SERUM UROMODULIN IS EARLY BIOMARKER OF INTERSTITIAL FIBROSIS/TUBULAR ATROPHY IN PATIENTS WITH GLOMERLOPATHIES

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OBJECTIVES

Uromodulin (Umo; also known as Tamm-Horsfall protein) is a 95 kDa protein represents the most abundant urinary protein exclusively produced in the tubular cells of the thick ascending limb and the early distal tubule. Most of the protein is released into the tubular lumen. Its physiological role is hypothesized to protect from ascending urinary tract infection and stone formation. Umo is also released on the basolateral side of the tubular cell into the interstitium and further in the blood. A reduced number of tubular cells, due to for example, interstitial fibrosis/tubular atrophy in chronic kidney disease (CKD), is paralleled by reduced urinary and serum concentrations of uromodulin. Therefore, uromodulin might represent a promising biomarker for the number of intact nephrons and therefore renal mass. Some data suggest that serum Umo (SUmo) may be more relevant index of kidney status than urinary Umo. However the exact role of Umo as a marker of degree of kidney lesions in patients (Pts) with CKD is not known. In this regard we studied the relationships between SUmo, kidney function and structure in Pts with glomerulopathies.

METHODS

Eighty one Pts with different glomerulopathies (M:F 41:40: age 18 – 78 yr) were included. Control group consisted of eleven healthy subjects. SUmo (ng/ml) was measured with ELISA ("Biovendor", Brno, Slovakia). Severity of glomerular lesions (GL) was evaluated as the percent of sclerosing glomeruli from the total number of glomeruli in the renal bioptate (light microscopy). The degree of tubular atrophy (TA) or interstitial fibrosis (IF) assessed by semiquantitative scale: from zero to three (null – absence of lesions; three – severe lesions). eGFR was estimated by CKD-EPI equation (creatinine). Results were presented as median [interquartile range]. Spearmen rank correlation coefficient and Mann-Whitney tests were used. False Discovery Rate (FDR) procedure has been applied to correct for multiple comparisons.

RESULTS

In Pts with glomerulopathies SUmo directly correlated with eGFR (RS=0.547, P<0.00001) and inverse with GL (RS=-0.293, P=0.0075), TA (RS=-0.422, P=0.00009), IF (RS=-0.446, P=0.00003). On the other hand it was found that in the absence of signs of tubular atrophy eGFR and SUmo was not significantly differ from control (Fig. 1, Table 1). In the TA-1 stage of tubular atrophy SUmo was significantly lower than in control, whereas eGFR - did not (Fig. 1, Table 1). In TA-2 and TA-3 stages of tubular atrophy SUmo and eGFR declined in parallel in relation to control (Fig.1, Table 1). The relationships between IF, SUmo and eGFR were practically the same (see Fig. 1 and 2; Table 1 and 2).

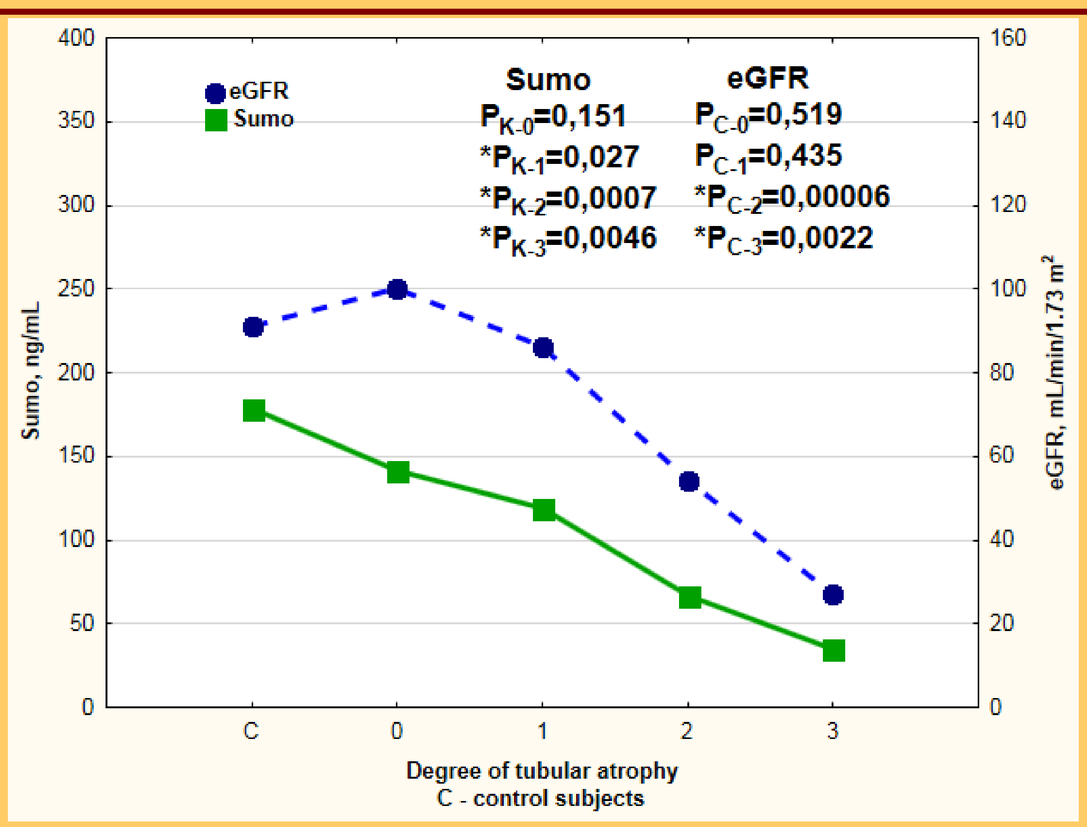

Fig. 1. Associations between tubular atrophy, Sumo and eGFR.
*** Confirm by FDR-procedure**

