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Risk of Intracerebral Hemorrhage after Emergency Department Discharges for Hypertension

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Abstract

Background—Recent literature suggests that acute rises in blood pressure may precede intracerebral hemorrhage. We therefore hypothesized that patients discharged from the emergency department with hypertension face an increased risk of intracerebral hemorrhage in subsequent weeks.

Methods—Using administrative claims data from California, New York, and Florida, we identified all patients discharged from the Emergency Department from 2005 through 2011 with a primary diagnosis of hypertension (*ICD-9-CM* codes 401-405). We excluded patients if they were hospitalized from the emergency department or had prior histories of cerebrovascular disease at the index visit with hypertension. We used the Mantel-Haenszel estimator for matched data to compare each patient's odds of intracerebral hemorrhage during days 8-38 after emergency department discharge to the same patient's odds during days 373-403 after discharge. This cohort-crossover design with a one-week washout period enabled individual patients to serve as their own controls, thereby minimizing confounding bias.

Results—Among 552,569 patients discharged from the emergency department with a primary diagnosis of hypertension, 93 (0.017%) were diagnosed with intracerebral hemorrhage during days 8-38 after discharge compared to 70 (0.013%) during days 373-403 (odds ratio 1.33, 95% confidence interval 0.96-1.84). The odds of intracerebral hemorrhage were increased in certain subgroups of patients (≥60 years of age and those with secondary discharge diagnoses besides hypertension), but absolute risks were low in all subgroups.

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Conclusions—Patients with emergency department discharges for hypertension do not face a substantially increased short-term risk of intracerebral hemorrhage after discharge.

Keywords

hypertension; intracerebral hemorrhage; emergency department; risk factors; stroke

Introduction

Chronic hypertension,(1) especially uncontrolled hypertension,(2, 3) is an established risk factor for intracerebral hemorrhage (ICH). The effect of acute hypertension on ICH has not been as well studied, despite a high proportion of emergency department (ED) patients presenting with hypertension – at least 25% have elevated blood pressure (over 140/90) and about 5% have severely elevated blood pressure (over 180/110).(4-8) Current guidelines recommend against the aggressive treatment of hypertensive ED patients without acute evidence of end-organ damage and instead recommend initiation of oral anti-hypertensives and outpatient follow-up.(9-11) In reality, however, these patients often receive inadequate follow-up care.(4, 7, 12)

The clinical significance of hypertension in the ED is uncertain. Recent Joint National Committee guidelines addressing the management of acute hypertension are based on studies that did not conclusively demonstrate an increased risk of vascular complications after episodes of hypertensive urgency.(10-14) However, a recent study of detailed ambulatory blood pressure data before and after ICH suggested that an acute rise in blood pressure might precede the diagnosis of ICH.(15) Furthermore, conditions that acutely increase blood pressure, such as cocaine ingestion, are well known to cause ICH, presumably through deleterious effects on cerebral autoregulation and vascular integrity.(16, 17)

We hypothesized that patients discharged from the ED with hypertension face an increased risk of ICH in subsequent weeks. Therefore, we performed a large population-based study evaluating the risk of ICH in patients discharged from the ED with a primary diagnosis of hypertension. In order to minimize confounding bias and to focus our study on the immediate effects of blood pressure elevation, we used a cohort-crossover design whereby patients served as their own controls. Specifically, we compared the risk of ICH soon after an ED diagnosis of hypertension to the rate of ICH in the same patient during a time period of similar length 1 year later.

Methods

Study Design and Setting

We performed a retrospective cohort-crossover study using administrative claims data on all discharges from nonfederal EDs and acute care hospitals in California, New York, and Florida. We identified all patients who were discharged from the ED with a primary diagnosis of hypertension from 2005 through 2010 in California, 2005 through 2011 in Florida, and 2006 through 2010 in New York. These dates were chosen to incorporate all

available data with longitudinal patient identifiers in these large and demographically heterogeneous states.(18) Trained analysts used standard methods to collect administrative data on all ED and hospital discharges. After a multistep review for quality-assurance purposes, these data were reported in a deidentified format to the Agency for Healthcare Research and Quality for its Healthcare Cost and Utilization Project. This study was approved by the Weill Cornell Medical College institutional review board; the right to informed consent was waived because of minimal risk to patients.

