



Factors associated with hospital readmissions among patients with COVID-19: A single-center experience

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Abstract

Identify factors associated with readmission after an index hospital admission for coronavirus disease 2019 (COVID-19) infection in a single center serving an underserved and predominantly minority population. This retrospective descriptive study included 275 patients who tested COVID-19 positive via reverse transcriptase-polymerase chain reaction assay at our institution and who survived the index hospitalization. The main outcomes were 1- and 6-month readmission rates after an index hospitalization for COVID-19. The mortality rate among the readmitted patients was also determined. Factors independently associated with readmission were investigated using multivariable logistic regression. A final sample of 275 patients was included. The mean age was 64.69 ± 14.64 (SD), 133 (48%) were female and 194 (70%) were African American. Their chronic medical conditions included hypertension 203 (74%) and diabetes mellitus 121 (44%). After the hospitalization, 1-month readmission rate was 7.6%, while 6-month readmission rate was 24%. Nine percent of patients who were readmitted subsequently died. Coronary artery disease (CAD) was significantly associated with 6-month readmission odds ratio (OR), 2.15 (95% confidence interval [CI]: 1.04–4.44; $p = 0.039$) after adjustment for age, gender, ethnicity, and comorbidities. Readmissions were due to cardiac, respiratory, and musculoskeletal symptoms. Hispanic ethnicity was associated with increased readmission OR, 3.16 (95% CI: 1.01–9.88; $p = 0.048$). No significant difference was found between inflammatory markers or clinical outcomes during the index hospitalization among patients who were readmitted compared to those who were not. A significant number of patients hospitalized for COVID-19 may be readmitted. The presence of CAD is independently associated with high rates of 6-month readmission.

KEYWORDS

COVID-19, mortality, novel coronavirus, readmission

1 | INTRODUCTION

Based on the World Health Organization records, the most number of deaths during the first peak in April 2020 was already exceeded by December 11, 2020, with a record of 13,141 deaths in a day worldwide.¹ As the pandemic continues to unfold, the world is learning more about the long-term outcomes after a coronavirus disease 2019 (COVID-19) infection. However, as of now, literature is scarce regarding the long-term outcomes among patients who had COVID-19. There is also limited data on the characteristics of patients who get readmitted after an index hospitalization for COVID-19. Looking into this is significant, as readmissions may further pull resources from an already overwhelmed healthcare system.² Information on long-term outcomes may help guide physicians and even policy makers in making decisions on discharge, hospital-capacity planning, and possibly patient monitoring after discharge for COVID-19 patients.³ Readmission rates remain an important indicator of patient safety and a hospital's quality performance.⁴ Thus, this study aims to identify factors associated with rates of readmission after hospital admission for COVID-19. Understanding these patterns can help guide clinicians as they manage factors that can help curb readmissions, especially in a high-risk patient population.

2 | PATIENTS AND METHODS

2.1 | Study design, participants, and data collection

This study was a single center retrospective analysis of all patients ≥ 18 years of age who were admitted to Einstein Medical Center Philadelphia from March 1 to April 24, 2020, with a confirmed diagnosis of COVID-19 via reverse transcriptase-polymerase chain reaction (RT-PCR) assay performed on nasopharyngeal swab specimens. Our institution is an inner-city tertiary hospital serving predominantly African American patients as well as patients from a lower socioeconomic stratum. There are other nearby hospitals in the area but usually emergency medical services bring patients to the hospital nearest their current location. In-house COVID-19 PCR tests were done using Abbott m2000. A single positive COVID-19 PCR test was considered confirmatory. This time period was selected as it was the first COVID-19 surge in our area. Patients receiving Remdesivir or convalescent plasma were not included in the analyses as these treatments were still relatively new at the time of initial cohort data collection and utilization during the early phase of the pandemic was nonexistent. Data on patient readmissions were collected retrospectively at 1-month (30 days) and 6-month (180 days) postindex admission. This spanned the time period from March 2020 to October 31, 2020 and 6-month outcomes were only obtained up to this date. Final data extraction was done at the end of the desired follow-up period starting from November 2020. Demographic and clinical factors, including age, gender, race, and comorbidities were extracted from electronic medical records with a standardized data

collection form. Laboratory and clinical parameters were all derived during the very first index admission for COVID-19. Laboratory admission values were the first values obtained at the time of the index admission while peak laboratory values were the highest values recorded across the entire index admission. This study was approved by the institutional review board.

