



Opinion Paper

Managing ACS during COVID-19 infection: Do not follow the traditional route

Santanu Guha ^{a,*}, Somnath Mukhopadhyay ^a, Avik Karak ^a, Basabendra Choudhury ^a, Aditya Kapoor ^b, Rakesh Yadav ^c

^a Department of Cardiology, Medical College, Kolkata, West Bengal, India

^b Department of Cardiology, Sanjay Gandhi PGIMS, Lucknow, India

^c Department of Cardiology, A.I.I.M.S, New Delhi, India



ARTICLE INFO

Article history:

Received 7 April 2020

Accepted 9 April 2020

Available online 15 April 2020

Keywords:

Acute coronary syndrome

COVID-19

ABSTRACT

COVID-19 pandemic is creating havoc in the world. It is also spreading in India creating a massive healthcare problem. Few major hospitals were closed down because of the spread among healthcare personnel. Management of several commonly occurring diseases needed modifications to a lesser or greater extent because of this pandemic. Management of acute coronary syndrome (ACS) also requires certain modifications. In this opinion paper an attempt has been made to give an outline of ACS management in this changed scenario.

© 2020 Cardiological Society of India. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Humanity is about to be marooned in this beautiful world, courtesy to SARS-COV-2. China has witnessed the initiation. Developed countries are experiencing the devastating propagation and termination is yet to be seen. Pre-existing cardiovascular disease (CVD) patients, having COVID-19 infection, are at higher risk of adverse outcomes and increased mortality. This infection itself can be associated with many cardiovascular complications.^{1,2} Drugs used for treatment of COVID-19 infection have many interactions with cardiovascular drugs and can also cause significant adverse cardiovascular effects.³

Once this infection becomes more prevalent, all patients presenting with symptoms of severe emergent CVD should be managed as suspected cases of COVID-19.⁴

Acute coronary syndrome (ACS) in COVID-19 infection is primarily attributed to demand supply mismatch. But plaque destabilization may also contribute. Profound inflammatory response and altered hemodynamics associated with severe disease may confer risk for atherosclerotic plaque rupture in susceptible patients.⁵ Additionally, it is important to note the potential overlapping symptomatology between ACS and COVID-19. While the predominant presenting symptoms of COVID-19 are respiratory, reports suggest that a patient can present with chest pain and

electrocardiographic changes suggestive of ACS with normal coronaries.⁶

Considering the present pandemic, for a patient who presents with ACS and in whom the infection has not been ruled out, isolation in a separate room is preferred with hemodynamic monitoring till COVID-19 is excluded. Transfer to different areas of hospital for various tests and investigations should be minimized. Appropriate guideline based personal protection equipment (PPE) is of utmost importance for the protection of medical personnel, as it will not only avoid them getting infected but also prevent nosocomial infection and transmission. Echocardiography should be done only if it contributes to decision making and TEE should be avoided unless absolutely necessary. Personal equipments like stethoscope, BP machine, cellphones have to be decontaminated after each examination.

The management strategy of ACS patients should be determined by a) risk stratification and b) whether patient is confirmed COVID-19, suspected COVID-19 or low risk of COVID-19.⁷ In general, the total number of PCI procedures should be minimised in order to conserve healthcare resources and limit the risk of infection and its transmission among healthcare personnel. So, a conservative approach can be recommended for all ACS patients who are stable. Fibrinolysis may be considered as a reasonable option for stable STEMI patients presenting within stipulated time frame, without contra-indications as per standard protocols. Invasive interventions may be limited to STEMI and NSTEMI with hemodynamic instability. Intervention should be done in a CCL (cardiac catheterization

* Corresponding author. Department of Cardiology, Medical College, Kolkata, India.

E-mail address: guhas55@gmail.com (S. Guha).

laboratory) if proper PPE is available in an institute with proper infection control unit. The CCL or operating room should preferably have negative pressure ventilation, with strict vigil on post-procedural disinfection. If negative pressure ventilation is not available, air conditioning (laminar flow and ventilation) should be stopped. Minimal equipment in the CCL should be used for procedures.

Ideally all efforts should be made to perform diagnostic testing for COVID-19, prior to considering for PCI. It is recommended that sick patients with definite or suspected COVID-19 be intubated prior to arrival to the catheterization laboratory to reduce aerosol exposure in lab. Efforts should be made to avoid emergent intubation in the catheterization laboratory as this can result in aerosolization of respiratory secretions with increased exposure risk to the cath lab personnel.

