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Renal Preservation Increases Survival Rate in Critically Ill COVID-19 Patients

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Abstract

BACKGROUND: COVID-19 infection tends to cause organ dysfunction and disrupts immunity due to cytokine storm. In addition to pulmonary distress and myocarditis due to the aforementioned cytokine storm, another prominent clinical feature of this disease is kidney failure. Maintaining good kidney function, normal creatinine levels, removing cytokine, avoiding fluid overload, and implementing higher level additional measures such as early (renal replacement therapy) are expected to increase survival in critically ill COVID-19 patients.

AIM: We aimed to analyze whether renal preservation increases survival rate in critically ill COVID-19 patients

METHODS: An observational analytic study was conducted in 53 critically ill COVID-19 patients treated in the ICU (Intensive Care Unit). All patients were treated with either standard therapy with additional renal-focused fluid evacuation and cytokine removal method such as CRRT (continuous RRT) or cytokine removal only with plasmapheresis.

RESULTS: investigation through Cox regression analysis revealed that only cumulative balance an creatinine have a significant relationship with mortality ($p < 0.05$).

CONCLUSION: Maintenance of cumulative balance and serum creatinine will increase survival rates.

Introduction

COVID-19 infection tends to cause organ dysfunction and disrupts immunity due to cytokine storm. In addition to pulmonary distress and myocarditis due to the aforementioned cytokine storm, another prominent clinical feature of this disease is kidney failure [1], [2].

Kidneys are emergency marker organs that are quite challenging to manage. Septic acute kidney injury has been known to be triggered by inflammation due to cytokine storm, causing acute tubular necrosis. Serum creatinine, a typical marker of kidney failure, will only show an increase within 24–48 h after the insult, too late for drastic and meaningful interventions to take place. Maintaining good kidney function, normal creatinine levels, removing cytokine, avoiding fluid overload, and implementing higher level additional measures such as early RRT (renal replacement therapy) are expected to increase survival in critically ill COVID-19 patients [3], [4], [5].

Materials and Methods

An observational analytic study was conducted in 53 critically ill COVID-19 patients treated in the ICU (Intensive Care Unit). All patients were treated with either standard therapy with additional renal-focused fluid evacuation and cytokine removal method such as CRRT (continuous RRT) or cytokine removal only with plasmapheresis. We observed the survival rate, cumulative balance, creatinine serum, and RRT types. Standard therapy consists of conservative fluid management and active fluid removal with negative cumulative balance; ventilation using PEEP level of 5–12 targeting 92–95% SpO_2; early feeding; antimicrobial stewardship without ECMO; prone positioning; or intravenous immunoglobulin. Statistical analysis was conducted using SPSS version 21, with Chi-square test for categorical variables and Cox regression for inferential analysis.

Results

We collected data from 53 patients including age, gender, RRT types, added adsorbent, cumulative balance, as well as serum urea and creatinine levels (Tables 1 and 2).

Table 1: Frequencies and characteristics

Variables	Frequency, *n* (%)
Gender	
Male	44 (83.0)
Female	9 (17.0)
Age (year old)	
18–65	32 (60.4)
>65	21 (39.6)
RRT type	
None	25 (47.2)
CVVH	15 (28.3)
TPE	10 (18.9)
CVVH and TPE	3 (5.7)
Adsorbent type	
None	39 (73.6)
Oxiris™	10 (18.9)
M100	2 (3.8)
Oxiris™ and M100	2 (3.8)
Outcome	
Survived	25 (47.2)
Did not survive	28 (52.8)

RRT: Renal replacement therapy, Continuous Venous-Venous Hemofiltration, TPE: Therapeutic Plasma Exchange

Table 2: Descriptive analyses

Variables	Median
Cumulative balance	−2202.25
Urea	61
Creatinine	1.653

Several analyses were conducted to observe the relationship between those variables and mortality. Chi-square test (Table 3) revealed that age, gender, type of RRT, and additional adsorbent had no statistically significant relationship with mortality.

Table 3: Chi-square test of categorical variables

Variables	Value	Significance
Age	1.149	0.284
Gender	0.032	0.857
RRT type	4.846	0.183
Adsorbent type	4.074	0.254

RRT: Renal replacement therapy.

Further, investigation through Cox regression analysis (Table 4) revealed that only cumulative balance and creatinine have a significant relationship with mortality ($p < 0.05$). Those two variables are depicted more clearly in the Kaplan–Meier charts in Figures 1 and 2. When the cumulative balance was maintained negative and the creatinine level was maintained at <1.6 mg/dL, the survival rates were higher compared to when the two parameters were not maintained.

