Trends in Clinical and Medical Sciences

PSR Press

Article

Clinical outcomes of patients with ACS associated with concomitant Covid-19 infection

Dr. Sunil Kumar Sharma[1], Dr. Sibaram Panda[2] and Dr. Jagannath Hati[3,*]

[1] Professor and HOD, Department of Cardiology, India.
[2] Assistant Professor Department of Cardiology, India.
[3] Assistant Professor, Department of Medicine, India.
* Correspondence: jagaajagaa.jagaa@gmail.com

Received: 13 October 2022; Accepted: 5 May 2023; Published: 20 May 2023.

Abstract: Introduction: The coronavirus 2019 (COVID-19) pandemic has significantly impacted the management of cardiovascular emergencies across the world. Early in the pandemic, an unforeseen decline in hospital admissions of patients with acute cardiovascular emergencies was noted. Furthermore, the overall reduction in respiratory infections and vigorous exercise related to social isolation may have contributed to a decrease in the incidence of acute coronary syndrome (ACS). However, a significant number of patients have presented with late-stage cardiac diseases, such as late-presenting ACS, and with serious cardiac complications including cardiac arrests and out-of-hospital death.
Material and Methods: A retrospective cross-sectional study of all consecutive COVID-19 infected ACS patients admitted during the period April 1st, 2021 to March 1st, 2022, at VIMSAR BURLA. The cases could be ACS patients shown to be COVID-19 positive during routine screening after admission or referred from elsewhere as COVID positive or ACS developing in the hospital after admission for the treatment of COVID-19 infection. All consecutive COVID-19 (RT-PCR) positive patients above the age of 18 years with ACS admitted to VIMSAR Burla. Data of patients with age and sex-matched COVID-19 free ACS patients treated in the same period in VIMSAR Burla was enrolled as the control group for comparison in a 1:3 ratio. Data about baseline characteristics, electrocardiographic findings, clinical findings, and outcomes of patients were compared between the case and control groups.
Results: Once ACS is suspected, medical therapy should be instituted immediately along with a decision on whether to proceed with an invasive strategy. Medical therapy for ACS in COVID-19 patients is identical to patients without COVID-19. This includes dual antiplatelet therapy (aspirin and a P2Y12 inhibitor), intravenous or subcutaneous anticoagulation, statins, and beta-blockers (if no contraindications). However, only one in vitro study has shown that SARS-CoV-2 downregulates the ACE2 expression, and further studies are needed to confirm this pathophysiological pathway.
Conclusion: Despite the overall reduction in cases admitted to the emergency departments during the early phase of the pandemic, ACS is a potential life-threatening complication of COVID-19. The pathophysiological mechanisms are multiple and include atherosclerotic plaque rupture, overactivation of the coagulation system, platelet hyperreactivity, abnormal systemic inflammatory response, and oxygen supply/demand imbalance. When compared to non-COVID-19 cases, patients with ACS and SARS-CoV-2 infection present distinctive clinical and anatomical features, including the absence of obstructive CAD, the higher burden of thrombus, and the angiographic evidence of multiple thrombotic lesions.

Keywords: COVID-19; Patients; Infection; ACS.

1. Introduction

The coronavirus 2019 (COVID-19) pandemic has significantly impacted management of cardiovascular emergencies across the world. Early in the pandemic, an unforeseen decline in hospital admissions of patients with acute cardiovascular emergencies was noted [1]. A survey conducted by the Society for Cardiovascular Angiography and Interventions (SCAI) showed that people considered going to a hospital a high-risk behavior for contracting COVID-19, and people over the age of 60 years were more afraid of

contracting the disease than of having a heart attack [2]. This along with extensive public health campaigns promoting staying at home has, in part, led to fewer patients seeking care for symptoms [3].