1. Issues which require special attention for ACS management during COVID-19 pandemic

1. Training of medical and paramedical staffs regarding early recognition of COVID-19 infection, disinfection measures for facilities and medical equipment and training for PPE are essential.
2. Myocardial injury and acute myocarditis due to COVID-19 infection can mimic ACS. Raised troponin results are very common specially with high sensitivity cardiac troponin assays. So routinely ordered increased troponin values may not be helpful in diagnosis of ACS during COVID 19 infection.⁸
3. Rapid antibody detection test can reduce the time delay, and may be helpful for quick triage of COVID-19 positivity in ACS.
4. Patients may be diagnosed as having this infection during the course of hospital stay. Hence collaboration with ID Department on regular basis is important. Regular assessment of risk benefit ratio for intervention and ongoing medical treatment is mandatory.
5. In every city, at least a few CCUs (coronary care units) and CCLs should be developed in hospitals caring for COVID-19 positive cases, where patients from other hospitals may be transferred.
6. Delayed presenters of STEMI will significantly increase due to lack of proper transport, lack of routine medical services, reluctance to attend hospital in present conditions and fear of getting infection from healthcare systems. Even in a hospital equipped with CCL, stipulated 'door-to-balloon time' for primary PCI may not be maintained due to delay in ruling out the COVID-19 diagnosis. So thrombolysis is preferred even in hospitals with CCL facilities.
7. Coagulation parameters are deranged during severe COVID infection, which need to be kept in mind before giving thrombolysis or antiplatelets.⁵ Close monitoring of bleeding parameters should be done in such situations.
8. Anti-viral drugs: Ribavirin has no direct toxicity over CV system. Lopinavir/ritonavir may result in QT and PR interval prolongation, mainly in those having baseline abnormality (long QT) or those who are at risk for conduction abnormalities including those taking other QT prolonging drugs.⁹
9. Anticoagulant dosing: Ribavirin has variable effects on warfarin dosing.¹⁰ Lopinavir/ritonavir may need dose reductions or avoidance of CYP3A4 mediated drugs such as rivaroxaban and apixaban.¹¹
10. Lopinavir/ritonavir, through CYP3A4 inhibition, causes increased serum concentrations of ticagrelor.¹² Hence, concomitant use of ticagrelor should be discouraged due to excess bleeding risk as has been done in USA and Canada.³ Conversely, clopidogrel may not provide sufficient platelet

inhibition during concomitant administration of lopinavir/ritonavir but this was not the case with prasugrel.^{13,14} In case prasugrel cannot be used, testing guided approach with platelet function assays is strongly recommended.

11. Co-administration of lopinavir/ritonavir with statins can result in myopathy due to elevated statin levels. Lovastatin and simvastatin are contraindicated for co-administration with lopinavir/ritonavir for the risk of rhabdomyolysis. Atorvastatin or rosuvastatin, should be administered at the lowest possible dose.³
12. Being a QT prolonger, cautious use of hydroxychloroquine (HCQ)¹⁵ is needed in ACS patients. Same is true for azithromycin and its combination with HCQ. Careful use with more frequent assessment of QT interval is needed for anti-arrhythmic drugs known to cause QT prolongation, especially amiodarone.
13. Angiotensin Converting Enzyme Inhibitor (ACEI)/Angiotensin Receptor Blockers (ARB) are usually used in post ACS setting. It is recommended to continue use of ACEI/ARB in the treatment of HTN, HF, post MI and other scenarios during COVID-19 pandemic¹⁶ although there is a debate regarding their use during this pandemic, as they increase the ACE-2 levels.
14. **Follow up with telephonic or telehealth care systems should be extended for all stable patients** to minimize hospital visits and if possible avoid them. As per new Indian guidelines,¹⁷ medical practitioners are entitled to provide telemedicine consultation to patients while upholding the same professional and ethical norms and standards as applicable to traditional in-person care. All practitioners are also encouraged to get familiar with these guidelines by online programs developed and made available by the Board of Governors of MCI.

