

ORIGINAL RESEARCH

Neurology

Antihypertensive use for stroke in United States emergency departments

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Abstract

Objective: Timely emergency department (ED) control of hypertension in the acute phase of stroke is associated with improved outcomes. It is unclear how emergency physicians use antihypertensive medications to treat severe hypertension associated with stroke. We sought to determine national patterns of antihypertensive use associated with ED visits for stroke in the United States.

Methods: We analyzed data from the National Hospital Ambulatory Medical Care Survey (NHAMCS) 2008–2017. We included ED visits associated with ischemic stroke (ICD9 433–434, ICD10 I630–I639) or hemorrhagic stroke (ICD9 430–432, ICD10 I600–I629). We estimated the number and proportions of stroke ED visits with triage blood pressure meeting treatment thresholds (triage systolic blood pressure [SBP] ≥ 180 mm Hg). We identified the frequency of antihypertensive use, as well as the most commonly used agents.

Results: Between 2008–2017, of a total 135,012,819 ED visits, 619,791 were associated with stroke (78.3% ischemic strokes and 21.7% hemorrhage strokes). Of all stroke visits, 21.8% received antihypertensive medications. Of the identified visits, 9.0% (95% confidence interval [CI] = 6.0%, 13.1%) ischemic stroke visits and 58.2% (95% CI = 49.0%, 66.9%) hemorrhagic stroke visits met criteria for BP reduction. A total of 47.6% (95% CI = 29.1%, 66.7%) of eligible ischemic stroke visits and 41.5% (95% CI = 30.5%, 53.3%) of eligible hemorrhagic strokes visits received antihypertensives. The most common agents used in ischemic stroke were beta-blockers, calcium-channel blockers, and ACE inhibitors. The most common agents used in hemorrhagic stroke included calcium-channel blockers, beta-blockers, and vasodilators.

Conclusion: In this national sample, less than half of strokes presenting to the ED with hypertension received antihypertensive therapy.

KEYWORDS

acute stroke, antihypertensives, hemorrhagic stroke, hypertension, ischemic stroke

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1 | INTRODUCTION

1.1 | Background

By 2030, epidemiologic projections indicate the prevalence of stroke to increase by 20.5%, adding over 3 million new stroke cases in the United States (US) alone.^{1,2} Hypertension, a common risk factor for all-cause strokes,³ undoubtedly will contribute to this increase. Ischemic and hemorrhagic stroke are commonly present (~60% of patients) with hemodynamic instability, usually, in an acute hypertensive response.⁴ This response directly impacts cerebrovascular autoregulation and propagates secondary neurological damage following an initial ischemic insult.⁵

To mitigate secondary damages such as cerebral edema, hemorrhagic transformation, and hematoma expansion, consensus recommendations suggest reducing stroke-associated hypertension.⁶⁻⁸ Current guidelines by the American Heart Association/American Stroke Association (AHA/ASA) recommend BP reduction to below 185/110 mm Hg for fibrinolytic use eligibility using agents such as labetalol, nicardipine, clevidipine, hydralazine, and enalapril.⁷ For patients not eligible for fibrinolytic therapy, the guidelines recommend judicious BP reduction for SBP ≥ 220 or diastolic blood pressure (DBP) ≥ 120 .⁷ The AHA/ASA also recommends acute BP treatment in spontaneous intracerebral hemorrhage in patients with systolic BP (SBP) between 150 and 220 if there are no imminent contraindications to BP reduction.⁸

1.2 | Importance

In the United States, rescue stroke care usually starts in the emergency department (ED). Although the literature has suggested that earlier BP control may positively impact patients' outcomes following acute stroke,^{9,10} the extent and type of antihypertensive medication used for stroke in the ED are unknown. An understanding of antihypertensives use in stroke in the United States could identify areas for quality improvement and research.

1.3 | Goals of this investigation

We sought to determine the frequency and types of antihypertensives used to treat acute stroke in the ED in the United States.