2.2 | Statistical analysis

Demographic variables were presented using descriptive statistics and frequencies. Categorical variables were analyzed with χ^2 testing. Patients were stratified according to those with readmission events and those without. Demographic, laboratory, and clinical variables were tabulated. χ^2 was used to analyze the association between categorical variables while Independent *t* test was used to test differences between continuous variables. Mann-Whitney *U* test was used to identify differences between skewed variables. Multivariable logistic regression was used to determine factors associated with both 1- and 6-month readmissions. Comorbidities found to have trends toward significant differences ($p < 0.3$) in univariate analyses were selected to be included in the multivariable model together with other common demographic variables. Odds ratios (ORs) and 95% confidence intervals (CIs) were used and are presented when appropriate. A *p* value of less than 0.05 was considered significant. All analyses were performed using IBM's SPSS Statistics for Windows, Version 23.0.

3 | RESULTS

A total of 355 hospitalized patients were evaluated and tested positive via RT-PCR for COVID-19 during the first COVID-19 peak in our institution from March to April 2020. We excluded 80 patients who died during the index hospitalization limiting the readmission analysis to a final sample of 275 patients. The mean age ($\pm SD$) was 64.69 ± 14.64 , 133 (48%) were female and 194 (70%) were African American. Chronic medical conditions of these patients included hypertension 203 (74%), diabetes mellitus 121 (44%), chronic obstructive pulmonary disease (COPD) 33 (12%), and asthma 22 (8%) (see Table 1 for other demographic, clinical, and laboratory data).

Of the 275 patients, 21 (7.6%) were readmitted within 1 month while 66 (24%) were readmitted within 6 months of the initial hospitalization. Six (9%) of the patients who were readmitted subsequently died. Of the reasons for readmissions, cardiac causes were the most common at 14 (21%) followed by respiratory 12 (18%), musculoskeletal 12 (18%), and neuropsychiatric causes 12 (18%). Infectious causes other than COVID-19 were 9 (14%) with other causes at 7 (11%). Of the various comorbidities, there was a significantly higher rate of coronary artery disease (CAD) among those readmitted versus those without readmission (32% vs. 15%, $p = 0.007$) while being on hemodialysis had a trend toward being significant (17% vs. 9%, $p = 0.07$).

TABLE 1 Demographic and clinical factors among patients with and without readmissions

	Readmission (n = 66)	No readmission (n = 209)	p value
Age (mean ± SD)	66.92 ± 14.45	63.98 ± 14.67	0.155
Gender, n (%)			
Female	35 (53)	98 (47)	0.400
Ethnicity, n (%)	0.300		
African American		46 (69)	148 (71)
Caucasian		7 (11)	15 (7)
Hispanic		10 (15)	23 (11)
Other		3 (5)	23 (11)
Comorbidities			
BMI (mean ± SD)	29.79 ± 9.26	29.90 ± 9.21	0.931
COPD	11 (17)	22 (11)	0.195
Asthma	5 (8)	18 (9)	1.000
Heart Failure	14 (21)	26 (12)	0.107
Atrial fibrillation	10 (15)	21 (10)	0.267
Chronic kidney disease	13 (20)	31 (15)	0.342
End-stage renal disease on dialysis	11 (17)	18 (9)	0.070
Coronary artery disease	21 (32)	32 (15)	0.007
Hypertension	51 (77)	153 (73)	0.629
HIV	1 (2)	4 (2)	1.000
Clinical and lab parameters (mean ± SD)			
FiO ₂ % requirement on admission	21 (21–29)	28 (21–33)	0.012
Serum ferritin on admission	579 (194–1707)	713 (334–1685)	0.257
Peak ferritin	1061 (244–2907)	1006 (378–2628)	0.563
D-Dimer on admission	1855 (835–3292)	1580 (813–3262)	0.678
Peak D-dimer	3110 (1490–5080)	2460 (1188–5895)	0.637
CRP on admission	78 (42–140)	121 (51–180)	0.122
Peak CRP	133 (53–193)	141 (71–216)	0.597
Procalcitonin	0.16 (0.07–0.71)	0.19 (0.08–0.50)	0.710
Peak procalcitonin	0.33 (0.09–1.52)	0.19 (0.09–0.67)	0.533
LDH on admission	320 (245–427)	397 (256–530)	0.062
Peak LDH	386 (306–639)	480 (335–634)	0.233
COVID-19 treatment			
Hydroxychloroquine	30 (46)	122 (58)	0.088
Steroids	13 (20)	45 (22)	0.863
Tocilizumab	4 (6)	23 (11)	0.343
Clinical outcomes			
Need for RRT/HD	10 (15)	20 (10)	0.256
Need for vasopressors	8 (12)	16 (8)	0.316
Need for intubation	9 (14)	18 (9)	0.240

