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Long Term Effects of Acute Kidney Injury on Chronic Kidney Disease and Patient Outcomes: 3-year Results from a Large Prospective Parallel Group Cohort Study

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Introduction
Acute Kidney Injury (AKI) is associated with adverse long-term outcomes, but most of our current knowledge arises from retrospective studies. Prospective studies with deep patient pheno-typing and long-term follow up are required, to avoid biases inherent in retrospective studies, to identify strategies to predict those at highest risk, and with the capability to investigate mechanistic pathways. Here we report three-year outcomes from one such large prospective parallel group cohort study.

Methods
In a single UK centre, hospitalised patients who sustained AKI were recruited and matched 1:1 with controls (hospitalised patients without AKI) for age, baseline eGFR stage and diabetes. Biochemical parameters including renal function and proteinuria were measured at 3 months, 1 year and 3 years following index hospitalisation. CKD progression was defined as ≥25% decline in eGFR with decline in eGFR stage, and a composite renal endpoint as a doubling of serum creatinine, eGFR<15ml/min or initiation of renal replacement therapy.

Results
1125 patients were recruited of whom 866 were successfully matched. There was no difference between AKI and control groups in age (71 yrs (IQR 14) vs. 71 yrs (IQR 13), p=0.7) or baseline eGFR (70.3±20ml/min vs 69.6±20ml/min, p=0.58). AKI episodes were predominantly stage 1 with median duration 3 days (IQR 3). Mean eGFR was lower at all-time points in AKI group. At 3 years, eGFR was 61□20ml/min in AKI group versus 70□20ml/min in controls (p<0.001), and CKD progression occurred in 26.7% of the AKI group, as compared to 6.6% in the control group (p<0.001). The greatest odds of CKD progression rates were seen at three months, with progressive attenuation over time. Proteinuria was also more common and more severe in the AKI group at each time point. The composite renal endpoint occurred less frequently, but at a significantly higher rate in the AKI group (3% versus 0.7%; OR 4.4, 95% CI 1.3-15.7, p=0.012). Mortality rates were also significantly higher in the AKI group (15.7% versus 9.7%, p=0.008). In addition to presence of AKI, binary logistic regression analysis identified factors that were independently associated with CKD progression at 3 years including severity of AKI, proteinuria and CKD progression at 3 months.

Conclusions
AKI is associated with long term renal dysfunction, proteinuria, higher rates of ESKD and increased mortality. This is true even in a general hospitalised population in which a majority of patients had AKI stage 1. Early non-recovery of renal function is a key determinant, and a potential therapeutic target, of long-term outcomes post AKI