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# The Impact of COVID-19 Patients With Troponin Elevation on Renal Impairment and Clinical Outcome

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ABSTRACT

*Background:* Cardiac involvement in coronavirus disease 2019 (COVID-19) is known, manifested by troponin elevation, and these patients have a worse prognosis than patients without myocardial injury.
*Methods:* We analyzed COVID-19-positive patients who presented to the MedStar Health system (11 hospitals in Washington, DC, and Maryland) during the pandemic (March 1–September 30, 2020). We compared renal function and subsequent in-hospital clinical outcomes based on the presence or absence of troponin elevation. The primary outcome was the incidence of acute kidney injury in COVID-19 patients with troponin elevation. We also evaluated in-hospital mortality, overall and based on the presence and absence of both troponin elevation and renal dysfunction.
*Results:* The cohort included 3386 COVID-19-positive admitted patients for whom troponin was drawn. Of these patients, 195 had troponin elevation (defined as ≥1.0 ng/mL), mean age was 61 ± 16 years, and 51% were men. In-hospital mortality was significantly higher (53.8%) in COVID-19-positive patients with concomitant troponin elevation than in those without troponin elevation (14.5%; $p < 0.001$). COVID-19-positive patients with troponin elevation had a higher prevalence of renal dysfunction (58.5%) than those without troponin elevation (23.4%; $p < 0.001$). Further analysis demonstrated that having both troponin elevation and renal dysfunction carried the worst in-hospital prognosis (in-hospital mortality 57.9%; intensive-care-unit admission 76.8%; ventilation requirement 63.2%), as compared to the absence or presence of either.
*Conclusion:* COVID-19 patients with troponin elevation are at higher risk for worsening renal function, and these patients subsequently have worse in-hospital clinical outcomes. Efforts should focus on early recognition, evaluation, and intensifying care of these patients.



## 1. Introduction

Patients infected with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), resulting in coronavirus disease 2019 (COVID-19), can develop cardiac damage due to the virus directly injuring myocardial cells or as part of the systemic inflammatory response to the virus resulting in myocardial oxygen supply/demand mismatch [1] and precipitating vulnerable-plaque rupture, resulting in acute coronary syndrome [2]. In the United States, during the early stages of the pandemic, the Centers for Disease Control and Prevention recommended deferral of elective coronary angiography and percutaneous coronary intervention (PCI) [3] to maximize hospital capacity. Next, guidelines reinforced primary PCI as the standard of care for ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) patients [4,5]. These guidelines are important, as cardiac involvement in COVID-19 patients is common, and these patients have a worse prognosis than patients without myocardial injury [6–8]. However, there are limited data evaluating outcomes of COVID-19 patients with both troponin elevation and renal dysfunction. In this study, we describe our healthcare system's experience of COVID-19-positive patients with troponin elevation and its impact on renal function. Furthermore, we evaluated how the combination of myocardial injury and renal dysfunction impacts in-hospital clinical outcomes.

*Abbreviations:* COVID-19, coronavirus disease 2019; GFR, glomerular filtration rate; ICD-10, International Classification of Diseases, Tenth Revision; ICU, intensive care unit; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; STEMI, ST-elevation myocardial infarction.

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## 2. Material and methods

We analyzed COVID-19-positive patients who presented to the MedStar Health system (11 hospitals in Washington, DC, and Maryland) during the pandemic era. The "pandemic era" (our study time period) was identified as March 1 through September 30, 2020. The positive test for the infection was based on polymerase-chain-reaction testing and the patient having respiratory symptoms and/or chest x-ray or computed tomography findings. We then divided COVID-19-positive patients into 2 cohorts based on whether or not troponin-I was elevated. Investigators identified significant presence of troponin-I as an elevation ≥1.0 ng/mL. In our healthcare system, this equates to 5 times the upper limit of normal. For our analysis, the maximum troponin-I during the patient's hospitalization was included. The study was conducted with the approval of our institutional review board.

Baseline characteristics (age, sex, gender, race) 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, intensive-care-unit (ICU) admission, ICU length of stay, and use of ventilation were compared between the two groups. The primary outcome was the incidence of acute kidney injury and the minimum glomerular filtration rate (GFR). Acute kidney injury was identified using International Classification of Diseases, Tenth Revision (ICD-10) codes. Renal dysfunction was defined as GFR ≤30 mL/min. Secondary outcomes included in-hospital mortality, ICU admissions, time on ventilator, and length of stay.

