Received: 23 April 2020 | Accepted: 20 May 2020

DOI: 10.1111/eci.13309

EDITORIAL

WILEY

Challenges in COVID-19 medical response: A nephrology perspective

1 | COVID-19 AND END-STAGE RENAL DISEASE

The new coronavirus disease, named by World Health Organization as COVID-19 brought great challenges to patients with end-stage renal disease (ESRD). In general, ESRD patients have higher number of comorbidities and are at age risk for severe pulmonary presentation of this disease. Another important issue is that haemodialysis (HD) clinics are usually not located in small towns, and these frail patients often travel to their dialysis centre in groups and also cannot keep the 6-feet safe distance during their HD session.[1]

The total number of patients on dialysis in Brazil was estimated at 126 583 in 2017. Peritoneal dialysis (PD) was used by 6.9% of patients, the majority of whom were on automated peritoneal dialysis (APD); frequent (>4 times a week) HD by 1.3% and conventional HD by 91.8%. The distribution of active dialysis centres was 46% in the Southeast region, 20% in the South, 10% in the Midwest, 19% in the Northeast and 5% in the North. Fifty per cent of them were located outside hospitals, and 73% were entitled to attend patients from both public health system and private health insurance companies.[2]

Some strategies to minimize the risk of spreading SARS-CoV-2 throughout the dialysis units are simple such as a phone call to the patients just before their HD session asking about any signs of fever or respiratory symptoms. Despite patients are highly stimulated to minimize public transportation and if possible use private means, this option is often unavailable in developing countries. Furthermore, the social distance measures are not so easy to follow, as it depends on unit's architectural characteristics as well as on staff resources.

In a rapid-testing scenario, testing HD patients who present fever on nondialysis days would be reasonable, but with the lack of rapid diagnostic kit tests this is not that feasible. For the dialysis days, screening fever and symptoms before entering the room is mandatory and should help installing a cohort-dialysis session, preferably at the last session of the day. Dialysis facilities with hepatitis B isolation rooms are used for COVID-19-infected patients and should be the first choice if there is no hepatitis B on that session. Selected dialysis personnel is assigned exclusively to these patients and must wear complete personnel protective equipment (PPE) including face shields (Figure 1). Routine dialysis cleaning and disinfection procedures are appropriate for COVID-19 in dialysis settings, but a second cycle of surface cleaning is recommended before using the equipment on another patient. At the end of daily use of the equipment, a final cycle of thermal disinfection should be performed, with citric acid or sodium hypochlorite, according to the manufacturer's recommendations.

Dialysis staff must undergo respiratory symptoms surveillance and remain isolated if presenting febrile symptoms. In a region where the ascending curve of cases is just at the beginning, this strategy could work, but in a staff-shortening period, testing symptomatic personnel will be crucial to minimize lack of healthcare workers. The nontesting strategy recommended by Center of Disease Control should be used if there is rapid-tests shortage. After three days of recovered symptoms plus seven days after the symptoms first appeared, personnel should return to work.[3]

Regarding PD remote patient management is the best option to keep patients away from medical facilities. PD patients must have a 2-week supply bags in case of hospitalization as recommended by International Society of Peritoneal Dialysis. When these patients become positive for COVID-19, the prescription must be revaluated in order to keep patients dry, since positive fluid balance could worsen respiratory symptoms. There is lack of evidence if PD-drained dialysate fluid could spread virus, but caution for accidental splash when disposing PD-drained fluid is reinforced. Nevertheless, PD could be a strongly recommended strategy during COVID-19 pandemic, for its special characteristics on limiting social contact and minimizing hospital visits.

As part of the high-risk group, ESRD patients must wear face masks. As shortage of PPE becomes a worldwide

Correction added on [26 October 2020], after initial online publication. A duplicate of this article was published under the DOI 10.1111/eci.13328. This duplicate has now been deleted and its DOI redirected to this version of the article.