Furthermore, the overall reduction in respiratory infections and vigorous exercise related to social isolation may have contributed to a decrease in the incidence of acute coronary syndrome (ACS). However, a significant number of patients have presented with late-stage cardiac diseases, such as late-presenting ACS, and with serious cardiac complications including cardiac arrests and out-of-hospital death [4]. With improved awareness of the disease and public messaging, subsequent COVID-19 waves have not correlated with a similar decline in acute myocardial infarction-related hospitalizations [5]. The pandemic has further given rise to an immense demand for resources, leading to diversion and deferral of essential preventive and elective medical services for patients with stable cardiac problems [6].

Increased morbidity and mortality were noted secondary to ACS and were thought to be related to a significantly longer time from symptom onset to hospital presentation in addition to the delay in performing primary percutaneous coronary interventions (PPCI) [7]. Managing late-presenting myocardial infarction (MI) has always been challenging and complex, and COVID-19 has added another layer of complexity [8]. Early in the pandemic, prospective data from 55 international centers was used to create a "COVID-ACS" registry that included patients who were either COVID-19 positive or had a high index of clinical suspicion for the infection [9].

Analysis of registry data showed that mortality and complications were significantly higher in COVID-ACS patients compared to the same population in the pre-pandemic era (COVID–ST-elevation myocardial infarction [STEMI]: 23% vs 6%, $P < .001$; COVID–non-ST-elevation ACS: 7% vs 1%, $P < .001$; cardiogenic shock in COVID-STEMI: 20% vs 9%, $P < .001$) [10]. For this reason, it is important to address ACS in patients with COVID-19 differently to improve morbidity and mortality while protecting the treatment staff [11].

To date, there is a paucity of data about the presentation, clinical outcomes in COVID infected ACS patients. Hence there is an urgent need to address important care processes for COVID-19 infected ACS patients to mitigate adverse outcomes. Therefore we are planning a retrospective observational study to evaluate clinical outcomes of COVID-infected ACS patients.

The objective of this is to find out differences in the composite of in hospital mortality, heart failure, shock, stroke and systemic embolisation in COVID-19 infected ACS patients compared to age and sex-matched non-infected ACS patients treated during the same period.

2. Materials and Methods

The study was conducted at VIMSAR, Burla, specifically in the VIMSAR Covid Hospital. It employed a retrospective record-based design.

The study population comprised patients aged 18 years and above who were diagnosed with Acute Coronary Syndrome (ACS) and tested positive for COVID-19 (RT-PCR).

All consecutive COVID-19 positive patients with ACS were included in the study using purposive sampling.

To estimate the sample size, the prevalence (P) of the target population was determined as 4% based on a previous study. The complementary probability (Q) was calculated as 96%. Using a 95% confidence level and an allowable error (L) of 0.16 (40% of the prevalence), the sample size (N) was determined as 576.

Inclusion criteria consisted of all consecutive COVID-19 positive patients aged 18 years and above with ACS admitted to VIMSAR Burla. Patients aged above 18 years with ACS who tested negative for COVID-19 were excluded.

The study variables included baseline characteristics such as age, sex, and body mass index, as well as comorbidities such as diabetes, hypertension, dyslipidemia, chronic kidney disease, chronic obstructive pulmonary disease, bronchial asthma, and history of invasive or noninvasive ventilation. The study tools used were a predesigned proforma and registered records.

A retrospective cross-sectional study design was employed, including all consecutive COVID-19 infected ACS patients admitted to VIMSAR Burla between April 1st, 2021, and March 1st, 2022. This included ACS patients who tested positive for COVID-19 during routine screening after admission, those referred from other facilities as COVID positive, or those who developed ACS after admission for COVID-19 treatment. Data

regarding baseline characteristics, comorbid conditions, clinical presentation, medical treatment, reperfusion methods, clinical course, management of COVID-19 infection, and outcomes of ACS patients were retrieved from the medical record system. A control group comprising age and sex-matched COVID-19 negative ACS patients treated at VIMSAR Burla during the same period was enrolled in a 1:3 ratio for comparison. Patient anonymity and confidentiality were maintained throughout the study. Baseline characteristics, electrocardiographic findings, clinical presentation, and outcomes were compared between the case and control groups.

