Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Efficacy of Paxlovid in patients with acute kidney injury who developed COVID-19

Dear Editor,

The coronavirus disease 2019 (COVID-19) pandemic has affected public health on a global scale.[1] Recently, a letter in your journal analyzes the efficacy of Paxlovid on death and hospitalization for COVID-19 patients and shows that Paxlovid for COVID-19 is effective and safe.[2] Paxlovid, an oral protease inhibitor, is significantly effective in high-risk patients with SARS-Cov-2.[3] Older patients who received Paxlovid had lower hospitalization and mortality rates. Patients with acute kidney injury (AKI) who developed COVID-19 are at high risk of worse outcomes than those without AKI.[4] However, evidence on the efficacy of Paxlovid in high-risk patients such as those with AKI is limited. In part because of these findings, the current study aimed to evaluate the efficacy of Paxlovid in improving outcomes in patients with AKI.

We performed a retrospective, observational study on patients with AKI aged between 18 and 103 years who developed COVID-19 from April 7, 2022, to June 21,2022, in Shanghai. The study protocol was approved by the ethics committee of Renji Hospital, Shanghai JiaoTong university, school of medicine. All patients provided a written informed consent. The primary endpoints were viral elimination, which was defined as negativity for ORF1ab and N genes (a cycle threshold value of ≥35 based on real-time polymerase chain reaction) on 2 consecutive days, according to local guidelines, and CVD-related and all-cause mortality. The secondary endpoints were length of hospital and ICU stay, lung infection, and renal replacement treatment (RRT). Of 3311 patients,1083 were excluded due to do not have at least two serum creatinine, 881 due to age<18 years old, 3 due to mental illness. Total 1344 sample were enrolled and screen AKI patients. 69 due to hemodialysis and peritoneal dialysis,1171 due to non-AKI patients. A total of 104 individuals were enrolled in the final analytic sample (Supplementary Fig. S1).

The mean age of 104 patients with AKI was 76.14 ± 13.47 years (Supplementary Tables S1-2). In total, 61 (58.65%) patients received Paxlovid. Compared with patients who did not receive Paxlovid, those who received Paxlovid had a lower incidence of lung infection (60.6% vs 81.4%, P=0.031), shorter length of hospital stay (18.15 ± 6.85 vs 22.70 ± 11.91 days, P=0.015) and viral elimination time (9.00 [6.00-11.00] vs 17.00 [11.00-22.50] days, $P < 0.001$), and less need for RRT(1 [1.6%] vs 6 [14.0%],P=0.019) (Supplementary Table S3). Compared with the no received Paxlovid group, the group of received Paxlovid were similar in terms of all-cause and CVD-related mortality rates, Charlson Comorbidity Index, and baseline estimated glomerular filtration rate. Univariate and binary logistic regression analyses were performed to identify the risk factors of lung infection. Results showed that Paxlovid treatment were independent predictors of lung infection (Supplementary Table S4). Multiple linear regression analysis showed that Paxlovid was correlated with the length of hospital stay in AKI patients with COVID-19(Supplementary Table S5). The patients who receive Paxlovid can effectively reduce the hospital stay and in cadence of lung infection.

In total, 64 patients presented with stage I AKI and 40 with stage II and III AKI. Patients with stage I AKI who received Paxlovid had a lower lung infection rate than those who did not receive Paxlovid (22 [55%] vs 20 [83.3%], P=0.030). However, there was no significant difference in terms of the incidence of lung infection in patients with stage II and III AKI. Patients with stage I AKI who received Paxlovid had a significantly shorter length of hospital stay (16.93 ± 6.78 vs 21.86 ± 11.10 days, P=0.031) than those who did not receive Paxlovid. Patients with stage II and III AKI who received Paxlovid had a lower length of hospital stay than those who did not receive Paxlovid. Nevertheless, the results did not significantly differ. Patients with stage II and III AKI received renal RRT. The Paxlovid group had a lower proportion of patients requiring RRT than the without Paxlovid group (1 [4.8%] vs 6 [31.6%], P=0.026). Regardless of AKI stage I or stage II and III, patients who received Paxlovid had a significantly shorter viral elimination time than those who did not receive Paxlovid (9.00 [6.75,11.25] vs 17.5 [11.00,21.00] days, $P < 0.001$; 7.00 [6.25,17.00] vs 17.00 [14.00,25.00] days, $P < 0.001$) (Table 1).