In addition, we evaluated clinical outcomes based on the presence, or absence, of troponin elevation and evidence of renal dysfunction. This was done by dividing the COVID-19-positive patient population into 4 cohorts: 1) Troponin Elevation and Renal Dysfunction, 2) Troponin Elevation and Normal Renal Function, 3) No Troponin Elevation and Renal Dysfunction, and 4) No Troponin Elevation and Normal Renal Function.

### 2.1. Statistical analysis

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 test was used to compare categorical variables. Statistical significance was considered as a *p*-value <0.05 for all study endpoints. SAS 9.4 (SAS Institute Inc., Cary, North Carolina) was used for statistical analyses.

## 3. Results

In our medical system, 3386 COVID-19-positive patients were admitted from March 1 through September 30, 2020. Of these patients, 195 had troponin elevation (5.76%). Baseline characteristics can be found in Table 1. The majority of patients were men (51.1%), with a mean age of 62 ± 16 years. Patients with troponin elevation tended to be older than those without. Co-morbidities, including hyperlipidemia, diabetes, chronic kidney disease, hemodialysis, asthma, chronic obstructive pulmonary disease, coronary artery disease, stroke, congestive heart failure, and atrial fibrillation, were more frequently seen in patients with COVID-19 and concomitant troponin elevation. In the troponin-elevation arm, the mean minimum troponin was 2.6 ± 9.94 ng/mL, and the mean maximum elevation was 13.82 ± 35.12 ng/mL (Table 1).

In terms of our primary outcome, patients with COVID-19 and troponin elevation had a higher rate of renal dysfunction (Table 2). Acute kidney injury was seen in 48.7% of patients with troponin elevation versus 28.5% of patients without troponin elevation ($p < 0.001$). Furthermore, GFR ≤30 mL/min was seen in 58.5% of patients with troponin elevation as compared to only 23.4% of patients without troponin elevation ($p < 0.001$). Conversely, GFR ≥60 mL/min was seen in only 21.5% of patients troponin elevation as compared to 55.9% of patients without troponin elevation ($p < 0.001$) (Table 2).

With regard to our secondary endpoint, in-hospital mortality was significantly higher (53.8%) in COVID-19-positive patients with concomitant troponin elevation than in COVID-19-positive patients without troponin elevation (14.5%; $p < 0.001$) (Table 3). Our data demonstrate that the majority of COVID-19-positive patients with troponin elevation were admitted into the ICU, and over half required mechanical ventilation.

Finally, after the COVID-19 patient population was divided into 4 subgroups, based on the presence of absence of troponin elevation or renal dysfunction, the following outcomes were observed. The combination of both troponin elevation and renal dysfunction carried the worst prognosis, with an in-hospital mortality rate of 57.9%, 76.8% requiring an ICU admission, and 63.2% requiring mechanical ventilation.

**Table 1**
Baseline characteristics. Baseline characteristics of all COVID-19-positive patients during the pandemic era overall and based on troponin elevation.

| | Overall | Troponin elevation | No troponin elevation | p-Value |
|---|---|---|---|---|
| | n = 3386 | n = 195 | n = 3191 | |
| Demographics | | | | |
| Age (years) ± SD | 61.9 ± 16.4 | 68.6 ± 14.5 | 61.45 ± 16.4 | <0.001 |
| Male | 51.1% | 53.8% | 50.9% | 0.428 |
| Ethnicity | | | | |
| Caucasian | 17.7% | 21.8% | 17.4% | 0.124 |
| African American | 61.6% | 66.3% | 61.3% | 0.165 |
| Asian | 1.0% | 0.5% | 1.1% | 0.474 |
| Native American | 0.2% | 0.5% | 0.2% | 0.417 |
| Other | 19.5% | 10.9% | 20.0% | 0.002 |
| Co-Morbidities | | | | |
| Hypertension | 52.9% | 47.7% | 53.2% | 0.135 |
| Hyperlipidemia | 41.8% | 56.9% | 40.9% | <0.001 |
| Diabetes | 44.3% | 53.3% | 43.8% | 0.009 |
| Chronic kidney disease | 25.1% | 42.1% | 24.0% | <0.001 |
| Hemodialysis | 8.1% | 19.5% | 7.5% | <0.001 |
| Chronic obstructive pulmonary disease | 9.8% | 13.8% | 9.5% | 0.048 |
| Asthma | 9.8% | 4.6% | 10.1% | 0.013 |
| Coronary artery disease | 14.5% | 37.4% | 13.1% | <0.001 |
| Stroke | 9.4% | 19.5% | 8.8% | <0.001 |
| Congestive heart failure | 16.5% | 39.5% | 15.1% | <0.001 |
| Atrial fibrillation | 10.1% | 19.0% | 9.6% | <0.001 |
| Prior pulmonary embolism | 0.1% | 0.0% | 0.1% | 0.727 |
| Troponin max ng/mL | 0.85 ± 9.00 | 13.82 ± 35.12 | 0.06 ± 0.14 | <0.001 |
| Troponin min ng/mL | 0.18 ± 2.45 | 2.6 ± 9.94 | 0.03 ± 0.08 | <0.001 |

