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Factors associated with prompt recovery among hospitalised patients with coronavirus disease 2019

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Abstract

Background: Patients who survived hospitalisation for COVID-19 experienced varying durations of illness but the factors associated with prompt recovery are unknown. This study identifies factors differentiating hospitalised patients who recovered promptly versus survived a prolonged course of illness because of COVID-19.

Methods: This was a retrospective study from March-August 2020 of hospitalised adults with COVID-19 which were grouped based on time to recovery: short (≤3 days), intermediate (4-10 days) and prolonged (>10 days). Recovery was defined as resolution of fever, tachypnea, hypotension, extubation and return of mental status at baseline. Multivariate analysis was used to evaluate factors associated with prompt recovery.

Results: Among 508 patients hospitalised for COVID-19, 401 (79%) survived. Of those, prompt recovery (within 3 days) was achieved in 43% (174/401), whereas 23% (92/401) recovered after a prolonged period of >10 days. Overall, median age was 64 years with 73% admitted from home and 25% from a skilled nursing facility. Predictors for prompt recovery upon admission included female sex (OR, 1.8; 95% CI, 1.1-2.7; $P = .01$), no fever (OR, 1.6; 95% CI, 1.1-2.6; $P = .03$), longer time from symptom onset to hospitalisation (OR, 1.1; 95% CI, 1.0-1.1; $P = .001$), no supplemental oxygen (OR, 1.9; 95% CI, 1.2-3.0; $P = .004$), no direct ICU admission (OR, 41.7; 95% CI, 2.4-740.4; $P = .01$) and absence of bacterial co-infections (OR, 2.5; 95% CI, 1.5-4.0, $P = .0003$).

Conclusions: Our study provides relevant data that could help clinicians triage competing resources in health systems that are challenged by the ebb and flow of COVID-19 cases by identifying clinical features of COVID-19 patients who may require less intensive management including avoidance of unnecessary antibacterial therapy.

1 | INTRODUCTION

The novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), caused an initial outbreak in Wuhan, China in December 2019 and has spread resulting in a global pandemic with significant mortality and strain on healthcare operations.[1-3] To date, most of the published work focuses on the epidemiological, clinical, laboratory and radiological characteristics of patients infected with SARS-CoV-2 along with risk factors associated with mortality. Less is known about the varying durations of illness among those who survived hospitalisation for COVID-19. With many health systems challenged by the demands from the ebb and flow of COVID-19 cases

nationwide and globally, our study aims to identify features associated with prompt recovery to help clinicians triage management of patients hospitalised for COVID-19.

What's known

- Patients who survived hospitalisation for COVID-19 experienced varying durations of illness but the factors associated with prompt recovery are unknown.

What's new

- Our study provides relevant data that could help clinicians triage competing resources in health systems that are challenged by the ebb and flow of COVID-19 cases by identifying clinical features of COVID-19 patients who may require less intensive management including avoidance of unnecessary antibacterial therapy.

2 | METHODS

This retrospective cohort study was conducted on adult patients (age ≥18 years) who survived hospitalisation for symptomatic COVID-19 confirmed by positive polymerase chain reaction (PCR) result for SARS-CoV-2 from March to August 2020 at a 625-bed community teaching hospital in Los Angeles. The study was approved by the hospital's Institutional Review Board (Date: June 24, 2020; Number: 00000971); informed consent was waived.

Medical charts were reviewed to obtain demographic, laboratory and clinical information, and details of antiviral and antibacterial therapy. All data were recorded on a structured data collection form and managed using REDCap electronic data capture tools hosted at the University of Southern California.[4] Sepsis-3 criteria were used to define sepsis and septic shock.[5] Outcome measures included development of acute kidney injury (AKI) and acute respiratory distress syndrome (ARDS) and hospital length of stay (LOS).

2.1 | Data analysis

Patients were grouped based on short (≤3 days), intermediate (4-10 days), prolonged (>10 days) time to recovery defined by achievement of clinical stability (TTS): resolution of fever <38°C, respiratory rate <22 breaths/min, systolic blood pressure >100 mmHg, extubated and return of mental status to baseline. Study groups were compared on demographic and clinical characteristics, pharmacologic management and outcomes. Descriptive analyses were performed using Kruskal–Wallis and chi-square test where appropriate. The model outcome, prompt recovery defined by short TTS was compared with combined intermediate and prolonged TTS to determine the predictability of each factor for the prompt recovery of COVID-19 patients. Univariate logistic regression analyses were performed to determine the candidates of the predictors for prompt recovery with P value <.20. Only the factors found to be potentially significant by univariate analysis were included in the multivariate logistic regression analysis using forward model selection method. A P value <.05 was considered significant. Statistical analyses were performed using GraphPad Prism v6.07 (San Diego, CA, USA) or SAS version 9.4 (SAS Institute, Cary, NC).