2 | METHODS

2.1 | Study design and setting

This study was a secondary data analysis from the National Hospital Ambulatory Medical Care Survey (NHAMCS) 2008–2017.¹¹ The NHAMCS is a national multistage sampled data set designed to characterize ED care patterns in the United States. The NHAMCS collected

The Bottom Line

While often important in the management of acute stroke, the ED patterns of antihypertensive use are unknown. In this analysis of 10 years of ED visits from the National Hospital Ambulatory Medical Care Survey (NHAMCS), 48% of hypertensive ischemic stroke visits and 42% of hypertensive hemorrhagic stroke visits received antihypertensives. These observations provide important perspectives of stroke care in the United States.

information from EDs in non-institutional general and short-stay hospitals in the 50 states and the District of Columbia using a 3-stage probability sampling design. Each ED was randomly assigned to a 4-week period during which a systematic random sample of visits was obtained. Information extracted from each visit included patient characteristics, visit characteristics, diagnoses, and treatments, and ED facility characteristics. More information about the NHAMCS can be found at the Center for Disease Control and Prevention (CDC) website (<http://www.cdc.gov/nchs/ahcd.htm>).

2.2 | Selection of patients

Visits related to stroke were identified from ED diagnoses using the International Classification of Diseases Version 9 (ICD 9) for 2008–2015 and ICD10 for 2016–2017. We categorized these visits into ischemic stroke (ICD9 433–434, ICD10 I630–I639) and hemorrhagic stroke (ICD9 430–432, ICD10 I600–I629). Because of the small sample size of visits related to stroke each year, we combined 10 years of data to provide sufficient numbers of observations; per NHAMCS guideline, samples < 30 and with $> 30\%$ standard error are considered unreliable.

2.3 | Outcomes

The primary outcome measured was the use rate of antihypertensive medication. NHAMCS provides information on the use of up to 30 medications in each ED encounter. Each drug was coded in the database by the generic component and therapeutic categories using Lexicon Plus. Each drug may have up to 4 therapeutic categories, and each category classified into 3 levels. For example, furosemide has a Level 3 designation of loop diuretics, a Level 2 designation of diuretics, and a Level 1 designation of cardiovascular agents. Initially, we identified all antihypertensive medications by their generic and brand names, then their therapeutic classes. A total of 12 Level 2 class antihypertensives were identified among stroke-related visits. Alteplase usage was also identified during a visit for ischemic stroke.

2.4 | Measurements

We included systolic and diastolic BPs and heart rate at obtained at triage. Subsequent BP measurements were not available in the data other than the BP at ED disposition. The data also included patient characteristics: age, sex, race, ethnicity, insurance, metropolitan statistical areas (MSA), and region. Also included was whether a patient arrived via an ambulance. Notably, the data set did not include information about the time of onset of the symptoms precluding conclusions on the acuity of the patient's presentation to the ED.

2.5 | Primary analysis and statistical methods

We estimated total number and proportions of ischemic stroke and hemorrhagic stroke. We determined the distributions of triage SBP for each type of stroke. To investigate whether antihypertensives use for stroke visits were based on AHA/ASA recommendations,^{7,8} we identified ischemic stroke visits that received alteplase with SBP ≥ 185 or DBP ≥ 110 and those that did not receive alteplase with SBP ≥ 220 or DBP ≥ 120 . The proportion of this subgroup was then estimated to characterize the rate of adherence to guidelines/recommendations by the AHA/ASA. For hemorrhagic stroke, we set the BP cutoff at SBP of 150 per recommendation.⁸ We determined and estimated the frequencies of each of the 12 classes of medications for ischemic stroke and hemorrhagic stroke, respectively. Statistical software Stata (StataCorp, College Station, TX) was used. We accounted for the complex sampling strategy of NHAMCS in the analysis using the "svy" commands with "subpop" in Stata. The weights used in the analyses were adjusted for 10 years of data to provide annualized averages.

