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

Kasparas Briedis, MD, MSc[a,b,*], Ali Aldujeli, MD, MSc[a,b], Montazar Aldujeili, MD[c], Kamilija Briede, MD, MSc[a,b], Remigijus Zaliunas, MD, PhD[a,b], Anas Hamadeh, MD[d,e], Robert C. Stoler, MD[d,e], and Peter A. McCullough, MD, MPH[d,e]

Accumulating evidence suggests that influenza and influenza-like illnesses can act as a trigger for acute myocardial infarction. Despite these unprecedented times providers should not overlook acute coronary syndrome (ACS) guidelines, but may choose to modify the recommended approach in situations with confirmed or suspected COVID-19 disease. In this document, we suggest recommendations as to how to triage patients diagnosed with 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. **(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.[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.

[a]Hospital of Lithuanian University of Health Sciences Kaunas Clinics, Kaunas, Lithuania; [b]Lithuanian University of Health Sciences, Kaunas, Lithuania; [c]University of Brescia, Brescia, Italy; [d]Baylor University Medical Center, Dallas, Texas; and [e]Baylor Scott and White Heart and Vascular Hospital, Dallas, Texas. Manuscript received May 1, 2020; revised manuscript received and accepted June 16, 2020.

See page 118 for disclosure information.

*Corresponding author: Tel: 0037069654230.

E-mail address: kasparas.briedis@kaunoklinikos.lt (K. Briedis).

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Table 1
Groups at high risk for severe illness (adopted from Centers of Disease Control and Prevention CDC)[5]

A patient with one or more of the following: - Age ≥65 years
- BMI ≥40 kg/m^2
- 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

Noncontact COVID-19 cases are managed as per standard institutional policies and protocols.

Some of the porter services can be transformed to dedicated COVID transfer teams who have everyday experience and skills on proper donning and doffing sequences for PPE.

When performing cardiac procedures on confirmed and suspected COVID-19 cases, procedures should be performed in a dedicated COVID catheterization laboratory.[6] It should contain COVID dedicated lead aprons, conventional equipment with the most commonly used balloon and stent sizes, wires, catheters and other equipment.[7] 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.[7] Cleaning procedures before and after the cases must be strictly followed according to the institutional policies.[8] Intense cleaning of lead aprons should be added to the protocols.[9] Cardiac procedures for all other cases should be performed per usual protocols with standard equipment in non-COVID dedicated catheterization laboratory.[10]

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.[7] 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.

Table 2
Sample donning and doffing steps for personal protective equipment (PPE) for catheterization laboratory[7]

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

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 3
Very high-risk features (according to 2018 ESC Guidelines on Myocardial revascularization)[11]

- 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 intermitted ST-segment elevations

department, if the patient is a suspected or contact COVID-19 case, SARS-CoV-2 PCR should be immediately performed. If there is no option for rapid nucleic acid testing and if the patient is still stable, any invasive procedure should be delayed until PCR testing has resulted. If the result is positive, patients should be transferred to an infectious zone and can be admitted to a room with other COVID-19 positive cases if needed. If the result is negative in a suspected COVID-19 case, a stable low-risk patient with a clear diagnosis, can be transferred to ordinary Cardiology ward for standard care. There is no need for further isolation in this case. If the initial COVID test is negative, in a stable patient with unclear diagnosis or high-risk features, a second SARS-CoV-2 PCR test for suspected COVID-19 case should be performed. The patient should be admitted to an infectious zone and may later be transferred to a non-infectious zone based on the second PCR test result, for further ACS management. In contact cases, patients can be transferred to the appropriate ward and zone after the first SARS-CoV-2 PCR test result.

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.[13] 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.[12] 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.[14] However, this may not hold true in severe COVID-19 cases as they are commonly complicated by coagulopathy,[15,16] 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)[12]

Severe pneumonia
Adolescent or adult: fever or suspected respiratory infection, plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO_2 ≤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. echocardiography) to exclude hydrostatic cause of infiltrates/edema if no risk factor present
Oxygenation impairment in adults:
- Mild ARDS: 200 < PaO_2/FiO_2a ≤ 300 (with PEEP or CPAP ≥ 5 cmH_2O, or nonventilated)
- Moderate ARDS: 100 < PaO_2/FiO_2 ≤200 (with PEEP ≥ 5 cmH_2O, or nonventilated)
- Severe ARDS: PaO_2/FiO_2 ≤100 (with PEEP ≥ 5 cmH_2O, or nonventilated)
- When PaO_2 is not available, SpO_2/FiO_2 ≤315 suggests ARDS (including in nonventilated patients)

ARI = acute respiratory infection; CPAP = continuous positive airway pressure; FiO_2 = fraction of inspired oxygen; PaO_2 = partial pressure of oxygen; PEEP = positive end-expiratory pressure.

Table 5
Doses of fibrinolytic agents[13]

Drug	Initial treatment
Tenecteplase (TNK-tPA)	Single IV bolus:
	30 mg bolus (6000 IU) if < 60 kg
It is recommended to reduce to half-dose in patients ≥75 years of age	35 mg bolus (7000 IU) if 60 to 69 kg
	40 mg bolus (8000 IU) if 70 to 79 kg
	45 mg bolus (9000 IU) if 80 to 89 kg
	50 mg bolus (10000 IU) if ≥ 90 kg
Alteplase (tPA)	15 mg IV bolus
	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 > 67kg
Reteplase (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.[9] There is a higher risk of patient exposure and contamination in the hospital even if in noninfectious zones.[8] 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.[17] 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.[9]

All face-to-face follow-up appointments in outpatient clinics after the discharge during the pandemic should be postponed.[17] Teleconsultation services with online drug prescription options for follow-up should be established and encouraged to avoid unnecessary patient contamination.[10]

Table 6
World Health Organization (WHO) definition of mild illness clinical syndrome associated with COVID-19[12]

Mild illness
Patients with uncomplicated upper respiratory tract viral infection may have nonspecific symptoms such as fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnea, nasal congestion, or headache. Rarely, patients may also present with diarrhea, nausea, and vomiting.
The elderly and immunosuppressed may have atypical presentations.
Symptoms due to physiologic adaptations of pregnancy or adverse pregnancy events, such as dyspnea, fever, GI-symptoms or fatigue, may overlap with COVID-19 symptoms.

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

The authors declare that they have no known competing financial interests or personal relations that could have appeared to influence the work reported in this study.

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