Online supplement

Factors associated with prolonged viral shedding and impact of Lopinavir/Ritonavir treatment in hospitalized non-critically ill patients with SARS-CoV-2

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Take home message: Risk factors for prolonged viral shedding included older age and lack of Lopinavir/Ritonavir treatment. Earlier administration of Lopinavir/Ritonavir treatment could shorten the duration of SARS-CoV-2 RNA shedding.

Table E1. Characteristics of included patients and excluded patients with SARS-CoV-2 infection in Wuhan

Characteristic	Included patients (n=120)	Excluded patients (n=40)	P value
Age, year	52 (35-63)	54 (46-65)	0.21
Male sex	54 (45)	17 (42.5)	0.78
Current smoker	12 (10)	2 (5)	0.33
Comorbidity			
Hypertension	32 (26.7)	11 (27.5)	0.92
Diabetes	10 (8.3)	6 (15)	0.22
Cardiac disease	7 (5.8)	4 (10)	0.54
Stoke	3 (2.5)	1 (2.5)	1
COPD or asthma	2 (1.6)	0 (0)	
Chronic renal insufficiency	1 (0.8)	0 (0)	
Malignancy	7 (5.8)	1 (2.5)	0.68
Disease severity			0.67
General	89 (74.2)	28 (70)	
Severe	30 (25.0)	11 (27.5)	
Critical	1 (0.8)	1 (2.5)	
Laboratory finding on admission			
White blood cell count, × 10^9 cells/L			0.75
<4	27 (22.7)	7 (17.5)	
4-10	82 (68.9)	30 (75)	
>10	10 (8.4)	3 (7.5)	
Lymphocyte count, × 10^9 lymphocytes/L			
<0.8	29 (24.3)	12 (30)	0.48
Platelet count, × 10^9 platelets/L			
<100	7 (5.9)	1 (2.5)	0.68
Creatinine level, μmol/L			
>133	4 (3.4)	1 (2.5)	1
AST level, U/L			
>40	33 (27.7)	16 (40)	0.15
Treatment			
Corticosteroid therapy	54 (45.0)	17 (42.5)	0.78
Lopinavir/Ritonavir treatment	78 (65)	19 (47.5)	0.05
Antibiotics	102 (85.0)	26 (67.5)	0.006
High-flow nasal canula oxygen therapy	21 (17.5)	5 (12.5)	0.46
No-invasive mechanical ventilation	2 (1.7)	1 (2.5)	1
Invasive mechanical ventilation	1 (0.8)	1 (2.5)	0.44

Abbreviations: AST=aspartate aminotransferase; COPD=chronic obstructive pulmonary disease; d=day
IQR=interquartile range.
Data presented as n (%) or median (IQR) unless otherwise noted.
*Data were available for 119 patients except D-dimer (n=101)
[a]includes congestive heart disease and coronary atherosclerotic heart disease.

Table E2. Multivariable Logistic Regression Model Analysis of Factors Associated with Duration of SARS-CoV-2 RNA detection in 120 Hospitalized Patients in Wuhan

Variables	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P[a]
Demographic characteristic				
Age	1.02 (1.00-1.04)	0.04	1.03 (1.00-1.05)	0.03
Age ≥50 years	2.13 (1.02-4.44)	0.04	2.26 (1.07-4.78)	0.03
Male sex	0.71 (0.34-1.46)	0.35	0.60 (0.28-1.28)	0.19
Healthcare workers	1.14 (0.50-2.64)	0.75		
Symptoms				
Fever	1.36 (0.53-3.52)	0.53		
Cough	1.11 (0.52-2.36)	0.80		
Short of breath	0.76 (0.16-3.57)	0.73		
SpO2≤93%	1.62 (0.71-3.70)	0.25		
Comorbidity				
Current smoking	0.86 (0.23-3.18)	0.82		
Hypertension	0.63 (0.28-1.42)	0.26		
Cardiac disease	1.41 (0.30-6.57)	0.67		
Diabetes	2.60 (0.64-10.59)	0.18		
Malignancy	0.76 (0.16-3.57)	0.73		
Severe COVID-19	1.53 (0.67-3.52)	0.32		
Drug treatment				
Corticosteroid	0.90 (0.44-1.85)	0.78	0.80 (0.38-1.70)	0.57
Lack of Lopinavir/Ritonavir	2.59 (1.19-5.62)	0.02	2.42 (1.10-5.36)	0.03
Immunoglobulin	1.41 (0.58-3.43)	0.44	1.40 (0.55-3.56)	0.48

Abbreviation: OR=odd ratio; CI=confidence interval.