3 | RESULTS

Between 2008–2017, on a yearly average, there were 619,791 ($n = 1,208$ of NHAMCS visits) ED stroke visits. Of those, 78.3% ($n = 956$, 95% CI = 74.3%, 81.5%) were ischemic stroke and 21.70%

TABLE 1 Patient characteristics

	Sample(n)	%/mean ^a	95% CI
Type of stroke			
Ischemic	956	78.30	(74.73, 81.49)
Hemorrhagic	252	21.70	(18.51, 25.27)
Tachycardia ^b at triage	233	19.36	(16.27, 22.88)
Age (in years)		67.53	(66.22, 68.84)
Female	631	53.58	(49.12, 57.99)
Race			
White	948	78.2	(74.22, 81.72)
Black	202	18.05	(14.58, 22.14)
Other races	58	3.75	(2.52, 5.54)
MSA	937	83.26	(74.91, 89.23)
Region			
Northeast	255	18.55	(14.24, 23.80)
Midwest	301	24.96	(19.30, 31.62)
South	422	36.73	(30.43, 43.51)
West	230	19.76	(15.71, 24.56)
Ambulance arrival	641	52.33	(47.58, 57.04)
Insurance			
Private	256	22.50	(19.35, 25.98)
Public	826	71.91	(68.10, 75.42)
No insurance	68	5.60	(3.81, 8.15)

Abbreviations: CI, confidence interval; MSA, metropolitan statistical areas. Sample of $n = 1,208$ represents 0.50% of total emergency department visits nationally.

^aThe percentages are population proportions, not sample proportions.

^bHeart rate ≥ 100 beats/min.

($n = 252$, 95% CI = 18.5%, 25.3%) hemorrhage stroke. Table 1 includes the descriptive statistics of patient characteristics including age, sex, race, insurance, region, urban/rural, and whether the visits were an ambulance arrival. Of all ED stroke visits, 21.8% ($n = 270$, 95% CI = 18.8%, 25.2%) received any antihypertensive medications.

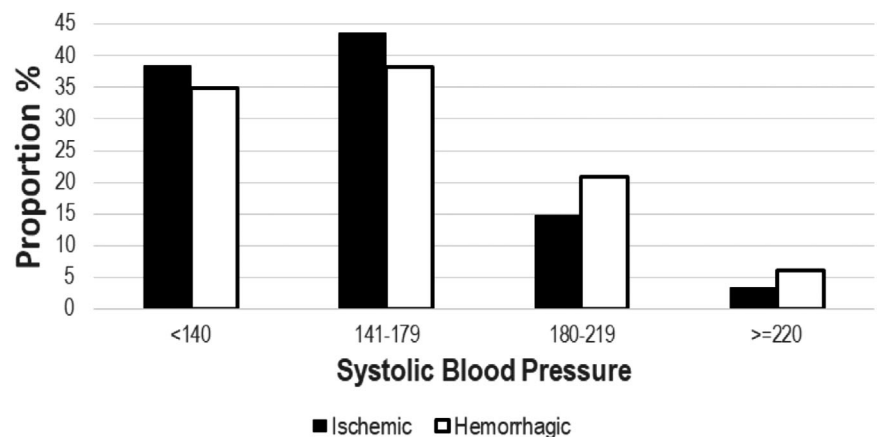


FIGURE 1 Triage systolic blood pressure by stroke type ($N = 1,208$). The percentages reflect the total population, not sample proportions