The collected data was managed by entering it into MS Excel after thorough data cleaning. The compiled data was then tabulated and analyzed.

2.1. Data analysis

Categorical variables were reported as frequencies and percentages. Continuous variables were expressed as mean and standard deviation. Clinical and demographic variables were reported using mean +/- SD or as median when appropriate. Continuous and categorical variables were assessed using appropriate tests and P value >0.05 was considered statistically significant.

3. Results

Table 1. Distribution of Age

Variable	Mean	SD
Mean Age (years)	59.3	5.31
Body mass index (kg/m2)	24.7	3.54

Table 2. Distribution of Gender

Gender	Frequency	Percentage
Male	112	58.94
Females	78	41.05

Table 3. Distribution of Comorbidities

Comorbidities	Frequency	Percentage
Diabetes mellitus	93	48.94
Hypertension	117	61.57
Dyslipidaemia	64	33.68
Chronic kidney disease	19	10
Chronic obstructive pulmonary disease	71	37.36
Bronchial asthma	39	20.52
History of invasive or non-invasive ventilation	21	11.05

Table 4. Distribution of Clinical presentation

Clinical presentation	Frequency	Percentage
STEMI	81	42.63
NSTE-ACS	74	38.94
LVEF,%,	20	10.52
GRACE score,	21	11.05
Acute pulmonary edema	9	4.73
Shock	7	3.68
Cardiac arrest	4	2.10
SARS-CoV-2 infection	5	2.63

STEMI: ST-elevation myocardial infarction, **NSTE-ACS:** Non-ST elevation acute coronary syndrome, **LVEF:** Left ventricular ejection fraction, **GRACE:** Global Registry of Acute Coronary Events score.

Table 5. Distribution of Coronary angiography and revascularization

Coronary angiography and revascularization	Frequency	Percentage
Coronary angiography	139	73.15
STEMI	158	83.15
NSTE-ACS	146	76.84
Radial artery access	132	69.47
PCI	126	66.31
CABG	12	6.31
Complete revascularization	104	54.73
IABP	9	4.73
PMCS	3	1.57

PCI: Percutaneous coronary intervention, CABG: Coronary artery by-pass grafting, **IABP:** Intra-aortic ballon pump, **PMCS:** Percutaneous mechanic circulatory support

Table 6. Distribution of Management

Management	Frequency	Percentage
Aspirin	168	88.42
P2Y12 inhibitors	143	75.26
Glycoprotein IIb/IIIa inhibitors	31	16.31
Inotropic drugs	24	12.63

4. Discussion

Once ACS is suspected, medical therapy should be instituted immediately along with a decision whether to proceed with an invasive strategy. Medical therapy for ACS in COVID-19 patients is identical to patients without COVID-19. This includes dual antiplatelet therapy (aspirin and a P2Y12 inhibitor), intravenous or subcutaneous anticoagulation, statins, and beta blockers (if no contraindications). Oxygen is only administered in the setting of hypoxia. Reports from the early pandemic phase showed that angiotensin converting enzyme inhibitors and angiotensin-receptor blockers might be harmful, but further investigations negated these findings [12–18]. In addition, a recent randomized controlled trial confirmed that there was no difference in short-term outcomes for patients with mild-to-moderate COVID-19 symptoms, regardless of whether such medications were continued or discontinued.

COVID-19 is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), a novel β-coronavirus infecting human cells of the respiratory tract, vascular endothelium, heart, gut, and immune system [19]. The virus binds the angiotensin-converting enzyme 2 (ACE2) receptor, highly expressed on the target host cells, through a spike (S) protein that enables the fusion of membranes and viral internalization [20]. In particular, endothelial cells and cardiac pericytes express abundant ACE2, making them highly susceptible to SARS-CoV-2 interaction and internalization.