**Table 2**
Primary outcome. Renal function based on troponin elevation, kidney function, and glomerular filtration rate of COVID-19-positive patients during the pandemic era overall and based on troponin elevation.

| | Overall | Troponin Elevation | No Troponin Elevation | p-Value |
|---|---|---|---|---|
| | n = 3389 | n = 195 | n = 3194 | |
| Acute kidney injury[a] | 29.6% | 48.7% | 28.5% | <0.001 |
| Glomerular filtration rate ≤ 30 mL/min/1.73m$^2$ | 25.4% | 58.5% | 23.4% | <0.001 |
| Glomerular filtration rate ≥ 60 mL/min/1.73m$^2$ | 53.9% | 21.5% | 55.9% | 0.226 |

[a] Acute kidney injury diagnosis based on International Classification of Diseases (ICD) code.

**Table 3**
Secondary outcomes. In-hospital outcomes of COVID-19-positive patients during the pandemic era overall and based on troponin elevation.

| | Overall | Troponin elevation | No troponin elevation | p-Value |
|---|---|---|---|---|
| | n = 3389 | n = 195 | n = 3194 | |
| Overall in-hospital mortality | 16.8% | 56.9% | 18.0% | <0.001 |
| Intensive care unit admission | 33.8% | 74.4% | 31.3% | <0.001 |
| Ventilator requirement | 20.2% | 56.9% | 18.0% | <0.001 |
| Length of stay in intensive care unit (days) (± SD) | 9.70 ± 10.87 | 8.80 ± 9.39 | 9.83 ± 11.07 | 0.226 |

The second worst combination was the presence of troponin elevation and normal renal function followed by no troponin elevation and renal dysfunction. As expected, the combination of no troponin elevation and normal renal function carried the best prognosis, with an in-hospital mortality rate of 9.4%, and with only 25.4% requiring ICU admission and 13.0% requiring mechanical ventilation (Table 4; Fig. 1).

## 4. Discussion

The primary findings of our analysis suggest that COVID-19-positive patients with concomitant troponin elevation have a significantly increased risk of renal dysfunction. This leads to worse in-hospital outcomes, including in-hospital mortality, ICU admission, and the need for mechanical ventilation. In addition, having the combination of both troponin elevation and renal dysfunction carries the worst in-hospital prognosis as compared to the presence or absence of either of the two.

It is known that patients with pre-existing co-morbidities are at an increased risk of SARS-CoV-2-related adverse outcomes [9,10]. It is not surprising that in our study, underlying co-morbidities (hyperlipidemia, diabetes, asthma, known coronary artery disease, stroke, congestive heart failure, and atrial fibrillation) were more frequently seen in COVID-19-positive patients with troponin elevation. What is more interesting is that COVID-19-positive patients with troponin elevation can possibly represent an even sicker cohort, as they have a higher rate of renal dysfunction.

Furthermore, 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.) [11]. Our analysis demonstrates that troponin and renal function should be checked along with the above laboratory data, irrespective of classic cardiac symptoms. If a provider is concerned about a COVID-19-positive patient, it is imperative that inflammatory markers, including troponin, are checked, as this can be an indication of both infection and overall severity of the illness [12]. In addition, providers should consider the patient's renal function (GFR), as this can be a further predictor of adverse outcomes. Alternatively, if a patient has a history of chronic kidney disease, cardiac involvement should be ruled out given the higher prevalence of chronic kidney disease seen in the troponin-elevation cohort. The increased rate of in-hospital mortality for patients who have troponin elevation and renal dysfunction probably reflects that these patients tend to be older, with more co-morbidities. In addition, these patients tend to be admitted to the ICU more frequently and require intubation.

