Technical note and clinical instructions for Acute Kidney Injury (AKI) in patients with Covid-19: Brazilian Society of Nephrology and Brazilian Association of Intensive Care Medicine

Nota técnica e orientações clínicas sobre a Injúria Renal Aguda (IRA) em pacientes com Covid-19: Sociedade Brasileira de Nefrologia e Associação de Medicina Intensiva Brasileira

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ABSTRACT

We produced this document to bring pertinent information to the practice of nephrology, as regards to the renal involvement with COVID-19, the management of acute kidney injury cases, and practical guidance on the provision of dialysis support.
As information on COVID-19 evolves at a pace never before seen in medical science, these recommendations, although based on recent scientific evidence, refer to the present moment. The guidelines may be updated when published data and other relevant information become available.

Keywords: Acute Kidney Injury; Coronavirus Infections; Covid-19; Critical Care.

RESUMO

Este documento foi desenvolvido para trazer informações pertinentes à prática nefrológica em relação ao conhecimento sobre o acometimento renal da COVID-19, conduta frente aos casos de injúria renal aguda e orientações práticas sobre a provisão do suporte dialítico.
Como as informações sobre a COVID-19 evoluem a uma velocidade jamais vista na ciência médica, as orientações apresentadas, embora baseadas em evidências científicas recentes, referem-se ao momento presente. Essas orientaços poderão ser atualizadas à medida que dados publicados e outras informações relevantes venham a ser disponibilizadas.

Palavras-chave: Lesão Renal Aguda; Infecções por Coronavirus; Covid-19; Cuidados Críticos.

CONTEXT

The Covid-19 pandemic is a global threat with the potential to deplete national healthcare systems. The colossal volume of reports and discussions produced in such a short term is an unprecedented fact in medicine, not only in traditional vehicles of scientific dissemination, but also in blogs, websites, social networks and conversations between peers. Evidence is published at a rapid pace and no recommendation can be considered definitive. Like the first version, made available online, this second edition is based on information available until the moment of its publication. The objective is to inform, recommend practices and assist in decision-making, recognizing that the situation does not allow for establishing strict guidelines.

The Brazilian Society of Nephrology (SBN) and the Brazilian Association of Intensive Care Medicine (AMIB) understand that there are different scenarios of assistance to patients with Acute Kidney Injury (AKI) in our country. It is inevitable that there will be variations in practice, resulting from individualities in the clinical picture, the availability of human and material resources and other aspects, associated with the resources of each healthcare institution, including the type of organization and the type of contracting of nephrological care.

Every professional involved in nephrological care must provide the best possible assistance to the patients under their responsibility, adopt practices that minimize their personal risk of contamination, that of their patients and the whole range of other professionals who participate in hospital kidney support, including nurses and technicians, dialysis staff, healthcare professionals from all areas (for example, doctors and nurses in intensive care medicine), laboratory and radiology technicians, cleaning and transport staff, etc.

Each institution must define its bed allocation policy for patients with Covid-19, as well as that of the professionals responsible for the treatment, either by isolation of a cohort in a specific physical area, in a general inpatient unit or in a general hospital intensive care unit. Protocols for the entry and circulation of nephrology team members in the environment of patients with Covid-19 must be defined in advance, in order to minimize the use of personal protective equipment (PPE) and to limit nonessential traffic in isolation environments.

Since a larger contingent of patients with AKI will be under intensive or semi-intensive care, interaction and collaboration between nephrologists and intensivists is essential. It is advisable to adapt visiting routines to digital format and all documentation/prescription to electronic format, avoiding the movement of papers and documents between the inpatient unit and other institutional sectors.

It is imperative, during interactions with patients, that nephrologists and other members of the dialysis team follow the guidelines for safety and use of PPE.

Covid-19 clinical phenotypes

As Covid-19 spreads, awareness of its manifestations also increase. It is now evident that Covid-19 has different clinical phenotypes[1], not necessarily sequential, which may have direct implications in the risk of AKI.