[a]By use of the Logistic Regression model and the cut-off was determined according to the median duration of SARS-CoV-2 RNA shedding (23 days). An odd ratio (OR)>1 indicates that the variable increases the duration of SARS-CoV-2 RNA shedding. ORs in multivariable analysis were adjusted for age and sex.

Table E3. Multivariable Cox Hazard Model Analysis of Factors Associated with Duration of SARS-CoV-2 RNA detection in 120 Hospitalized Patients in Wuhan

Variables	Unadjusted HR (95% CI)	P	Adjusted HR (95% CI)	P[a]
Demographic characteristic				
Age	0.98 (0.97-0.99)	0.002	0.98 (0.97-0.99)	0.001
Age ≥50 years	0.59 (0.41-0.85)	0.005	0.57 (0.39-0.83)	0.003
Male sex	1.18 (0.82-1.69)	0.39	1.43 (0.96-2.10)	0.10
Healthcare workers	0.82 (0.53-1.25)	0.35		
Symptoms				
Fever	0.83 (0.52-1.34)	0.44		
Cough	1.20 (0.81-1.76)	0.37		
Short of breath	1.04 (0.48-2.23)	0.93		
SpO2≤93%	0.82 (0.54-1.24)	0.34		
Comorbidity				
Current smoking	1.53 (0.79-2.98)	0.21		
Hypertension	1.42 (0.94-2.14)	0.10		
Cardiac disease	1.36 (0.62-2.93)	0.45		
Diabetes	0.72 (0.37-1.38)	0.32		
Malignancy	0.64 (0.30-1.39)	0.26		
Sever COVID-19	0.81 (0.53-1.24)	0.34		
Drug treatment				
Corticosteroid	1.04 (0.72-1.49)	0.84		
Lack of Lopinavir/Ritonavir	0.61 (0.42-0.90)	0.012	0.60 (0.41-0.89)	0.01
Immunoglobulin	1.19 (0.76-1.87)	0.45	1.17 (0.74-1.86)	0.50

Abbreviation: HR=hazard ratio; CI=confidence interval.

