P0360 **URINARY PEPTIDOMIC ANALYSIS IN PROLIFERATIVE VERSUS NON-PROLIFERATIVE LUPUS NEPHRITIS : RESULTS OF THE PEPTIDU-LUP STUDY.**

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Background and Aims: Lupus nephritis (LN) is a frequent manifestation of Systemic Lupus Erythematosus (SLE). The therapeutic strategy relies on the result of kidney biopsy, which differentiates proliferative LN (PLN) from non-proliferative LN (NPLN). The analysis of the urinary peptidome has led to the identification of prognostic biomarkers in chronic kidney disease (CKD, namely the CKD273 classifier), or, as a liquid biopsy, for the diagnosis of glomerulonephritides. We verified whether urinary peptidomics could predict the severity of renal pathological injury and damage in LN.

Method: Urine samples, collected before kidney biopsy, were analyzed by capillary-electrophoresis coupled to mass-spectrometry (CE-MS). Urinary peptide profiles were compared between PLN and NPLN. Predictive values for chronic pathological lesions (glomerulosclerosis and interstitial fibrosis/tubular atrophy (IF/TA)), response to therapy and development of CKD were also assessed. Clinical characteristics, routine laboratory parameters and immunological SLE markers were collected at inclusion and prospectively for at least 24 months.

Results: We collected 100 urinary samples from patients with LN, forming a discovery (n=67) and an independent validation (n=33) cohort. Overall there were 69 patients with PLN (class III or IV +/-V with active lesions) and 31 patients with NPLN (class II or V or chronic lesions). In the discovery cohort, the abundance of 36 urinary peptides differed between PLN and NPLN (Mann-Whitney test). However, these peptides did not resist multiple testing correction. Among them, 17 could be sequenced (fragments of collagen-I, -II, -III, apolipoprotein A-I, Fibrinogen alpha chain and Histone H2B). Of the 17 sequenced peptides, 7 were also part of the CKD273 classifier. A mathematical model combining the 36 peptides classified PLN and NPLN patients from the validation cohort with an AUC of 0.75 and sensitivity and specificity of 0.81 and 0.53, respectively. Positivity of anti-dsDNA antibodies had the best sensitivity (0.96) and sterile pyuria the best specificity (0.68) to differentiate PLN from NPLN, and including the CKD273 score did not improve the accuracy of the predictive models. No urinary peptidomics profile was identified to predict early response to therapy in patients with LN.

Glomerulosclerosis was observed in 63/100 biopsies. In the discovery cohort, the abundance of 38 urinary peptides (including 22 sequenced) differed between patients with vs without glomerulosclerosis (Mann-Whitney test). Again, these peptides did not resist multiple testing correction. Of the 22 sequenced peptides, 7 (different from the peptides associated with PLN) belonged to the CKD273 classifier. A mathematical model combining the 38 peptides classified patients from the validation cohort with an AUC of 0.75 and sensitivity and specificity of 0.82 and 0.54, respectively, for the presence of glomerulosclerosis. Although the quantification of IF/TA was correlated to the pre-existing CKD273 classifier, including the CKD273 score did not improve the prediction of IF/TA when tested in combination with simple clinical parameters. Only 3 patients developed CKD after a mean follow-up of 4 years, therefore contribution of urinary peptidomics for the prediction of CKD in LN could not be evaluated.

Conclusion: Different urinary peptidomics signatures were identified among patients with LN, according to the presence of active proliferative lesions or chronic lesions. However, these panels did not resist multiple testing correction, and did not improve the diagnostic accuracy when combined with clinical or immunological markers. The contribution of urinary peptidomics to predict CKD in patients with LN, or as an early predictor of renal flares, could not be evaluated. Kidney biopsy remains central for the care of patients with LN.