Video abstract transcript

Renal Histopathology Associated With Kidney Failure and Mortality in Patients With Lupus Nephritis: A Long-Term Real-World Data Study

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Hello, I am Dr. Yu-Wan Liao. On behalf of my co-authors, I would like to thank the Journal of Rheumatology for inviting us to discuss our article, entitled “Renal Histopathology Associated With Kidney Failure and Mortality in Patients With Lupus Nephritis: A Long-Term Real-World Data Study.”

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Lupus Nephritis, commonly referred to as LN, greatly impacts a significant proportion of SLE patients. The importance of understanding lupus nephritis lies in its potential to lead to kidney failure and increased mortality. Among the six subtypes, proliferative LN (classes III & IV) displays greater inflammatory characteristics. Prior studies have identified associations between specific LN classes and histologic findings with renal outcomes and mortality. Our study seeks to further explore these associations, aiming to provide a clearer picture of the implications of lupus nephritis on patient outcomes."

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We initiated a retrospective cohort, enrolling 537 SLE patients receiving renal biopsy, spanning from 2006 to 2019. The diagnosis of SLE was based on the 1997 American College of Rheumatology criteria and specific ICD codes.

Nine patients were excluded and a total of 526 patients were analyzed eventually. Regarding renal histopathology, these samples were examined by an experienced renal pathologist using the International Society of Nephrology/Renal Pathology Society (ISN/RPS) classifications. For our clinical assessments, we had regular follow-ups every 1 to 3 months. Variables we used in our analysis included kidney function, proteinuria level and disease activity. Our primary outcomes were kidney failure and mortality.

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Our study encompassed an analysis of 526 patients diagnosed with LN. The distribution of each histologic class showed 50.8% with class IV, which was the most, followed by class V and III. The median follow-up time was 7.5 years. Furthermore, we noticed a predominant female representation across all classes without significant age differences. Proteinuria was most significant in patients of Class IV + V, followed by those in classes IV and V. There was a more pronounced decline in renal function in patients with class III or IV LN compared to those with class V. Lastly, patients in Class IV + V had higher SLEDAI scores and increased anti-dsDNA antibody levels.

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Histopathologically, patients with class IV lupus nephritis exhibited elevated activity and chronicity index scores. Tubulointerstitial inflammation was more prevalent in this class. In terms of therapeutic interventions, cyclophosphamide emerged as the predominant choice for induction therapy in class IV ± V. For maintenance therapy in class IV ± V, mycophenolate was favored, whereas cyclosporine was the preferred choice for class V. Nephrotic flares, defined as nephrotic-range proteinuria, were predominantly observed in class IV + V, followed sequentially by classes IV and III + V.

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In this study, 58 patients progressed to kidney failure. The Cox regression analysis identified several predictors for kidney failure. In the first multivariate analysis, the presence of tubular atrophy with a Hazard Ratio (HR) of 2.28, tubulointerstitial inflammation with an HR of 3.13, and nephrotic flares with an HR of 2.55 were significant predictors. In the second multivariate analysis, tubular atrophy, tubulointerstitial inflammation, and nephritic flares were identified as significant prognostic factors.

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To investigate the impacts of renal histology on kidney failure, we conducted a Kaplan-Meier survival analysis, according to the combination of tubular atrophy and tubulointerstitial inflammation. Notably, the worst renal outcomes were observed in patients who had both tubular atrophy and tubulointerstitial inflammation.

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Out of 526 patients, 64 (12.2%) passed away during the follow-up period. Notably, 9 (14.1%) of these patients developed kidney failure before their demise. The Cox regression analysis highlighted sex as a significant predictor of mortality. Specifically, among male patients, the presence of cellular crescent was a predictor of mortality with a hazard ratio of 1.91. On the other hand, for female patients, the presence of fibrous crescent increased the risk of mortality with a hazard ratio of 5.70.

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Kaplan-Meier survival curves revealed that female patients generally had a more favorable long-term survival compared to their male counterparts. In detail, the existence of cellular crescent in male patients was linked to the worst outcomes, while in the female subgroup, the presence of fibrous crescent indicated a higher risk of mortality.

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Clinical and renal histopathologic variables are linked to kidney failure and death in lupus patients. From previous literatures, both glomerular pathology and tubulointerstitial inflammation predicted renal outcomes. Our study highlighted that both activity and chronicity indices in histology were predictors of kidney failure and death. Specifically, Tubular Atrophy (TA) and tubulointerstitial inflammation were independent predictors of renal survival. Our study also revealed a gender difference in mortality predictors, suggesting that male lupus nephritis patients with cellular crescents might have increased risks of mortality. In conclusion, renal histopathology serves as a determinant for kidney failure and mortality. It's imperative for physicians to recognize these predictors and implement optimal management strategies to avert potential adverse outcomes.

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Thank you for your time and interest. For a comprehensive view of this manuscript, please visit the Journal of Rheumatology's website. Thank you very much for listening.

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