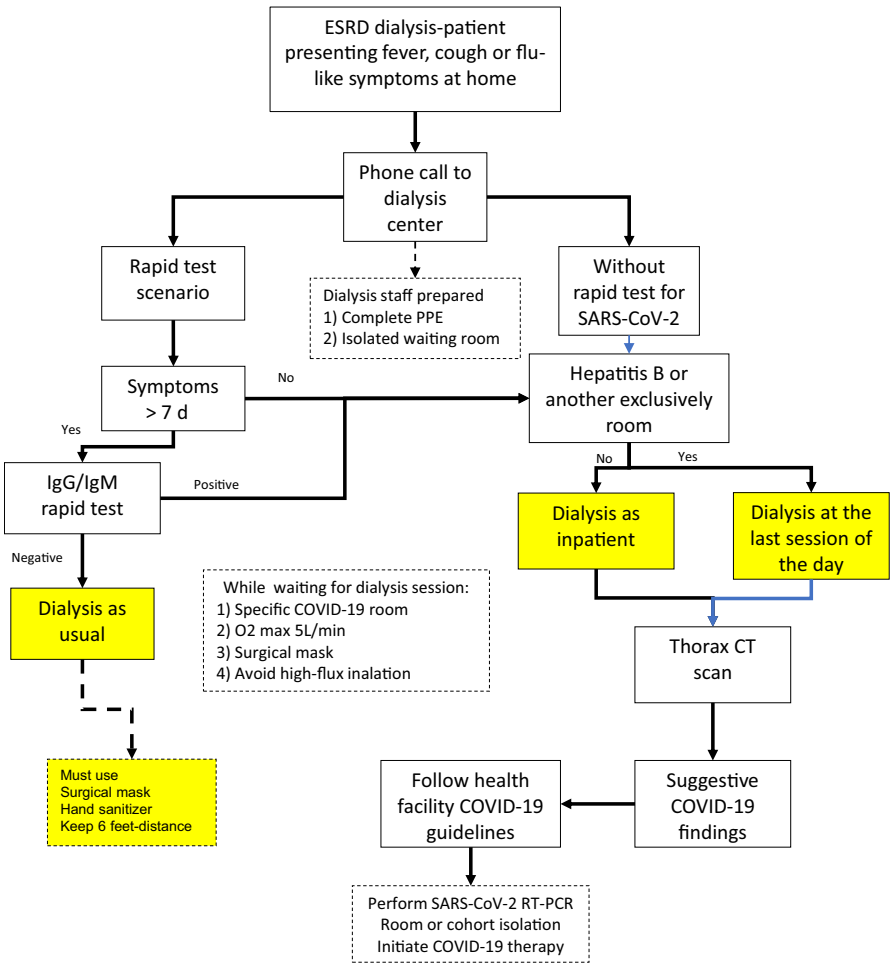

FIGURE 1 Managing haemodialysis patients to prevent COVID-19 in dialysis centres. Hepatitis B isolation rooms should only be used if the facility does not have any Hepatitis B patients

problem, homemade masks can be recommended for outpatient at home and should offer more protection than using any mask, preserving approved-masks for healthcare professionals.[4]

2 | COVID-19 AND ACUTE KIDNEY INJURY

Patients infected with COVID-19 often present clinical markers of kidney injury. In 710 patients evaluated by Cheng et al,[5] haematuria was present in 26.7% and the association of haematuria/proteinuria was found in 44% of patients. According to the available reports, acute kidney injury (AKI) occurs in approximately 3%-15% of patients with COVID-19 infection.[6] Most patients with COVID-19 are affected by mild or asymptomatic renal disease, but those who develop AKI usually share the most severe phenotype of the disease, characterized by cytokine storm, acute lung injury and, eventually, hypercoagulability. Clinical and experimental models of organ cross-talk are well described and could justify AKI in this scenario, in addition of a possible kidney tropism of the SARS-CoV-2.[6,7] In a necropsy study, it was demonstrated that SARS-CoV-2 infection induces severe acute tubular necrosis and lymphocyte infiltration associated with the presence of virus antigens in renal tubules.[8] A case report of collapsing glomerulopathy in a patient infected with COVID-19 was recently published. Although the viral antigen was not detected in the renal tissue, there is a possibility that the virus may have been the trigger for the development of the glomerular lesion.[9]

