Study of early and late readmissions with COVID-19: A retrospective analysis

Tariq Z, Vahia A, Grover K, Ignacio S, Kaur I, Talari G, Chaudhry Z, Bhargava P

Henry Ford Health System, Michigan

Abstract

- Michigan was one of the severely impacted regions during the initial COVID-19 surge[1]
- An institutional protocol with early corticosteroids to treat COVID-19 patients requiring supplemental oxygen was implemented[2]
- We sought to study characteristics of these patients who were readmitted with infectious and non-infectious complications

Methods

- A retrospective analysis of 21 COVID-19 readmitted patients initially admitted between 3/10/2020 and 4/20/2020 (early 0-7, late 8-30 days) was done
- Total of 455 COVID-19 patients, confirmed by a positive nasopharyngeal RT-PCR were admitted during this time period
- Demographic data, clinical characteristics, laboratory and radiographic results, treatment, outcomes of initial and the subsequent admissions were compared among the early and late readmission groups
- Univariate and logistic regression analysis were performed to study the risk factors associated with early readmission and worsening of COVID-19 pneumonia
- Secondary analyses were performed comparing worsening COVID-19 pneumonia with other readmission diagnoses

Table 1. Readmission Diagnoses in early and late readmissions of COVID-19 patients

Readmission Diagnosis COVID-19 Related	Early n	Late n
Worsening of COVID-19 pneumonia	7	0
COVID-19 pneumonia resolving	2	2
Secondary bacterial infections	1	0
Pulmonary Embolism	1	0
Arterial Thrombosis	0	1

Readmission Diagnosis COVID-19 unrelated	Early n	Late n
Infections	4	3
Gout	1	0
Atrial arrhythmia	0	2
Congestive heart failure	1	2
Ascites	0	1
Failure to thrive	1	1
Acute Kidney Injury	2	2

Table 2a. Characteristics of early versus late readmissions of COVID-19 patients

Characteristic	Early Readmits N = 14	Late Readmits N = 7	P Value
Median Age (IQR)	75 (59-81)	65 (49-86)	0.9404
Male Gender N (%)	8 (57)	5 (71)	0.6557
Median BMI (IQR)	28.6 (25-32.4)	26 (23-32.6)	0.3509
Length of Stay First Admission	6.5 (3-9)	6 (5-7)	0.9699
Median Days of Symptoms Prior to Presentation (IQR)	6.5 (3-8)	7 (3-7)	0.7027
Readmission Symptoms			
Fever	3 (21.4)	0 (0)	0.5211
Cough	8 (57.1)	2 (28.6)	0.3615
Shortness of Breath	10 (71.4)	3 (42.9)	0.3458
Worsening O2 Requirement	9 (64.3)	6 (85.7)	0.6126
Labs			
D-Dimer Discharge	1.14 (0.57-1.68)	2.95 (1.34-8.6)	0.0305
D-Dimer Readmit	1.2 (1.07-2.26)	3 (1.44-3.40)	0.3429
CRP Discharge	2.15 (0.5-4.3)	1.4 (0.7-4.4)	0.8805
CRP Readmit	7 (1.4-16.6)	3.7 (1.2-6)	0.2035
Ferritin Discharge	417.5 (219-895)	503 (52-678)	0.9109
Ferritin Readmit	572 (330-827)	341 (111-547)	0.2035
ALC Discharge	0.85 (0.5-1.67)	0.5 (0.2-1.1)	0.2458
ALC Readmit	0.75 (0.6-1.6)	0.7 (0.5-1.2)	0.7649
Initial Therapies			
Solumedrol Given	12 (85.7)	6 (85.7)	1
Solumedrol Dose	80 (64-112)	80 (48-80)	0.1856
Hours to Solumedrol Administration	13.5 (4-19)	22.5 (6-32.3)	0.2919
Solumedrol Duration	4.5 (3-6)	6 (5-7)	0.4297
Discharged on O2	2 (14.29)	1 (14.29)	1
Readmitted requiring NC	7 (50)	6 (85.7)	0.5265
Readmit Requiring HFNC	1 (7.14)	0 (0)	
Readmitted and Intubated	1 (7.14)	0 (0)	
Readmission Treatment			
Readmission Pulmonary Related	10 (71.4)	2 (28.6)	0.1588
Diagnosis Worsening COVID	7 (50)	0 (0)	0.0468
Second Round Steroids	14 (100)	0 (0)	<.0001

Abbreviations: BMI, body mass index; O2, oxygen; CRP, C reactive protein(mg/dL); Ferritin (ng/mL); D-dimer (ug/mL) ALC, absolute lymphocyte count; NC, nasal canula; HFNC, high flow nasal canula; COVID, Novel Corona virus disaease 2019.

