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The burden of COVID-19 on the population with kidney disease

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While early reports on COVID-19 did not clearly mention chronic kidney disease (CKD) as a risk factor for a severe cause of the disease, this changed after publication of data from the OpenSAFELY project which analyzed factors associated with COVID-19 death in 17 million patients in the UK. This study demonstrated significantly increased mortality risk for dialysis patients (HR 3.69), organ transplant recipients (HR 3.53) and patients with CKD (HR 2.52 for patients with eGFR<30 ml/min/1.73 m^2). The CKD-associated risk was higher than the risk associated with diabetes mellitus (HR range 1.31-1.95, depending upon glycaemic control) or chronic heart disease (HR 1.17).

In March 2020, the ERACODA database was established to collect data on adult patients with a functioning kidney allograft or being on long-term dialysis. More than 100 centers, mostly from Europe, have contributed to this database. Analysis after inclusion and follow-up of more than 1500 patients showed 28-day mortality of 16,9% (95% CI: 13.9-20.5%) in kidney transplant recipients and 23.9% (95% CI: 21.6-26.5%) in dialysis patients. The unadjusted 28-day mortality risk was 33% lower in kidney transplant recipients compared with hemodialysis patients (HR: 0.67, 95%CI: 0.52-0.85). However, in an age, sex and frailty adjusted model, mortality risk was 29% higher in kidney transplant recipients (HR: 1.29, 95%CI: 1.00-1.68), whereas in a fully adjusted model the risk was 43% higher (HR: 1.43, 95%CI: 1.06-1.93). Results were similar for other endpoints (e.g. hospitalization, ICU admission, mortality beyond 28 days) and across subgroups.

There are limited data available on longer term clinical, functional and mental health outcomes in kideny transplant recipient and dialysis patients who survived COVID-19. Data on vital status, hospitalization and/or intensive care unit (ICU) admission at three-month follow-up were retrieved from the ERACODA database. Of 912 kidney transplant recipients, 26.4% were not hospitalized, 57.5% were hospitalized without need for ICU admission, and 16.1% were hospitalized and admitted to the ICU. Three-month survival was 82.3% overall, and 98.8%, 84.2% and 49.0% respectively in each group. Three-month acute rejection, need for renal replacement therapy, and graft failure occurred in the overall group in 1.0%, 2.6% and 1.8% respectively, and in 2.1%, 10.6% and 10.6% of ICU-admitted patients, respectively. Of the surviving patients, 83.3% had reached their pre-COVID-19 functional status within three months according to the opinion of the treating physician. Of patients

who had not yet reached their prior functional status, their treating physicians expected that 79.6% still would do so within the coming year. Regarding the mental health outcome, 94.4% had reached their pre-COVID-19 status. 80% of patients who had not yet reached their prior mental health status were expected to do so within the coming year. ICU admission was independently associated with a low likelihood to reach prior functional and mental health status. Since similar data on recovery were found in dialysis patients, it can be concluded that in patients alive at three-months follow-up after COVID-19, clinical, functional and mental health recovery was good for both non-hospitalized and hospitalized patients. Recovery was however less favorable for patients who had been admitted to the ICU.

The high COVID-19 associated mortality rates In patients with severely impaired kidney function, patients on dialysis and kidney transplant recipients neceesitates the availability of effective vaccination strategies for these patients who were excluded from the large phase 3 registration trials with mRNA vaccines. A Dutch REnal patients COVID-19 VACcination (RECOVAC) consortium performed a multicenter investigator-initiated study to assess the immunogenicity at the humoral as well as cellular level, tolerability and safety of the mRNA-1273 COVID-19 vaccine (®Moderna) in patients with severely impaired kidney function, patients on dialysis, kidney transplant recipients, and control subjects without known kidney disease. The primary endpoint was seroconversion, i.e. reaching a SARS-CoV-2 Spike S1-specific IgG antibody concentration at day 28 following the second vaccination of ≥10 BAU/ml. This prospective study showed that kidney transplant recipients had a significantly lower seroconversion rate when compared to controls (56.9% versus 100%, P<0.001). Use of mycophenolic acid, not using steroids, higher age, lower lymphocyte concentration, lower eGFR, and shorter time after transplantation were associated with being a non-responder. Transplant recipients also showed significantly lower titers of neutralizing antibodies and T cell responses when compared to controls. Although a high seroconversion rate was observed for participants with CKD G4/5 (100%) and on dialysis (99.4%), mean antibody concentrations in the CKD G4/5 cohort and dialysis cohort were lower than in controls (2405 [Interquartile Interval 1287-4524] and 1650 [698-3024] versus 3186 [1896-4911] BAU/ml, P=0.06 and P<0.001, respectively). Dialysis patients and especially kidney transplant recipients experienced less systemic vaccination related adverse events, such as fever, chills and myalgia. No specific safety issues were noted. The low response rate in kidney transplant patients urges for an effective booster vaccination. The RECOVAC consortium will perform a randomized trial to investigate the efficacy and safety of several booster vaccination strategies.