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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Renal replacement therapy in critically ill patients with COVID-19: A retrospective study investigating mortality, renal recovery and filter lifetime

Dear editor,

Acute Kidney Injury (AKI) complicates a COVID-19 infection in up to 30% of the patients [1-7]. The need for Renal Replacement Therapy (RRT) varied from 2 to 22% [8-12]. Reported mortality rates for patients with RRT varies from 51.6–100% [6-8,13,14]. These mortality rates might suggest that renal replacement therapy appears to be prognostically important, especially when resources are limited. In addition, due to the thrombogenicity of the patients suffering from COVID-19, filter life may be shorter due to filter clotting [15]. The aim of this study was to investigate the mortality-rate and renal recovery in patients with AKI due to COVID-19. A secondary aim was to investigate the filter life times and the effect of different anticoagulants.

All patients admitted to the Intensive Care Unit (ICU) of the Rijnstate Hospital in Arnhem, The Netherlands from March 16th 2020 to May 10th 2020 were retrospectively studied. Follow-up lasted until May 13th 2020. Inclusion criterium was a positive COVID-19 Polymerase Chain Reaction (PCR). Exclusion criterium was an admission shorter than 24 h. Ethical approval and requirement for written informed consent was not required due to the retrospective and non-interventional nature of the study.

All patients with COVID-19 were admitted to the ICU for respiratory failure. All patients received thromboprophylaxis with daily nadroparin 2800 IE s.c., which was increased to 5600 IE s.c. daily following national guidelines on April 10th, 2020.When AKI occurred, post-renal and pre-renal causes were excluded. CRRT was started on indication, such as hyperkaliemia, fluid overload unresponsive to diuretics and severe metabolic acidosis. RRT was not an indication for ICU-admission, since a dialysis unit is available.

In our institution the primary method of RRT is Continuous VenoVenous Hemofiltration (CVVH) anticoagulated with citrate. When patients receive systemic anticoagulation with heparin for another indication, a bicarbonate-buffered substitution fluid is chosen and heparin is targeted at an APTT of 50–70 s. A filter change is scheduled routinely after 72 h. Intermittent Hemodialysis (IHD) is the secondary modality.

The indication for RRT is evaluated with every filter change. RRT is only restarted if clearance or diuresis, with diuretics if needed, is deemed insufficient by the treating physician.

The patients were categorized in a AKI-group, defined by a KDIGO-stage 1, 2 and 3 and a non-AKI-group. The patients from the AKI-group were categorized in a RRT-group and a non-RRT-group. All data are presented as median (interquartile range)[minimum-maximum]. 95% Confidence Interval (95%CI) was calculated for proportions. The Mann-Whitney-*U* test was used to compare continuous data between groups, the Fisher's exact test was used for categorical data. A $p < 0.05$ was considered significant.

A total of 39 patients were admitted to the ICU for COVID-19. 37 patients were included for analysis, of which 6 (16%) patients were still admitted to the ICU on May 13th.

Twenty-two (60%, 95%CI: 42–75) patients developed AKI. Hypertension, diabetes mellitus and chronic kidney disease were more frequent present in the AKI group, albeit not reaching significance. The severity of illness was comparable between the AKI and non-AKI group, except for a higher level of creatinine in the AKI-group upon admission. Mortality tended to be increased in the AKI-group (41%, 95%CI: 20–64) compared to the non-AKI-group (20%, 95%CI: 0–40). Of the AKI-group patients, renal function recovered in 64% to a KDIGO-stage 1 upon discharge from ICU.

Thirteen of the 22 patients with AKI (59%, 95%CI, 36–79) were treated with RRT. The patients in the RRT-group were younger, had higher levels of creatinine and BUN and oliguria was more frequently present compared to the non-RRT group. RRT was initiated a median of 6 days (4–12)[2–19] after ICU admission and lasted for 7 days (4–9)[1–19]. All patients received CVVH and five received at least one session of IHD. The indication for starting RRT were acidosis ($n = 4$), hyperkaliemia ($n = 7$) and fluid overload ($n = 2$).

Comparable mortality rates were seen in the RRT (39%, 95% CI:14–68) versus non-RRT group (44%, 95%CI:14–79), $p = 1.000$. Four patients that did not survive in the RRT-group needed RRT until death. The KDIGO-stages on discharge were comparable between the groups. None of the patients required RRT after ICU discharge.

Fifty-three filters were used for CVVH and filter lifetime was 27 h (14–63) [2–78], 35 (66%) of which were regional anticoagulated with citrate. Thirty filters (57%) failed prematurely and the lifetime of these filters was 21 h (13−33)[4–71]. No data were available regarding cause of failing. No correlation was found between the filter lifetime and dose of LMWH as thromboprophylaxis (2800 IE: 25 h (18–61) [4–72] versus 5600 IE: 26 h (13–66)[5–72], $p = 0.905$), therapeutic or prophylactic anticoagulation (20 h (14–30)[7–48] versus 21 h (9–40) [4–71], $p = 0.950$) or citrate versus bicarbonate-buffered substitution fluid (21 h (13–27)[4–71] versus 21 h (12–40)[7–48], $p = 0.801$). Prone position showed a non-significant lower filter lifetime than supine position (20 h (8–51)[2–72] versus 40 h (20–64)[6–78], $p = 0.071$).

