organ transplantation                              |
| - Recent treatment with general or selective chemotherapy or radiotherapy (last treatment <2 years) | - Corticosteroid therapy of doses higher or equal to methylprednisolone to 10 mg/kg (last treatment dose within last 6 months) |
| - Conditions requiring prolonged use of corticosteroids and other immune suppressants | - Immunodeficiency                                                        |

### Table 2
Sample donning and doffing steps for personal protective equipment (PPE) for catheterization laboratory

| Sequence | Donning                                      | Doffing                                      |
|----------|----------------------------------------------|----------------------------------------------|
| 1        | Hand hygiene                                | Hand hygiene                                 |
| 2        | Leaded glasses                              | Remove sterile gown with second gloves       |
| 3        | First head cover                            | 3. Hand hygiene                              |
| 4        | Disposable shoe covers                      | 4. Remove goggles or face shield             |
| 5        | COVID dedicated lead apron                  | 5. Remove FFP2/FFP3 (N95) mask               |
| 6        | FFP2/FFP3 (N95) mask                        | 6. Remove disposable surgical mask           |
| 7        | Goggles or face shield                      | 7. Remove second head cover                  |
| 8        | Disposable surgical mask                    | 8. Remove nonsterile gown                    |
| 9        | Second head cover                           | 9. Hand hygiene                              |
| 10       | Nonsterile gown                             | 10. Remove first pair of gloves              |
| 11       | Hand hygiene                                | 11. Remove disposable shoe covers in between nonsterile and sterile zone |
| 12       | First pair of sterile gloves                | 12. Hand hygiene                             |
| 13       | Sterile gown                                | 13. Remove FFP2/FFP3 (N95) mask             |
| 14       | Second pair of sterile gloves               | 14. Remove first head cover                  |
| 15       | Remove COVID dedicated lead apron and glasses | 15. Hand hygiene                             |
| 16       | Remove COVID dedicated lead apron and glasses | 16. Step out to sterile zone                 |

### Table 3
Very high-risk features (according to 2018 ESC Guidelines on Myocardial revascularization)

- Hemodynamic instability or cardiogenic shock
- Recurrent/ongoing chest pain refractory to medical treatment
- Life-threatening arrhythmias or cardiac arrest
- Mechanical complication of myocardial infarction
- Acute heart failure
- Recurrent dynamic ST-segment or T-wave changes, particularly with intermittently ST-segment elevations
ACS presentations. Fibrinolytic therapy should be higher CPR and intubation rates compared with other
reduce the possible exposure risks to the staff given onsets, PCI as first line therapy may be deferred to
19 disease presenting within 12 hours of symptom
In stable patients with confirmed or suspected COVID-
tary infection (Table 4) are recommended to be managed
severe pneumonia with or without severe acute respira-
Origin of pulmonary infiltrates: respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. echo-cardiography) to exclude hydrostatic cause of infiltrates/edema if no risk factor present
Oxygenation impairment in adults:
- Mild ARDS: 200 < PaO2/FiO2a ≤ 300 (with PEEP or CPAP ≥ 5
- Moderate ARDS: 100 < PaO2/FiO2 ≤ 200 (with PEEP ≥ 5 cmH2O, or nonventilated)
- Severe ARDS: PaO2/FiO2 ≤ 100 (with PEEP ≥ 5 cmH2O, or nonventilated)
- When PaO2 is not available, SpO2/FiO2 ≤ 315 suggests ARDS (including in nonventilated patients)
ARI = acute respiratory infection; CPAP = continuous positive airway
pressure; FiO2 = fraction of inspired oxygen; PaO2 = partial pressure of oxygen; PEEP = positive end-expiratory pressure.

Patients who test negative for SARS-CoV-2 should undergo standard ACS treatment aiming for an early discharge within 24 hours to minimize the potential risk of be infected. Patients who test positive for COVID-19 should continue medical treatment and be scheduled for an elective coronary angiography after full recovery from COVID-19 disease (2 negative consecutive SARS-CoV-2 PCR tests more than 24 hours apart) to minimize possible exposure and contamination.

- Patients diagnosed with non-ST elevation ACSs (NSTEMI) AND one or more very high-risk features for ongoing myocardial ischemia.

In this category of patients, there is no time to wait for the result of SARS-CoV-2 PCR test. The decision needs to be made at the time of presentation of symptoms of ongoing myocardial ischemia. In confirmed or suspected COVID-19 cases a prompt decision-making meeting should be attempted with other senior colleagues to weigh the benefits and risks of urgent percutaneous coronary intervention (PCI) for the patient with possible exposure risk to the staff. If an urgent invasive strategy is chosen, the procedure should be performed within 2 hours of presentation. Patients who have already tested positive for COVID-19 disease and are diagnosed with severe pneumonia with or without severe acute respiratory infection (Table 4) are recommended to be managed with conservative medical therapy for ACS.

- Patients diagnosed with ST elevation myocardial infarction.