3 | RESULTS

Survival rate was 79% (401/508) among patients hospitalised for COVID-19 during the study period. Overall, median age of COVID-19 survivors was 64 years; majority (73%) were admitted from home with 25% from a skilled nursing facility (SNF). The overall median TTS was 4 days (IQR: 2-10) for survivors, with 43% (n = 174) within 3 days, 34% (n = 135) between 4-10 days and 23% (n = 92) after a prolonged period exceeding 10 days. More females achieved prompt versus prolonged time to recovery (51% vs 37%; Table 1).

At time of admission, significantly less patients in the short TTS group experienced fevers (47% vs 58% vs 63%, $P = .0214$), required supplemental oxygen (55% vs 73% vs 77%, $P < .0001$), while none had septic shock (vs 4% vs 16%, $P < .0001$), required direct ICU admission (vs 7% vs 25%, $P < .0001$) or mechanical ventilation (vs 2% vs 16%, $P < .0001$) compared with the intermediate and prolonged groups, respectively (Table 1). Therapy directed against COVID-19 was less frequently prescribed to patients with short compared with intermediate and prolonged TTS: hydroxychloroquine ± azithromycin (13% vs 32% vs 37%, $P < .0001$), remdesivir (14% vs29% vs 48%, $P < .0001$), tocilizumab (0.6% vs 0.7% vs 12%, $P < .0001$), corticosteroids (34% vs 31% vs 58%, $P < .0001$) and convalescent plasma (10% vs 24% vs 40%, $P < .0001$).

Patients with prompt recovery were less likely to have co-bacterial infections at time of admission (presumed 13% vs 24% vs 39%, $P = .0001$; culture-positive 11% vs vs 21% vs 28%, $P = .0013$), especially in the respiratory site (0% [0/19] vs 10% [3/29] vs 46% [12/26], $P = .0002$) compared withintermediate and prolonged TTS groups, respectively. Nonetheless, 86% of the patients in the short TTS group who did not have co-bacterial infections were prescribed broad-spectrum antibacterial therapy for a median duration of 4 days. A notable proportion of the prolonged TTS cohort were co-infected with multidrug-resistant pathogens such as *Pseudomonas aeruginosa* (15%) and carbapenem-resistant organisms (4%) compared with none in the short TTS group; patients who resided in a SNF prior to admission accounted for 56% (5/9) of those with *Pseudomonas aeruginosa* and all three cases involving carbapenem-resistant organisms. Interestingly, co-infection with ESBL-producing isolates (mostly urine) occurred in 4% of patients overall, irrespective of TTS. Compared withthe intermediate and prolonged TTS cohorts,

TABLE 1 Characteristics and outcomes of patients surviving hospitalisation with COVID-19[a]

Characteristics	All patients N = 401	Short TTS (≤3 d) N = 174	Intermediate TTS (4-10 d) N = 135	Prolonged TTS (>10 d) N = 92	*P*-value
Demographics					
Female	180 (45)	89 (51)	57 (42)	34 (37)	.0644
Age, median (IQR), y	64 (50-77)	64 (49-78)	66 (51-77)	64 (50-73)	.5982
Residence prior to admission					.0300
Home	291 (73)	135 (78)	93 (69)	63 (68)	
Skilled nursing facility	102 (25)	37 (21)	41 (30)	24 (26)	
Outside hospital/other	8 (2)	2 (1)	1 (0.7)	5 (5)	
Current/former smoker	52 (13)	21 (12)	21 (16)	10 (11)	.5261
Top 5 comorbidities					
Hypertension	213 (53)	86 (49)	74 (55)	53 (58)	.3958
Diabetes	116 (29)	46 (26)	42 (31)	28 (30)	.6251
Hyperlipidaemia/dyslipidaemia	107 (27)	46 (26)	39 (29)	22 (24)	.7040
Dementia	71 (18)	26 (15)	30 (22)	15 (16)	.2316
Chronic kidney disease	44 (11)	15 (9)	16 (12)	13 (14)	.3622
None	76 (19)	39 (22)	23 (17)	14 (15)	.2843
Time from symptom onset to hospitalisation, median (IQR), d	4 (1-7)	5 (2-10)	3 (1-7)	5 (2-7)	.0114
Top 3 COVID-19 symptoms					
Fever	217 (54)	81 (47)	78 (58)	58 (63)	.0214
Dyspnoea	222 (55)	87 (50)	78 (58)	57 (62)	.1379
Non-productive cough	205 (51)	88 (51)	64 (47)	53 (58)	.3142
Disease severity upon admission					
Septic shock	20 (5)	0 (0)	5 (4)	15 (16)	<.0001
Direct ICU admission	33 (8)	0 (0)	10 (7)	23 (25)	<.0001
Required supplemental O_2	265 (66)	95 (55)	99 (73)	71 (77)	<.0001
Mechanical ventilation	18 (4)	0 (0)	3 (2)	15 (16)	<.0001
Presumed or culture-positive co-bacterial infection[b]	138 (34)	36 (21)	50 (37)	44 (47)	<.0001
Receipt of antibacterial therapy upon admission	370 (92)	149 (86)	129 (96)	92 (100)	<.0001
Duration of antibacterial therapy	7 (4-11)	4 (2-6)	7 (6-10)	15 (11-20)	<0.0001
Outcomes					
Developed AKI	72 (18)	18 (10)	23 (17)	31 (34)	<.0001
Developed ARDS	18 (4)	0 (0)	2 (1)	16 (17)	<.0001
Hospital LOS, median (IQR), d	9 (5-15)	5 (3-7)	9 (8-13)	22 (16-29)	<.0001

