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Can we diagnose diabetes-related kidney disease without kidney biopsy using proteomics?

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Objectives : This study aimed to identify potential proteome in the serum and urine that could aid in diagnosing kidney disease solely attributed to diabetes mellitus, without the need for a kidney biopsy.

Methods : A retrospective review was conducted on patients with type 2 diabetes (T2D) who underwent kidney biopsy between 2010 and 2020. The most frequently coexisting glomerulonephritis were IgA nephropathy (IgAN) and membranous glomerulonephritis (MN). Based on this, we selected age- and sex-matched patients from the enrolled cohort for proteomic analysis, including those with pure diabetic nephropathy (DN, n = 11) and those with pure non-DN (IgAN, n = 11; MN, n = 11). A control group comprised living kidney transplant donors (n = 11). Comparative quantitative proteomic analysis was conducted using high-resolution mass spectrometry in combination with nanoflow liquid chromatography. Protein quantification for each group was performed in a label-free manner, followed by statistical analysis to identify potential biomarkers specific to each group.

Results : In the serum dataset, a total of 1,220 proteins were identified, among which 15 proteins were found to be distinct in the DN group compared to the non-DN and control groups. Random forest analysis effectively differentiated DN from the entire cohort (out-of-bag error of 0, accuracy 100%). Gene ontology analysis revealed that DN-specific serum proteins were predominantly associated with processes such as wound healing response, antibacterial humoral defense, cell development, chemotaxis, and vascular formation. In the urine dataset, 1,579 proteins were identified, with 15 proteins showing distinct clustering in the DN group relative to the non-DN and control groups. Random forest analysis successfully classified DN cases (out-of-bag error 0.159, accuracy 84.1%).

Conclusions : Serum and urine proteome can be useful to diagnose diabetes-related kidney disease without the need for a kidney biopsy. Additionally, it can help determine the appropriate indications for kidney biopsy in T2D patients with kidney damage.