[a]By use of the Cox hazard proportional model. A hazard ratio (HR)<1 indicates that the variable increases the duration of SARS-CoV-2 RNA shedding. HRs in multivariable analysis were adjusted for age and sex.
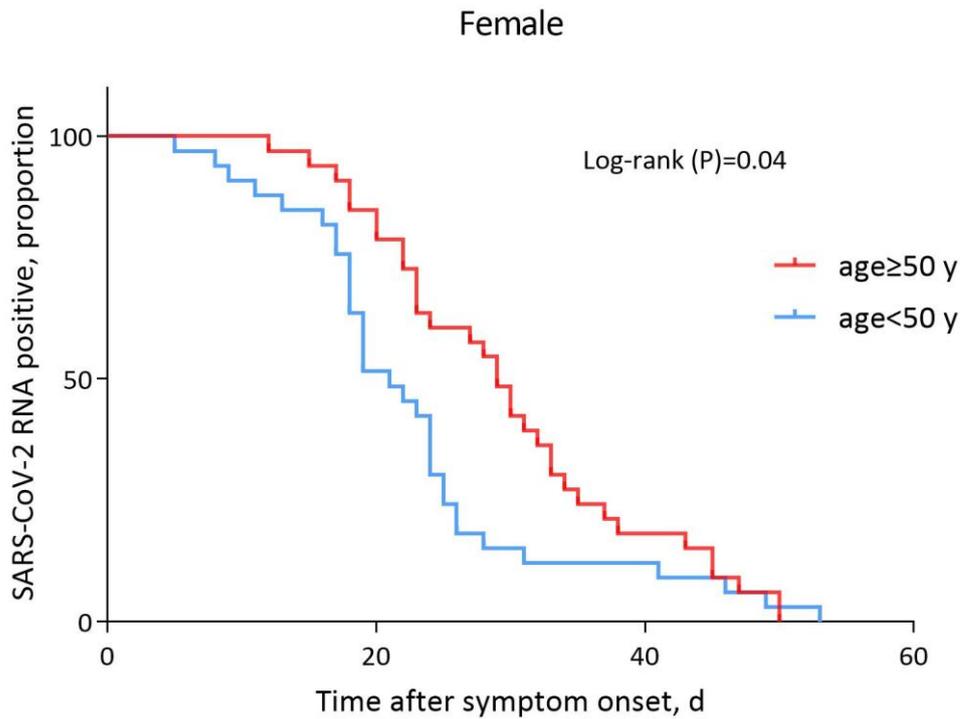
Figure E1: Cumulative proportion of patients with detectable SARS-CoV-2 by day after symptom onset between women with age ≥50 years and those with age <50 years.
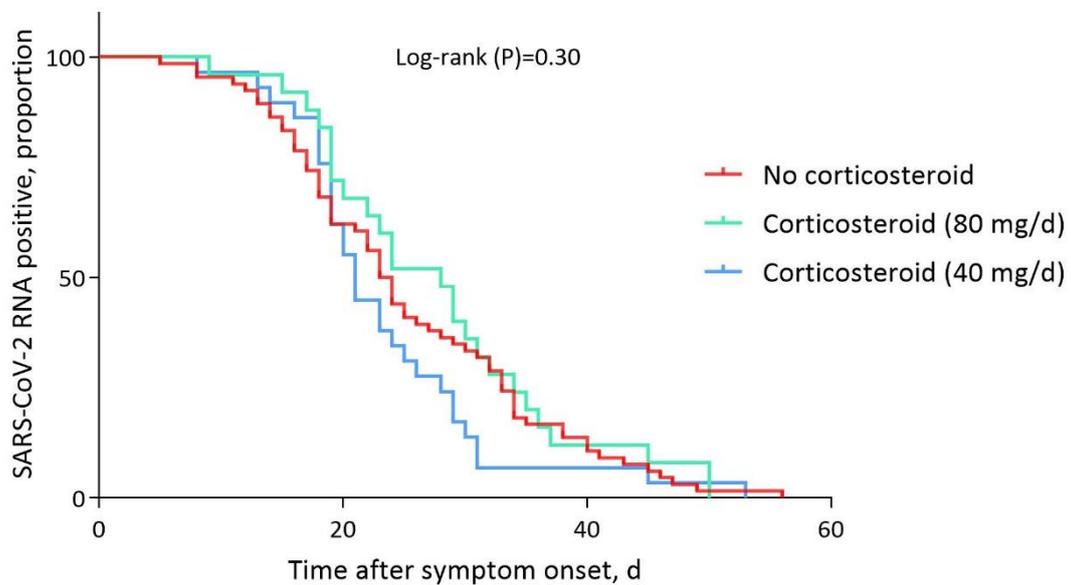
Figure E2: Cumulative proportion of patients with detectable SARS-CoV-2 by day after symptom onset among patients with maximum daily corticosteroid dose 80mg, 40mg and those without corticosteroid use.
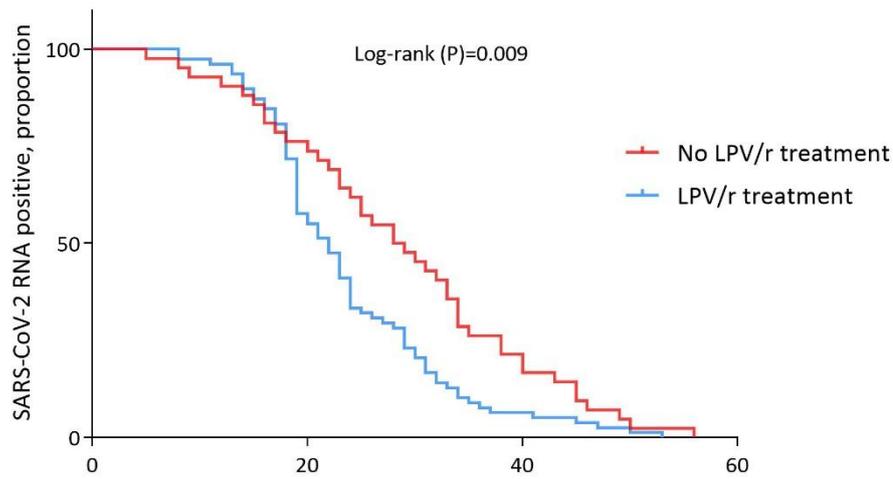
Figure E3: Cumulative proportion of patients with detectable SARS-CoV-2 by day after symptom onset between patients with Lopinavir/Ritonavir treatment and those without.