2. Conclusion

We are in the midst of a pandemic of unprecedented magnitude infecting more than a million people globally and causing nearly sixty thousand deaths. This has overwhelmed the medical infrastructure worldwide and compelled to make modifications in the management of some commonly occurring diseases. A more conservative approach in the management of ACS is mandated by certain compulsions. Setting up of a few dedicated CCUs and CCLs in hospitals taking care of COVID-19 positive cases in every city is the need of the hour to combat the pandemic if it propagates in our country. This pandemic has asked for several modifications like modification in our lifestyle, modification in our social behavior, modification in our clinical practice. We have to live with these modifications till we can get rid of this menace.

Conflicts of interest

All authors have none to declare.

References

1. Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clin Res Cardiol*. 2020. <https://doi.org/10.1007/s00392-020-01626-9>.
2. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. *Nat Rev Cardiol*. 2020 Mar 5. <https://doi.org/10.1038/s41569-020-0360-5>.
3. Driggin Elissa, Madhavan Mahesh M, Bikdeli Behnood, et al. Cardiovascular considerations for patients, health care workers, and health systems during the coronavirus disease 2019 (COVID-19) pandemic. *JACC (J Am Coll Cardiol)*. 2020. <https://doi.org/10.1016/j.jacc.2020.03.031>.

4. Beck Debra L. New guidance on management of acute CVD during COVID-19. *Circulation*. 2020;48:189–194. Published online March 27,2020.
5. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020 March 28;395(10229):1054–1062. [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3).
6. Wood S. COVID-19 and the heart: Insights from the front lines. *tctMD/ the heartbeat*. 2020 March 12.
7. Jing Zhi-Cheng, Zhu Hua-Dong, Yan Xiao-Wai, Chai Wen-Zhao, Zhang Shuyang, COVID-19 & AMI Committee of Peking Union Medical College Hospital. Recommendations from the Peking Union Medical College Hospital for the management of Acute Myocardial Infarction during the COVID-19 outbreak. *Eur Heart J*. 2020 March 31. <https://doi.org/10.1093/eurheartj/ehaa258>.
8. Bansal M. *Diabetes Metab Syndr*. 2020 Mar 25;14(3):247–250. <https://doi.org/10.1016/j.dsx.2020.03.013>.
9. Soliman EZ, Lundgren JD, Roediger MP, et al, INSIGHT SMART Study Group. Boosted protease inhibitors and the electrocardiographic measures of QT and PR durations. *AIDS*. 2011 Jan 28;25(3):367–377. <https://doi.org/10.1097/QAD.0b013e328341dcc0>.
10. De Carolis DD, Westanmo AD, Chen YC, Boese AL, Walquist MA, Rector TS. Evaluation of a potential interaction between new regimens to treat hepatitis C and warfarin. *Ann Pharmacother*. 2016;50:909–917.
11. Egan G, Hughes CA, Ackman ML. Drug interactions between antiplatelet or novel oral anticoagulant medications and antiretroviral medications. *Ann Pharmacother*. 2014 Jun;48(6):734–740. <https://doi.org/10.1177/1060028014523115>. Epub 2014 Mar 10.
12. *Product monograph. Brilinta (Ticagrelor)*. Mississauga, Ontario, Canada: Astra-Zeneca Canada Inc.; May 2011.
13. Itkonen MK, Tornio A, Lapatto-Reiniluoto O, et al. Clopidogrel increases dasabuvir exposure with or without ritonavir, and ritonavir inhibits the bio-activation of clopidogrel. *Clin Pharmacol Ther*. 2019;105:219–228.
14. Marsousi N, Daali Y, Fontana P, et al. Impact of boosted antiretroviral therapy on the pharmacokinetics and efficacy of clopidogrel and prasugrel active metabolites. *Clin Pharmacokinet*. 2018;57:1347–1354.
15. Morgan ND, Patel SV, Dvorkina O. Suspected hydroxychloroquine-associated QT-interval prolongation in a patient with systemic lupus erythematosus. *J Clin Rheumatol*. 2013 Aug;19(5):286–288. <https://doi.org/10.1097/RHU.0b013e31829d5e50>.
16. *HFSA/ACC/AHA statement addresses concerns re: using RAAS antagonists in COVID-19*. American College of Cardiology News Story; 2020 March 17. acc.org/latest-in-cardiology/articles/2020/03/17/08/59.
17. BOARD OF GOVERNORS. In supersession of the Medical Council of India Telemedicine Practice Guidelines Enabling Registered Medical Practitioners to Provide Healthcare Using Telemedicine [Appendix 5 of the Indian Medical Council (Professional Conduct, Etiquette and Ethics Regulation, 2002)]. 25 March 2020.