	Control	CKD 1&2	CKD 3	CKD 4&5
Total IxS (mg/l)	0.857 ± 0.86	1.01 ± 0.60	1.192 ± 0.54	3.887 ± 3.25 [a,b,c]
Free IxS (mg/l)	0.018 (0.014)	0.041 (0.040)	0.031 (0.017) [d]	0.083 (0.075) [a,c,e]
Sdc-1 (ng/ml)	2.33 ± 0.31	3.11 ± 0.42	3.22 ± 0.45	5.69 ± 1.26 [f,g,h]
MMP-7 (ng/ml)	4.38 (0.82)	6.03 (1.33) [f]	7.78 (5.50) [f,e]	7.62 (2.15) [f,e]
Ang-2 (ng/ml)	1.60 (0.89)	2.50 (0.61) [d]	2.47 (0.35) [d]	3.36 (1.08) [b,c,f]
VCAM-1 (ng/ml)	688 (557)	682 (479)	634 (148)	1030 (708)
ICAM-1 (ng/ml)	230 (318)	331 (276)	248 (678)	279 (209)
E-selectin (ng/ml)	20.1 ± 7.44	27.5 ± 8.08	25.1 ± 8.54	31.4 ± 9.46 [d]
P-selectin (ng/ml)	18.3 ± 3.58	22.3 ± 3.46	23.9 ± 3.58 [d]	24.8 ± 4.99 [a]

Variables are presented as median (interquartile range) or as mean ± SD.
[a] p<0.01 vs control, [b] p<0.01 vs CKD 1&2, [c] p<0.05 vs CKD 3, [d] p<0.05 vs control, [e] p<0.05 vs CKD 1&2,
[f] p<0.001 vs control, [g] p<0.001 vs CKD 1&2, [h] p<0.001 vs CKD 3

Despite the rather low predicitive power at the level of the individual patient, correlations were observed between Total IxS and Sdc-1 ($r = 0.664$, $p < 0.001$) and MMP-7 ($r = 0.410$, $p = 0.01$) and between Free IxS and Sdc-1 ($r = 0.566$, $p < 0.001$), Ang-2 ($r = 0.516$, $p < 0.01$) and MMP-7 ($r = 0.405$, $p < 0.01$).

CONCLUSIONS: Notwithstanding the low number of patients, these data confirm a possible link between IxS and eGC damage and strengthen the hypothesis that the negative impact of IxS on composite cardiovascular outcomes could be mediated by damage to the eGC. In the near future, we will expand this cohort and link these data to cardiovascular events and mortality.

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ENDOTHELIAL GLYCOCALYX DAMAGE IN CKD: ROLE OF THE UREMIC TOXIN INDOXYL SULFATE

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INTRODUCTION AND AIMS: Damage to the endothelial glycocalyx (eGC) is a crucial step in the development of cardiovascular disease (CVD). By using a rat model, we were able to link the protein-bound uremic toxin indoxyl sulfate (IxS) to eGC disruption as indicated by shedding of its fragments into the circulation. We therefore hypothesize that eGC damage could be one of the mechanisms by which IxS contributes to an increased risk of CVD in chronic kidney disease (CKD) patients. To test this hypothesis in the clinical setting, the present study investigates whether the increase in IxS with CKD progression was accompanied by changes in markers for endothelial dysfunction and eGC disruption.

METHODS: Plasma samples were obtained from matched healthy donors (n=13) and patients from CKD stage 1&2 (n=10), CKD stage 3 (n=7) and CKD stage 4&5 (n=11). Concentrations of IxS were determined by UPLC. Circulating syndecan-1 (Sdc-1; one of the major components of the eGC), Matrix metalloproteinase 7 (MMP-7; an eGC degrading enzyme) and different markers of endothelial dysfunction (Angiotensin 2 [Ang-2], Vascular Cell Adhesion Molecule 1 [VCAM-1], Intercellular Adhesion Molecule 1 [ICAM-1], E-selectin, P-selectin) were simultaneously detected with a Luminex assay (R&D systems).

RESULTS: Concentrations of IxS and Sdc-1 are both significantly higher in patients with CKD stage 4&5 compared to the other groups. P-selectin and E-selectin were significantly upregulated from CKD stage 3 and stage 4&5 on, respectively. Plasma levels of MMP-7 are significantly increased at all stages of CKD compared with healthy controls, and moreover precedes the shedding of eGC degradation fragments. An increment of Ang-2 levels was observed throughout the consecutive CKD stages.