In stable patients with confirmed or suspected COVID-19 disease presenting within 12 hours of symptom onset, PCI as first line therapy may be deferred to reduce the possible exposure risks to the staff given higher CPR and intubation rates compared with other ACS presentations. Fibrinolytic therapy should be considered a first line option in the absence of contraindications (Table 5). Fibrinolytic therapy is considered effective if pain is relieved with resolution of ST segments by more than 50% within 60 to 90 minutes after the last dose has been administered. In this case further medical treatment should be continued and elective coronary angiography may be scheduled after full recovery from COVID-19 disease. If fibrinolytic therapy is ineffective, prompt decision-making meeting with a senior colleague should be undertaken to discuss the benefits and risks of PCI relative to the possible high exposure risk to the staff. Rescue PCI should be attempted as soon as a COVID dedicated catheterization laboratory is available. If medical treatment is selected, patient should be initiated on Aspirin, P2Y12 receptor blocker, intravenous unfractionated heparin for at least 48 hours, angiotensin-converting enzyme (ACE) inhibitors and beta blockers. In confirmed COVID-19 cases with severe pneumonia with or without severe acute respiratory infection, conservative medical treatment versus fibrinolytic therapy without rescue PCI should be considered given the unfavorable prognosis of COVID-19 disease at that stage. In non-COVID-19 patients, there is evidence suggesting that systematic and early invasive revascularization is superior to a delayed or ischemic-guided revascularization approach. However, this may not hold true in severe COVID-19 cases as they are commonly complicated by coagulopathy, which may pose a higher risk for in-stent thrombosis if PCI is performed emergently in those patients.

### Table 4

| Definitions of severe pneumonia and Acute Respiratory Distress Syndrome (ARDS) for COVID-19 (World Health Organization) |
|---------------------------------------------------------------|
| **Severe pneumonia**                                          |
| Adolescent or adult: fever or suspected respiratory infection, plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO2 <93% on room air |
| **Acute respiratory distress syndrome (ARDS)**                |
| Onset: within 1 week of a known clinical insult or new or worsening respiratory symptoms. |
| Chest imaging (radiograph, CT scan, or lung ultrasound): bilateral opacities, not fully explained by volume overload, lobar or lung collapse, or nodules |
| Origin of pulmonary infiltrates: respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. echo-cardiography) to exclude hydrostatic cause of infiltrates/edema if no risk factor present |
| **Oxygenation impairment in adults:**                         |
| - Mild ARDS: 200 < PaO2/FiO2a ≤ 300 (with PEEP or CPAP ≥ 5 cmH2O, or nonventilated) |
| - Moderate ARDS: 100 < PaO2/FiO2 ≤ 200 (with PEEP ≥ 5 cmH2O, or nonventilated) |
| - Severe ARDS: PaO2/FiO2 ≤ 100 (with PEEP ≥ 5 cmH2O, or nonventilated) |
| - When PaO2 is not available, SpO2/FiO2 ≤ 315 suggests ARDS (including in nonventilated patients) |

ARI = acute respiratory infection; CPAP = continuous positive airway pressure; FiO2 = fraction of inspired oxygen; PaO2 = partial pressure of oxygen; PEEP = positive end-expiratory pressure.
Doses of fibrinolytic agents

| Drug                   | Initial treatment                                                                 |
|------------------------|-----------------------------------------------------------------------------------|
| Tenecteplase (TNK-tPA) | Single IV bolus:                                                                  |
|                        | 30 mg bolus (6000 IU) if < 60 kg                                                  |
|                        | 40 mg bolus (8000 IU) if 60 to 69 kg                                               |
|                        | 50 mg bolus (10000 IU) if ≥ 70 kg                                                 |
|                        | Then 0.75 mg/kg IV over 30 min (up to 50 mg) over 30 min then 0.5 mg/kg IV over 60 min (up to 35 mg) Maximum total dose is 100 mg for patients > 67 kg |
| Alteplase (tPA)        | 15 mg IV bolus                                                                    |
|                        | 30 kg bolus (6000 IU) if < 30 kg                                                  |
|                        | 35 mg bolus (7000 IU) if 30 to 69 kg                                               |
|                        | ≥ 60 kg                                                                            |
|                        | ≥ 90 kg                                                                            |
| Retepase (rPA)         | 10 U + 10 U IV boluses given 30 min apart                                          |

Discharge and Follow-Up

Patients treated for ACSs during pandemic who have tested negative for COVID-19 disease should be discharged as early as the condition of the patient allows. There is a higher risk of patient exposure and contamination in the hospital even if in noninfectious zones. We recommend aiming for very early discharge for NSTEMI cases within less than 24 hours and less than 48 hours for ST elevation myocardial infarction patients. Patients diagnosed with ACS and have tested positive for COVID-19 disease with mild illness can be discharged within the same timeframes (Table 6). After discharge, patients should self-isolate for at least 14 days or until full recovery from COVID-19, whichever is longer. Patients with positive COVID-19 and ACS who have a moderate to severe presentation such as pneumonia, severe pneumonia, Acute Respiratory Distress Syndrome, or even sepsis with or without septic shock should be managed primarily for the viral illness as inpatients for as long as the condition requires.

All face-to-face follow-up appointments in outpatient clinics after the discharge during the pandemic should be postponed. Teleconsultation services with online drug prescription options for follow-up should be established and encouraged to avoid unnecessary patient contamination.

Limitations

The proposed strategies and algorithms are based on limited available data and might change as the epidemiologic conditions and transmission routes change. This document provides recommendations that may not be applicable to all institutions, and each center may need to modify these recommendations to survive with the resources that they may or may not have. Appropriate treatment strategies for ACSs in patients diagnosed with COVID-19 disease during pandemic are not well understood due to lack of clinical trials or large studies to date. In addition, testing turnaround times are long for most centers and availability is not present in all institutions for in-house services.

Conclusion

The key proposed recommendations of this document are: (1) Early and on-time risk stratification at the time of presentation based on COVID-19 probability must be obtained in all patients diagnosed with ACS. (2) Every staff member must be acquainted with the strict protocols and policies of management of ACS patients during this pandemic. (3) Patient selection criteria must be well established with algorithms to simplify the workflow in these life-threatening conditions. (4) All elective nonurgent procedures should be rescheduled to reduce potential risk for the patient and the staff members. (5) Proper training in donning and doffing sequences is crucial to reduce contagion between healthcare workers.

Disclosures

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