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A protein dilution against metabolic dysfunction and kidney injury in human type 2diabetic kidney disease and Wistar fatty rats, an animal model of type 2 diabetes and obesity

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We assessed whether a low-protein diet (LPD) could prevent the progression of type 2 diabetic nephropathy. The participants (n=112) were randomly assigned to either LPD (0.8 g kg/day) or normal-protein diet (1.2 g kg/day), and were followed for 5 years. The primary outcomes were the annual change in estimated GFR, the incidence of doubling of sCr and the time to doubling of sCr. The difference in mean annual change in eGFR between the LPD and the normal-protein diet groups was −0.3 ml/min/1.73 m2 (p = 0.93). A doubling of sCr and the time to doubling of sCr was similar in both groups. Although in the LPD group overall protein intake was slightly lower, it did not confer renoprotection (ClinicalTrials.gov NCT00448526).
We next investigate the preventative effects of a LPD on diabetes and renal injury in a rat model of type 2 diabetes and obesity. Diabetic male Wistar fatty (fa/fa) rats (WFRs) were fed a standard diet (23.84% protein) or an LPD (5.77% protein) for 24 weeks beginning at 6 weeks of age .Increases in BW/FW in WFRs were prevented by the LPD, and the LPD in WFRs suppressed the elevation of glucose levels through improvement of insulin resistance, which were possibly related tohigher plasma FGF21 and HMW adiponectin. T-CHO/TG levels in WFRs were also reduced by the LPD. Renal hypertrophy, albuminuria, renal histological changes, increased expression of p62 and p-S6RP were observed in WFRs compared with those in WLRs. The LPD ameliorated all renal damage in the diabetic kidneys. We further examined the interventional effect of LPD on the advanced diabetic kidney injury from 24 weeks age for 20 weeks. Similarly, a LPD improved not only metabolic dysfunction, but advanced diabetic renal injuries, including tubulointerstitial damage by restoring autophagy dysfunction.