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The coronavirus disease 2019 (COVID-19) pandemic has greatly impacted the US healthcare system. Cardiac involvement in COVID-19 is common and manifested by troponin and natriuretic peptide elevation and tends to have a worse prognosis. We analyzed patients who presented to the MedStar Health system (11 hospitals in Washington, DC, and Maryland) with either an ST-elevation myocardial infarction or non-ST-elevation myocardial infarction early in the pandemic (March 1, 2020 to June 30, 2020) using the International Classification of Diseases, Tenth Revision. Patients’ clinical course and outcomes, including in-hospital mortality, were compared on the basis of the results of COVID-19 status (positive or negative). The cohort included 1533 patients admitted with an acute myocardial infarction (AMI), of whom 86 had confirmed severe acute respiratory syndrome coronavirus 2 infection, during the study period. COVID-19-positive patients were older and non-White and had more co-morbidities. Furthermore, inflammatory markers and N-terminal-proB-type-natriuretic peptide were higher in COVID-19-positive AMI patients. Only 20.0% (17) of COVID-19-positive patients underwent coronary angiography. In-hospital mortality was significantly higher in AMI patients with concomitant COVID-19-positive status (27.9%) than in patients without COVID-19 during the same period (3.7%; p < 0.001). Patients with AMI and COVID-19 tended to be older, with more co-morbidities, when compared to those with an AMI and without COVID-19. In conclusion, myocardial infarction with concomitant COVID-19 was associated with increased in-hospital mortality. Efforts should be focused on the early recognition, evaluation, and treatment of these patients. © 2020 Published by Elsevier Inc. (Am J Cardiol 2021;144:8–12)
body mass index) and co-morbidities (hypertension, hyperlipidemia, diabetes, chronic kidney disease, hemodialysis, chronic obstructive pulmonary disease, asthma, coronary artery disease, cerebrovascular disease, congestive heart failure, atrial fibrillation, and history of pulmonary embolism) were collected for each cohort. Laboratory data (inflammatory makers, troponin I, natriuretic peptide) were collected, and the peak value was used for our analysis. In addition, clinical outcomes, including inhospital mortality, coronary angiography with subsequent revascularization, length of stay, intensive care unit (ICU) admission, ICU length of stay, and use of ventilation, were compared between the 2 groups.

Descriptive statistics such as frequencies, means, and standard deviations were used to describe the study population. Student’s t test or analysis of variance was used to compare mean values of normally distributed data. Cox-regression methods were used to evaluate risk factors for the primary outcome. Two-tailed Fisher’s exact test or chi-squared tests were used to compare categorical variables. Statistical significance was considered as a p value of <0.05 for the primary end point. The study was conducted under the approval of our institutional review board.

Results

In our medical system, 1533 patients were admitted with an AMI from March 1 through June 30, 2020. Of these patients, 86 were confirmed to be COVID-19-positive. Of the 86 COVID-19-positive AMI patients, 10 (11.6%) presented with STEMI, while the rest presented with NSTEMI. The majority of patients were men, with a mean age of 66 years. There was evidence of potential racial disparity in our analysis. The majority of White AMI patients tended to be COVID-19-negative, while the vast majority of COVID-19-positive AMI patients were Black. A larger proportion of Black patients with AMI were COVID-19-positive in comparison with White patients with AMI. Co-morbidities, including diabetes, chronic kidney disease, hemodialysis, coronary artery disease, stroke, atrial fibrillation, and history of pulmonary embolism, were more frequently seen in patients with AMI and COVID-19.

Inflammatory markers, including white blood cell count, lactate dehydrogenase, ferritin, and c-reactive protein were all statistically higher in the AMI patients with COVID-19. N-terminal-proB-type-natriuretic peptide (NT-proBNP) was statistically higher in the COVID-19-positive patients, while troponin levels were similar between the 2 groups (Table 2).

With regard to our primary end point, in-hospital mortality was significantly higher (27.9%) in the AMI patients with concomitant COVID-19 than in AMI patients without COVID-19 (3.7%; p < 0.001) (Figure 1). Secondary analysis of the AMI patients with COVID-19 demonstrated that fewer than 1/4 of the patients underwent coronary angiography, with an even smaller percentage being revascularized. None of the AMI COVID-19 patients received thrombolysis as their primary treatment strategy. Furthermore, a majority of patients were admitted into the ICU and a third required mechanical ventilation. Finally, the average length of stay in the ICU was 3.8 ± 7.4 days (Table 3).

Discussion

The primary findings of our analysis suggest that AMI patients with concomitant COVID-19 have a significantly increased risk of mortality as compared to those AMI patients without COVID-19. There was a racial and age disparity, as patients with STEMI/NSTEMI tend to be Black and older, with multiple co-morbidities. Additionally, AMI patients with COVID-19 have higher levels of inflammatory markers and increased levels of NTproBNP. Furthermore, given this sicker cohort, coronary angiography and subsequent revascularization are often not performed.

