Editorial

# Pathology and Prognosis of Type 2 Diabetes Mellitus with Renal Involvement

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Type 2 diabetes (T2D) is the most common cause of chronic kidney disease (CKD) and end-stage renal disease worldwide. In China, approximately 21.3% of diabetes was estimated to accompany with CKD and the number of diabetes-related CKDs was 24.3 million, of whom 60.5% preserved renal dysfunction with slightly increased albuminuria.[1,2] In the light of the prevalence and massive health and financial toll, the pathologic diagnosis and prognosis of diabetes-related CKD are of great clinical and societal relevance. Therefore, based on the different pathological types of diabetes with renal impairment, appropriate therapeutic schedules largely impacted on the prognosis of diseases. It was well worthy to summarize the relationship between pathology and prognosis for T2D with renal involvement in the study.

The National Kidney Foundation/Kidney Disease Outcomes Quality Initiative guideline (2007) defined CKD related to diabetes as diabetic kidney disease (DKD). As for T2D related to renal involvement, there were three pathological types: DKD, nondiabetic renal disease (NDRD), and DKD superimposed on NDRD. If without the help of renal biopsy, pathologic types were difficult to diagnose and classify, which even be misdiagnosed. Therefore, the prerequisite to the further investigation for pathology and prognosis of DKD was renal biopsy. Although several research centers launched long-term follow-up to T2D with renal function, the number of samples was still insufficient, which was attributed to the inconsistency to execute renal biopsy. Wong *et al*.[3] followed up 68 diabetic patients with renal damage nearly for 74 months and found that these DKD or DKD superimposed on NDRD had more rapid renal function deterioration and lower renal survival rate than those of NDRD. Defined 5-year renal survival rate and doubling of serum creatinine as the endpoints of renal outcomes, the data of 328 T2D patients undergone renal biopsy from our center of West China Hospital, showed that DKD had a poorer renal prognosis (5-year renal survival rates of 55.21% and doubling of serum creatinine rates of 63.54%), and NDRD had a better prognosis (96.72% and 4.92%, respectively), which was consistent with the study by Wong *et al*. Interestingly, the outcomes of DKD superimposed NDRD from our center revealed that the prognosis of mixed types was better than that of NDRD (100% and 0%, respectively).[4] There was a disparity in the prognosis of DKD superimposed NDRD between our results and other similar investigations, which should be attributed to the proportion and sample size and may not represent the real prognosis of those patients. However, the ongoing study of the incidence, development, and prognosis of DKD launched by the First Hospital Affiliated Peking University, which covered more than 10,000 diabetic patients, may reveal a reliable consequence.[5]

On the guidance of Renal Pathology Society for the pathological classification of DKD, the severity of renal damage was evaluated by the lesions of glomeruli, tubulointerstitium, and renal vessels. Specifically, glomerular lesions were classified as class I, class IIa, class IIb, class III, and class IV, and tubulointerstitial and vascular lesions are assessed by scoring. A 52-month follow-up to 69 pure DKD patients (lack of Class I) performed by Okada *et al*.[6] found that Class IIa of patients had the lowest rate of initiation of chronic dialysis or doubling of serum creatinine level (54.5%), and the rate of renal endpoint events were notably increased (>71%) if the renal pathological changes

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were progressed to Class IIb or higher levels. A recent study by An *et al*.[7] including 396 DKD patients showed that the 5-year renal survival rates gradually declined with the severity of glomerular lesions (Class I: 100%, Class IIa: 90.1%, Class IIb: 75.4%, Class III: 39%, and Class IV: 15.3%). Similarly, 178 were diagnosed with pure DKD from the 328 patients of our center, and the follow-up results displayed the consistent trend (Class I: 100%, Class IIa: 84.62%, Class IIb: 60%, Class III: 47.5%, and Class IV: 33.3%) with the previous study. Furthermore, the results of our center revealed the rates of doubling serum creatinine from Class I to Class IV were 0%, 23.1%, 66.7%, 72.5%, and 87.5%.[4] From the previous studies, Class I and IIa of glomerular lesions had a good prognosis, and Class IIb or higher classes had a poor prognosis, so that we speculated that the progress from Class IIa to IIb might be a significant watershed to the prognosis of DKD. Previously, several studies evaluated the relationship between tubulointerstitial lesions and renal outcomes in DKD patients; however, these were conflicted. Okada *et al*.[6] found that interstitial lesions, including interstitial fibrosis and tubular atrophy (IFTA) and interstitial inflammation, were significative predictors for renal prognosis. An *et al*.[7] reported that IFTA but not interstitial inflammation was the independent risk factor for renal outcomes. In contrast to those studies, the data of our center exhibited that tubulointerstitial lesions were not independently associated with the prognosis of DKD. The limitation of sample size might be the primary cause of these inconsistent results. The severity of vascular lesions was a part of evaluation criteria for the pathology of DKD. Interestingly, efferent arteriolar hyalinosis was reported that specific kidney changes to DKD had a clear correlation with urine albumin excretion and disease progression.[8-10] However, there was still lack of proofs to confirm that vascular lesions were directly associated with the prognosis of DKD. Therefore, large sample size and long-term follow-up studies are required to reflect the authenticity between the pathology and prognosis of DKD.[4,6,7]

In summary, there is a close relationship between the pathology and prognosis of T2D-related CKD. Noteworthily, renal biopsy and pathological classification to DKD are of great importance in early diagnosis and personalized treatment, and to evaluate the prognosis of disease. The renal biopsy was positively advised to carry out and avoid the misdiagnosis and improved the treatment accuracy of diabetes related to kidney damage. At the same time, sensitive biomarkers should be discovered to prevent renal injury of diabetic patients and only by these means could improve the prognosis.


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