The vast majority of symptomatic cases are benign, with flu-like syndrome and mild pulmonary involvement. Phenotypes that are more serious include acute respiratory distress syndrome (ARDS) with alveolar damage due to viral cytopathic effect, systemic hyperinflammation syndrome (or cytokine storm) and hypercoagulability syndrome with micro and macrovascular manifestations[2].

Causes of acute kidney injury with Covid-19

There is ample literature on the association of acute respiratory distress syndrome (ARDS) with AKI, within the pathophysiological model of the crosstalk between the organs. It is not surprising to see the development of AKI in patients with the extensive pulmonary damage that characterizes the severe forms of Covid-19 and the adverse renal effects of the highly complex ventilatory support that these patients need. In a large series in New York, the main cause attributed to the development of AKI was the systemic collapse that follows orotracheal intubation and the beginning of mechanical ventilation[3].

In some cases, disease progression is much more severe, with hyperinflammation, often associated with acute cardiac injury. The striking feature of these cases is the significant increased circulating levels of inflammatory cytokines, notably IL-6, IL-18 and IFN-γ, and other markers, such as troponin, ferritin and D-dimer[4,5]. These patients have a poor prognosis and evidently difficult-to-manage AKI.

Autopsy studies have produced variable findings. One of the first series reported severe tubular necrosis, associated with lymphocytic tubulointerstitial nephritis, with macrophages and tubular deposition of the complement membrane attack complex[6]. Immunohistochemistry demonstrated direct renal infection by SARS-CoV-2, which is not surprising, given the high expression of ACE2 receptor in the renal tubular epithelium. The possibility of cytopathic action by direct viral invasion of the renal epithelium has been reinforced with ultrastructural and molecular studies[7-9]. As these samples are skewed for the patients that died, it is not possible to assess the relevance of the findings in relation to the AKI cases reported in clinical studies.

In conclusion, the term AKI is used for a wide variety of diseases that result in acute and subacute decrease in renal function, including, among others, processes of mechanical, ischemic, toxic, infectious origin and the branches of innate, adaptive humoral and cellular immunity. It is interesting to note that AKI cases with Covid-19 seem to reproduce this diversity. The etiologic factors involved are multiple and include direct viral cytopathic effect, decreased blood oxygen content and renal plasma flow, angiotensin II activation, glomerulopathies, crosstalk injury, inflammatory deregulation, hyperviscosity, thrombotic microangiopathy, secondary sepsis and drug toxicity[3,6-8, 10-14].

Epidemiology of acute kidney injury in patients with Covid-19

In the first published series, almost all from China, the average incidence of AKI associated with Covid-19 was relatively low. On average, only 5.8% (0.5 to 23%) affecting severe cases and only 2.1% of patients (0.8 to 11.0%) needing renal replacement therapy (RRT)[4,5.15-24]. These data did not suggest a higher incidence of AKI in patients with Covid-19 when compared to other patients with the same severity profile[17]. In publications, the existence of two AKI patterns was also highlighted; one early and one late. The latter was assigned a worse prognosis[5,17]. In late cases, the average time from admission to AKI was seven days[5,25].

The experience in the West seems to be diverse and still in the process of being published. However, in a large series from New York, AKI in the three KDIGO stages was seen in 37% of 5449 patients[3]. Of these, 14% required artificial renal support. Of the patients who died, 34% were in the KDIGO stage1; 64%, in stage 2; and 91% in KDIGO stage 3.

In particular, there was a strong association with ventilatory support, with 98% of patients on mechanical ventilation developing AKI, versus 22% of those not ventilated.[3] Again in opposition to the initial publications, the majority of cases seen in the New York large serie occurred in the first two days of hospitalization, 52% in the first 24 hours[3]. Anecdotal reports from European and Brazilian centers also point to a high incidence of AKI in patients on mechanical ventilation, between 20% to 50% of cases.

This information is especially important to plan the allocation of dialysis machines and supplies as well as human resources to face the epidemic in places where the pandemic is still in the initial phase of dissemination through the population.