Table 1
Baseline characteristics of all acute myocardial infarction patients during the pandemic era overall and based on Coronavirus Disease 2019 status

| Variable                      | Overall (n = 1533) | COVID-19 (+) AMI (n = 86) | COVID-19 (−) AMI (n = 1447) | p value |
|-------------------------------|-------------------|--------------------------|-----------------------------|---------|
| Age ± SD (years)              | 66.7 ± 14.6       | 70.8 ± 14.7              | 66.5 ± 14.6                 | 0.008   |
| Men                           | 55.2% (846)       | 55.8% (48)               | 55.1% (798)                 | 0.904   |
| Height (cm)                   | 169.4 ± 12.0      | 169.3 ± 10.3 (64)        | 169.4 ± 12.13(623)          | 0.928   |
| Weight (kg)                   | 85.5 ± 37.0       | 80.5 ± 22.7 (70)         | 86.1 ± 38.2 (664)           | 0.075   |
| White                         | 42.5% (652)       | 23.3% (20)               | 43.7% (632)                 | <0.001  |
| Black                         | 49.1% (753)       | 64% (55)                 | 48.2% (698)                 | 0.005   |
| Other Race                    | 4.7% (72)         | 10.5% (9)                | 4.4% (63)                   | 0.009   |
| Hypertension                  | 57.2% (877)       | 47.7% (41)               | 57.8% (836)                 | 0.066   |
| Hyperlipidemia                | 59.2% (908)       | 58.1% (50)               | 59.3% (858)                 | 0.832   |
| Diabetes Mellitus             | 40.7% (624)       | 57% (49)                 | 39.7% (575)                 | 0.002   |
| Chronic Kidney Disease        | 27.1% (415)       | 44.2% (38)               | 26.1% (377)                 | <0.001  |
| Hemodialysis                  | 8% (122)          | 22.1% (19)               | 7.1% (103)                  | <0.001  |
| Asthma                        | 5.2% (79)         | 3.5% (3)                 | 5.3% (76)                   | 0.472   |
| Coronary Artery Disease       | 64.9% (995)       | 51.2% (44)               | 65.7% (951)                 | 0.006   |
| Stroke                        | 9.1% (139)        | 16.3% (14)               | 8.6% (125)                  | 0.017   |
| Congestive Heart Failure      | 35.4% (543)       | 44.2% (38)               | 34.9% (505)                 | 0.080   |
| Atrial Fibrillation           | 11% (169)         | 19.8% (17)               | 10.5% (152)                 | 0.008   |
| Prior Pulmonary Embolism      | 0.1% (2)          | 1.2% (1)                 | 0.1% (1)                    | 0.006   |

AMI = acute myocardial infarction; COVID-19 = coronavirus disease 2019.

The boldface on the numbers indicates that they are statistically significant (p<0.05).
Finally, two-thirds of AMI patients with COVID-19 are admitted into the ICU, with one-third of patients admitted to the ICU requiring mechanical ventilation. Underlying co-morbidities (diabetes, chronic kidney disease, hemodialysis, known coronary artery disease, stroke, atrial fibrillation, and prior pulmonary embolism) were more frequently seen in AMI patients who were COVID-19-positive. These findings reinforce previous studies that demonstrate an increased risk of SARS-CoV-2 infection in the presence of pre-existing co-morbidities.\textsuperscript{10,11} Furthermore, our healthcare system demonstrated a racial disparity. White AMI patients were more likely to be COVID-19-negative, while Black AMI patients were more likely to be COVID-19-positive. These findings are consistent with previous studies.\textsuperscript{12,13}

It is known that patients infected with SARS-CoV-2 have elevated inflammatory markers (white blood cell count, ferritin, lactate dehydrogenase, c-reactive protein, etc.).\textsuperscript{14} Our analysis demonstrated similar findings in AMI patients. If a provider is concerned that an AMI patient has SARS-CoV-2 infection, it is imperative that inflammatory markers are checked, as this can be an indication of infection and overall disease severity.\textsuperscript{15} Furthermore, NT-proBNP was statistically higher in the COVID-19-positive AMI patients, while troponin levels were consistent between the 2 cohorts. NT-proBNP should be checked in concordance with the inflammatory markers to determine severity of illness.

The increased rate of in-hospital mortality for patients who have an AMI and concomitant COVID-19 likely reflects that these patients tend to be older, with more co-morbidities and elevated inflammatory markers. In addition, these patients tend to be admitted to the ICU more frequently and require intubation.

The severe form of COVID-19 occurs in about 15% of patients requiring hospitalization, with 5% of patients requiring intensive care. The current mortality rate is estimated to be between 2% and 5% of all patients with COVID-19.

