patients progressed to kidney failure, and 85 died. For each doubling of baseline plasma KIM-1, hazard ratio (HR) for kidney failure was 1.19. Plasma KIM-1 was not significantly associated with mortality after multivariate adjustment.

In the CRIC study, higher plasma KIM-1 was associated with non-White race, higher prevalence of diabetes and cardiovascular disease, higher systolic blood pressure, and lower hemoglobin. Plasma KIM-1 was negatively correlated with estimated glomerular filtration rate and positively correlated with urinary albumin-to-creatinine ratio.

At a median follow-up of 11.5 years in CRIC, 1153 patients had progressed to kidney failure, whereas 1356 died. For each doubling of plasma KIM-1, HR for kidney failure was 1.10. In the highest quintile of plasma KIM-1, HR for progression was 1.58. Again, there was no significant association with mortality.

Plasma KIM-1 is a sensitive marker of tubular injury, which may contribute to development or progression of CKD. The new analysis finds that higher plasma KIM-1 is associated with tubulointerstitial and mesangial lesions and is an independent risk factor for progression to kidney failure. The investigators conclude: "Collectively, the findings suggest that plasma KIM-1 may serve as a non-invasive tool to assess histopathologic lesions and has prognostic value across a variety of kidney diseases" [Schmidt IM, et al. Plasma kidney injury molecule 1 in CKD: Findings from the Boston Kidney Biopsy Cohort and CRIC studies. A*m J Kidney Dis*, published online ahead of print June 24, 2021. doi: 10.1053/j.ajkd.2021.05.013; https://www.ajkd.org/article/S0272-6386(21)00694-6/fulltext]. ■

Do Some Diabetes Drugs Reduce the Risk of Severe or Fatal COVID-19?

For patients with COVID-19, two newer classes of antihyperglycemic medications are associated with lower rates of death and other adverse outcomes, according to a study in *Diabetes Care*.

The observational study included 12,466 adult patients with polymerase chain reaction-diagnosed SARS-CoV-2 infection, drawn from the US National COVID Cohort Collective. Included patients had an ambulatory prescription for at least one of three antihyperglycemic medication classes over 24 months before diagnosis: glucagon-like peptide-1 receptor agonist (GLP1-RA), sodium-glucose cotransporter-2 inhibitor (SGLT2i), or dipeptidyl peptidase 4 inhibitor (DPP4i). The patients' mean age was 58.6 years, 53.4% were women, and 62.5% were White race.

Sixty-day mortality and other severe outcomes were compared for patients with premorbid GLP1-RA or SGLT2i use versus DPP4i use. Associations were analyzed with targeted maximum likelihood estimation (TMLE) using a super learner approach, accounting for baseline characteristics.

Patients taking DPP4i drugs were older and had a lower body mass index (BMI) compared to GLP1-RA or SGLT2i users. Patients in the DPP4i group were also more likely to have chronic or end-stage kidney disease, myocardial infarction, congestive heart failure, cancer, dementia, or stroke.

Crude 60-day mortality was 2.06% for patients with premorbid GLP1-RA use and 2.32% for those with SGLT2i use, compared to 5.67% for DPP4i users. Total mortality over the observation period was 2.29%, 2.48%, and 6.18%, respectively. In propensity score-weighted analyses, 60-day mortality was 2.31% in GLP1-RA users versus 4.86% in DPP4i users and 2.70% in SGLT2i users versus 4.74% in DPP4i users. Differences in total mortality also remained significant.

On TMLE analysis, odds ratio (OR) for 60-day mortality was 0.54 for GLP1-RA users versus DPP4i users. Secondary outcome ORs were 0.56 for total mortality, 0.81 for emergency department (ED) visits, 0.73 for hospitalization, and 0.73 for mechanical ventilation. For GLP1-RA versus DPP4i use, ORs were 0.66 for 60-day mortality, 0.63 for total mortality, 0.90 for ED visits, and 0.82 for hospitalization.

Patients with diabetes are at increased risk of death and other adverse outcomes of COVID-19. The newer antihyperglycemic medications GLP1-RA and SGLT2i have been shown to reduce cardiorenal events in high-risk groups. The new study explored the possible impact of these drug classes on COVID-19 outcomes.

The results show lower odds of mortality and other adverse events among COVID-19 patients with premorbid GLP1-RA and SGLT2i use, compared to those prescribed DPP4i medications. The authors note some important limitations of their study, including the older age and higher comorbidity of the DPP4i group. Anti-inflammatory effects of GLP1-RA and SGLT2i drugs might account for the associated improvement in COVID-19 outcomes [Kahkoska AR, et al. Association between glucagon-like peptide 1 receptor agonist and sodium-glucose cotransporter 2 inhibitor use and COVID-19 outcomes. *Diabetes Care* 2021; 44:1564–1572. doi: 10.2337/dc21-0065]. ■

Moral Distress in Nephrology Fellowship Programs

Nephrology fellows experience high rates of moral distress during their fellowship training, according to a survey study in *American Journal of Nephrology*.