Prognosis of acute kidney injury in patients with Covid-19

As with other causes for ARDS, the development of AKI in patients with Covid-19 correlates with a worse overall prognosis and impacts mortality.[5,17] In a series with AKI staging by the KDIGO system (Table 1), there was a progressive increase in the odds ratio for lethality, reaching 9.8 in patients staged as KDIGO 3. In the American series mentioned above, the mortality initially reported was 35%, although 39% of the patients were still hospitalized[3].

When to call the nephrologist

Even though it is always necessary, in the current situation it is essential to reinforce the need for close collaboration between intensivists and nephrologists, sharing opinions at the bedside, and reviewing hemodynamic parameters and volume status. In the discussion of each case, priorities and the best treatment strategies are expected to be established in a shared way.

Within this perspective, the nephrologist shall be contacted in any situation of need, even with discrete degrees of renal dysfunction, since the nephrological involvement in intensive care is not limited to AKI. The nephrologist's contribution includes additional situations, such as electrolyte disturbances, adjustment of medication doses, etiological diagnosis and management of kidney diseases of various etiologies.

KDIGO qualifies the severity of AKI in stages (Table 1). In this sense, we recommend that patients

Table 1 KDIGO classification for acute kidney injury

Stage	Serum creatinine (Cr)	Score the largest deviation (diuresis or creatinine)	Hourly diuresis
1	↑ ≥ 0,3 mg/dl in 48h or ↑ 1,5-1,9 x Cr within 7 days	or	< 0,5 mL/kg/h for 6-12h
2	↑ 2,0-2,9 x Cr of baseline	or	< 0,5 mL/kg/h for ≥ 12h
3	↑ ≥ 3,0 x Cr of baseline or ↑ Cr ≥ 4,0 mg/dl or RRT	or	< 0,3 mg/kg/h for ≥ 24h or Anuria ≥ 12 h

with Covid-19 in stage 2 be already the subject of communication and discussion between the intensive care team and the nephrologist.

Patients classified as stage 3 have a high probability of requiring artificial renal replacement therapy (RRT), justifying the immediate call of the nephrology team. Practical details on the possible prescription/performance of RRT will be discussed below.

Protection of the workforce in nephrology and RRT

Healthcare professionals are at increased risk of exposure to SARS-CoV-2, which is reflected in multiple morbidity and mortality reports. Even when the infection evolves favorably, the mandatory temporary medical leave can overwhelm the remaining staff. For this reason, there was an initial recommendation to restrict the entry of nephrologists and dialysis nurses in the cohorts allocated Covid-19 patients. The RRT prescription (and subsequent adjustments) was to be done remotely, as long as close contact with the medical team within the isolated cohort was assured. In the same way, the management of RRT procedures by ICU nurses were encouraged, as long as they were properly trained.

The experience with this strategy proved to be adequate while the number of cases remained relatively low. However, the excess of patients with Covid-19 complicated by AKI has caught many centers by surprise. In many places, the strategy of restricting the access of nephrology personnel proved to be inadequate by overburdening intensive care teams, which were already overwhelmed with other priorities. There was also occasional compromise in the exchange of information between doctors inside and outside the isolation units, and the impact on logistics that involved the insertion of vascular access and the flow of orders for the beginning, postponement, conduction and/or discontinuation of procedures.

Thus, in settings with a high prevalence of AKI, we recommend that the direct participation of the nephrologist and nephrology nursing in the care within isolated areas is convenient, giving preference to professionals who have already developed antibodies against SARS-CoV-2. For better operational capacity, we also recommend that patients be installed in contiguous, frontal or close beds, to enable simultaneous procedures to be carried out, supervised by the same dialysis technician or nurse.

Whenever possible, portable reverse osmosis equipment and systems should be exclusive and remain in the areas allocated to Covid-19 patients, avoiding their displacement to other areas of the hospital. Throughout the procedure, we recommend keeping the equipment outside or close to the bed access entrance. By the same perspective, we recommend that dialysis nurses remain in proximity and not inside the box/room.

The use of standard procedures for disinfecting RRT equipment is suitable for the elimination of SARS-CoV-2, including systems with a glass tank, which uses peracetic acid. There is no evidence of significant passage of SARS-CoV-2 across RRT filters.