### Table 2

| Variable          | Overall (n) | COVID + AMI (n) | COVID − AMI (n) | p value |
|-------------------|------------|----------------|---------------|---------|
| WBC (k/uL)        | 11.0 ± 5.2 | 13.8 ± 7 (83)  | 10.7 ± 4.9 (815) | <0.001  |
| LDH (U/L)         | 687.4 ± 1005.1 | 873.2 ± 1329.7 (54) | 486.6 ± 363.5 (50) | 0.044   |
| Ferritin (ng/mL)  | 1689.4 ± 4599.8 | 3417.7 ± 6647.1 (68) | 570.1 ± 1819.2 (105) | <0.001  |
| CRP (mg/dL)       | 48.9 ± 59.7 | 125.5 ± 58.3 (43) | 31.2 ± 44.0 (186) | <0.001  |
| NTproBNP (pg/mL)  | 10955.8 ± 28323.8 | 23028.9 ± 47608.2 (53) | 9327.6 ± 24242.0 (393) | 0.044   |
| Troponin (ng/L)   | 22.2 ± 44.6 | 22.9 ± 52.8 (77) | 22.1 ± 43.7 (786) | 0.908   |

cm = centimeter; CRP = C-reactive protein; kg = kilogram; LDH = Lactate dehydrogenase; NTproBNP = N-terminal (NT)-pro hormone B-type natriuretic peptide; WBC = white blood cell.

The boldface on the numbers indicates that they are statistically significant (p<0.05).
COVID-19. The major cause of death in COVID-19 is acute respiratory distress.\textsuperscript{1,16} However, other organ involvement is common, including cardiac involvement.\textsuperscript{13} Previous studies have demonstrated that having cardiac co-morbidities places a patient at an increased risk of developing both the infection and the more severe form.\textsuperscript{14} However, our analysis demonstrates that cardiovascular involvement greatly increases a patient’s likelihood of death. The rate of mortality for patients who develop AMI with concomitant COVID-19 is much higher than what is estimated for patients with COVID-19 without AMI. Healthcare providers need to be aware of this deadly combination.

Finally, our analysis demonstrates that in these patients with AMI and COVID-19, coronary angiography is performed in fewer than one-fourth of patients. In patients who underwent coronary angiography, coronary artery disease was present, with revascularization commonly being performed. The deferral of performing an invasive strategy for treating these STEMI and NSTEMI patients reflects a sicker cohort, with more co-morbidities and a higher percentage in the ICU. In our analysis, we are unable to capture the reason why the angiography was not performed, but this real-world analysis is important. Previous studies have demonstrated that up to 60\% of STEMI patients with COVID-19 had true culprit lesion vessel disease, while the others had STEMI-mimicking disease.\textsuperscript{18} The impact of primary PCI on time to reperfusion and outcomes during the pandemic remains to be determined. Every effort needs to be made to make an early diagnosis of this potential complication. Guidelines of performing primary PCI for STEMI and NSTEMI need to be followed, even during a pandemic, to help treat these critically ill patients.

There are limitations to our analysis. First, the analysis is retrospective and relies on ICD-10 codes to identify the patient population. Our analysis does not distinguish between Type I and Type II NSTEMI. In addition, we did not capture patients who underwent coronary angiography, or subsequent PCI, to identify those patients who had a true plaque rupture as the etiology of their AMI versus another etiology (myocarditis, stress-induced cardiomyopathy, etc.).\textsuperscript{19} Furthermore, we did not capture how these patients were treated (pharmacology, mechanical support, etc.). Third, only a small percentage of patients who were COVID-19-negative had inflammatory markers drawn given the retrospective nature of our analysis. This can introduce a change for sampling bias. These findings should be hypothesis generating in nature. Finally, our data capture patients in the Mid-Atlantic region of the United States, where the pandemic was most impactful in March and April. Our findings may not represent the broader United States.

In conclusion, patients with both an AMI and COVID-19 tended to be older, with more co-morbidities, as compared to patients with an AMI without COVID-19. This led to a substantially higher rate of in-hospital mortality in this cohort. Efforts should be focused on the early recognition, evaluation, and treatment of these patients.

Authors’ contributions
Brian C. Case: Conceptualization, Formal analysis, Writing original draft, Writing (review and editing). Charan Yerasi: Validation, Writing (review and editing). Brian J. Forrestal: Validation, Writing (review and editing). Corey Shea: Methodology, Formal analysis. Hank Rappaport: Methodology, Formal analysis. Giorgio A. Medranda: Validation, Writing (review and editing). Cheng Zhang: Methodology, Validation, Formal analysis, Writing (review and editing). Lowell F. Satler: Validation, Writing (review and editing). Itsik Ben-Dor: Validation, Writing (review and editing). Hayder Hashim: Validation, Writing (review and editing). Toby Rogers: Validation, Writing (review and editing). Ron Waksman: Conceptualization, Writing (review and editing), Supervision.

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Disclosures
Ron Waksman – Advisory Board: Amgen, Boston Scientific, Cardioset, Cardiovascular Systems Inc., Medtronic, Philips, Pi-Cardia Ltd.; Consultant: Amgen, Biotronik, Boston Scientific, Cardioset, Cardiovascular Systems Inc., Medtronic, Philips, Pi-Cardia Ltd.; Grant Support: AstraZeneca, Biotronik, Boston Scientific, Chiesi; Speakers Bureau: AstraZeneca, Chiesi; Investor: MedAlliance. Toby Rogers – Consultant and Proctor: Medtronic, Edwards Lifesciences; Advisory Board: Medtronic. All other authors – None.

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