Acute Kidney Injury Is Associated with Increased Hospital Mortality after Stroke

Minesh Khatri, MD,* Jonathan Himmelfarb, MD,† Derk Adams, BS,‡ Kyra Becker, MD,‡ W. T. Longstreth, MD,‡ and David L. Tirschwell, MD, MSc‡

Background: Acute kidney injury (AKI) is common and is associated with poor clinical outcomes. Information about the incidence of AKI and its effect on stroke outcomes is limited. *Methods:* Data were analyzed from a registry of subjects with ischemic stroke and intracerebral hemorrhage (ICH) hospitalized at a single academic medical center. Admission creatinine was considered to be the baseline. AKI was defined as a creatinine increase during hospitalization of 0.3 mg/dL or a percentage increase of at least 50% from baseline. Multivariate logistic regression models were created for both stroke types, with hospital mortality as the outcome. Covariates included gender, race, age, admission creatinine, National Institutes of Health Stroke Scale score at admission, the performance of a contrast-enhanced computed tomographic scan of the head and neck, and medical comorbidities. *Results:* There were 528 cases of ischemic stroke with 70 deaths (13%), and 829 cases of ICH with 268 deaths (32%). The mean age was 64 years; 56% of patients were men and 71% were white. AKI complicated 14% of ischemic stroke and 21% of ICH hospitalizations. In multivariate analysis stratified by stroke type, AKI was associated with increased hospital mortality from ischemic stroke (odds ratio [OR] 3.08; 95% confidence interval [CI] 1.49-6.35) but not ICH (OR 0.82; 95% CI 0.50-1.35), except for those surviving at least 2 days (OR 2.11; 95% CI 1.18-3.77). *Conclusions:* AKI occurs frequently after stroke and is associated with increased hospital mortality. Additional studies are needed to establish if the association is causal and if measures to prevent AKI would result in decreased mortality. **Key Words:** Acute kidney injury—intracerebral hemorrhage—ischemic stroke—kidney disease.

Acute kidney injury (AKI) is defined as an abrupt deterioration in kidney function that is manifested by an increase in serum creatinine, a decrease in urine output, or both. Multiple recent studies using national administrative data, electronic health record analysis, and hospital chart review all indicate that the prevalence of AKI is high, and that it may be increasing in hospitalized patients.[1-3] In one analysis of Medicare beneficiaries, AKI occurred in 23.8 cases per 1000 hospital discharges, and was increasing at 11% per year.[2] The incidence is even greater in high acuity states, such as sepsis, where AKI has complicated up to 51% of hospitalizations.[4]

The development of AKI portends a higher risk of in-hospital death, which has been demonstrated in both general medical and surgical hospitalizations and specific settings, such as after acute myocardial infarction and cardiac surgery, and in the intensive care unit.[5-8] For instance, in studies involving septic patients, the development of AKI is associated with a 2- to 3-fold higher risk of in-hospital mortality.[9-11] However, data

From the *Division of Nephrology, Department of Internal Medicine, Columbia University, New York, New York; †Division of Nephrology, Department of Internal Medicine; and ‡Department of Neurology, University of Washington, Seattle, Washington.

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Address correspondence to Minesh Khatri, MD, Division of Nephrology, Department of Internal Medicine, 622 West 168th St, PH4-124, New York, NY 10032. E-mail: minesh.khatri@gmail.com.

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are lacking on the frequency and prognosis of AKI in the setting of stroke, the third leading cause of death in the United States.[12] Moreover, current studies have been limited by the lack of an objective measure of stroke severity (such as the National Institutes of Health Stroke Scale [NIHSS] score), data concerning the frequency of computed tomographic (CT) angiography performed at admission (which can cause contrast-induced nephropathy), lack of racial and ethnic diversity, and lack of data specifically pertaining to intracerebral hemorrhage (ICH).[13,14]

Our goals were to determine the frequency of AKI in patients hospitalized with ischemic stroke or ICH, to characterize the association between AKI and in-hospital mortality, and to determine the risk factors for AKI in this setting.

Methods

Study Population

Subjects were selected from a stroke registry maintained at Harborview Medical Center, a tertiary care and teaching hospital of the University of Washington (Seattle, WA). The registry consists of all cases of ischemic stroke, transient ischemic attack, nontraumatic ICH, and nontraumatic subarachnoid hemorrhage admitted to Harborview Medical Center between October 2004 and December 2008. Subjects 18 years of age and older with ischemic stroke or ICH were eligible for inclusion into this study (n = 2029). Subjects were excluded if: (1) they were missing any key covariate data listed below (n = 618 missing admission NIHSS scores; n = 12 missing admission creatinine), or (2) if the estimated glomerular filtration rate (eGFR)[15] at admission was <15 mL per minute, in order to exclude those with end stage renal disease (n = 42). The Institutional Review Board of the University of Washington approved this study.

Data Collection and Outcomes

All data were collected retrospectively from medical records available from hospital admission to discharge by trained abstractors in the quality improvement program. Medical comorbidities, including a history of atrial fibrillation, heart failure, diabetes, coronary artery disease, hypertension, hyperlipidemia, stroke or transient ischemic attack (TIA), and smoking within the past year were abstracted based on documentation in the medical record alone and were assigned binary values. Race was categorized as white, African American, Asian/Pacific Islander, or other/unknown. Stroke subtype was determined based on interpretation of the clinical records, including discharge summaries and codes from the *International Classification of Diseases, 9th revision*. Serum creatinine values were measured on admission and routinely thereafter (typically every day) during the course of hospitalization. NIHSS scores were measured on admission or estimated retrospectively using data from admission physical examinations by a validated method.[16] Data were also collected regarding CT angiography of the head and neck performed during hospitalization, if applicable. The primary outcome of this study was all-cause in-hospital mortality.

Estimation of Kidney Function and Definition of AKI

A subject's admission kidney function was considered to be baseline and was estimated using serum creatinine and the Modification of Diet in Renal Disease formula for eGFR[15] as follows:

$$\begin{aligned}\text{eGFR} = {} & 186.3 \times (\text{creatinine}^{\wedge} - 1.154) \\ & \times (\text{age}^{\wedge} - 0.203) \\ & \times (1.21 \text{ if African American}) \\ & \times (0.742 \text{ if female})\end{aligned}$$

AKI was classified and graded based on severity according to a widely used definition: the Acute Kidney Injury Network (AKIN) criteria.[17] The AKIN criteria has 3 stages: stage 1 is a 50% to 99% increase in creatinine from baseline or an absolute increase in creatinine of ≥0.3 mg/dL; stage 2 is a 100% to 199% increase in creatinine from baseline; and stage 3 is a 200% increase in serum creatinine, or a rise in serum creatinine of 0.5 mg/dL to at least 4.0 mg/dL, or the initiation of renal replacement therapy.[18] Criteria involving urine output were not used in this study because urine output was not routinely recorded in all patients. A subject's highest creatinine during hospitalization was compared to admission creatinine to determine if a subject met criteria for AKI. AKI defined by AKIN stage 1 or greater was used in the models. Data on prevalent or incident renal replacement therapy were not available in this cohort.

Statistical Analysis

Multivariate logistic regression models testing the association between AKI and all-cause in-hospital mortality were constructed. In the overall cohort, there was a significant interaction between stroke type and AKI; stratified analyses were therefore performed by stroke type (ICH or ischemic stroke). Potential confounders were included in the models if strong evidence existed in the literature of an association with either outcome or AKI. Differences in covariates based on AKI status and stroke type were tested using Chi-square tests for categorical variables and 2-sample *t* tests for continuous variables. A 2-sided