In bedside hemodialysis procedures, the dialysate waste should be drained in the hospital wastewater system. Peritoneal dialysate can be discarded in the same way, keeping the PPE on throughout the process. Although infrequent, there was a first report of detection, and persistence for more than 40 days, of SARS-CoV-2 in the peritoneal effluent of a patient with Covid-19[26]. Bags of wasted peritoneal dialysate can also be depleted in the sanitary network, with particular care to prevent spilling and the dispersion of its contents.

Vascular access

In compliance with the policy of restricting non-essential entry of personnel in Covid-19 isolated areas, and to prevent wasting by having the nephrologist donning PPE solely for the purpose of catheter insertion, we advise that RRT access insertion ought to be performed the intensivist. However, with the work overload represented by the almost total occupation of ICUs by patients with Covid-19, experience has shown that the nephrologist must enter the isolated environment to insert dialysis catheters and perform other activities.

The selection of catheters with adequate length and diameter is of paramount importance to ensure optimal blood flow. Dialysis accesses with inconsistent or unsatisfactory flow promote clotting of the system, which results in blood loss and interruption of RRT. One should not insist on repeated flushing or other maneuvers. The most cost-effective solution is usually to replace the catheter. Table 2 shows dialysis catheter lengths recommended for

Table 2 Optimum catheter length for ARS, according to the venipuncture site (adults)

Venous territory	ARS catheter length (cm)
Right jugular	15-18
Left jugular	18-24
Left or right femoral	20-30
Right subclavian	15-18
Left subclavian	20-24

different sites of central venipuncture. The different ranges stem from the diversity of biotypes in the population.

Catheters and dialysis lines are not a contraindication the placement of the patient in the prone position, but requires specific attention to avoid traction during pronation and supination maneuvers. Whenever possible, particularly in the case of intermittent hemodialysis, it is recommended to temporarily disconnect the circuit. Immediately after these maneuvers, the access must be inspected for traction, twisting and patency.

The preferred site for vascular access implantation for RRT is the right internal jugular vein. It is common, however, that this route is no longer available due to the need of multiple simultaneous vascular lines in patients with severe Covid-19. The left internal jugular vein is the second option. The femoral access, which is easier to cannulate, may be inappropriate for patients under pronation protocols or ECMO. Depending on the room layout, femoral access can reduce the risk of professional contamination at the time of insertion[27] and facilitate the positioning of the equipment in an area that minimizes the risk of contamination by professionals.

Dialysis access through subclavian veins is often discouraged, because of the risk of accidents and of residual stenosis. However, they carry a lower risk of infection and may be the only remaining option for patients with inaccessible femoral internal jugular veins, under ECMO, or following a pronation protocol.

Due to the risks and difficulties associated with performing bedside chest x-rays, its routine use should be reconsidered. In services with availability and proper training, chest ultrasonography can be used to confirm the central positioning of the line and the absence of complications[27].

Chlorhexidine antisepsis is associated with a lower incidence of local and bloodstream infections. When available, the use of transparent dressings with chlorhexidine gluconate gel (CHG) can reduce the number of exchanges and the need for handling.

The routine of access care must also include the daily inspection of the insertion site and the integrity of the fixation points. In the absence of contraindications, all patients with Covid-19 and a central vascular line should receive prophylaxis with low molecular weight heparin[1], in order to reduce the thrombotic risk[27].

Renal replacement modalities

RRT modalities include continuous renal replacement therapy (CRRT), prolonged intermittent hemodialysis (PIRRT), conventional intermittent hemodialysis (IHD) and peritoneal dialysis (PD). The modality choice must be individualized, considering logistical aspects and the experience of each institution. It is not advisable to implement a new protocol or treatment modality in the midst of the Covid-19 emergency. Unfamiliarity increases the risk of adverse effects, increases the likelihood of errors, is detrimental to patient safety, and poses a higher risk of contamination to the team.

Continuous renal replacement methods

CRRT represent an efficient and safe treatment strategy, have an excellent stability profile, is performed in a closed system, and reduce physical contact with the patient. Its preferential use, when available, can decrease the number of nurses and technicians exposed to SARS-CoV-2.

