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Statin Use and Survival After Acute Kidney Injury

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Introduction: The incidence of acute kidney injury (AKI) in hospitalized patients is rising, and survivors are at high risk for cardiovascular events and mortality. Effective strategies that improve long-term outcomes of AKI are unknown.

Methods: A retrospective cohort study was performed between 2008 and 2011. All subjects were followed until 31 March 2013, with a minimum follow-up of 2 years. Participants were adults 18 years of age or older, who developed AKI during a hospitalization and had chronic kidney disease (CKD) following discharge (n = 19,707 mean age 69.9 years, mean postdischarge estimated glomerular filtration rate (eGFR) 43.0 ml/min/1.73 m^2). Exposure to statins was examined prior to the index hospitalization as well as within 2 years following hospital discharge. The primary outcome was mortality; secondary outcomes included all-cause re-hospitalization and cardiovascular events.

Results: Within 2 years of discharge, only 38.3% of the participants were prescribed a statin. After adjustment for comorbidities, statin use prior to admission, demographics, baseline kidney function, and a number of other factors, statin use was associated with lower mortality (hazard ratio, 0.74; 95% confidence interval, 0.69, 0.79) in AKI survivors with CKD. Patients who received a statin also had a lower risk of all cause rehospitalization (adjusted hazarad ratio, 0.90; 95% confidence interval, 0.85, 0.94). Statin use was not associated with a reduction in cardiovascular events.

Discussion: Among AKI survivors with CKD, statin use was associated with a lower risk of mortality and rehospitalization rates. This finding suggests that there is an opportunity to improve postdischarge care in AKI survivors.

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Acute kidney injury (AKI) is a common complication in hospitalized patients, and has been consistently associated with an increased risk of death, *de novo* or worsening chronic kidney disease (CKD), and end-stage renal disease (ESRD).[1–5] Patients discharged after an episode of AKI have a 40% increased risk of death in the 2 years following hospitalization,[6] and a 50% to 60% increased risk of cardiovascular events, compared to patients who do not develop AKI.[7] There are currently no effective therapies targeting established AKI; however, identifying and treating patients with CKD following an episode of AKI may improve health outcomes. Although recently published data suggested that nephrologist follow-up was associated with a 24% reduction in risk of death after hospitalization with severe AKI requiring dialysis,[8] little is known about processes of care that modify outcomes after episodes of AKI.

Statins are effective for reducing cardiovascular morbidity and mortality in patients with CKD.[8–18] We sought to evaluate whether the use of statins was associated with better outcomes among patients with CKD after AKI.

METHODS

Study Population and Data Sources

We used the Alberta Kidney Disease Network population-based database, which has been described in detail elsewhere.[19] The study cohort[20] included all adults 18 years or older residing in Alberta who were

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admitted to the hospital between 1 July 2008 and 31 March 2011 and had an episode of AKI during hospitalization. To be eligible for inclusion, patients had to have at least 1 outpatient serum creatinine (Scr) measurement within 180 days prior to hospitalization to establish baseline kidney function, ≥ 1 measurement during the hospitalization to establish AKI, and ≥ 1 SCr, urine dipstick (udip), urine albumin to serum creatinine ratio (ACR), or urine protein to serum creatinine ratio (PCR) measurement in the follow-up period after hospital discharge to establish CKD. If participants had more than 1 hospitalization during this period, only the first was considered (index hospitalization). Participants who died or progressed to ESRD (estimated GFR [eGFR] < 15 ml/min per 1.73 m^2, chronic dialysis, prior kidney transplantation) before or during the index hospitalization were excluded. The cohort was restricted to patients who had CKD after an AKI episode. All subjects were followed up from the discharge date of their index hospitalization until 31 March 2013, with a minimum follow-up of 2 years.

The study was reviewed and approved by the institutional review boards at the Universities of Alberta and Calgary.

Assessment of Baseline Kidney Function

The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used to determine the estimated glomerular filtration rate (eGFR).[21] Baseline kidney function was defined as the mean outpatient Scr in the 180 days prior to the index hospitalization.

Identification of Acute Kidney Injury

AKI was identified by changes between baseline (prehospital) and peak in-hospital Scr. AKI was defined as an increase in serum creatinine by 50% or greater within 7 days or by 26.5 μmol/L within 48 hours and/or requirement for acute dialysis within 7 days of the index hospitalization. AKI severity was determined using the consensus criteria for AKI staging from the recently published Kidney Disease Improving Global Outcomes (KDIGO) AKI guidelines.[22] Requirement for acute dialysis for AKI was determined using a validated approach, based on diagnosis and procedural administrative codes.[23]

Assessment of CKD After AKI

The presence of CKD was assessed using Scr, urine ACR, urine PCR, or udip measured 90 days or more after the AKI episode to allow sufficient time for recovery of renal function (Supplementary Figure S1). A 90-day time frame for recovery was chosen based on the Kidney Disease Outcomes Quality Initiative guidelines,[24] which define CKD as a persistent decline in kidney function lasting >90 days. If subjects had more than 1 outpatient SCr measurement, the measurement closest to 90 days was considered. Postdischarge CKD was defined as eGFR < 60 ml/min/1.73 m^2, ACR > 30 mg/g, PCR > 150 mg/g, or Udip > trace, consistent with the KDIGO CKD guidelines.[25]

Assessment of Medication Use After Discharge

Prescription drug information was obtained from the Pharmaceutical Information Network (PIN) database. We classified statin exposure into the following groups: no previous prescription, new prescription (defined as at least 1 prescription within 2 years after discharge from the index hospitalization), stopping a previous prescription, and continuing a prescription. Patients were classified in the continuing prescription group if they had at least 1 prescription in the 6 months prior to admission and at least 1 prescription within 2 years postdischarge. High-dose statin was defined as the highest dosage for each statin drug (Supplementary Table S1).

Assessment of Comorbid Conditions

Relevant demographic characteristics, preexisting comorbid conditions (defined using validated algorithms),[20,26] hospitalizations and outpatient physician visits (general practitioner as well as specialist visits), details of the index hospitalization including primary admission diagnosis, and intensive care unit stay were obtained using hospitalization data, claims files, and ambulatory care classification system files. We obtained primary International Classification of Diseases (10th revision) codes and used these to classify primary admission diagnoses using a previously published approach.[26] Resource intensity weight, similar to diagnostic related group weight, was used to categorize acuity and severity of illness.[27,28] Cholesterol level was defined as the mean outpatient total cholesterol in the 1 year prior to the index hospitalization. The cholesterol levels were classified into 5 risk categories according to the Framingham coronary heart disease risk score.[29] Patients who did not have a cholesterol measurement during this time period were classified in an unknown group.

Outcomes

The primary outcome was mortality; secondary outcomes included all-cause re-hospitalization and cardiovascular events. All outcomes were assessed after the discharge date of the index hospitalization. All-cause re-hospitalization was defined as any hospitalization occurring after the index hospitalization. All hospitalizations were identified using AH data. All-cause mortality was identified using administrative data sources. Cardiovascular events were defined as myocardial infarction, stroke, or revascularization procedure, as defined by validated algorithms.[30–32]