Arch Nephrol Urol 2021; 4 (1): 023-030 *DOI: 10.26502/anu.2644-2833033*

Research Article

Covid-19 and Renal Replacement Therapy: A Single-Center Perspective from Southern Italy

Piero Lisi[1], Luigi Rossi[1], Bianca Covella[1], Simone Corciulo[1], Annalisa Teutonico[1], Pasquale Libutti[1], Elisabetta Manno[1], Clorinda Derosa[2], Giovanni Larizza[2], Franco Mastroianni[2], Carlo Lomonte[1*]

[1]Nephrology Unit, Miulli General Hospital, Acquaviva delle Fonti, Bari, Italy

[2]Medicine Unit, Miulli General Hospital, Acquaviva delle Fonti, Bari, Italy

[*]**Corresponding Author:** Carlo Lomonte, Nephrology Unit, Miulli General Hospital, SP per Santeramo km 4.1, 70021 - Acquaviva delle Fonti, Bari, Italy, E-mail: c.lomonte@miulli.it

Received: 01 December 2020; **Accepted:** 28 December 2020; **Published**: 09 February 2021

Citation: Piero Lisi, Luigi Rossi, Bianca Covella, Simone Corciulo, Annalisa Teutonico, Pasquale Libutti, Elisabetta Manno, Clorinda Derosa, Giovanni Larizza, Franco Mastroianni, Carlo Lomonte. Covid-19 and Renal Replacement Therapy: A Single-Center Perspective from Southern Italy. Archives of Nephrology and Urology 4 (2021): 023-030.

Abstract

Introduction: The outbreak of cases of coronavirus disease (COVID-19), a very contagious disease, poses a serious threat to human health, especially in the elderly and in co-morbid populations like patients with kidney disease requiring renal replacement therapy (RRT). Furthermore, data about HD patients and how to best dialyze them during the COVID-19 pandemic are scarce. The aim of the study is to describe the organizational model and clinical outcomes of patients confirmed COVID-19 needing RRT, admitted in a COVID Hospital in Southern Italy.

Methods: This study is a cohort study of hospitalized patients with COVID-19 enrolled at Miulli General Hospital, one of the major designated hospitals providing medical care for COVID-19 patients in the Apulia Region.

We included all consecutive patients requiring RRT, either due to ESKD or AKI. Demographic data, information on clinical symptoms or signs at presentation, and laboratory results were extracted by the electronic medical record. A group of pair-matched COVID-19 patients, with normal renal function, were considered as controls. All the RRT sessions were performed with the Genius system.

Results: From March 10 through May 24, 2020, Miulli Hospital admitted 217 patients with COVID-19 infection, including 11 (5%) maintenance HD and 29 critically ill patients (13.3%) referred for ICU admission, of whom 3 with AKI. Overall, 140 bedside treatments were performed in the COVID Hospital, 122 bicarbonate standard in 11 HD patients, and 18 sustained low-efficiency daily dialysis (SLEDD) in 3 patients with AKI. Mean session time and mean weekly sessions were 3.64 ± 0.40 hours, and 3.4 ± 0.45 HD/week; while session time has been 7.4 ± 0.58 hours for SLEDD. The phenotype and clinical symptoms at the admission were not different between HD patients and controls. Compared to non-HD, HD patients showed lower serum levels of inflammatory markers, but only C-reactive protein reached significant levels (p=0.030), and lower hospital stay (p=0.020). In-hospital mortality was not different between the two groups. All AKI patients showed a severe systemic hyperinflammation at the admission and died in ICU.

Conclusions: Our data show that an organizational model based on the HD bedside with the Genius system, adopting the strict protocol, allows a personalized treatment with efficacy and safety for the patients and staff. The HD patients, SARS-Cov-2 infected, seem to have a lower inflammatory profile and shorter in-hospital stay compared with non-HD COVID-19 patients.