The challenge for the intensive care nephrology community, especially in developing countries, is to be able to provide dialysis care and adequate support during the pandemic. In Brazil, as most part of the world, the model of AKI care involves mainly the nephrologist. The nephrologist exposition can be minimized through collaboration with the intensive care unit (ICU) team to provide reports of physical examination, perception of hypervolemia, hemodynamic and ventilatory parameters. This strategy can minimize the exposure of health professionals and permit rational use of PPE. However, with the burden of cases and patients in ICU, an increasing risk for the nephrology team is inevitable.

In the general population, outside pandemic scenario, about 15% of AKI patients require dialysis. It is possible that the same occurs in COVID-19 patients. Recently in a series with 2249 COVID-19 patients reported in England, Wales

and Northern Ireland up to 3 April 2020, ICU outcomes have been documented in 690 patients and renal support was necessary in 107 (18.5%) patients.[10] In case series of 151 critically ill adult patients admitted to the ICU in São Paulo city (12 million inhabitants) hospital up to 23 April 2020, 60 (40%) required mechanical ventilation and 26 (17.2%) patients received dialysis due to AKI. The authors report that dialysis was needed early in some of these cases (around 48 hours after ICU admission), and AKI was not clearly associated with septic shock.[11]

In general, dialysis indications in COVID-19 patients follow the same recommendations as in other acute kidney injuries. One of the greatest concerns in AKI COVID-19 patients is the time of dialysis initiation. As the evidence is not yet sufficient to establish whether early or late start of dialysis has a mortality impact on AKI patients, the indication should be—as always—shared between the nephrologist and intensivist. In COVID-19, due to ventilatory issues, hypervolemia is a leading cause of early dialysis indication and intensivists should be aware of minimizing volume resuscitation in these patients. For safety reasons, if there is no very clear indication of dialysis, one should consider the nonexposure of machines, health professionals and patients to the procedure.

The choice of dialysis modality for patients with COVID-19 should take into account logistical issues and experience of each institution. Likewise in non-COVID-19 patients, continuous (CVVHD, CVVH or CVVHDF), intermittent methods (conventional HD) or even hybrids ones (SLED) may be used. Due to cytokine storm, some authors advocate the use of membranes or methods with the ability to remove inflammatory mediators, however, at daily care this is not a stablished routine.[12]

Intensive care unit and nephrology team must be aware whenever a COVID-19 patient needs prone position ventilation. The presence of dialysis catheters and lines does not contraindicate this position but requires specific attention during pronation maneuvers and returning to the supine position. Whenever possible, particularly in intermittent procedures, it is recommended to return the blood and temporarily disconnect the circuit. Immediately after these maneuvers, dialysis equipment should be inspected for pulls, twists and patency. Regarding fluid management, as far as possible a restrictive strategy should be used targeting reduction of extravascular pulmonary water. In the absence of shock, volume replacement should be restricted and hypotension that usually develops after the onset of mechanical ventilation should initially be approached with vasopressors. All this volume-restricted protocols in COVID-19 patients must keep ICU staff aware of avoiding some typical intensive care maneuvers, as maintenance hydration, high-volume nutritional support, and repeated use of volume responsiveness tests.[13,14]

Depending on each local reality and expertise, APD using a cycler may be an option to reduce exposure of health professionals. However, most COVID-19 patients who are on mechanical ventilation necessitates high PEEP and FiO_2 values, and this method may restrict lung expansion.

