INTRODUCTION AND AIMS: Acute kidney injury (AKI) is characterized by a high prevalence in hospital patients and unfavorable clinical courses. Novel biomarkers such as neutrophil gelatinase-associated lipocalin (NGAL) improve the early detection of AKI, but they are sensitive to stimuli other than kidney injury. In addition, NGAL remains elevated for long periods. We identified glutathione specific gamma-glutamylcyclotransferase 1 (CHAC1) as a potential new biomarker for early AKI in a mouse model of ischemia-reperfusion injury (IRI). In mice, CHAC1 is produced in injured proximal tubules in the early phase after ischemia. Our goal was to evaluate the utility of urinary CHAC1 in a cohort of patients who underwent unilateral clamping of the renal artery during partial nephrectomy.

METHODS: The study population consisted of 37 patients. 27 underwent partial nephrectomy with unilateral clamping of the renal artery inducing a median renal ischemia of 4.5 (IQR 3-6) minutes. CHAC1 was measured in the urine by ELISA at baseline and at a median of 1.49 hours (IQR 1.25-2.28) post-ischemia. Controls were 5 healthy volunteers. Differences were analyzed by non-parametric tests.

RESULTS: CHAC1 was significantly increased at post-ischemia in the renal ischaemia group compared to baseline and control. CHAC1 expression correlated with ischemia time (rho = 0.32, p = 0.04) and was higher than in healthy controls (p = 0.0009). Concentrations were above the expected range in all patients with AKI compared to all healthy controls (p = 0.0002).

CONCLUSIONS: CHAC1 levels increased significantly after renal ischemia in partial nephrectomy. This highlights the potential of CHAC1 as a biomarker for AKI.
ischemia time of 18 minutes (Group 1). 10 patients underwent partial nephrectomy without renal ischemia (Group 2). Urinary samples were collected before surgery and serially after surgery. Urinary CHAC1 was detected by Western blotting using anti-CHAC1 antibody (Abcam ab155533). Semiquantitative analysis of band intensity was performed using ImageJ calibrating to known quantities of recombinant CHAC1 loaded onto adjacent lanes. Urinary NGAL and calprotectin were measured using enzyme-linked immunosorbent assay.

RESULTS: Urinary CHAC1 concentration was significantly increased compared to preoperative baseline in group 1 from 6h up to 3 days after surgery, but not in group 2. Highest CHAC1 concentrations in group 1 were reached 6h after surgery. There was a significant correlation between CHAC1 concentrations 6h after surgery and renal ischemia time in group 1 (p=0.023). CHAC1 on postoperative day 1 correlated positively with NGAL and calprotectin in group 1.

CONCLUSIONS: Urinary CHAC1 is a promising new biomarker for the detection of AKI after renal ischemia. CHAC1 increases early after renal ischemia and shows a rapid normalization. Future studies in different clinical settings must now further evaluate the diagnostic value of urinary CHAC1.