Keywords: COVID-19; Hemodialysis bedside; Genius System; SLEDD; Organizational model

1. Introduction

A novel human coronavirus that is now named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China, in late 2019 and is now causing a pandemic [1]. The outbreak of cases of coronavirus disease (COVID-19), a very contagious disease, poses a serious threat to human health, especially in the elderly and in co-morbid populations like hemodialysis patients. Uremic patients on dialysis combine an intrinsic fragility and a very frequent burden of co-morbidities [2, 3] and could be considered as a highly susceptible population; in addition, the HD centers are high-risk areas in the outbreak of COVID-19 epidemic. Measures of prevention, protection, and mitigation are essential in epidemic management and should be taken in the early stage [2, 3]. Furthermore, the management of patients with endstage kidney disease (ESKD), or COVID-19 associated AKI needing RRT, is even more challenging; the intensity of dialysis requiring specialized resources and staff is further complicated by requirements for isolation. It was recommended to set up designated dialysis hospitals to centrally isolate and manage the numerous patients with COVID-19 on hemodialysis [4]. However, there are limited data in the literature regarding how to best dialyze these patients during COVID-19 pandemic, and what are the appropriate dialysis schedules, membranes, organization models of care, as well as the clinical features of infection and outcomes in patients needed RRT. We described our

experience in treating patients with laboratory-confirmed COVID-19 needing RRT, implementing an organizational model of care based on bedside RRT treatments.

2. Methods

We included a cohort of consecutive hospitalized patients with laboratory-confirmed COVID-19 requiring RRT, either due to ESKD or Covid-19 associated AKI, admitted to Miulli General Hospital, one of the major designated hospitals providing medical care for COVID-19 in the Apulia Region (Southern Italy), from March 10 to May 24, 2020. A confirmed case of Covid-19 was defined by a positive result on a reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay of a specimen collected on a nasopharyngeal swab. Coexisting conditions were ascertained from medical records. The patient's phenotype at admission was evaluated according to a 3-stage classification system: Stage I (mild) early infection; Stage II (moderate), pulmonary involvement (IIa) without and (IIb) with hypoxia; Stage III (severe), systemic hyperinflammation [5]. The outcomes are presented for patients who completed their hospital course at the study end. All the RRT sessions utilized the Genius (Fresenius Medical Care, Bad Homburg, Germany) single-pass batch dialysis system. Genius therapy system gained interest for application in sustained low-efficiency daily dialysis (SLEDD) in acute bedside setting, due to its portability and battery runtime [6]. Genius provides 90 L of bicarbonate dialysate per dialysis session. It uses a double-sided roller pump that generates equal blood and dialysate flow up to 350 mL/min, as in the case of the 4-h HD sessions. The excess body water that is ultrafiltered out of the patient plasma is collected in an ultrafiltrate recipient. The medium cutoff dialyzer for expanded HD (Theranova 400, Baxter, U.S.) was utilized in all hemodialysis sessions, with the aim of increasing the efficiency of removal of middle size molecules and inflammation mediators [7]. Unfractionated heparin was used as systemic anticoagulation. Dialysate composition was as follows: calcium (Ca++) 1.5 mmol/L; magnesium 0.5 mmol/L; K+ 2 - 3 mmol/L; Na+ 140 mmol/L; bicarbonate 35 mmol/L; chloride 113 mmol/L; glucose 5.55 mmol/L; citrate 0.10 mmol/L.

Genius machine was prepared in the Dialysis Unit and then transferred to the COVID Hospital. After treatment, the dialysis machine undergoes standard sterilization, and the monitor was carefully cleaned with chlorine wipes and re-transferred into the dialysis Unit to be prepared for the next dialysis. A group of pair-matched COVID-19 patients, with normal renal function, were considered as controls. Serum biochemistry samples were analyzed in a standard multi-channel analyzer. Demographic data, information on clinical symptoms or signs at presentation, and laboratory results during admission were extracted by the electronic medical record.

2.1 Statistical analysis

Descriptive statistics were used to summarize the data; results are reported as means and standard deviations, as appropriate. Categorical variables were summarized as counts and percentages. Student's *t*-test for unpaired data and Fisher's exact test were employed for categorical variables as appropriate. A p-value below 0.05 was considered statistically significant. Analysis was performed with Statgraphics 18 software. The study was approved by the local institutional review board and waived the requirement for informed consent.