Table 2 b. Comparison of lab parameters of worsening COVID-19 pneumonia patients versus other readmissions

COVID-19 readmissions	Worsening COVID (N=7)	Other readmissions (N=14)	P Value
D-Dimer Discharge	0.63 (0.56-1.04)	2.21 (1.34-5.56)	0.0032
D-Dimer Readmit	1.22 (1.07-1.79)	2.82 (1.11-3.40)	0.3416
D-Dimer Change (Final-Initial)	0.56 (0.17 (1.12)	-0.14 (-1.78 - 0.85)	0.2048
CRP Discharge	3.1 (0.6-5.5)	1.2 (0.5-4.3)	0.4301
CRP Readmit	13.2 (7-19.5)	1.7 (1.05-5.7)	0.006
CRP Change	9.5 (2.1-14)	0.95 (0.15-2.55)	0.0312
Ferritin Discharge	244 (219-429)	588 (155-895)	0.4785
Ferritin Readmit	495 (330-936)	454 (99-734)	0.422
Ferritin Change	99 (-85-331)	-11 (-160-55.5)	0.1632
ALC Discharge	0.58 (0.5-0.8)	1 (0.4-1.67)	0.5492
ALC Readmit	0.6 (0.4-0.7)	1.05 (0.5-1.79)	0.1348
ALC Change	-0.1 (-0.18-0.1)	0.3 (0.1-0.4)	0.0275

Table 3. Univariate and multivariate analyses of readmissions

Univariate Analysis: Odds of Early Readmission				
Variable	OR	Lower CI	Upper CI	P Value
Methylprednisolone Given First Admission	1	0.075	13.367	1
Hours to First Methylprednisolone Dose	0.959	0.892	1.03	0.2508
Methylprednisolone Duration First Admission	0.901	0.633	1.284	0.5656
Age - 1 Year Increase	1.007	0.953	1.064	0.8062
Male Sex	0.533	0.076	3.756	0.528
Length of Stay Previously (Days)	1.07	0.841	1.361	0.583
CRP at First Discharge - 1 Point Increase	1.117	0.825	1.512	0.4751
Multivariate Analysis: Odds of Readmission For Worsening COVID-19 Pneumonia				
Variables	OR	Lower CI	Upper CI	P Value
CRP at Discharge - 1 Point Increase	1.226	0.678	2.215	0.5007
Methylprednisolone Duration - 1 Day Increase	1.361	0.595	3.115	0.4657
Age - 1 Year Increase	1.033	0.953	1.119	0.4318
Male Sex	0.138	0.004	4.695	0.2714
Length of Stay First Admission - 1 Day Increase	0.303	0.098	0.936	**0.0381**

Table 3: Univariate and Multivariate Analysis of Readmissions

Results

- 4.6% (21/455) patients were readmitted. 14 early and 7 late. Median age was 75 versus 65 years
- 10/14 early readmissions were COVID-19 related and 7/14 were thought to have worsening COVID-19 pneumonia based on clinical picture, laboratory and imaging findings
- All patients with worsening COVID-19 pneumonia presented as early readmissions
- Readmitted patients with worsening COVID-19 related pneumonia had significantly elevated CRP and lower ALC compared to last discharge value
- CRP in patients with worsening COVID-19 pneumonia was elevated at discharge as compared to other readmissions but did not reach statistical significance
- All early readmission were given corticosteroids
- 6/7 late readmissions were short of breath but from reasons other than worsening COVID-19 pneumonia
- A total of 8 readmissions had bacterial coinfections (1/8 was COVID-19 related- MSSA pneumonia)
- Keeping all the other factors in multivariate model equal, each day of increased length of stay lowers the likelihood of admission by at least 7% [7-90%]
- Each increasing day of methylprednisolone duration during the first admission reduced the likelihood of early readmission by approximately 10%, although this did not achieve statistical significance (OR 0.90, 95% CI 0.63-1.2, p=0.56)
- Late readmissions had elevated D-dimer. 1/7 patients had arterial thrombosis requiring embolectomy
- In the worsening COVID-19 pneumonia, D-dimer was lower. CTA of 4 patients was negative for pulmonary embolism, 1 had pre-existing emboli and 2 had no new imaging available

Conclusion

- Optimal dose and duration of glucocorticoids in COVID-19 pneumonia needs to be defined. Patients with clinical improvement but elevated markers of inflammation may need longer duration of corticosteroids to prevent readmissions. A fixed dose and duration may not be applicable to all patients
- Lab values at discharge may help guide treatment at discharge to prevent an early readmission
- Early methylprednisolone in COVID-19 pneumonia was not associated with increased risk of early secondary bacterial infections in the readmitted patients
- Further studies comparing the readmitted patients to a control group of COVID-19 patients who weren't readmitted would be helpful to better discern the reasons leading to readmission
- Increased sample size would provide the statistical power to discern effect of steroids and other therapies in first admission to prevent readmissions
- Elevated D-dimer may reflect a continued prothrombotic state

References

1. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review. *JAMA*. 2020;324(8):782–793. doi:10.1001/jama.2020.12839
2. Raef Fadel, Austin R Morrison, Amit Vahia, Zachary R Smith, Zohra Chaudhry, Pallavi Bhargava, Joseph Miller, Rachel M Kenney, George Alangaden, Mayur S Ramesh, Henry Ford COVID-19 Management Task Force, Early Short-Course Corticosteroids in Hospitalized Patients With COVID-19, *Clinical Infectious Diseases*, , ciaa601, https://doi.org/10.1093/cid/ciaa601
3. Ponti G, Maccaferri M, Ruini C, Tomasi A, Ozben T. Biomarkers associated with COVID-19 disease progression. *Crit Rev Clin Lab Sci*. 2020;57(6):389-399. doi:10.1080/10408363.2020.1770685