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; HD, hemodialysis; HIV, human immunodeficiency virus; LDH, lactate dehydrogenase; RRT, renal replacement therapy.

In terms of laboratory and clinical parameters, these were all obtained and recorded during the very first index admission for COVID-19. Patients who had readmissions had significantly lower fractional inspired oxygen (FiO₂) requirements during the index admission (21% vs. 28%, *p* = 0.012) while no significant differences between the inflammatory markers, including ferritin, D-dimer, C-reactive protein, procalcitonin, and lactate dehydrogenase, were identified. There were also no significant associations between the need for vasopressors, intubation and mechanical ventilation, and renal replacement therapy among patients who were readmitted compared to those who were not (see Table 1).

To explore further factors related to readmission within our institution, multivariable logistic regression was done to look for factors independently associated with 1- and 6-month readmission risk. African American ethnicity was associated with fewer 1-month readmissions OR 0.37 (95% CI: 0.14–0.98; *p* = 0.045) while CAD was significantly associated with over two-fold higher odds of 6-month readmissions OR 2.15 (95% CI: 1.04–4.44; *p* = 0.039). In a subgroup analysis looking at ethnicity, only Hispanic ethnicity was significantly associated with higher rates of 1-month readmissions OR 3.16 (95% CI: 1.01–9.88; *p* = 0.048) with over 24% of Hispanic patients subsequently readmitted within the first 30 days (Table 2).

4 | DISCUSSION

The results of this single-center retrospective study showed significant readmission rates of 7.6% and 24% within the first and sixth months, respectively. Nine percent of patients who were readmitted subsequently died. These findings are similar to the study by Donnelly et al. who reported a 19.9% 2-month readmission rate among veterans affairs patients who survived their initial COVID-19 hospitalization.⁵ Meanwhile a large-scale study by Lavery et al.⁶

reported a 9% (9504 out of 106,543 patients) readmission rate within two months of discharge, while a study by Atalla et al. showed a readmission rate of 6.8% after a median of 5 days.⁷ So far, this study is one of the few to showcase more long-term 6-month readmission rates (Figure 1).

