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## Vocal assessment in patients with unilateral vocal cord paralysis pre and post vocal rehabilitation and their outcomes Urine Klotho in human acute kidney injury

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AKI is associated with increased mortality and carries increased risk for subsequent CKD. Klotho deficiency has been observed in experimental AKI and low Klotho post-AKI is associated with progression to CKD in rodents. We conducted a prospective study of 29 AKI patients and 29 controls without AKI in the ICU setting. We excluded patients with baseline eGFR<60 or kidney transplant. Urine samples were obtained within 24 hours of peak serum creatinine (SCr) or at RRT initiation in AKI cases and within 24 hours of ICU admission in frequency-matched controls (by baseline eGFR and age). AKI was defined by KDIGO stage  $\geq 2$  criteria. Longitudinal data from AKI cases were obtained throughout hospital stay. Renal recovery was defined as the ratio of follow-up SCr/baseline SCr  $\leq 1.5$ . Urine Klotho was measured by immunoprecipitation-immunoblot. Mean (SD) age was 58 (17) years, 62% were men and 75% white. Five (17.2%) patients died and 8 (27.6%) required RRT in the AKI group. Only 3.5% patients died in the control group. Urine Klotho adjusted by urine creatinine (uKlotho/Cr) was significantly lower in AKI cases than in controls, median 10 [IQR 4-20] vs. 28 [14-52] fmol/mg,  $p=0.003$ . Furthermore, uKlotho/Cr significantly increased with time in patients that exhibited renal recovery ( $n=7$ ,  $\Delta+216\%$ ,  $p=0.05$ ) but not in those that did not ( $n=7$ ,  $\Delta+8\%$ ,  $p=0.91$ ), mean follow-up 8 days. uKlotho/Cr is significantly lower in patients with AKI when compared to ICU controls without AKI. uKlotho/Cr recovered only in patients that recovered kidney function. Klotho may serve as a prognostic marker for AKI recovery.

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## The PTEN phosphatase in the development of diabetic nephropathy: Loss of PTEN promotes podocyte cytoskeletal rearrangement

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In diabetic nephropathy (DN), podocyte cytoskeletal rearrangement occurs followed by podocyte effacement and the development of proteinuria. PTEN (phosphatase and tensin homologue) is a ubiquitously expressed phosphatase that plays a critical role in cell proliferation, cytoskeletal rearrangement and motility. In mouse models of diabetes mellitus, PTEN expression is reportedly decreased in mesangial cells, contributing to expansion of the mesangial matrix but how PTEN in the podocyte influences the development of DN is unknown. We observed that PTEN expression is down-regulated in the podocytes of diabetic db/db mice and patients with DN. In cultured podocytes, PTEN inhibition caused actin cytoskeletal rearrangement and this response was associated with unbalanced activation of the small GTPases Rac1/Cdc42 and RhoA. In mice treated with PTEN inhibitor, actin cytoskeletal rearrangement occurred in podocytes and was accompanied by increased albumin excretion. We also created mice with an inducible deletion of PTEN selectively in podocytes. These mice exhibited increased albumin excretion and moderate foot process effacement. When the mice were challenged with a high fat diet, podocyte-specific knockout of PTEN resulted in substantially increased proteinuria and glomerulosclerosis compared to control mice fed a high fat diet or mice with PTEN deletion fed a normal diet. These results indicate that PTEN is involved in the regulation of cytoskeletal rearrangement in podocytes and that loss of PTEN predisposes to the development of proteinuria and DN.

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