Within 10 days after the diagnosis of viral infection, the viral load, which was measured based on ORF1ab viral gene replication, decreased significantly in patients with AKI who received Paxlovid. In addition, the correlation between the time to Paxlovid initiation and viral elimination is linear ($R^2 = 0.288$, $P < 0.001$) (Fig. 1). The viral load of patients with stage I AKI and those with stage II and III AKI decreased significantly on day 6th and 5th, respectively, after treatment. There was still a linear correlation between viral elimination and time to Paxlovid initiation ($R^2 = 0.256$, P=0.001; $R^2 = 0.402$, $P < 0.002$, respectively) (Fig. 1).

In conclusion, Paxlovid can effectively shorten the length of hospital stay in patients with AKI who developed COVID-19. Further, it can reduce the incidence of lung infection and shorten the length of hospital stay in patients with early-stage AKI. In patients with late-stage AKI, Paxlovid can reduce the rate of RRT. Early treatment may accelerate viral elimination, shorten hospital stay, and improve outcome in patients with AKI.

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Table 1
Outcome of patients with stage I AKI and those with stage II and III AKI who had Paxlovid prescription and those who did not.

	Patients with stage I AKI				Patients with stage II and III AKI			
	All patients (n = 64)	Paxlovid		P value	All patients (n = 40)	Paxlovid		P value
		Patients who received Paxlovid (n = 40)	Patients who did not receive Paxlovid (n = 24)			Patients who received Paxlovid (n = 21)	Patients who did not receive Paxlovid (n = 19)	
RRT (n, %)	0	0	0		7 (17.5)	1 (4.8)	6 (31.6)	0.026
Male sex (n, %)	32 (50)	19 (47.5)	13 (54.2)	0.582	20 (50)	10 (47.6)	10 (52.6)	1.000
Lung infection (n, %)	42 (65.6)	22 (55)	20 (83.3)	0.030	31 (77.5)	16 (76.2)	15 (78.9)	1.000
CVD-related mortality (n, %)	3 (4.7)	1 (4.2)	2 (5.0)	0.551	9 (22.5)	3 (15.8)	6 (28.6)	0.265
All-cause mortality (n, %)	13 (20.3)	8 (20)	5 (20.8)	1.000	19 (47.5)	10 (47.6)	9 (47.4)	1.000
Non-invasive ventilation (n, %)	10 (15.9)	8 (20)	2 (8.7)	0.297	13 (32.5)	6 (28.6)	7 (36.8)	0.738
Invasive ventilation (n, %)	3 (4.7)	2 (5.0)	1 (4.2)	1.000	12 (30)	6 (28.6)	7 (36.8)	0.738
ICU (n, %)	30 (46.9)	19 (47.5)	11 (45.8)	1.000	31 (77.5)	15 (71.4)	16 (84.2)	0.457
ICU (d, x ± s)	5.94 ± 9.25	5.74 ± 7.87	6.32 ± 11.63	0.814	11.08 ± 9.84	11.57 ± 10.12	10.53 ± 9.75	0.742
Length of hospital stay	18.63 ± 8.75	16.93 ± 6.78	21.86 ± 11.10	0.031	22.28 ± 10.29	20.05 ± 6.53	24.74 ± 13.04	0.153
CCI (x ± s)	6.97 ± 2.86	6.74 ± 2.90	7.41 ± 2.79	0.376	7.53 ± 2.81	7.00 ± 2.57	8.11 ± 3.02	0.219
CT value upon diagnosis (ORF 1ab gene)	10.50 (7.00-16.00)	9.00 (6.75-11.25)	17.5 (11.00-21.00)	<0.001	11.00 (6.25-17.00)	7.00 (6.00-11.00)	17.00 (14.00-25.00)	<0.001
Time to viral elimination (days)	25.06 (20.82-32.53)	25.06 (21.28-31.29)	25.94 (19.38-38.99)	0.804	21.74 (18.49-24.02)	21.74 (18.91-24.98)	21.19 (18.28-24.03)	0.907

CCI=charlson comorbidity index; RRT=renal replacement treatment; CVD=cardiovascular disease; ICU=Intensive Care Unit.