The interferon-mediated upregulation of ACE2 may facilitate the involvement of adjacent pneumocytes and the development of an uncontrolled inflammatory reaction, microvascular thrombosis, interstitial and alveolar edema, and eventual progression toward acute respiratory distress syndrome (ARDS), [21]. Moreover, it has been hypothesized that SARS-CoV-2, by interacting with ACE2 for the cell entry, causes a downregulation of the bound ACE2 and increases the circulating level of soluble ACE2. This deregulation affects the activity of bound ACE2, which is associated with several beneficial effects by regulating the inflammatory response, reducing oxidative stress, and promoting vessel relaxation via the production of angiotensin1-7 (Ang1-7) [22]. It seems reasonable to hypothesize that, similarly to SARS-CoV-1, SARS-CoV-2 promotes the cleavage of ACE2 receptors leading to lower Ang1-7 serum levels [23].

However, only one in vitro study has showed that SARS-CoV-2 downregulates the ACE2 expression, and further studies are needed to confirm this pathophysiological pathway [24]. SARS-CoV-2 is transmitted from

person to person via close contact through respiratory droplets and viral particles inhalation, with a mean incubation of about five days [25]. Viral load detected in the asymptomatic and symptomatic subjects appears to be similar, suggesting that asymptomatic subjects can transmit the virus as well as the symptomatic ones [26].

COVID-19 vaccinations have shown to be safe and effective in preventing cases and reducing the severity of the disease, hospitalization, and death [27]. However, there is significant vaccination hesitancy recorded in different parts of the country, and this—along with new emerging strains like the Delta, Delta-plus, Omicron, and Lambda variants—continues to pose risks for a wave of milder COVID-19 infections in the near future [28]. The factors that resulted in increased complications and mortality from ACS in past waves will continue to persist in future waves of milder disease. It is important for healthcare systems to evolve and create policies to ensure that treatment is not delayed and standard of care is maintained for patients presenting with ACS in future similar circumstances. The use of telemedicine played a major role in providing healthcare services during the pandemic [29]. The effectiveness of telemedicine for preventive cardiology and post-ACS care should be studied further since it could result in regular healthcare follow-up without visiting a cardiologist's office.

5. Conclusion

Despite the overall reduction in cases admitted at the emergency departments during the early phase of the pandemic, ACS is a potentially life-threatening complication of COVID-19. The pathophysiological mechanisms are multiple and include atherosclerotic plaque rupture, overactivation of the coagulation system, platelet hyperreactivity, abnormal systemic inflammatory response, and oxygen supply/demand imbalance. When compared to non-COVID-19 cases, patients with ACS and SARS-CoV-2 infection present distinctive clinical and anatomical features including the absence of obstructive CAD, the higher burden of thrombus, and the angiographic evidence of multiple thrombotic lesions. A deeper understanding of the ACS pathophysiology in COVID-19 may allow the application of translational notions in daily clinical practice. The use of pharmacological agents, namely, antiplatelets, anticoagulants, ACEi, β-blockers, and statins, seems a valuable strategy not only in the treatment of ACS but also as a preventive strategy in higher CV risk subjects with COVID-19.

Author Contributions: All authors contributed equally to the writing of this paper. All authors read and approved the final manuscript.

Conflicts of Interest: The authors declare that they do not have any conflict of interests.

References

[1] Grines, C. L. (2021). SCAI consumer survey comparing fear of COVID-19 versus heart attack or stroke (first publish date: September 4, 2020). *Catheterization and Cardiovascular Interventions, 97*(2), 193.

[2] Bhatt, A. S., Moscone, A., McElrath, E. E., Varshney, A. S., Claggett, B. L., Bhatt, D. L., ... & Vaduganathan, M. (2020). Fewer hospitalizations for acute cardiovascular conditions during the COVID-19 pandemic. *Journal of the American College of Cardiology, 76*(3), 280-288.

[3] Wadhera, R. K., Shen, C., Gondi, S., Chen, S., Kazi, D. S., & Yeh, R. W. (2021). Cardiovascular deaths during the COVID-19 pandemic in the United States. *Journal of the American College of Cardiology, 77*(2), 159-169.

