Prediabetes a Risk Factor for Hyperfiltration and Albuminuria

Prediabetes is independently associated with glomerular hyperfiltration and an increased albumin-to-creatinine ratio (ACR) at medium-term follow-up, reports a study in The New England Journal of Medicine.

The study included a general population sample of 1,261 white, middle-aged adults from the Renal Ischemic Clearance Study in Tooms 6 (RENIS-T6) and the RICA Study. Participants underwent a six-month run-in phase in which supportive care was adjusted according to proteinuria. In 94 patients, urinary protein excretion decreased to less than the target level of 0.75 g/d. One hundred sixty-two patients with IgA nephropathy were randomized, of which 82% had severe infections, impaired glucose tolerance, and weight gain of more than 5 kg. There was one case of fatal sepsis in the immunosuppression group. Some evidence supports the use of immunosuppressive therapy for patients with IgA nephropathy. This three-year trial finds no substantial kidney-related benefit of adding immunosuppression to intensive supportive care for high-risk IgA nephropathy. Immunosuppressive therapy also has significant adverse effects, including a risk of severe infections. [Rauen T, et al. Intensive supportive care plus immunosuppression in IgA nephropathy. N Engl J Med. 2015; 373:2225–2236.]

Kidney Failure Risk Scores Show Good Accuracy Worldwide

Although a calibration factor is sometimes needed, equations for predicting kidney failure risk developed in Canada perform well in widely varying world populations, concludes a study in The Journal of the American Medical Association.

Kidney failure risk equations developed and validated in Canada were further validated in 31 cohorts participating in the Chronic Kidney Disease Prognosis Consortium. These cohorts included more than 720,000 participants with stage 3 to 5 CKD from 30 countries, with data collected from 1982 through 2014. New pooled risk equations were developed to compare with the original risk equations for prediction of kidney failure (dialysis treatment or kidney transplant). Two calibration factors were developed to address regional variations in risk.

The analysis included nearly 24,000 cases of kidney failure developing over a median four-year follow-up. The original Canadian equations showed very high discrimination of patients who developed kidney failure, with C statistics of 0.90 at two years and 0.88 at five years. Discrimination was also excellent in subgroups defined by age, race, and diabetic status, and was not further improved with the use of the pooled equations.

The Canadian risk equations showed good calibration in North American populations, but overestimated risk in some cohorts from other continents. Use of a calibration factor that lowered baseline risk by 3.9% percent at two years and 16.5% percent at five years, calibration improved in most non-North American cohorts.


Sclerostin Predicts Arterial Calcification in ESRD

The osteocyte-derived bone formation inhibitor sclerostin predicts vascular calcification in patients with end-stage renal disease (ESRD), according to a study in Kidney International.

The researchers measured serum sclerostin levels in 89 patients with ESRD, mean age 48 years, who had undergone epidermal growth factor receptor-2 mutation testing. Measuring sclerostin levels were significantly higher in the 37 patients who had moderate to extensive vascular calcification, compared to the 52 with no or minimal calcification. Patients with a coronary artery calcification score of 100 or higher also had higher sclerostin levels: 559 versus 367 pg/ml, respectively. Serum sclerostin was correlated with patient age, intact parathyroid hormone and bone-specific alkaline phosphatase levels, and percent calcification. On multivariable analysis, older age, female sex and high-normal ACR were all independently associated with vascular calcification.

On receiver operating characteristic curve analysis, sclerostin was a significant predictor of vascular calcification, with an area under the curve of 0.68. There was little or no expression of vascular sclerostin mRNA and protein, suggesting that vascular-derived sclerostin in not a major contributor to circulating levels.

Recent evidence suggests that sclerostin may be an important contributor to vascular calcification in patients associated with chronic kidney disease—mineral and bone disorder (CKD-MBD). The new results show that high serum sclerostin levels are associated with several measures of increased vascular calcification in ESRD patients. Of several circulating CKD-MBD biomarkers evaluated, sclerostin is the only one that predicts vascular calcification. The authors discuss the implications for understanding the development of arterial calcification in kidney disease [Qureshi AR, et al. Increased circulating sclerostin in end stage renal disease predicts biopsy-verified vascular medial calcification and coronary artery calcification. Kidney Int 2015; 88:1356–1364].

Does Immunosuppression Improve Outcomes in IgA Nephropathy?

For high-risk patients with IgA nephropathy, adding immunosuppressive treatment to intensive supportive care doesn’t improve clinical outcomes—but does increase the rate of infections and other serious adverse effects, reports a trial in The New England Journal of Medicine.

The randomized, open-label trial included 337 patients with IgA nephropathy at 32 German nephrology centers. Three hundred nine patients completed a six-month run-in phase in which supportive care was adjusted according to proteinuria. In 94 patients, urinary protein excretion decreased to less than the target level of 0.75 g/d. One hundred sixty-two patients with IgA nephropathy were randomized, of which 82% had severe infections, impaired glucose tolerance, and weight gain of more than 5 kg. There was one case of fatal sepsis in the immunosuppression group. The new study, using measured rather than estimated GFR, suggests an independent role of prediabetes in the development of hypertension and albuminuria. If the results are confirmed by further studies, early treatment for prediabetes might help to lower the burden of CKD in diabetes [Melton T, et al. Prediabetes and risk of glomerular hyperfiltration in the general nondiabetic population: a prospective cohort study. Am J Kidney Dis 2015 Dec 16; pii: S0272-6386(15)01389-X. doi: 10.1053/j.ajkd.2015.10.025].

Findings