3. Results

During the period from March 10 through May 24, 2020, Miulli Hospital admitted 217 patients (58% M) with COVID-19 infection, including 11 (5%) HD patients and 29 (13.3%) referred for ICU admission, of whom 3 with AKI. Overall, 140 bedside treatments were performed in the COVID Hospital, 122 (87.1%) bicarbonate standard in 11 HD patients, and 18 (12.9%) SLEDD in 3 critically ill patients with AKI in ICU. The vascular accesses (VA) in ESKD patients consisted in 73% (8/11) of AVF and 27% (3/8) of a tunneled central venous catheter (CVC). A non-tunneled CVC was the VA utilized in AKI patients. Mean session time and mean weekly session was 3.64 ± 0.40 hours, and 3.4 ± 0.45 HD/week in HD patients; while session time has been 7.4 ± 0.58 hours for SLEDD in COVID-19 associated AKI. All the AKI patients showed a Stage III phenotype with a severe systemic hyperinflammation at the admission; they died in ICU and their data were not included in the analysis.

Table 1 shows the demographic characteristics, clinical presentation, and outcomes of 11 patients receiving HD treatment and 11 nondialysis pair-matched infected patients. The mean age was 78 years (range: 65-89); males were highly prevalent in the uremic subgroup (10/11; 90.9%.) Fever was present in 20/22 (90.9%) of patients on admission. The second most common symptom was cough 16/22 (72.7%); headache and fatigue 3/22 (13.6%), anosmia, and ageusia 3/22 (13.6%), gastroenteric symptoms were uncommon 1/22 (0.45%). Among the coexisting illnesses, hypertension was highly prevalent followed by CV diseases and diabetes. As expected, sCr and Hb showed significant differences between HD patients and controls ($p<0.0001$ and $p=0.010$). Mean lymphocyte was below the limit of normal in both groups, with lower levels in uremic patients, albeit not significant. Compared to non-dialysis, HD patients showed low levels of inflammatory markers as IL6 and C-reactive protein, although only the latter reached statistical significance ($p=0.030$), and higher levels of procalcitonin ($p<0.01$). The hospital stay was significantly higher in non-HD patients ($p=0.020$), while in-hospital mortality was not different between the two groups. Supportive pharmacologic treatments were administered in all cases. Thirteen patients received hydroxychloroquine/ azithromycin (7 HD patients and 6 controls), and eight lopinavir/ritonavir (2 HD patients and 6 controls) as a specific treatment. Tocilizumab has been administered only in three AKI patients admitted in ICU (data not shown). In-hospital death occurred in 18% (39/217) of the entire COVID-19 cohort and in 18.2% (2/11) in HD patients. Patients were discharged if they are free of symptoms and after that two consecutive testings collected on a nasopharyngeal swab conferred negative.

Characteristic	**All patients no. 22**	**HD patients no. 11**	**non-HD patients no. 11**	**p**
Age, years (range)	78 (65-89)	77.8 (69-85)	78.3 (71-89)	ns
Male patients no. (%)	20 (90.9)	10 (90.9)	10 (90.9)	ns
Dialysis Vintage, months (range)	-	71 (4-228)	-	-
Phenotype at admission - no. (%)				
Stage I (mild)	7 (32)	3 (27.3)	4 (36.3)	ns
Stage IIa (moderate) no hypoxia	7 (32)	4 (36.3)	3 (27.3)	ns
Stage IIb (moderate) hypoxia	5 (22.5)	3 (27.3)	2 (18.2)	ns
Stage III (severe)	3 (13.5)	1 (9.1)	2 (18.2)	ns
Symptoms - no. (%)				
Fever	20 (90.9)	9 (81.8.)	11 (100)	ns
Cough	16 (72.7)	7 (63.6)	9 (81.8)	ns
Headache and fatigue	3 (13.6)	1 (9.1)	2 (18.2)	ns
Anosmia and ageusia	3 (13.6)	1 (9.1)	2 (18.2)	ns
Gastroenteric symptoms	1 (0.45)	1 (9.1)	0 (0)	ns
Comorbidity - no. (%)				
Hypertension	19 (86.3)	10 (90.9)	9 (81.8)	ns
Diabetes	4 (18.2)	2 (18,1)	2 (18.2)	ns
CV disease	12 (54.5)	7 (63.6)	5 (45.4)	ns
Laboratory Data, mean ± sd				
sCr mg/dl	3.9 ± 3.0	6.8 ± 0.6	1.08 ± 0.4	0.000
Hemoglobin g/L	11.8 ± 0.6	10.8 ± 0.7	12.9 ± 0.5	0.010
Lymphocytes $x10^9$/L	982.93 ± 420.18	905.45 ± 420.88	1060.90 ± 419.48	ns
Albumin g/L	38 ± 5.2	37 ± 4.1	39 ± 6.2	ns
C-reactive protein, mg/L	4.74 ± 3.8	2.78 ± 2.15	6.70 ± 5.44	0.030
IL 6, pg/mL	51.9 ± 44.8	48.36 ± 35.74	55.45 ± 46.52	ns
Procalcitonin, ng/ml	0.55 ± 0.31	0.88 ± 0.46	0.23 ± 0.17	0.000
Therapy				
Need for oxigen supply, no. (%)	8 (36.4)	4 (36.3)	4 (36.3)	ns
Lopinavir/ritonavir, no. (%)	8 (36.4)	2 (18.2)	6 (54.5)	ns
Hydroxichloroquine/azithromycin, no.(%)	13 (59.1)	7 (63.6)	6 (54.5)	ns
Outcomes				