Selection of Participants

We identified all patients aged 18 years or older who were discharged from an ED with a primary discharge diagnosis of hypertension as defined by International Classification of Diseases, 9th Revision, Clinical Modification (*ICD-9-CM*) codes 401-405. Since we were primarily interested in capturing patients with an acute episode of hypertension rather than patients who frequently seek non-ambulatory care for hypertension, we counted only the first ED visit with a hypertension diagnosis. To minimize misclassification error (i.e., the primary outcome was present but misdiagnosed during the initial ED visit for hypertension), we excluded patients if they were hospitalized from the ED or had concomitant *ICD-9-CM* codes for cerebrovascular disease (430-438) at the time of the index hypertension visit. To maximize longitudinal follow-up, we excluded patients who did not permanently reside in California, New York, or Florida.

Measurements and Outcomes

To characterize our study population, we collected patient data on demographics and medical comorbidities, including diabetes mellitus, coronary artery disease, congestive heart failure, peripheral vascular disease, chronic kidney disease, chronic obstructive pulmonary disease, atrial fibrillation, tobacco use, and ethanol abuse. Our primary outcome was ICH, defined by a diagnosis code algorithm previously validated to have a specificity of 96% and a sensitivity of 85%.(19)

Statistical Analysis

After instituting a prespecified 1-week washout period to minimize the risk of misclassification error (i.e., ICH was present but missed at the index ED visit because symptoms or signs were minor or misconstrued), we compared each patient's risk of ICH during the 4-week period soon after discharge (days 8 through 38) with the risk of ICH in the same patient during the 4-week period one year later (days 373 through 403). Therefore, the cohort period comprised days 8 through 38 following the ED visit for hypertension, while the crossover period comprised days 373 through 403 following the index visit. The choice of a 4-week period was based on recent evidence about the time-course of blood pressure elevation before ICH.(15) Absolute risks and odds ratios (ORs) were calculated using a Mantel-Haenszel estimator for matched data.

Several prespecified subgroup analyses were performed to test the robustness of our results. First, we compared risks of ICH after malignant essential hypertension (401.0) versus all other hypertension diagnoses; previous studies using administrative data have defined malignant hypertension with this *ICD-9-CM* code.(20) Second, since national guidelines

recommend higher blood pressure goals for older patients,(10) we compared risks of ICH after hypertension visits in those aged 60 years or older versus those younger than 60 years of age. Third, we compared risks of ICH in those with a sole ED diagnosis of hypertension versus those with accompanying secondary discharge diagnoses. Statistical significance was defined using an alpha of 0.05. All analyses were performed with Stata/MP version 13 (College Station, TX).

Results

Subject Characteristics

During the study period, 552,569 patients were discharged from the ED with a primary diagnosis of hypertension, including 170,476 whose sole ED diagnosis was hypertension and 10,288 who had a diagnostic code for malignant hypertension. Compared to those without subsequent ICH, patients subsequently diagnosed with ICH had different insurance sources; were older; and more often had diabetes mellitus, congestive heart failure, and chronic kidney disease (Table 1).

Primary Outcomes

There were 93 patients (0.017%) diagnosed with ICH during the cohort period (days 8-38 after hypertension visit) versus 70 (0.013%) patients during the crossover period (days 373-403 after hypertension visit). This equated to an OR of 1.33 (95% confidence interval [CI] 0.96-1.84, p=0.09) (Table 2).

Subgroup Analyses

Among patients with a primary diagnosis of malignant hypertension, 3 (0.029%) were diagnosed with ICH during the cohort period versus 2 (0.019%) during the crossover period (OR 1.50, 95% CI 0.17-17.96, p=1.000); while among those with hypertension diagnoses other than malignant hypertension, 90 (0.017%) were diagnosed with ICH during the cohort period versus 68 (0.013%) during the crossover period (OR 1.32, 95% CI 0.96-1.84, p=0.09). Among patients whose sole ED diagnosis was hypertension, 18 (0.011%) were diagnosed with ICH during the cohort period versus 26 (0.015%) during the crossover period (OR 0.69, 95% CI, 0.36-1.31, p=0.29); while among patients with concomitant secondary diagnoses, 75 (0.020%) were diagnosed with ICH during the cohort period versus 44 (0.012%) during the crossover period (OR 1.70, 95% CI 1.16-2.53, p=0.006). Lastly, among patients 60 years of age or older, 57 (0.024%) were diagnosed with ICH during the cohort period versus 30 (0.013%) during the crossover period (OR1.90, 95% CI 1.20-3.06, p=0.005); while among patients younger than age 60, 36 (0.012%) were diagnosed with ICH during the cohort period versus 40 (0.013%) during the crossover period (OR 0.90, 95% CI 0.56-1.44, p=0.73).