The current study shows a mortality rate of 39% in patients with RRT for COVID-19 associated AKI, which strengthens the likelihood of a mortality around the lower limit of the reported 51.6–100% [6–8,13,14]. Second, renal function recovered to KDIGO-stage 1 in 64% of the patients with AKI when discharged from the ICU. This is merely a suggestion of renal recovery, since no long-term data are available. One can conclude, however, that RRT is a temporary intervention and associated with similar short term mortality rates as patients with AKI without RRT.

Furthermore, the low filter lifetimes were not associated with anticoagulation. Other reasons for a reduced filter lifetime may be

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Table 1
Characteristics and outcomes of the groups non-AKI, RRT and non-RRT.

	Non-AKI (n = 15)	RRT (n = 13)	Non-RRT (n = 9)	P[a]	P#
Patient characteristics					
Age (years)	68 (63−70)[42−81]	64 (59−69)[42−73]	71 (70−73)[60−76]	0.752	0.014
Gender (%male)	11 (73%)	10 (77%)	6 (67%)	1.000	0.655
BMI (kg/m^2)	27 (26−28)[20−43]	29 (26−31)[22−34]	27 (26−29)[21−34]	0.400	0.393
Comorbidities					
- *Hypertension*	2 (13%)	3 (23%)	5 (56%)	0.153	0.187
- *Diabetes Mellitus*	1 (7%)	2 (15%)	1 (11%)	0.633	1.000
- *Chronic Renal Failure*	0 (0%)	1 (8%)	2 (22%)	0.257	0.544
Severity of illness on admission					
SOFA-score	6 (6−7) [3−11]	8 (6−8) [3−11]	7 (6−8) [3−9]	0.161	0.471
P/F-ratio (kPa)	14.4 (11.1−25.6)[6.8−34.3]	16.0 (12.9−19.1)[7.7−28.9]	11.0 (9.1−15)[8−18.5]	0.547	0.104
PEEP (cmH2O)	12 (10−12)[10−16]	13 (10−16)[8−16]	14 (12−17)[10−18]	0.263	0.343
Creatinine (μmol/L)	63 (45−75)[35−90]	84 (74−92)[52−357]	92 (65−98)[48−159]	0.002	0.845
BUN (mmol/L)	6.6 (4.2−7.8)[3.1−14.0]	7.5 (6.5−10.3)[3.5−22.5]	7 (5.7−12.1)[4.8−18.6]	0.092	0.948
Mechanical ventilation	14 (93%)	13 (100%)	8 (89%)	1.000	0.409
Severity of AKI					
KDIGO-stage AKI		0 (0%)/ 0 (0%)/ 13 (100%)	5 (56%)/ 3 (33%)/ 1 (11%)		0.000
Highest creatinine (μmol/L)		390 (308−451)[178−500]	125 (98−150)[93−338]		0.000
Highest BUN (mmol/L)		42.1 (36.8−50.7)[17.6−66.2]	22 (19.8−28.1)[9.1−30.8]		0.004
Oliguria (<500 ml/24 h)		8 (62%)	1 (11%)		0.031
Duration of RRT		7 (4−9)[1−19]			
Outcomes					
Duration of ICU admission (days) (n = 31)	18 (9−27)[1−31]	24 (14−33)[8−37]	19 (7−37)[1−52]	0.258	0.762
Mortality (n = 31)	3 (20%)	5 (39%)	4 (44%)	0.257	1.000
Still in ICU	2 (13%)	3 (23%)	1(11%)	1.000	0.616
KDIGO-stage at discharge (1/2/3)		7 (54%)/ 2 (15%)/ 4 (31%)	7 (78%)/ 0 (0%)/ 2 (22%)		0.367
RRT after discharge		0 (0%)	0 (0%)		N/A

^: Difference between the Non-AKI and the AKI-group (combined RRT and non-RRT group), #: difference between RRT and non-RRT group.

increased filter clogging due to inflammatory proteins, a late response to alarms by the nursing staff due to personal protection equipment requirements or the decreased catheter performance due to prone positioning.

In conclusion, the need for RRT for AKI in critically ill patients with COVID-19 was often temporary in our cohort and was not associated with an increased mortality rate compared to AKI without the need for RRT. This could imply that no threshold for initiating RRT based on futility of treatment is warranted. This study found no support for the use of higher levels of anticoagulation to prolong the low filter lifetime (Table 1).

Ethics approval

Not deemed necessary by the Dutch law.

Consent to participate

All patients agreed on participation in retrospective studies in the study hospital.

Availability of data and material

Available upon reasonable request.

Declaration of Competing Interest

None of the authors have any conflicts of interests.

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