Another challenge for AKI dialysis is the anticoagulation during continuous or intermittent dialysis. The indications and methods are very similar from the ones already routinely used in each institution but it is worth remembering that hypercoagulability states have been described in these patients and a higher dose of heparin or regional anticoagulation with citrate may be required. It is important to remember that most ICUs in developing countries and even some units in developed countries do not have all the dialysis methods available. As far as literature can demonstrate, there is not a superior benefit of an specific dialysis method comparing to another one. Thus, the ICU and nephrology team must take expertise and experience into account whenever deciding the appropriated strategy for each situation.

CONFLICT OF INTEREST

All authors declare that they have no financial or ethical conflict of interest.

Gustavo Navarro Betônico[1,2]
Emerson Quintino Lima[3]
Ana Carolina Tome[3]

[1]*UNIFAI Medical School, Adamantina, Brazil*
[2]*FEMA Medical School, ASSIS, Brazil*
[3]*Nephrology Division, Medicine School of Sao Jose do Rio Preto, Sao Jose do Rio Preto, Brazil*

gustavonavarro@fai.com.br

ORCID

Gustavo Navarro Betônico https://orcid.org/0000-0001-6759-3910

REFERENCES

1. Meijers B, Messa P, Ronco C. Safeguarding the maintenance hemodialysis patient population during the coronavirus disease 19 pandemic. *Blood Purif*. 2020;49(3):259-264.
2. Thomé FS, Sesso RC, Lopes AA, Lugon JR, Martins CT. Brazilian chronic dialysis survey 2017. *J Bras Nefrol*. 2019;41(2):208-214.
3. CDC. Criteria for Return to Work for Healthcare Personnel with Confirmed or Suspected COVID-19 (Interim Guidance). 2020. https://www.cdc.gov/coronavirus/2019-ncov/healthcare-facilities/hcp-return-work.html. Accessed June 15, 2020.
4. Davies A, Thompson KA, Giri K, Kafatos G, Walker J, Bennett A. Testing the efficacy of homemade masks: would they protect in an influenza pandemic? *Disaster Med Public Health Prep*. 2013;7(4):413-418.
5. Cheng Y, Luo R, Wang K, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int*. 2020;97(5):829-838.

6. Durvasula R, Wellington T, McNamara E, Watnick S. COVID-19 and kidney failure in the acute care setting: our experience from Seattle. *Am J Kidney Dis*. 2020;76(1):4-6. https://doi.org/10.1053/j.ajkd.2020.04.001
7. Doi K, Rabb H. Impact of acute kidney injury on distant organ function: recent findings and potential therapeutic targets. *Kidney Int*. 2016;89(3):555-564.
8. Diao B, Feng Z, Wang C, et al. Human kidney is a target for novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection. *medRxiv*. 2020;2:1-17. https://doi.org/10.1101/2020.03.04.20031120
9. Kissling S, Rotman S, Gerber C, et al. Collapsing glomerulopathy in a COVID-19 patient. *Kidney Int*. 2020;98(1):228-231. https://doi.org/10.1016/j.kint.2020.04.006
10. ICNARC report on COVID-19 in critical care. 2020;1-9. https://www.icnarc.org/About/Latest-News/2020/04/04/Report-On-2249-Patients-Critically-Ill-With-Covid-19. Accessed June 15, 2020.
11. Sesso RC, Durão M. Management of hemodialysis patients with suspected or confirmed COVID-19 infection: perspective of two nephrologists in Brazil. *Kidney*. 2020;360:1-8.
12. AlbericiF, 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 International Reports*. 2020;5(5):580-585. http://dx.doi.org/10.1016/j.ekir.2020.04.001
13. SBN; AMIB. Brazilian Society of Nephrology & Brazilian Intensive Care Medicine Association.Nota técnica e orientações sobre a injúria renal aguda (IRA) empacientes com COVID-19. 2020. https://www.sbn.org.br/fileadmin/user_upload/sbn/2020/04/15/Nota_tecnica_e_orientacoes_sobre_a_injuria_renal_aguda__IRA__em_pacientes_com_COVID-19.pdf. Accessed June 15, 2020.
14. Phua J, Weng L, Ling L, et al. Review Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. *Lancet Respir*. 2020;2019(20):1-12.