Looking at factors associated with readmissions, our study found an independent association of increased odds of readmission among patients with CAD. In fact, there was a two-fold increase in 6-month readmission in these patients. This also somewhat coincides with the finding that patients who were readmitted had somewhat higher troponin levels during the index admission, although this was not statistically significant likely due to the small sample size. So far, this study is one of the first to present the association of CAD with higher readmission risk after an initial hospitalization due to COVID-19. There have not been many studies on hospital readmissions, most of which showed that the presence of cardiopulmonary and metabolic comorbidities, including COPD, heart failure, hypertension, diabetes mellitus with chronic complications, chronic kidney disease, malignancy, obesity, liver disease, and substance abuse, have higher rates of readmission.^{5–7} In a small study in Turkey, it was mentioned that malignancy was significantly associated with increased readmission risk,⁴ while in a study in Spain, an immunocompromised state was also linked to readmissions.⁸ The results of our study concur with these studies as some of the abovementioned comorbidities are also risk factors for CAD. COVID-19 infection per se can be potentially associated with myocardial injury as the virus may gain access via angiotensin-converting enzyme 2 receptor expression in the coronary vessels and myocardium. This may lead to local inflammation, hypercoagulability, and thrombosis. In addition, hypoxia from the primary disease process itself can also bring about a supply-demand mismatch potentially leading to a type II myocardial infarction.⁹ As the world faces the upslope of the second wave of COVID-19, this study provides valuable insight on the need for

TABLE 2 Multivariable logistic regression looking at factors associated with 1- and 6-month readmissions among patients with COVID-19

Characteristics	1-Month readmission odds ratio (95% CI)	<i>p</i> value	6-Month readmission odds ratio (95% CI)	<i>p</i> value
Age	1.03 (0.99–1.07)	0.130	1.01 (0.99–1.03)	0.553
Male	Referrant		Referrant	
Female	0.90 (0.35–2.30)	0.823	1.17 (0.66–2.08)	0.592
Non-African American	Referrant		Referrant	
African American	0.37 (0.14–0.98)	0.045	1.04 (0.57–1.92)	0.891
COPD	1.06 (0.26–4.30)	0.941	1.55 (0.68–3.58)	0.299
HF	1.13 (0.30–4.27)	0.860	1.10 (0.47–2.54)	0.833
Atrial fibrillation	0.41 (0.08–2.14)	0.288	1.15 (0.48–2.78)	0.754
ESRD on HD	2.59 (0.68–9.85)	0.162	1.38 (0.55–3.47)	0.500
CAD	1.98 (0.67–5.89)	0.220	2.15 (1.04–4.44)	0.039

Abbreviations: CAD, coronary artery disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; ESRD, end-stage renal disease; HD, hemodialysis; HF, haemofiltration.

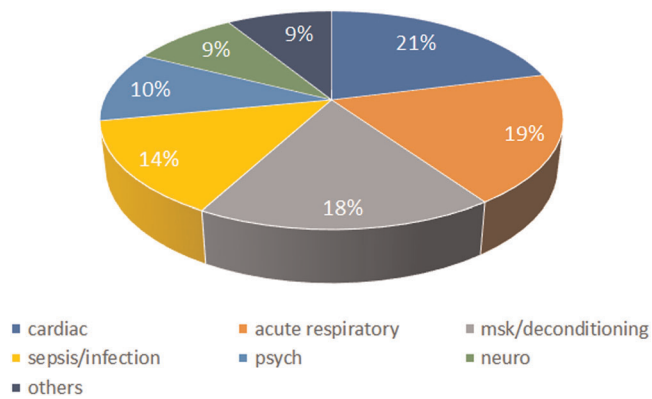


FIGURE 1 Causes of readmissions after the index hospitalization for COVID-19. COVID-19, coronavirus disease 2019

aggressive and optimal management of cardiopulmonary and metabolic comorbidities to help potentially decrease hospital readmissions and reduce the overall burden on the healthcare system.

Cardiac causes, mainly heart failure exacerbation and acute coronary syndrome, were the most common reasons for readmission followed by respiratory and musculoskeletal conditions. This can partly be accounted for by the higher rates of obesity and cardiovascular comorbidities, such as CAD, heart failure, and chronic kidney disease, predisposing to cardiac causes of readmission. Also, the majority of patients in our study were African American (70%). Genetic predisposition, metabolic risk factors, such as hypertension and dyslipidemia, together with socioeconomic factors can predispose these patients to a higher risk of cardiovascular disease.¹⁰ Our findings are somewhat consistent with the other studies by Leijte et al.,³ Atalla et al.,⁷ and Somani et al.,¹¹ although respiratory distress was cited as the most common cause for readmission. Given these findings, it may be justifiable to help establish closer follow-up or surveillance, especially for these high-risk patients with multiple comorbidities and cardiovascular disease after admission for COVID-19. Studies have shown that patients may develop cardiovascular complications, such as pericarditis and myocardial infarction several weeks after acute COVID-19.¹² This implies a management challenge, especially for the primary care setting to help differentiate symptoms of chest pain, shortness of breath, and cough as part of postacute COVID-19 symptoms versus actual cardiopulmonary complications.¹³ Therefore, closer surveillance and timely referral to specialist services and rehabilitation are crucial.¹³

