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## **Tertiary lymphoid tissues are associated with kidney function decline in patients with advanced diabetic kidney disease**

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**Objectives:** Tertiary lymphoid tissues (TLTs) are inducible ectopic lymphoid tissues that arise in chronic inflammatory conditions. Herein, we investigated the impacts of renal TLTs on kidney function decline in patients with diabetic kidney disease (DKD).

**Methods:** We retrospectively enrolled 180 patients with biopsy-proven isolated DKD and 53 controls (27 age/sex-matched thin basement membrane disease (TBMD) and 26 age/sex/estimated glomerular filtration rate (eGFR)-matched hypertensive nephrosclerosis). TLTs were defined as T and B cell infiltrations with signs of proliferation, and their stages were classified by the absence (stage I) or the presence (stage II) of follicular dendritic cells.

**Results:** Patients with DKD exhibited mean eGFR of 45.4 ml/min/1.73m<sup>2</sup> and mean urinary protein/creatinine ratio of 5.9 g/gCr. TLTs were observed in 5.0%, 32.0%, and 54.4% in patients with TBMD, hypertensive nephrosclerosis, and DKD, respectively ( $p < 0.001$ ), while stage II TLTs were exclusively detected in those with DKD (18.3%). Presence of stage II TLTs was independently associated with an increased risk of progression to end-stage kidney disease compared with patients with no TLT after multivariable adjustments (adjusted hazard ratio of 2.19, 95% confidence interval of 1.20 – 4.02). Stage II TLTs were associated with worse tubulointerstitial inflammation and fibrosis scores.

**Conclusions:** TLTs are commonly found in advanced diabetic kidneys. Presence of stage II TLTs are associated with rapid decline in kidney function in patients with DKD.