An online survey link was sent to the directors of 148 US nephrology fellowship programs, with a request to forward the survey to fellowship trainees. Adapted from a previous questionnaire, the survey focused on workplace scenarios relevant to nephrology training and practice in five domains: dialysis decision-making, futility of care, interdisciplinary communication, perceived powerlessness, and the institutional ethical environment.

Directors reported forwarding the survey to 386 nephrology fellows, of whom 142 responded: a rate of 37%. Ratings of 3 or higher, on a 0-to-4 scale, were considered to denote frequent or moderate to severe moral distress.

Respondents indicated moral distress in a wide range of scenarios involving all five selected domains. Scenarios most frequently rated as causing moderate to severe moral distress involved continuing dialysis in a hopelessly ill patient, 81% of respondents; initiating dialysis in situations perceived as futile, 77%; carrying a high patient census, 75%; and observing other practitioners give unduly optimistic descriptions of the benefits of dialysis, 64%.

Scenarios related to overly optimistic descriptions and futile kidney replacement therapy were cited as occurring often to frequently by more than one-half of respondents, as was following a family's wishes to continue dialysis in an incapacitated patient where the physician believes continued treatment is not in the patient's best interest.

Three-fourths of respondents perceived their fellowship program as stressful. Twenty-seven percent had considered quitting at some point during their fellowship training, including nine percent at the time they completed the survey.

Moral distress is a pervasive problem in healthcare settings. Nephrology fellows may experience uncertainty and constraint-related moral distress in many situations, including decisions about initiating, continuing, or withdrawing or withholding dialysis.

The new survey finds that nephrology fellows commonly experience situations involving moderate to high levels of moral distress. The authors discuss organizational and curricular changes and self-care opportunities to help address and reduce moral distress in fellowship programs [Saeed F, et al. Frequency of severity of moral distress in nephrology fellows: A national survey. *Am J Nephrol*, published online ahead of print June 21, 2021. doi: 10.1159/000516575; https://www.karger.com/Article/Abstract/516575]. ■

Final SPRINT Data Confirm Benefits of Intensive BP Lowering

Final results from the Systolic Blood Pressure Intervention Trial (SPRINT) support an intensive strategy targeting a systolic blood pressure (BP) of less than 120 mm Hg, reports *The New England Journal of Medicine*.

The analysis included patients, aged 50 years or older, with baseline systolic BP of 130 to 8 mm Hg and increased risk for cardiovascular disease, but without diabetes or a history of stroke. Patients were randomly assigned to intensive or standard treatment, with systolic BP targets of less than 120 or 140 mm Hg, respectively. The study was halted early in 2015—at a median follow-up of 3.33 years—due to overwhelming evidence of benefit in the intensive-treatment group. The current report presents final outcomes at a median 3.88 years' follow-up, including data from study close-out visits.

In the initial 2015 report, rates of a primary composite outcome of myocardial infarction, other acute coronary syndromes, stroke, heart failure, or cardiovascular death were 1.77% per year with the intensive-treatment strategy versus 2.40% per year with standard treatment: hazard ratio (HR) 0.73. All-cause mortality was 1.06% versus 1.41% per year: HR 0.75. Intensive treatment was associated with higher rates of some serious adverse events, including hypotension, electrolyte abnormalities, acute kidney injury or kidney failure, and syncope.

On analysis of the combined intervention and postintervention results, rates of both the primary outcome and all-cause mortality were lower with intensive treatment: HR 0.76 and 0.79, respectively. The lower systolic BP target remained associated with lower rates of myocardial infarction and cardiovascular death, although rates of heart failure events no longer differed significantly between groups.

Hypotension, electrolyte abnormalities, and acute kidney injury or kidney failure remained more common in the intensive-treatment group. Most kidney adverse events were solitary, mild, and followed by recovery of kidney function.

The final SPRINT results confirm significant reductions in major adverse cardiovascular events and all-cause mortality with intensive BP-lowering treatment targeting a systolic BP of less than 120 mm Hg. Some adverse events continue to be more frequent in the intensive-therapy group [SPRINT Research Group, et al. Final report of intensive versus standard blood-pressure control. *N Engl J Med* 2021; 384:1921–1930. doi: 10.1056/NEJMoa1901281]. ■