One theory behind the association between myocardial and renal involvement in COVID-19 patients is the pathological process of microthrombi [13]. In this analysis, Guagliumi et al. examined reports of autopsies that demonstrated that COVID-19 patients presenting with STEMI do not always have plaque rupture within the epicardial blood vessel. Up to 50% of these patients were found to have a myocarditis-like picture. When pathology was performed, they were found to have cardiac microthrombi, which contribute to myocardial

**Table 4**
Overall in-hospital outcomes in COVID-19 patients based on the presence or absence of troponin elevation and renal dysfunction.

| | Troponin elevation and renal dysfunction | Troponin elevation and normal renal function | No troponin elevation and renal dysfunction | No troponin elevation and normal renal function | p-Value |
|---|---|---|---|---|---|
| | n = 95 (2.81%) | n = 100 (2.95%) | n = 909 (26.85%) | n = 2282 (67.40%) | |
| Overall in-hospital mortality | 57.9% | 50.0% | 27.4% | 9.4% | <0.001 |
| Intensive care unit admission | 76.8% | 74.0% | 46.4% | 25.3% | <0.001 |
| Ventilation requirement | 63.2% | 51.0% | 30.6% | 13.0% | <0.001 |
| Length of stay in intensive care unit (days) (± SD) | 10.38 ± 10.50 | 7.24 ± 7.91 | 11.14 ± 12.29 | 8.87 ± 9.98 | 0.002 |

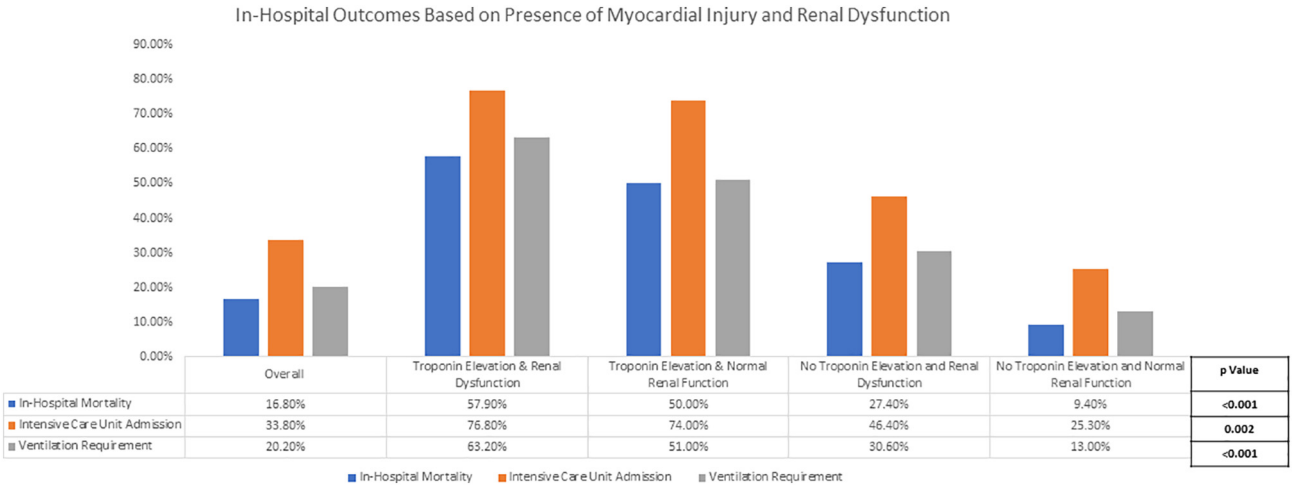


**Fig. 1.** Overall in-hospital outcomes in COVID-19 patients based on the presence or absence of troponin elevation and renal dysfunction.

damage and cell death. One could theorize that these microthrombi might occur in the glomeruli of the kidney as well, leading to cell death and renal dysfunction. Future studies are needed to validate this hypothesis and potential treatment options, such as anticoagulation, in COVID-19 patients with myocardial injury and renal dysfunction.

### *4.1. Limitations*

There are limitations to our study. 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 whether a patient underwent coronary angiography or had a subsequent PCI, which would have allowed us to identify those patients who had a true plaque rupture as the etiology of their acute myocardial infarction as opposed to another etiology, such as myocarditis or stress-induced cardiomyopathy [14]. We also did not capture how these patients were treated (pharmacology, mechanical support, etc.). Finally, our data capture patients in the Mid-Atlantic region of the US, where the pandemic was most impactful in March and April 2020. Our findings may not represent the broader US outcome data.

## 5. Conclusions

Patients with COVID-19 and troponin elevation are at a higher risk for worsening renal function and subsequent worse in-hospital clinical outcomes. Furthermore, the combination of troponin elevation and renal dysfunction carries the worst prognosis. Efforts should be focused on early recognition, evaluation, and treatment of patients with COVID-19 and both troponin elevation and renal dysfunction.

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## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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