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The Vascular-Renal Connection in Patients Hospitalized With Hypertensive Crisis: A Population-Based Study

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Abstract

Objective: To determine the risks of acute kidney injury development and long-term clinical outcomes of patients with hypertensive crisis.

Patients and Methods: This was a population study of Olmsted County residents with hypertensive crisis between January 1, 2000, and December 31, 2008, with follow-up until June 30, 2016.

Results: The results demonstrated that those with underlying chronic kidney disease upon admission for hypertensive crisis, defined as a systolic blood pressure above 180 mm Hg or diastolic blood pressure above 120 mm Hg, were more likely to develop acute kidney injury during hospitalization (odds ratio, 6.04; 95% CI, 1-26; $P=.02$). Hospitalization length of stay was increased when patients developed acute kidney injury during hypertensive crisis hospitalization (7.6 ± 9 vs 3.4 ± 4 days; $P=.04$). Furthermore, those who developed acute kidney injury had increased cardiac rehospitalization frequency over 10 years (87% vs 46%; $P=.009$). These results suggest that those with poor renal reserve are more likely to have further acute kidney damage in the setting of hypertensive crisis, likely due to decreased renal perfusion and neurohormonal dysregulation.

Conclusion: In patients hospitalized for hypertensive crisis, chronic renal insufficiency was a risk factor associated with acute kidney injury development during hospitalization. Those who developed acute kidney injury had longer hospitalizations with increased rehospitalization frequency. Future studies are warranted to further investigate whether the preservation of renal function will improve clinical outcomes in hospitalized patients with hypertensive crisis.

Both renal insufficiency and hypertension are extremely prevalent in the general population, and the occurrences of these conditions are intertwined. As many as 33% of adults in the United States have high blood pressure, and the prevalence of chronic kidney disease (CKD) in the United States is more than 16%.[1] Hypertension hospitalizations are also a large burden to the US health care system, with 579,000 patients in 2009 discharged from a hospital in the United States for hypertension as the primary diagnosis.[1]

While it has been well documented that chronic hypertension negatively impacts kidney function, the long-term outcomes of patients hospitalized for hypertensive crisis with acute kidney injury (AKI) remain undefined. Previous studies have shown that in the short term, hospitalized patients with CKD who develop AKI have associated increased mortality.[2-4] In the Studying the Treatment of Acute Hypertension registry, hospitalized acute severe hypertension patients with concurrent CKD and subsequent AKI had an increased risk of short-term mortality and morbidity.[5] However, the long-term outcomes following renal dysfunction after an acute episode of severe hypertension remain undefined.

This study aimed to identify the risk factors associated with AKI development in the hypertensive crisis population and how an episode of AKI in this population affects long-term mortality, morbidity, and rehospitalization. Clarifying this vascular-renal relationship can help the clinician provide a

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more accurate prognosis to patients as well as become more alert to patients at high risk for end-organ dysfunction, rehospitalization, or death.

PATIENTS AND METHODS

Study Setting

The study protocol was approved by the institutional review boards of both Mayo Clinic and Olmsted Medical Center, and data were obtained from the Rochester Epidemiology Project, which maintains a medical record database for residents of Olmsted County, Minnesota.[6] The Rochester Epidemiology Project database contains documentation of outpatient visits, emergency department visits, and hospitalizations.

In this retrospective analysis, we collected demographic, clinical, and laboratory data on adult residents of Olmsted County, Minnesota, who were hospitalized for hypertensive crisis between January 1, 2000, and December 31, 2008, with follow-up until June 30, 2016. Inclusion criteria were male and female adults, 18 years or older, who were hospitalized with a main discharge diagnosis of *hypertensive crisis*, defined as systolic blood pressure above 180 mm Hg or diastolic blood pressure above 120 mm Hg, and identified with *International Classification of Diseases, Ninth Revision* codes and confirmed with detailed review of the medical records. Selected 401-405 *International Classification of Diseases, Ninth Revision* codes corresponding to hypertensive crisis were used. Only those patients with repeated creatinine measurements during hospitalization were included.

Data Collection

Collection of baseline characteristics for the identified patients included age, sex, ethnicity, body mass index (calculated as the weight in kilograms divided by the height in meters squared), history of hypertension, tobacco use, known coronary artery disease, and history of heart failure (HF). Collection of admission laboratory values included lipid panel, liver function tests, serum urea nitrogen (BUN), and plasma creatinine. Vitals signs, including admission blood pressure and highest blood pressure during hospitalization, were collected. The highest BUN and plasma creatinine values during hospitalization were also collected. Outcome variables collected include mortality and date of death, length of hospitalization, date and reason of first rehospitalization, and posthospitalization BUN and creatinine. Mortality data were collected from the Mayo Clinic or Olmsted Medical Center electronic medical records. Data on echocardiographic parameters within 6 months of hospitalization and admission and discharge blood pressure medications were collected.

Acute kidney injury development was defined as an increase of 0.3 mg/dL or 25% in plasma creatinine during the hospitalization. Glomerular filtration rate (GFR) was calculated by the Modification of Diet in Renal Disease method: estimated GFR (eGFR; mL/min/1.73 m^2) = 175 × (Scr)$^{-1.154}$ × (Age)$^{-0.203}$ × (0.742 if female) × (1.212 if African American). *Chronic kidney disease* was defined by eGFR of less than 60 mL/min. *Cardiac rehospitalization* was defined as a rehospitalization with a main discharge diagnosis related to hypertension, coronary artery disease, arrhythmia, or HF.

Data Analysis and Outcomes

The primary analysis involved identifying risk factors for AKI development and determining the relationship between CKD and AKI among the hypertensive crisis population. Additional analyses included short- and long-term rehospitalization and mortality outcomes for the hypertensive crisis population with or without AKI development during hospitalization.

Continuous variables are presented as mean ± SD. Discrete variables are summarized as frequency (percentage). Comparisons between groups were made using the 2-sample t test for continuous variables and the Pearson χ^2 test for categorical variables. Further assessment of potential associations with renal failure was done using a logistic regression model, adjusting for age and sex on selected variables that showed statistical significance. Long-term follow-up event estimates were computed using the Kaplan-Meier method, with group comparisons made via the log-rank test. Modeling of long-term outcomes was assessed using Cox proportional hazards models, again adjusting for age and sex on selected variables that showed