[4] Garcia, S., Stanberry, L., Schmidt, C., Sharkey, S., Megaly, M., Albaghdadi, M. S., ... & Henry, T. D. (2021). Impact of COVID-19 pandemic on STEMI care: an expanded analysis from the United States. *Catheterization and cardiovascular interventions, 98*(2), 217-222.

[5] Ferreira, D., Graffen, S., Watkins, B., Peters, B., Lim, G. J., Kamalanathan, H., ... & Davies, A. (2021). Effects of lockdown on acute coronary syndrome incidence in an area without community transmission of COVID-19. *Open Heart, 8*(1), e001692.

[6] Solomon, M. D., Nguyen-Huynh, M., Leong, T. K., Alexander, J., Rana, J. S., Klingman, J., & Go, A. S. (2021). Changes in patterns of hospital visits for acute myocardial infarction or ischemic stroke during COVID-19 surges. *Jama, 326*(1), 82-84.

[7] Yong, C. M., Ang, L., Welt, F. G., Gummidipundi, S., Henry, T. D., Pinto, D. S., ... & Society for Cardiovascular Angiography and Interventions (SCAI) and the American College of Cardiology (ACC) Interventional Council. (2020). Cardiac procedural deferral during the coronavirus (COVID-19) pandemic. *Catheterization and Cardiovascular Interventions, 96*(5), 1080-1086.

[8] Wallace, D. W., Burleson, S. L., Heimann, M. A., Crosby, J. C., Swanson, J., Gibson, C. B., & Greene, C. (2020). An adapted emergency department triage algorithm for the COVID-19 pandemic. *Journal of the American College of Emergency Physicians Open, 1*(6), 1374-1379.

[9] Gramegna, M., Baldetti, L., Beneduce, A., Pannone, L., Falasconi, G., Calvo, F., ... & Cappelletti, A. M. (2020). ST-Segment–Elevation myocardial infarction during COVID-19 pandemic: insights from a regional public service healthcare hub. *Circulation: Cardiovascular Interventions, 13*(8), e009413.

[10] Kite, T. A., Ludman, P. F., Gale, C. P., Wu, J., Caixeta, A., Mansourati, J., ... & International COVID-ACS Registry Investigators. (2021). International prospective registry of acute coronary syndromes in patients with COVID-19. *Journal of the American College of Cardiology, 77*(20), 2466-2476.

[11] Butala, N. M., Patel, N. K., Chhatwal, J., Vahdat, V., Pomerantsev, E. V., Albaghdadi, M., ... & Elmariah, S. (2020). Patient and provider risk in managing st-elevation myocardial infarction during the COVID-19 pandemic: a decision analysis. *Circulation: Cardiovascular Interventions, 13*(11), e010027.

[12] Wee, L. E. I., Conceicao, E. P., Tan, J. Y., Magesparan, K. D., Amin, I. B. M., Ismail, B. B. S., ... & Ling, M. L. (2021). Unintended consequences of infection prevention and control measures during COVID-19 pandemic. *American journal of infection control, 49*(4), 469-477.

[13] Li, B., Yang, J., Zhao, F., Zhi, L., Wang, X., Liu, L., ... & Zhao, Y. (2020). Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clinical research in cardiology, 109*, 531-538.

[14] Guo, T., Fan, Y., Chen, M., Wu, X., Zhang, L., He, T., ... & Lu, Z. (2020). Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA cardiology, 5*(7), 811-818.

[15] Sandoval, Y., Januzzi Jr, J. L., & Jaffe, A. S. (2020). Cardiac troponin for assessment of myocardial injury in COVID-19: JACC review topic of the week. *Journal of the American college of cardiology, 76*(10), 1244-1258.

[16] Bangalore, S., Sharma, A., Slotwiner, A., Yatskar, L., Harari, R., Shah, B., ... & Hochman, J. S. (2020). ST-segment elevation in patients with Covid-19—a case series. *New England Journal of Medicine, 382*(25), 2478-2480.