Table 4: Cox regression analysis on variables

Steps	*B*	SE	Significant	Exp (B)	95.0% CI for Exp (B)	
					Lower	Upper
Step 1						
Gender	0.855	0.581	0.141	2.351	0.752	7.350
Age	−0.347	0.485	0.474	0.707	0.273	1.828
RRT type	−0.339	0.230	0.142	0.713	0.454	1.120
Adsorbent	0.014	0.333	0.967	1.014	0.528	1.946
Cumulative balance	0.000	0.000	0.053	1.000	1.000	1.000
Urea	0.001	0.006	0.906	1.001	0.989	1.012
Creatinine	0.238	0.117	0.042	1.269	1.008	1.596
Step 2						
Gender	0.857	0.580	0.140	2.355	0.756	7.341
Age	−0.347	0.485	0.475	0.707	0.273	1.831
RRT type	−0.336	0.224	0.133	0.714	0.461	1.108
Cumulative balance	0.000	0.000	0.053	1.000	1.000	1.000
Urea	0.001	0.006	0.908	1.001	0.989	1.012
Creatinine	0.238	0.117	0.042	1.268	1.008	1.595
Step 3						
Gender	0.881	0.539	0.102	2.414	0.839	6.947
Age	−0.322	0.431	0.455	0.725	0.312	1.687
RRT type	−0.331	0.218	0.129	0.718	0.469	1.102
Cumulative balance	0.000	0.000	0.049	1.000	1.000	1.000
Creatinine	0.247	0.081	0.002	1.281	1.092	1.501
Step 4						
Gender	0.814	0.531	0.125	2.256	0.797	6.384
RRT type	−0.280	0.210	0.182	0.755	0.500	1.141
Cumulative balance	0.000	0.000	0.057	1.000	1.000	1.000
Creatinine	0.225	0.075	0.003	1.252	1.080	1.451
Step 5						
Gender	0.795	0.528	0.132	2.214	0.786	6.231
Cumulative balance	0.000	0.000	0.028	1.000	1.000	1.000
Creatinine	0.208	0.072	0.004	1.231	1.069	1.418
Step 6						
Cumulative balance	0.000	0.000	0.019	1.000	1.000	1.000
Creatinine	0.194	0.070	0.006	1.214	1.058	1.394

RRT: Renal replacement therapy, SE: Standard error, CI: Confidence interval.

Discussion

It is really interesting that the result of this study showed that the type of RRT, age, gender, and the addition of sophisticated adsorbents did not have a significant effect in patient outcomes.

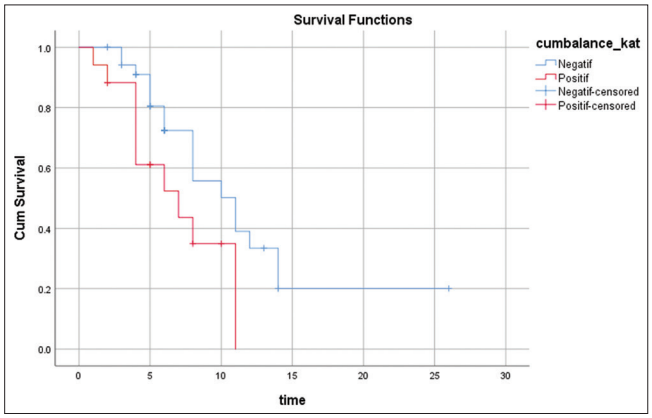

Figure 1: Cumulative balance in Kaplan–Meier survival functions

Maintaining the cumulative balance and the creatinine level in non-positive state and in normal range, respectively, would contribute better to patients' outcome.

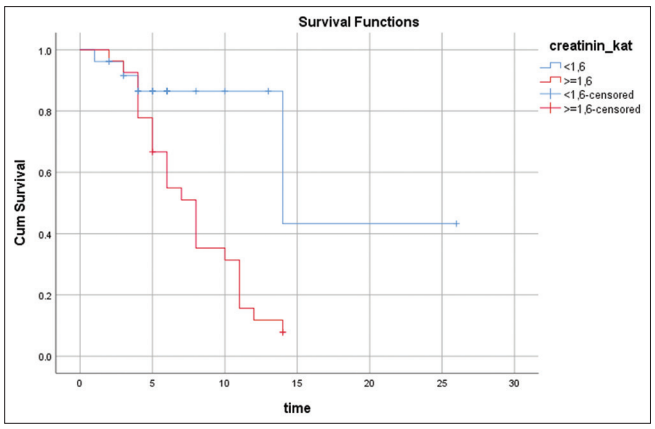

Figure 2: Serum creatinine levels in Kaplan–Meier survival functions

The limitation of this study lies in the difficulty to determine the role of effective therapy due to its wide variety, small sample size, and potential bias in timing of therapy. We also did not measure plasma and ultrafiltrate cytokine levels. However, this data provide a useful overview on the importance of protecting the excretory organs which are highly susceptible to insults in health-care facilities without specific cytokine examination.

Conclusion

Maintenance of cumulative balance and serum creatinine will increase survival rates.

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