As there is concern about the low worldwide availability of kits and supplies for CRRT, and to minimize the team's contact with infected patients, it is possible to skip scheduled exchange of filters, kits and systems, as long as these remain with optimal operational parameters.

In some settings, intensive care nurses have adequate training and routinely conduct continuous therapies. This type of organization can reduce the need for dialysis nurses to enter the isolated areas and help conserve PPE stocks. In other scenarios, the dialysis nurse prepares the equipment, connects lines and solutions and performs the procedure. In this situation, machine setup and preparation must be done outside the patient's room or outside the isolation ICU. Only afterwards, and properly protected with PPE, should the nurse or technician enter the box/room to start the procedure.

Once RRT starts, the assigned healthcare professional must constantly wear PPE, without leaving the treatment unit until the end of the work shift. Should such professional need to enter the box, he/she must wear personal protective clothing, as established by the institutional's infection control committee.

Units with different arrangements must follow official guidelines and develop strategies along the same safety lines. The underlying logic should always be to minimize the inflow and outflow of professionals and equipment.

Prolonged or conventional hemodialysis intermittent modalities

Most patients admitted to the ICU will not have access to CRRT, since the number of these machines in Brazil is relatively limited. In this sense, the main options for extracorporeal treatment will be PIRRT and IHD, evidently without reprocessing lines and capillaries.

PIRRT combines operational simplicity, reasonable cost, a good hemodynamic stability profile and excellent solute clearance, being widely used in the country. Adaptations to the procedure make it possible to couple a convection component or use high cut-off filters. IHD is the procedure most commonly performed in the hospital environment, especially after hemodynamic improvement of critically ill patients. However, both are not routinely performed by intensive care doctors and nurses.

Intermittent methods are usually prescribed by the nephrologist and conducted by dialysis nurses and/or technicians. In some institutions, these professionals are part of the hospital staff, while in others RRT is outsourced. Whichever the case, we recommend avoiding unwanted internal or interinstitutional circulation of machines and service providers.

When facing Covid-19, it is essential to develop strategies that minimize occupational exposure and spread of SARS-CoV-2. We strongly recommend the local stationing of equipment and advise against the relocation of the nursing staff from the Covid-19 cohort area for the treatment of uninfected patients during the same work shift.

During the procedure, we advise the nursing staff to avoid remaining inside the patient's box/room, rather controlling the procedure from the corridor or from a nearby area. If he/she needs to enter the box, we recommend proper paramentation, according to the routine established by the unit.

As previously mentioned, we recommend that nurses or dialysis technician perform simultaneous procedures, in order to save PPE in situations of high demand, to reduce the risk of widespread staff contamination and, particularly, to assure that RRT will not be denied to all patients who needs it.

It is advisable that the professional responsible for performing RRT eat meals in the ICU, avoiding going out and returning for food. At the end of the procedure, the professional must dispose of all supplies safely, by placing them in bags for infectious substances. Still inside the box/room and donning the PPE, he/she must perform the surface disinfection of the equipment and program a chemical disinfection cycle with peracetic acid.

We recommend a second surface cleaning cycle, in a common area, before using the equipment on another patient. At the end of the daily use of the equipment, a final thermal disinfection cycle must be carried out, using citric acid or sodium hypochlorite, according to the manufacturer's recommendations.

When using tank systems with central dialysate preparations, it must be brought to the ICU door by the professional responsible for the preparation, and delivered to the dialysis nurse. Before being transported to the patient's bed, the equipment must undergo surface disinfection. At the end of the procedure, there must be a new surface cleaning in the box/room, and the equipment must be brought to the ICU entrance to be collected by the professional responsible for its transport. We recommend a second surface cleaning cycle at the preparation center.

Peritoneal dialysis

In services with due experience, automated peritoneal dialysis with a flexible catheter, is a good treatment option, with the potential to reduce the length of stay of professionals at the bedside. To meet the needs of ultrafiltration, it may be necessary to work with hypertonic solutions (with a high glucose concentration), which can hinder glycemic control and require the addition of regular insulin to the dialysate bag.