Hospital stay - days, mean ± sd	26.15 ± 9.3	21.1 ± 10.8	31.2 ± 7.9	0.020
In-hospital mortality - no. (%)	4 (18.2)	2 (18.2)	2 (18.2)	ns
Discharge from hospital - no. (%)	18 (81.8)	9 (81.8.)	9 (81.8.)	ns

Table 1: Clinical Characteristics, laboratory data, and outcome in 11 hemodialysis patients and 11 pair-matched controls.

4. Discussion

Our study describes the organizational models of care and clinical outcomes in patients requiring RRT admitted to a COVID Hospital in Southern Italy from March 10 to May 24, 2020. Eleven HD patients and three critically ill patients with COVID-19 associated AKI were treated; all received a personalized bedside HD with Genius system. Demographic characteristics and clinical pattern in our small cohort of HD patients and controls were similar to data reported in other studies, and confirm the higher prevalence of older persons, men, and those with co-morbidities and pre-existing hypertension [8, 9]. Clinical symptoms and phenotype at the admission were not different between the two groups, while, the inflammatory biomarkers were slightly reduced in HD patients. In fact, it has been reported that HD patients display a remarkable lower serum level of inflammatory cytokines than other Covid-19 non-HD patients and mostly clinical mild [10-12]. A shorter hospital stay in HD patients seems to confirm this hypothesis. The elevated levels of procalcitonin, which are considered rare in Covid-19 [13], may reveal a bacterial co-infection. However, HD patients appear to have symptoms similar to the general population, but no studies until now have compared HD patients with the general population [14]. Finally, in-hospital mortality was not different between HD and non-HD patients, and it is very close to the mortality of the entire COVID-19 cohort and close to other reports regarding HD-patients [10, 15]. The management of HD patients affected by COVID-19 must be carried out according to strict protocols to minimize the risk for other patients and personnel taking care of these patients [3]. It is important to quickly devise plans to keep dialysis patients safe during COVID-19 pandemic and determine how to best dialyze them [12]. A real problem is a chosen modality of RRT necessitates thoughtful application to deliver the right therapy for the right patient at the right time [16]. Increasing the use of home dialysis with home HD or peritoneal dialysis has been also advocated [12, 17]. Dedicated dialysis hospitals to centrally isolate and manage numerous patients with COVID-19 on hemodialysis have been recommended [4]. In addition, for safety reasons, as experienced in some European centers, the dialysis machines should stay in the COVID-19 area that must be disinfected daily with efficient methods [18]. Still, practices may differ, and in a dynamic pandemic process, pro-active solutions are needed. In our hospital, we did not create a dedicated COVID-19 dialysis unit, as described in other Italian experiences [15], or moved the patients for the hemodialysis treatments. All patients were treated in COVID-19 ward; that could be advantageous in those patients who need continuous positive airway pressure [14]. Even more complex are the treatments in patients with COVID-19 associated AKI. An integrate multi-organ support platforms for personalized treatment has been advocated in critically ill patients with kidney involvement in COVID-19 [16]. Furthermore, team expert

recommendations encourage the use of continuous kidney replacement therapy [19], although forms of prolonged and conventional intermittent RRT may have an important role in the support of critically ill patients with COVID-19 infection [16]. The particular local resources, and logistics of our hospital, which is equipped with negative pressure in all rooms, allowed us to implement an organizational model based on the hemodialysis bedside, adopting strict protocol and personalized the treatment with Genius system, either for intermittent RRT or SLEDD, that represents a good compromise between continuous and intermittent modalities [16]. Importantly, Genius system doesn't require the installation of an in-room water supply, dialysate effluent drainage, or portable reverse osmosis. During the study period and until now, no virus transmission to doctors, uninfected HD outpatients, and nursing staff has been observed. Our study has some limitations. Firstly, the study only included a small number of HD patients, not large enough to exclude bias in the results of the analysis. However, it is a real-life experience that might be of interest to clinicians who manage patients who need RRT. Secondly, this is a single-center study, and the conclusions obtained need to be further verified by other centers.