Discussion

Using a cohort-crossover design in a large, heterogeneous, multi-state, population-based study, we found that patients' risk of ICH was not significantly increased soon after an ED discharge with a primary diagnosis of hypertension as compared to their risk 1 year later.

These findings were contrary to our prespecified hypothesis. We did, however, find a significantly increased risk in certain subgroups such as those ≥60 years of age and those with secondary discharge diagnoses. Regardless, the absolute risks overall and in all subgroups were very low (about 2 in 10,000 patients), so any potential increased relative risks are unlikely to be clinically significant.

There are few data about the risk of subsequent ICH in ED patients with elevated blood pressure. Most prior studies evaluating the short-term risk of hypertension in the ED have examined composite cardiovascular outcomes, particularly cardiac events, with some showing an increased risk in hypertensive ED patients.(13, 14, 21) In contrast, we chose to focus our study on ICH for two reasons: 1) it is one of the most feared complications of severe hypertension, resulting in death or severe disability in more than 50% of affected patients,(22, 23) and 2) we aimed to investigate recently published data suggesting that acute rises in blood pressure might precede the development of ICH.(15) Despite a sample size of over 500,000 patients, we did not find a significantly increased short-term risk of ICH in patients discharged from the ED with a primary diagnosis of hypertension. This supports the current real-world practice of discharging most patients with elevated blood pressure without acute complications in the ED.(6) Our findings also support the consensus recommendations of the American College of Emergency Physicians, which states that “patients with asymptomatic markedly elevated blood pressure should be referred for outpatient follow-up” and that in these patients, “routine emergency department medical intervention is not required.(9)” However, it should be noted that we *a priori* chose a conservative 7-day washout period to minimize the risk of misclassification error whereby minor or early ICH that was undetected at the index ED visit with hypertension was diagnosed within a few days at a different visit once clinical symptoms persisted or worsened. Therefore, our results should be considered in the context of this prespecified methodological design.

Our study has several noteworthy limitations. First and foremost, by using administrative claims data, we lacked data on actual blood pressure measurements. Therefore, we were unable to assess the severity or acuity of patients’ blood pressures. Additionally, we lacked data on what prompted patients to visit the ED. It is likely that some patients were referred to the ED from the ambulatory care setting because of concerns over, or symptoms from, increased blood pressure, while others self-presented because of concerns over high readings at home. Conversely, some patients may have presented for other conditions and noted to have hypertension incidentally or were ultimately coded as having hypertension because of inconclusive evaluations for nonspecific symptoms or signs that were unrelated to blood pressure. We tried to focus our study on the former group by restricting our analysis to patients with a primary discharge diagnosis of hypertension and by performing subgroup analyses of patients with diagnostic codes for malignant hypertension or those without secondary diagnoses. Even so, our lack of blood pressure data could have introduced misclassification that biased our study towards the null hypothesis of finding no relationship between elevated blood pressure in the ED and future ICH. Therefore, future prospective research with exact blood pressure measurements will be necessary to evaluate this relationship in more detail. Second, since we lacked outpatient data, our results may not generalize to patients diagnosed with hypertension in the clinic or patients with undiagnosed hypertension. Similarly, we only included outcomes that were diagnosed during subsequent

ED visits or hospitalizations. However, this is unlikely to have significantly affected our results since nearly all ICH leads to hospital admission in concordance with national guidelines.(24) Third, our dataset lacks information on prescriptions and outpatient management after discharge. Therefore, our results do not necessarily refute the findings of the recent literature suggesting that acute rises in mean blood pressure typically precede ICH by weeks;(15) it is possible that effective blood pressure control and risk factor modification resulting from the index ED visit mitigated subsequent ICH risk, thereby modifying the natural history of these hypertensive patients. In addition, our lack of data on anti-thrombotic agents prevented us from evaluating the effects of this potential confounder. Fourth, the results of our subgroup analyses had wide confidence intervals and therefore may have been underpowered and imprecise. Fifth, unrecorded emigration out of state or unrecorded out-of-hospital deaths may have mitigated our ability to capture cases of ICH in the crossover period. However, this would be expected to increase the apparent risk of ICH soon after the index visit for hypertension, and therefore this bias only underlines our finding that there was no elevated risk of ICH.