When available, the installation of a flexible catheter using the Seldinger technique can reduce the risk of team contamination, enabling the procedure to start more quickly and allowing the adoption of the prone position, if necessary.

In theory, the increase in abdominal pressure determined by the infusion of dialysate may interfere with the dynamics of mechanical ventilation in patients with ARDS that are difficult to manage. In such cases, we recommend reserving the PD for a later period, after the improvement of the ventilatory parameters.

Other extracorporeal therapies

There is the potential to treat Covid-19's severe hyperinflammatory phenotype with more sophisticated extracorporeal modalities, which have been shown to decrease the circulating levels of proinflammatory mediators and other harmful substances, at least in experimental studies.

These therapies include devices capable of adsorbing cytokines and high-volume hemofiltration techniques. At present, it is not possible to endorse the use of these approaches, which are in the process of clinical experimentation.

RRT indication and dosage

The ideal timing for RRT initiation in patients with critical illness, whether early or according to conventional indications at a later moment, is under intense investigation. The theoretical rationale for the early start of RRT consists in preventing homeostatic imbalances caused by renal dysfunction, which could help prevent or mitigate AKI complications.

In contrast, the "early" start may be unnecessary and harmful for some patients. In the two largest published multicenter studies, AKIKI and IDEAL-ICU, the result was indifferent in relation to survival. However, among patients allocated to the late strategy, 49% of AKIKI and 38% of IDEAL-ICU patients never came to need RRT[28].

During the Covid-19 epidemic, the decision about the initiation of RRT must necessarily be shared between the nephrologist and intensivist, and individualized for the patient's particularities. However, we recommend considering whether it is opportune to expose workers and deplete supplies in the absence of a strong indication for RRT, seeking the unproven benefit of early intervention.

Until further information, it is our recommendation that the conventional indicators for RRT implementation prevail in treating patients with Covid-19. These include volume control, prolonged anuria/oliguria, metabolic acidosis, uremia and electrolyte disturbances, notably hyperkalemia.

In view of the risk that RRT intensification could result in greater contact and contamination of healthcare workers, cause depletion of consumables and compromise the availability of equipment, it is advisable to pay attention to the lack of evidence concerning improvements in AKI prognosis when using high doses of RRT[29,30].

Regarding the AKI of Covid-19 patients, our recommendation is that each institution maintains its policy on RRT dose, without seeking further increments. Evidently, sub-dialysis, whether due to a reduction in treatment time or spacing in the interval between sessions, should not be practiced.

Volume management

The clinical picture of severe Covid-19 is fundamentally dominated by severe acute respiratory syndrome (SARS) and associated complications[4,25]. In addressing these cases, there is no consistent information to guide optimal fluid management. The tendency is to be based on strategies recommended for classic ARDS, where only a fraction of the lung parenchyma is aerated and the inflammatory lung injury is characterized by increased vascular permeability and diffuse alveolar damage, with an increase in physiological dead space and decreased pulmonary compliance.[31,32]

Since volume overload and hydrostatic pulmonary edema are frequent reasons for indicating RRT, it should be considered that excessive fluid resuscitation might precipitate its need, increase the risk of exposure of the workforce and consume resources in a situation of scarcity. In this context, it makes sense to approach volume management in a conservative way, which is associated with improved lung function and less time on mechanical ventilation and intensive care, while not increasing the risk of AKI[33]. This strategy has been recommended in pandemic-related consensuses[34,35].

Nonetheless, there is concern about the possibility that volume restriction strategies may not be suitable for all patients. In fact, there seems to be heterogeneity of clinical presentation on arrival at healthcare services, which implies in some patients presenting with classic ARDS, while others, even with extensive pulmonary opacities, due to low intake, vomiting or diarrhea, are hypovolemic[36]. In these patients, adopting a “zero” water balance policy can worsen renal perfusion, accelerate functional loss and increase the need for RRT.

