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Heart failure and AKI after hospital admission with AKI among patients taking ACE inhibitors and ARBs

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Introduction:
Angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARBs) are believed to be associated with a higher risk of acute kidney injury (AKI). The drugs are often temporarily or permanently withheld following AKI. However, the effects of discontinuing these drugs on outcomes like subsequent AKI and heart failure (HF) are uncertain.

Objectives:
We aimed to describe the rates of HF and AKI following an initial AKI hospitalisation among a cohort of patients prescribed ACEI/ARBs. In addition, we aimed to determine the rate of admission with HF, or re-admission with AKI, among patients who were re-prescribed ACEI/ARBs following discharge after AKI, compared to patients who stopped the drugs.

Methods:
We conducted a cohort study using linked primary and secondary care data from the Clinical Practice Research Datalink (CPRD) and the Hospital Episodes Statistics (HES). We included patients with AKI recorded as a primary cause of hospital admission between 2010-2016, and were prescribed an ACEI/ARB within 60 days prior to the AKI admission. The primary outcomes were re-admission to hospital with HF, or (separately) AKI. We calculated rates of re-admission (per 1000 person-years at-risk) stratified by time post-discharge. We also compared rates of re-admission for each outcome among patients prescribed or not prescribed ACEI/ARBs post-discharge (excluding the first 60 days post-discharge to capture prescriptions) using Cox regression adjusted for multiple confounders. We stratified hazard ratios for HF admission by spironolactone prescription prior to baseline AKI admission.

Results:
The study population included 18,816 patients with a mean age of 78 years (SD 11). Of these, 9,099 were female (48%), 8,533 (45%) had diabetes, 16,169 (86%) had hypertension and 5,722 (30%) had pre-existing HF. During total follow-up, after discharge from AKI hospitalisation, 2,691 (14%) were re-admitted with HF and 3,260 (17%) with AKI. Rates of admission with outcomes following AKI are shown in Figure 1.

Comparing patients who stopped ACEI/ARBs post-discharge with those re-prescribed the drugs within 60 days, among patients not prescribed spironolactone pre-admission, the hazard ratio (HR) for admission with HF after 60 days was 0.98 (95% CI 0.88-1.11), and was 1.11 (95% CI 0.90-1.36) for those prescribed spironolactone at baseline (p-value for interaction 0.34). For subsequent AKI after 60 days, the adjusted HR was 0.88 (95% CI 0.81-0.97).

Discussion:
Rates of admission with HF and AKI are high following an initial AKI hospitalisation, reflecting a substantial burden on health services. After 60 days post-discharge following the initial AKI hospitalisation there is no

increase in risk of re-admission with HF among patients not re-prescribed ACEI/ARBs after AKI, including among those prescribed spironolactone. There is a potential protective effect of ACEI/ARB cessation on subsequent re-admission with AKI. Further work is ongoing to explore the impact of potential limitations of these results including survivor bias and confounding by indication and frailty.