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CONFLICT OF INTEREST STATEMENT

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COVID-19 and policy changes for kidney disease: the need for a ‘decade of the kidney’

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In this issue of *Nephrology Dialysis Transplantation*, a timely analysis and call to action by the Council of the European Renal Association – European Dialysis and Transplant Association (ERA-EDTA) and the European Renal Association COVID-19 Database (ERACODA) working group [1] highlights the extremely high burden of coronavirus disease 2019 (COVID-19) infection in chronic kidney disease (CKD) patients, who, compared with patients suffering from other major disorders, are at

the highest risk to develop severe COVID-19 and to die from it [2].

Although it could be anticipated that the pandemic would take a heavy toll on the CKD population, as COVID-19 caused severe problems in populations with notorious CKD risk factors like diabetes and cardiovascular disease, the initial publications from China reported a prevalence of CKD below 1% in hospitalized COVID-19 patients [3], and it took some time before

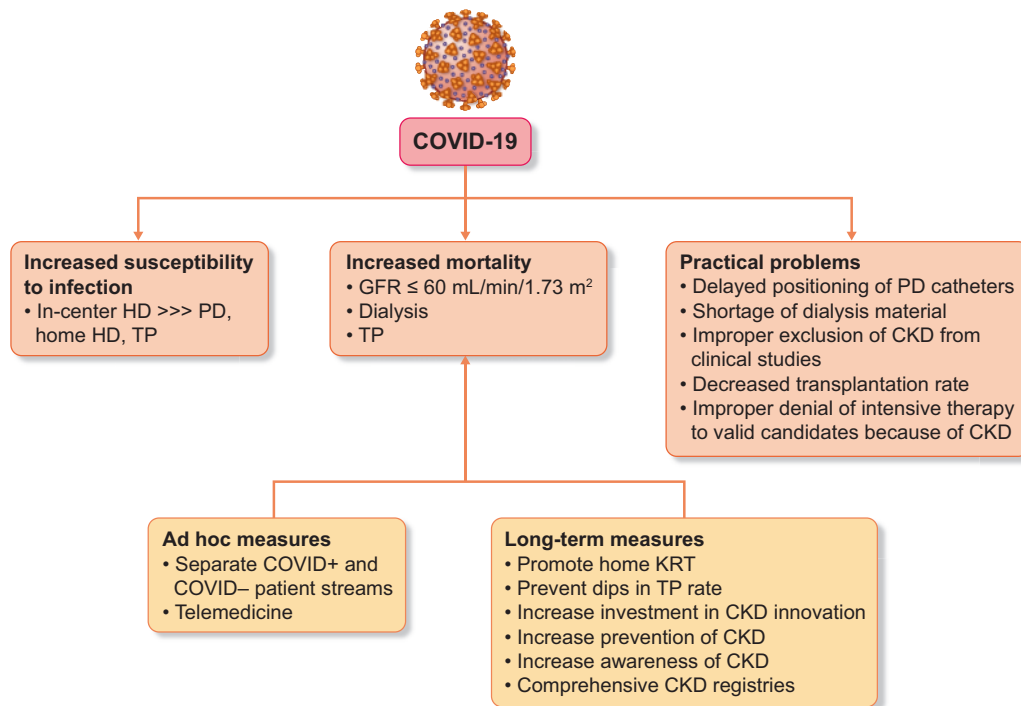


FIGURE 1: Clinical effects of COVID-19 on the population with CKD, and *ad hoc* and long-term measures to counteract them. HD, haemodialysis; TP, transplantation.

reports on large series highlighted the alarming impact of COVID-19 in CKD [4, 5].

The picture that emerges from the call to action under discussion [2] and other literature is complex and multifaceted (Figure 1). The overall modelled risk for severe COVID-19 disease (defined as need for hospitalization) and analysed over different age strata was higher for CKD than for any other risk factor, and notably more than for diabetes, cardiovascular disease, chronic respiratory and liver disease, HIV/AIDS and cancer [5]. In a UK study assessing the hazard ratio to die with COVID-19 and including more than 10 000 fatalities, CKD with estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m² and a history of dialysis or transplantation had the highest hazard ratios [4], in excess of those of diabetes (even uncontrolled), cancer, chronic heart disease, obesity (even severe—body mass index >40 kg/m²), stroke, dementia, chronic respiratory and liver disease and all <70 -year-old age strata. Of note, also in the CKD group with eGFR $30\text{--}60$ mL/min/1.73 m², mortality risk was significantly higher than in the reference population [2, 4].