In view of this new knowledge, we recommend that the volume management be individualized, with assessment on a case-by-case basis. Hypervolemia should not be tolerated, to avoid or minimize the expansion of extravascular pulmonary water. Care should be taken with routine maneuvers in intensive care, such as hydration maintenance, nutritional support with high volume and repeated use of volume responsiveness tests[37]. In contrast, hypovolemia can decrease pulmonary perfusion, increase dead space, worsen hypoxemia and increase the adverse effects of positive pressure ventilation on renal blood flow. In selected patients, if possible based on consolidated strategies for guiding volume management, it may be necessary to resort to volume expansion maneuvers[34,38].

Anticoagulation

The purpose of anticoagulation during RRT is to maintain patency of the extracorporeal circuit. Anticoagulation seeks to balance the risk of bleeding against the activation of coagulation by the underlying disease and by the contact of the blood with the artificial surfaces of the circuit.

Severe Covid-19 cases can present with hypercoagulation, which has been correlated with more unfavorable progress[39]. This coagulopathy can also interfere with RRT provision. Decreased filter and extracorporeal circuit lifespan has been reported frequently with Covid-19[12].

In patients with Covid-19, we recommend that, initially, each service follow its usual anticoagulation routine. When there is concern about a possible hypercoagulable condition and in order not to waste consumables, we do not recommend to perform repeated saline flushing maneuvers to maintain circuit patency without the use of anticoagulants.

Like any patient with AKI treated with RRT, the first measure in cases of recurrent filter loss is to check the adequacy of vascular access. If this is not the case, it may be necessary to intensify anticoagulation, increasing the dose of conventional or low molecular weight heparin. During citrate anticoagulation, the post-filter ionised calcium target level can be decreased.

Nephrotoxicity And Drug Dose Adjustments

Many patients with severe Covid-19 are treated with complex empirical or experimental protocols, which combine drugs in poorly studied associations. There is a clear risk of toxicity to the kidneys and to other organs and systems. We recommend daily monitoring of renal function biomarkers, including biochemical parameters, acid-base, fluid and electrolytic balance, and urine volume and composition.

Nephrotoxicity is not a frequent effect of chloroquine or hydroxychloroquine, but there is a risk of serious pharmacological interactions[40]. There is no evidence from a solid source to guide the eventual need to adjust the doses of these drugs in patients with kidney disease. After analyzing the available evidence, the Brazilian Society of Nephrology recommended a 50% reduction in the dose of chloroquine or hydroxychloroquine for patients with advanced kidney dysfunction[41].

Every patient with AKI requires a daily prescription review, discontinuing drugs that are no longer needed, identifying undesirable drug interactions and adjusting medication doses.

Recovery of renal function and discontinuation of RRT

The patient flow after recovery from Covid-19 in patients that remains dialysis-dependent is still unclear, notably the transfer from Covid-19 isolation areas to conventional hospital sectors and/or hospital discharge for outpatient dialysis treatment. The provisional guideline issued by the CDC is not always applicable to Brazilian hospitals[42]. In many units, transfer to Covid-19 free areas have occurred after 48 hours of absence of fever and respiratory symptoms, in association with negative oral/nasopharyngeal RT-PCR for SARS-CoV-2.

Apparently, most patients who manage to overcome the critical phase of Covid-19 appear to regain independent kidney function, but little information is available on renal outcomes in patients with Covid-19 complicated by AKI. In AKI associated with ischemia/sepsis, patients remain for approximately two weeks on RRT[43-45]. In 2003, in patients with SARS, the period of dialysis dependence was longer, three weeks on average[46]. Perhaps patients with AKI associated with Covid-19 also need a longer time to wean from RRT. In a French series, a third of the patients were still on dialysis, even three weeks after treatment onset. More time is needed to confirm these preliminary impressions.

Weaning strategies for ARS for patients with good urine output and adequate biochemistry should follow the usual practice of each service. Many patients are discharged with improving kidney function but still without complete recovery. However, the long-term risk of chronic residual kidney disease is still unknown. Only over the months will it be possible to establish whether there will be a persistent effect of COVID-19 on residual renal function.

Outside collaborators

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