RISK FACTORS

Hyperfiltration—a risk factor for renal function decline

In a paper recently published in *Diabetes Care*, the GFR Study Investigators show that persistent glomerular hyperfiltration is an independent risk factor for accelerated renal function loss and development or progression of nephropathy in patients with type 2 diabetes. “We decided to do this research to address whether and to what extent glomerular hyperfiltration predicts faster glomerular filtration rate (GFR) decline or increased risk of onset or progression of nephropathy, and whether amelioration of hyperfiltration may be renoprotective in the long-term”, explains investigator Piero Ruggenenti.

Patients with type 2 diabetes and normoalbuminuria or microalbuminuria were included in this *post hoc* analysis. Of the 600 patients, 15% were categorized as hyperfiltrating (GFR >120 ml/min/1.73 m²) at baseline. Despite intensified treatment, kidney function among participants declined by 3.37 ml/min/1.73 m² per year from baseline to study end (median follow-up 4 years), a rate of decline up to fivefold faster than that reported in the

general population. At 6 months, GFR decline was 13-fold greater in patients with hyperfiltration than in patients without hyperfiltration. This rapid short-term reduction in GFR was, however, followed by slower subsequent GFR decline, and the long-term reduction in kidney function was similar in the two groups.

“...persistent glomerular hyperfiltration is an independent risk factor for accelerated renal function loss...”

Compared with patients in whom hyperfiltration was ameliorated at 6 months (defined as a GFR reduction >10%) by metabolic or blood-pressure control or in those who were nonhyperfiltrating at baseline, patients with persistent hyperfiltration tended to have faster GFR decline (4.19 ml/min/1.73 m² versus 3.23 ml/min/1.73 m² per year) and were more likely to develop microalbuminuria or macroalbuminuria

(23.4% versus 10.6% of patients). The above differences in disease outcomes were partly explained by less effective metabolic control and blood-pressure control in those with persistent hyperfiltration, despite similar treatment in both groups. Higher GFR at inclusion, older age and higher systolic blood pressure predicted a faster GFR decline throughout the whole study period.

“We are planning to take this work forward by evaluating whether insulin resistance is a cause of hyperfiltration and whether its amelioration translates into amelioration of hyperfiltration and protection from renal disease in the long-term”, says Ruggenenti. “We are also evaluating genetic factors that may predispose to hyperfiltration and onset and progression of diabetic renal disease.”

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