The dismal outcomes of end-stage kidney disease (ESKD) patients affected by COVID-19 were confirmed in an analysis of the ERA-EDTA Registry, pointing to a mortality of $>20\%$ among European dialysis and kidney transplant patients, with the mortality risk of transplant recipients being slightly higher [hazard ratio 1.28 (1.02–1.60)] than that of dialysis patients [6]. The dialysed population included a small fraction of peritoneal dialysis (PD) patients with similar mortality as the group on haemodialysis [6]. In the ERACODA database, enrolling 1073 patients on kidney replacement therapy (28% transplanted),

28-day probability of death was 21.3% for transplant patients and 25.0% for dialysed patients [7].

On the other hand, the risk of developing COVID-19 differed markedly among ESKD therapies, with the highest risk for dialysis patients [6], and among dialysis patients, for in-centre haemodialysis as compared with PD ($\times 2.6$) and transplantation ($\times 4.1$) [8]. The high susceptibility of in-centre dialysis patients is plausible as they are members of a closed community where infections spread easily, a situation closely resembling that of nursing homes, which were also heavily struck by COVID-19. By contrast, PD and transplant patients are markedly less dependent on hospital visits. Also, personnel of in-centre dialysis units were at risk of infection, especially in cases where there was insufficient protection. This also increased the workload in the remaining non-infected personnel and in turn caused burnout related to stress, fear of infection and exhaustion.

COVID-19 infection was also strongly linked to the development of acute kidney injury (AKI) [9], which in some series occurred in more than half of hospitalized patients, with a mortality rate above 30% [10]. AKI especially affected patients with previous CKD [11]. As in pre-COVID-19 studies about one-third of patients surviving AKI develop CKD, it is likely that after severe COVID-19-related AKI, a similar evolution to CKD will occur, next to other expected chronic diseases, like chronic respiratory disease and heart failure.

In the margin of the above-described dramatic outcomes, logistic and organizational problems in nephrology care occurred (Figure 1), which likely contributed to the negative impact.

Unfortunately, these problems also reflect the low level of awareness and understanding of kidney disease outside the nephrology community, including administrators and health authorities, and even non-nephrology medical professionals. Examples of such problems are: (i) peritoneal dialysis catheter positioning was classified as a non-urgent intervention, resulting in postponement of the start of dialysis or the transfer of PD patients to the potentially less safe in-centre haemodialysis milieu; (ii) occasional shortage of dialysis material was at least in some places related to the use of continuous dialysis strategies for AKI, leading to more clotting in hypercoagulable diseases like COVID-19 and allowing only one patient to be treated per device; (iii) kidney failure is an exclusion criterion in most drug and vaccination studies, leaving the nephrology community with therapeutic and dosage uncertainties when necessitated to treat COVID-19; (iv) overwhelmed intensive care units were forced to focus on the massive influx of COVID-19 patients, slowing down living donation and causing a dramatic decline in deceased transplant donation, which increased the risk of death on the waiting list; and (v) CKD patients were at risk of being denied intensive treatment, e.g. in case of patient overflow, although the large majority had a chance of survival when treated properly.

For all those reasons, there is a need for a shift of paradigm (Figure 1), as also formulated by the European Kidney Health Alliance (EKHA) in a recent open letter to European Union (EU) key policy makers [12]. EKHA is a Brussels-based non-governmental organization advocating for the needs of kidney patients and the nephrological community at the level of the EU and from there top to bottom also at the national level. EKHA represents not only the nephrologists but also kidney nurses, patients and foundations, and uses fora in the European Parliament, sensibilization campaigns among Members of European Parliament, European policymakers and the community at large, publications, position statements, press releases and social media to emphasize the burden of kidney disease.

Action should be based on a long-term vision, to protect kidney patients against the negative consequences of the currently raging coronavirus waves, until enough efficient vaccines become available. However, the paradigm shift is also needed in case the anti-COVID-19 vaccines fail (which is more likely in CKD patients due to their immune suppression), or when novel epidemics with other infectious agents may occur in the future. Many of those mostly organizational measures will at the same time be potentially beneficial for non-COVID-19-related patient outcomes, including quality of life, and will also reduce the health-economic and societal cost of CKD, hopefully resulting in a more sustainable and resilient treatment of CKD.