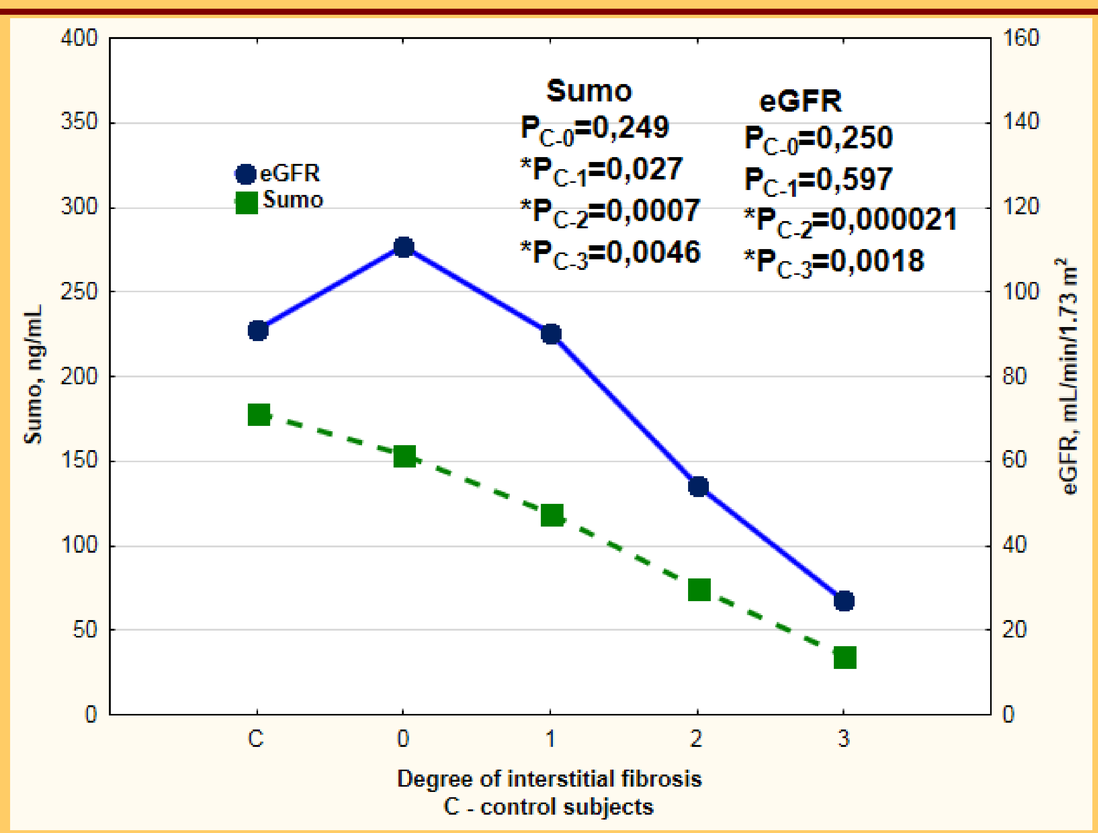

Fig. 2. Associations between interstitial fibrosis, Sumo and eGFR
*** Confirm by FDR-procedure**

Table 1. Relations between TA, eGFR and SUmo (P -significance vs control)

Parameters	Control (n=11)	TA-0 (n=23)	TA-1 (n=34)	TA-2 (n=19)	TA-3 (n=5)
SUmo	178.5[104.5-267.4]	142.0[79.4-183.0], P=0.151	119.3[72.5-164.4], P=0.027	66.8[56.8-97.6], P=0.0007	34.9[34.2-54.8], P=0.0046
eGFR	91.0[88.7-98.0]	100.2[82.4-123.0], P=0.519	86.2[67.6-105.8], P=0.435	54.2[35.2-69.7], P=0.00006	27.0[5.8-27.1], P=0.0022

Table 2. Relations between IF, eGFR and SUmo (P - significance vs control)

Parameters	Control (n=11)	IF-0 (n=21)	IF-1 (n=32)	IF-2 (n=23)	IF-3 (n=5)
SUmo	178.5[104.5-267.4]	153.5[84.7-202.8], P=0.249	119.3[70.7-164.0], P=0.027	75.0[56.8-115.5], P=0.007	34.9[34.2-54.8], P=0.0046
eGFR	91.0[88.7-98.0]	110.6[83,6-123.0], P=0.250	90.2[74.2-106.1], P=0.597	54.2[32.6-69.2], P=0.00002	27.1[27.0-30.3], P=0.0018

CONCLUSIONS

Our data suggests that in patients with glomerulopathies SUmo may be more earlier marker of interstitial fibrosis/tubular atrophy than eGFR.

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