5. Conclusions

Our data show that an organizational model based on the HD bedside with the Genius system, adopting the strict protocol, allows a personalized treatment, with efficacy and safety for the patients and staff. The HD patients, SARS-Cov-2 infected, seem to have a lower inflammatory profile and shorter in-hospital stay period compared with non-HD COVID-19 patients.

Conflict of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Disclosures of Grants or other Fundings

None.

References

1. Coronavirus disease (COVID-2019) situation reports. Geneva: World Health Organization (2020).
2. Rombolà G, Heidempergher M, Pedrini L, et al. Practical indications for the prevention and management of SARS-CoV-2 in ambu-latory dialysis patients: lessons from the first phase of the epidemics in Lombardy. J Nephrol 2 (2020): 193-196.
3. Basile C, Combe C, Pizzarelli F, et al. Recommendations for the prevention, mitiga-tion and containment of the emerging SARS-CoV-2 (COVID-19) pandemic in hae-modialysis centres. Nephrol Dial Transplant 5 (2020): 737-741.
4. Junhua Li and Gang Xu. Lessons from the Experience in Wuhan to Reduce Risk of COVID-19 Infection in Patients Undergoing Long-Term Hemodialysis. Clin J Am Soc Nephrol 5 (2020): 717-719.
5. Siddiqi HK, Mehra MR. COVID-19 Illness in Native and Immunosuppressed States: A Clinical-Therapeutic Staging Proposal. J Heart Lung Transplant 5 (2020): 405-407.
6. Vanholder R, Van Biesen W, Lamiere N. What is the renal replacement method of first choice for intensive care patients? J Am Soc Nephrol 12 (2001): 40-43.

7. Alberici F, Delbarba E, Manenti C, et al. Management of patients on dialysis and with kidney transplant during COVID-19 coronavirus infection. Kidney Int Rep 5 (2020): 580-585.
8. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA 20 (2020): 2052-2059.
9. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 395 (2020): 1054-1062.
10. Ma Y, Diao B, Lv X, et al. 2019 novel coronavirus disease in hemodialysis (HD) patients: Report from one HD center in Wuhan, China. medRxiv (2020).
11. Wang R, Liao C, He H, et al. COVID-19 in Hemodialysis Patients: A Report of 5 Cases. Am J Kidney Dis 76 (2020): 141-143.
12. Rabb H. Kidney diseases in the time of COVID-19: major challenges to patient care. J Clin Invest 6 (2020): 2749-2751.
13. Cheng Y, Luo R, Wang K, et al. Kidney disease is associated with in-hospital death of patients with Covid-19. Kidney Int 97 (2020): 829-838.
14. Gallieni M, Sabiu G, Scorza D. Delivering hemodialysis in patients with suspected or confirmed COVID-19 infection: a single-center perspective from Italy. Kidney360 1 (2020): 403-409.
15. Alberici F, Delbarba E, Manenti C, et al. Management of Patients on Dialysis and With Kidney Transplantation During the SARS-CoV-2 (COVID-19) Pandemic in Brescia, Italy. Kidney Int Rep 5 (2020): 580-585.
16. Ronco C, Bagshaw SM, Bellomo R, et al. Extracorporeal Blood Purification and Organ Support in the Critically Ill Patient during COVID-19 Pandemic: Expert Review and Recommendation. Blood Purif 26 (2020): 1-11.
17. Tz-Heng C, You-Hua W, Chun-Fan C, et al. The advantages of peritoneal dialysis over hemodialysis during the COVID-19 pandemic. Semin Dial 33 (2020): 369-371.
18. Meijers B, Messa P, Ronco C. Safeguarding the Maintenance Hemodialysis Patient Population during the Coronavirus Disease 19 Pandemic. Blood Purif 3 (2020): 259-264.
19. Ronco C, Reis T. Kidney involvement in COVID-19 and rationale for extracorporeal therapies. Nat Rev Nephrol 6 (2020): 308-310.