A number of *ad hoc* measures, like strict separation of COVID-19-positive and COVID-19-negative patient streams and a rapid transition to telemedicine, are already broadly implemented. However, not all CKD patients own a computer or are computer literate, creating problems for the elderly, the deprived, the health illiterate, minorities and refugees. Thus, focus on telemedicine should be accompanied by policy measures promoting computer literacy.

The risk for COVID-19 was the highest for the in-centre haemodialysis population [8]. This problem can be

circumvented by a move to more home haemodialysis or PD [13]. Telemedicine is certainly a helpful tool that favours this evolution. To make this change sustainable for the broad array of valid candidates, such a large-scale shift needs careful planning and preparation, considering patient and professional education, infrastructural changes and elimination of reimbursement inequities among dialysis strategies.

Likewise, transplantation is also associated with a lower infectious risk despite immunosuppression. Transplantation is an EU priority and was actively promoted between 2009 and 2015 by the Action Plan on Organ Donation and Transplantation, but this promotion needs new momentum. A Joint Statement on increasing transplantation by a Thematic Network of European stakeholders has been developed by the EKHA, advising the European Commission to upgrade transplant-promoting policies [14]. An exchange of strategic measures to cope with dips in transplantation rate in case of pandemics is also needed.

In contrast to several other invalidating chronic diseases, not many advances were made in the past for the treatment of both non-ESKD CKD and ESKD. More research and investment should bend the current status quo into a positive project, focusing on patient quality of life (including prevention of CKD progression, home dialysis and transplantation), personalized medicine (involving big data analysis, treatment of rare diseases and promoting informed patient choice), patient education and empowerment, and regenerative medicine (implying bioartificial organs and stem cell treatment). Many of those optional changes will also be protective against the negative aspects of devastating pandemics. It is the duty of the kidney disease community to create awareness for these problems, leading to greater investment in kidney diseases.

The best way to forestall problems in kidney patients is to prevent the development or the progression of the disease. This includes also prevention and adequate treatment of many other chronic diseases, which share several causative factors with kidney disease and cause kidney disease on their own. However, investment in prevention of chronic diseases remains minimal. In general, a shift of healthcare financing from the curative towards the preventive sector should be advocated.

Finally, the COVID-19 pandemic underscores the need for overarching health registries including chronic diseases. Nephrology initiatives like ERACODA on outcomes in ESKD patients illustrate the value of such actions. Nephrology registries might, however, be extended beyond COVID-19 and ESKD, to non-ESKD CKD and if possible AKI. In addition, there is a need for an even broader pan-European database including both communicable and non-communicable diseases (also comprising CKD) allowing rapid epidemiologic alert and guidance.

In summary, the call to action [2] discussed here underscores how the COVID-19 pandemic is causing a great deal of stress in patients with CKD because of the risk they run, while they deserve attention because of the scarcity of therapeutic improvements. EKHA advocates for a policy shift towards innovation, prevention and home therapy, and more transplantation, which will not only protect kidney patients from infectious threats but will also improve their outcomes and quality of life

as well as benefit society at large, bringing along the urgently needed health-economic advancement in kidney care. Patients are correctly asking for an initiative echoing the successful European investment in cancer registration and treatment. We therefore strongly advocate to make the coming 10 years ‘the decade of the kidney’ focusing on innovation improving cure and care for all kidney patients.

CONFLICT OF INTEREST STATEMENT

None declared.

(See related article by ERA-EDTA Council and the ERACODA Working Group. Chronic kidney disease is a key risk factor for severe COVID-19: a call to action by the ERA-EDTA. *Nephrol Dial Transplant* 2021; 36: 87–94)

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DATA AVAILABILITY STATEMENT

This publication includes no original data except those extracted from the cited publications.

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Rituximab in fibrillary glomerulonephritis: fumble or forward progress?

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While prospective, double-blind, randomized controlled trials continue to be regarded as the holy grail and hard endpoints such as progression to end-stage kidney disease (ESKD) or

death are considered the gold standard, there has been increasing effort in the research arena to limit costs and patient burden. With support from federal agencies to help