Abbreviations: AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; LOS, length of stay.

[a]Data are presented as number (percentage) of patients unless otherwise indicated.

[b]Presumed bacterial co-infection was defined as a procalcitonin level ≥0.25 ng/mL upon admission.

less patients with a short TTS developed AKI (10% vs 17% vs 34%, $P < .0001$) and none developed ARDS (vs 1% vs 17%, $P < .0001$) (Table 1). Ultimately, those who recovered fastest experienced a shorter hospital stay (median 5 vs 9 vs 22 days, $P < .0001$; Table 1).

By multivariable logistic regression analysis, independent predictors for prompt recovery from COVID-19 were female sex, absence of fever, longer time from symptom onset to hospitalisation, no direct ICU admission, not requiring supplemental oxygen upon presentation and absence of presumed or documented co/secondary bacterial infections (Table 2).

4 | DISCUSSION

Patients who survived hospitalisation with COVID-19 experienced varying time to achieve clinical stability before hospital discharge.

TABLE 2 Predictors of prompt recovery by multivariable logistic regression[a]

Variables	OR (95% CI)	*P*-value
Female	1.76 (1.13-2.74)	.01
Time from symptom onset to hospitalisation	1.08 (1.03-1.13)	.001
No Fevers upon admission	1.64 (1.06-2.57)	.03
No supplemental O_2 upon admission	1.95 (1.23-3.07)	.004
No direct ICU admission	41.73 (2.35-740.35)	.01
No presumed or culture-positive co-bacterial infection	2.46 (1.51-4.01)	.0003

[a]The model dependent variable is prompt recovery (short TTS vs combined intermediate and prolonged TTS cohorts).

While much of the focus has been on the severity of COVID-19 among those who required hospitalisation, less is known regarding the characteristics of patients who recovered promptly. Clinical features associated with a favourable hospital course could help clinicians triage competing resources in the care of patients especially at institutions challenged by the demands from the ebb and flow in COVID-19 cases.

Our findings indicate that female sex, longer time from symptom onset to hospitalisation, less severe presentation upon admission (fevers, septic shock, ICU, supplemental oxygen) and absence of bacterial co-infection are factors favouring prompt recovery. We observed a similar prevalence of COVID-19 requiring hospitalisation between male and female sex in our study. Although literature has shown a correlation between men with COVID-19 and worse outcomes including death, our data is the first to show an association between female sex and shortened recovery time.[6,7] Our data is also the first to show that an extended time from symptom onset to hospital admission is a predictor for prompt recovery.

We found that significantly less patients with prompt recovery had bacterial co-infections especially concurrent pneumonia compared with those in the prolonged TTS group. Nonetheless, 86% of patients in the short TTS group were prescribed antibacterial therapy for a median duration of 4 days despite the absence of bacterial co-infection. This finding underscores the need for continued antimicrobial stewardship to minimise indiscriminant antibacterial use in hospitalised COVID-19 patients. As expected, those with a short TTS had a less complicated course with less than one week length of hospital stay in this cohort. While we identified distinguishing clinical features between groups with varying time to achieve clinical stability, our study is limited by the relatively small number of patients at a single centre and the lack of viral load or host immune response measurements to provide a biological basis to our clinical observations.

5 | CONCLUSION

Health system resources may be triaged accordingly based on clinical features associated with prompt recovery in patients hospitalised for COVID-19. Concurrent antibacterial therapy needs to be judiciously prescribed to minimise the selection of antimicrobial resistance and untoward adverse effects (eg *C difficile* diarrhea).

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DISCLOSURES

The authors declared no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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