Can Endostatin Predict Renal Risk in Type 2 Diabetes?

Plasma endostatin might provide a useful biomarker of the risk of renal dysfunction in patients with type 2 diabetes, according to a study in Kidney International.

The study included banked specimens from 187 matched cases and controls) from the Action to Control Cardiovascular Disease (ACCORD) trial as well as samples from a contemporary cohort of 871 patients with type 2 diabetes from the Mount Sinai Biobank. Plasma endostatin – a fragment of collagen XVIII that may reflect endothelial dysfunction, matrix remodeling after kidney injury, and angiogenesis – was evaluated for association with a composite outcome of 40% decline in estimated glomerular filtration rate (eGFR) or end-stage renal disease.

Participants who met the composite renal outcome had higher baseline plasma endostatin levels. Log2-transformed endostatin levels were associated with similar and significant increases in risk in both groups: adjusted odds ratio 2.5 in ACCORD and hazard ratio 2.6 in BioMe. Risk was also elevated for those in the highest versus lowest quartile of plasma endostatin: OR 3.6 in ACCORD and HR 4.4 in BioMe.

In the BioMe data, adding information on endostatin to a baseline clinical model improved the area under the curve for the combined renal outcome at the cutoff of a 45 ng/mL, corresponding to the fourth quartile value, elevated plasma endostatin had a sensitivity of 50%, specificity of 71%, and positive and negative predictive values of 21% and 90%, respectively.

New biomarkers are needed to predict renal function decline associated with type 2 diabetes, particularly in patients with preserved GFR at baseline. This study suggests that plasma endostatin is associated with decline in kidney function over time in patients with type 2 diabetes.


Combined Rituximab-Cyclophosphamide for AAV

A combined regimen of rituximab and cyclophosphamide improves long-term outcomes in patients with renal anti-neutrophil cytoplasm antibody-associated vasculitis (AAV), reports a study in Nephrology Dialysis Transplantation. The study included 66 patients with AAV and biopsy-confirmed renal involvement. All were treated with a regimen of oral corticosteroids and rituximab plus low-dose pulsed intravenous cyclophosphamide. Maintenance therapy consisted of azathioprine and tapered steroid.

Disease activity was assessed using the Birmingham Vasculitis Activity Score (BVAS), along with monitoring of estimated glomerular filtration rate (eGFR). Median follow-up was 56 months. Outcomes were compared with those of 198 propensity-matched patients from previous European Vasculitis Study Group trials.

At baseline, median BVAS score was 19 and eGFR 25 mL/min. By 6 months, patients had received median cumulative doses of 2 g of rituximab and cyclophosphamide, and 4.2 g of corticosteroids. At that time, 94% had achieved disease remission, defined as a BVAS score of 0. At 5 years, the patient survival rate was 84% and renal survival 95%. Eighty-four percent of patients became ANCA-negative. Fifty-seven percent of patients remained B-cell-depleted (less than 10 cells/μL) through 2 years; this group had a 19% rate of major relapse at 5 years. Serious infections occurred at a rate of 1.24 per 10 patient-years. Compared to controls from previous trials, the combined rituximab-cyclophosphamide regimen was associated with lower rates of death, hazard ratio (HR) 0.29; progression to end-stage renal disease, HR 0.20; and relapse, HR 0.49.


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