1-2020

Spectrum of Renal Biopsy Findings in TRIDENT Cohort

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SI/CTR Abstract

Word count: 250 words

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Introduction: Diabetic kidney disease is the most common cause of chronic end stage renal failure in the USA. Kidney biopsy is the gold standard diagnostic criteria; however, it is an invasive procedure; not everyone undergoes diagnostic biopsy. The relationship between histological and clinical parameters and prognosis in DKD is incompletely understood. TRIDENT, (Transformative research in diabetic nephropathy) plans to enroll 400 diabetic subjects undergoing clinically indicated renal biopsies and performs multi-omics characterization of subjects to identify pathways associated with kidney function decline. Genetic studies indicated that podocytes influence albuminuria and diabetic kidney disease development. We seek to understand whether podocyte and basement membrane changes correlate with kidney function, degree of albuminuria, and histopathologic features of diabetic nephropathy using electron microscopy and digital light microscopy.

Methods: I performed quantitative characterization of podocyte foot process morphology using TRIDENT subject biopsies. Podocyte foot process width (FPW) was measured using

electron micrographs in ImageJ and calculated: FPW = (π/4) × (ΣGBM length/Σfoot process).

Results: In our cohort, the average FPW was 1.624μm, and the glomerular basement membrane (GBM) average thickness was 773.27μm. The average FPW and GBM thickness ranged from 519μm-4.806μm and 200μm-3230μm per patient, respectively. Using a Pearson's correlation coefficient: GBM thickness positively correlates with RPS Class (.424240229), %interstitial fibrosis (.203720183), arteriolar hyalinosis (0.307801899), proteinuria (.639114291).

Discussion: Podocyte features such as FPW and GBM thickness showed stronger correlation with proteinuria than other parameters. Some samples were collected in patients with advanced DKD; collecting samples earlier in the disease process may represent more accurate correlations between EM findings and disease severity. Overall podocyte structural changes strongly correlate with proteinuria, indicating the key role of podocytes in proteinuria.