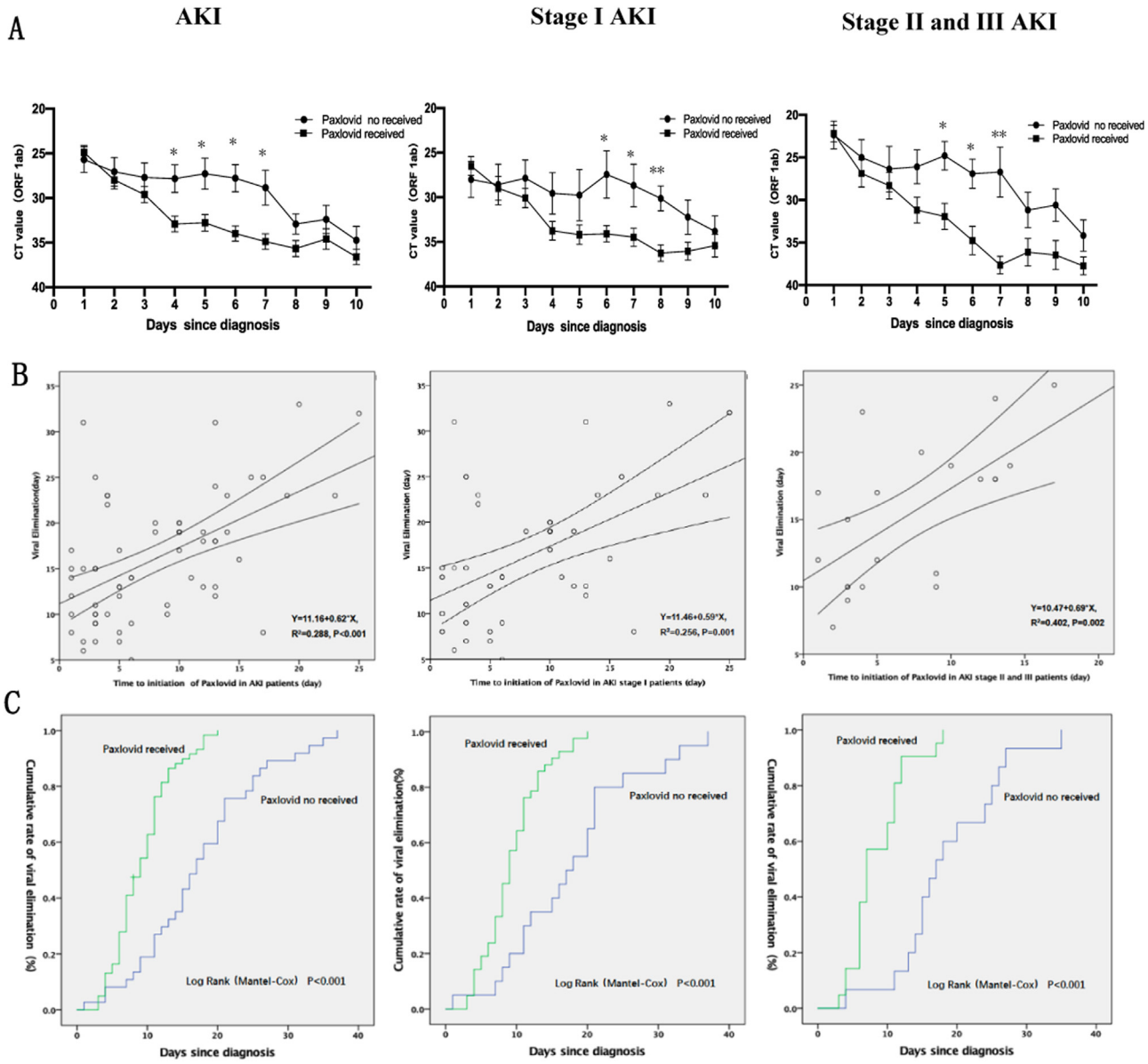

Fig. 1. Attenuation of viral load in patients with AKI who developed COVID-19 according to Paxlovid treatment. A) Changes in ORF1ab CT value in patients with AKI who received Paxlovid and those who did not. In total, 61 patients received Paxlovid, and an ORF1ab gene CT value of ≥35 based on real-time PCR was considered an indicator of virus elimination. The viral load of the Paxlovid group was significantly lower than that of the without Paxlovid group on the 4th day. The viral load of patients who received Paxlovid decreased significantly faster than that of patients who did not receive Paxlovid in the stage I, II and III subgroups, and the significant differences were observed between the two subgroups on the 6th and 5th days, respectively. B) Correlation between the timing of Paxlovid treatment and the duration of virus elimination in patients who received Paxlovid and those who did not. To validate the association between the time to Paxlovid initiation after viral positivity and the time of viral elimination, a correlation analysis was performed. The correlation between the time to Paxlovid initiation and viral elimination is liner in patients with AKI who developed COVID-19 ($R^2 = 0.288$, $P < 0.001$). There was still a liner correlation between viral elimination and the time to Paxlovid initiation in patients with stage I AKI and those with stage II and III AKI who developed COVID-19 ($R^2 = 0.256$, P=0.001; $R^2 = 0.402$, $P < 0.002$, respectively). C)
Cumulative rate of viral elimination in after Paxlovid treatment in patients with AKI who developed COVID-19. Patients with AKI who received Paxlovid had a short viral elimination time. Paxlovid had a better efficacy in patients with stage II and III AKI than in those who did not receive Paxlovid.

Declaration of Competing Interest

None declared

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2022.10.002.

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