[17] Garcia, S., Dehghani, P., Grines, C., Davidson, L., Nayak, K. R., Saw, J., ... & Society For Cardiac Angiography and Interventions, the Canadian Association of Interventional Cardiology, and the American College of Cardiology Interventional Council. (2021). Initial findings from the North American COVID-19 myocardial infarction registry. *Journal of the American College of Cardiology, 77*(16), 1994-2003.

[18] Mihatov, N., & Kirtane, A. J. (2020). Standards of Care in Crisis: ST-Segment–Elevation Myocardial Infarction Management in COVID-19. *Circulation: Cardiovascular Interventions, 13*(11), e010143.

[19] Kuster, G. M., Pfister, O., Burkard, T., Zhou, Q., Twerenbold, R., Haaf, P., ... & Osswald, S. (2020). SARS-CoV2: should inhibitors of the renin–angiotensin system be withdrawn in patients with COVID-19?. *European heart journal. 41*(19):1801-1803.

[20] Danser, A. J., Epstein, M., & Batlle, D. (2020). Renin-angiotensin system blockers and the COVID-19 pandemic: at present there is no evidence to abandon renin-angiotensin system blockers. *Hypertension, 75*(6), 1382-1385.

[21] Lopes, R. D., Macedo, A. V., Silva, P. G. D. B. E., Moll-Bernardes, R. J., Dos Santos, T. M., Mazza, L., ... & BRACE CORONA Investigators. (2021). Effect of discontinuing vs continuing angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers on days alive and out of the hospital in patients admitted with COVID-19: a randomized clinical trial. *Jama, 325*(3), 254-264.

[22] Mahmud, E., Dauerman, H. L., Welt, F. G., Messenger, J. C., Rao, S. V., Grines, C., ... & Henry, T. D. (2020). Management of acute myocardial infarction during the COVID-19 pandemic: a position statement from the Society for Cardiovascular Angiography and Interventions (SCAI), the American College of Cardiology (ACC), and the American College of Emergency Physicians (ACEP). *Journal of the American College of Cardiology, 76*(11), 1375-1384.

[23] Choudry, F. A., Hamshere, S. M., Rathod, K. S., Akhtar, M. M., Archbold, R. A., Guttmann, O. P., ... & Jones, D. A. (2020). High thrombus burden in patients with COVID-19 presenting with ST-segment elevation myocardial infarction. *Journal of the American College of Cardiology, 76*(10), 1168-1176.

[24] Elbadawi, A., Mahtta, D., Elgendy, I. Y., Saad, M., Krittanawong, C., Hira, R. S., ... & Jneid, H. (2020). Trends and outcomes of fibrinolytic therapy for STEMI: insights and reflections in the COVID-19 Era. *Cardiovascular Interventions, 13*(19), 2312-2314.

[25] Richterman, A., Meyerowitz, E. A., & Cevik, M. (2020). Hospital-acquired SARS-CoV-2 infection: lessons for public health. *Jama, 324*(21), 2155-2156.

[26] Polack, F. P., Thomas, S. J., Kitchin, N., Absalon, J., Gurtman, A., Lockhart, S., ... & Gruber, W. C. (2020). Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *New England journal of medicine, 383*(27), 2603-2615.

[27] Kadri, S. S., & Simpson, S. Q. (2021). Potential implications of SARS-CoV-2 delta variant surges for rural areas and hospitals. *Jama, 326*(11), 1003-1004.

[28] Kichloo, A., Albosta, M., Dettloff, K., Wani, F., El-Amir, Z., Singh, J., ... & Chugh, S. (2020). Telemedicine, the current COVID-19 pandemic and the future: a narrative review and perspectives moving forward in the USA. *Family medicine and community health*, *8*(3): e000530.

[29] Mahmud, E., Dauerman, H. L., Welt, F. G., Messenger, J. C., Rao, S. V., Grines, C., ... & Henry, T. D. (2020). Management of acute myocardial infarction during the COVID-19 pandemic. *J Am Coll Cardiol96*:336–45.