In summary, the risk of ICH does not appear substantially increased in the immediate period after patients are discharged from the ED with a primary diagnosis of hypertension. Furthermore, the absolute risk of ICH in these patients is low at about 2 in 10,000 per month. These findings may reflect optimal risk factor modification prior to ED discharge and during subsequent outpatient visits, or a lack of association between hypertension in the ED and ICH; future prospective research using actual blood pressure measurements and data on anti-hypertensive treatments will be needed to make this determination. Regardless, our data support current real-world practice and national guidelines for the management of uncomplicated ED patients with elevated blood pressure by initiation of oral anti-hypertensives and outpatient follow-up.(10)

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Table 1

Baseline Characteristics of Patients with an Emergency Department Visit for Hypertension, Stratified by the Subsequent Diagnosis of Intracerebral Hemorrhage[*,†]

Characteristic	Intracerebral Hemorrhage (N = 163)	No Intracerebral Hemorrhage (N = 552,406)
Age, mean (SD), y	62.7 (16.8)	57.5 (16.4)
Female	84 (51.5)	324,170 (58.7)
Race[‡]		
White	68 (43.6)	237,877 (44.8)
Black	53 (34.0)	154,049 (29.0)
Hispanic	21 (13.5)	94,028 (17.7)
Asian	8 (5.1)	20,937 (4.0)
Other	6 (3.9)	23,600 (4.4)
Payment source		
Medicare	71 (43.6)	177,118 (32.1)
Medicaid	15 (9.2)	56,033 (10.2)
Private insurance	38 (23.3)	184,164 (33.4)
Self-pay	34 (20.9)	100,787 (18.3)
Other	5 (3.1)	33,995 (6.2)
Vascular risk factors		
Diabetes	31 (19.0)	70,165 (12.7)
Coronary heart disease	10 (6.1)	24,285 (4.4)
Congestive heart failure	9 (5.5)	9,104 (1.7)
Peripheral vascular disease	2 (1.2)	2,387 (0.4)
Chronic kidney disease	20 (12.3)	17,549 (3.2)
Chronic obstructive pulmonary disease	3 (1.8)	8,805 (1.6)
Atrial fibrillation	5 (3.1)	7,490 (1.4)
Tobacco use	1 (0.6)	5,146 (0.9)
Ethanol abuse	5 (3.1)	31,098 (5.6)

Abbreviations: SD, standard deviation.

[*] Refers to intracerebral hemorrhage diagnoses occurring during days 8-38 after hypertension visit (cohort period) and days 373-403 after hypertension visit (crossover period).

[†] All data are presented as number (%) unless otherwise specified.

[‡] Percentages may not add up to 100 because of rounding

Table 2

Risk of Intracerebral Hemorrhage soon after Emergency Department Diagnosis of Hypertension*

Model	Odds Ratio (95% CI)
Primary analysis	1.33 (0.96-1.84)
Subgroup analyses	
Malignant essential hypertension†	1.50 (0.17-17.96)
Hypertension diagnosis besides malignant hypertension	1.32 (0.96-1.84)
Age ≥ 60 years	1.90 (1.20-3.06)
Age < 60 years	0.90 (0.56-1.44)
Sole discharge diagnosis of hypertension	0.69 (0.36-1.31)
Concomitant secondary discharge diagnoses	1.70 (1.16-2.53)

Abbreviations: CI, confidence interval.

*Mantel-Haenszel estimator for matched data was used to compare each patient's risk of ICH during the 4-week period soon after an ED visit with a primary discharge diagnosis of hypertension (days 8-38 or cohort period) with the risk of ICH in the same patient during the 4-week period one year later (days 373-403 or crossover period).

†Identified by *International Classification of Diseases, 9th Revision, Clinical Modification* code 401.0.