In a subgroup analysis, readmission rates were surprisingly higher among Hispanics relative to other ethnicities; this could potentially explain seemingly lower odds of readmission associated with African American ethnicity. Prevalence of cardiometabolic disease risk factors, such as diabetes mellitus, were found to be higher among Hispanics and Mexican Americans, which can potentially lead to higher rates of cardiovascular disease.¹⁴

In this analysis, the severity of COVID-19 disease during the index admission showed no significant association with hospital readmissions. There were no significant differences in inflammatory

markers and clinical outcomes, such as the need for intubation and the need for renal replacement therapy, among those readmitted compared to those who were not. These findings are in contrast to previous studies by Uyaroglu et al.⁴ and Parra et al.⁸ wherein patients with higher O₂ requirements and D-dimer levels during the index hospitalization were found to have higher rates of readmission. Differences in sample size, duration of follow-up, socioeconomic factors, and comorbidities, and lack of capturing of hospitalizations readmitted to other institutions, may potentially explain this finding. Longer follow-up farther along the course after hospital admission for COVID-19 may allow for better assessment of the influence of patient comorbidities and severity of the initial COVID-19 infection on readmission rates and outcomes.

5 | LIMITATIONS

This study is limited by the nature of its retrospective single-center descriptive design. Other factors that may possibly influence hospital readmissions, including compliance to outpatient follow-up and medications, were not taken into account. The majority of our study population were considered high risk with multiple comorbidities and were predominantly of African American ethnicity, which may limit the generalizability of findings. This may also explain the higher rates of hospital readmissions, which may not necessarily be comparable to other areas. Recording of comorbidities was based on actual manual chart review, which takes into consideration the diagnoses from the primary team, history, laboratory values, and previous diagnostic tests. Due to the relatively small sample size, this study might not be powered to detect differences in outcomes in patients who needed mechanical ventilation or who received other specific interventions, such as corticosteroids. Patients who were readmitted outside of the hospital system may potentially be missed and may also influence the results of the study. At the time that this study was conducted, the newer COVID-19 variants were not yet recognized, and as such, the disease patterns of the newer variants would be beyond the scope of this study. The follow-up period of this study was only 6 months and longer-term outcomes and effects may need to be studied further. However, this study remains hypothesis generating as to the role of comorbidities and ethnicity in postdischarge outcomes among patients with COVID-19. This study perhaps is one of the few with more long-term 6-month readmission data.

CONCLUSION

A significant number of patients hospitalized for COVID-19 get readmitted for several reasons. The presence of coronary artery disease seems to be independently associated with high rates of 6-month readmissions.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

All of the authors contributed to the conceptualization of this study project, including determining which variables to collect and account for: Glenn Eiger and Janani Rangaswami assumed a supervisory role in the final editing of this paper. Geneva Guarin, Kevin Bryan Lo, Ruchika Bhargav, Grace Salacup, Ammaar Wattoo, Jean-Gabriel Coignet, and Robert DeJoy III were involved in data collection. Geneva Guarin, Kevin Bryan Lo, Ruchika Bhargav, Grace Salacup, Zurab Azmaiparashvili, and Gabriel Patarroyo-Aponte played a role in the interpretation and analysis of data, and in writing up of the preliminary version of this paper.

DATA AVAILABILITY STATEMENT

The data supporting the results of this study are available upon request from the corresponding author. The data are not publicly available due to privacy and ethical restrictions.

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