TABLE 2 Most frequently used medication combinations in ED stroke visits^a

	Ischemic(n = 956)			Hemorrhagic(n = 252)		
	Sample(n)	%	95% CI	Sample(n)	%	95% CI
Any BP meds	189	19.20	(15.60, 23.39)	81	31.21	(24.14, 39.26)
Beta blockers	101	57.02	(46.03, 67.36)	42	36.75	(23.28, 52.67)
Calcium-channel blockers	46	22.70	(14.41, 33.86)	34	49.12	(34.39, 64.01)
ACE inhibitors	36	20.21	(12.87, 30.30)	12 ^b	12.97	(5.90, 26.15)
Diuretics	28 ^b	13.40	(8.41, 20.69)	14 ^b	17.38	(8.78, 31.52)
Vasodilators	17 ^b	8.95	(4.62, 16.62)	15 ^b	26.82	(13.24, 46.80)

Abbreviations: ACE, angiotensin converting enzyme; CI, confidence interval; ED, emergency department.

Sample of n = 1,208 represents 0.50% of total ED visits nationally.

^aThe percentages reflect the total population, not sample proportions. Except for the first row, the percentages were calculated among the visits during which at least one antihypertensive medication was given.

^bPer NHAMCS guidelines, estimates with cell size <30 may not be reliable.

The average ED triage SBP and DBP for all stroke visits were 153 (95% CI = 150, 156) and 80 (95% CI = 77, 82), respectively. Figure 1 depicts the distribution of SBP for each type of stroke. Note that the BPs were measured at triage, not necessarily at the medical decisionmaking time. For all stroke visits, 19.6% (95% CI = 16.2%, 23.6%) were above the AHA/ASA antihypertensive treatment threshold as discussed in the Methods section, and 43.7% (95% CI = 33.6%, 54.3%) of the visits above the treatment threshold received antihypertensives. For ischemic and hemorrhagic stroke visits, the proportions above the treatment threshold were 9.0% (95% CI = 6.0%, 13.1%) and 58.2% (95% CI = 49.0%, 66.9%), respectively. The proportions of visits that received antihypertensive medications among those above the treatment thresholds were 47.6% (95% CI = 29.1%, 66.7%) and 41.5% (95% CI = 30.5%, 53.3%) for ischemic and hemorrhagic strokes, respectively.

Table 2 reports the 5 most frequently used antihypertensive classes. For ischemic stroke, the most commonly used medications were beta-blockers, calcium-channel blockers, and ACE inhibitors. For hemorrhagic stroke, the most frequently used drugs were calcium-channel blockers, beta-blockers, and vasodilators.

4 | LIMITATIONS

There are several limitations to the current study. First, this was a study based on a secondary data set. Any biases that are inherent with secondary data analyses may be present. Prior studies noted several limitations of the NHAMCS data, such as the accuracy of disposition and some demographic information.^{12–14} NHAMCS is a sampled data set, and the observations presented may not represent the true national distributions. Furthermore, the decision to give antihypertensives may depend on the actual BP reading while the emergency physician was at the bedside instead of the 1 measured at triage. Some medication estimates may also not be reliable because of small cell sizes (<30) noted in the text and tables.

5 | DISCUSSION

In this study, approximately one-half of patients presenting to the US EDs with stroke and hypertension received antihypertensive treatment. Although no national guidelines guide the selection of antihypertensive class or BP reduction speed, these results hint at the gap between national recommendations and current clinical practice.

It is unclear from current data whether elevated BP associated with stroke requires immediate treatment.¹⁵ Randomized trials of BP reduction in ischemic stroke concluded that BP reduction either does not provide a benefit or leads to worse neurological and functional outcomes.^{16,17} Hemorrhagic stroke trials also fail to conclusively demonstrate a treatment benefit of BP reduction in patient outcomes.^{9,18} In the INTERACT-2 and ATACH-2 trials, the safety of intensive BP lowering was based on findings of no significant difference when comparing death or serious adverse event between patient groups.^{9,18} Further adding complexity to the debate, the idea of inducing hypertension in non-candidates for revascularization therapy improves neurological and functional outcomes in ischemic stroke recently is gaining ground.^{19,20}

Our study found that the most frequently used medications in EDs are in line with AHA's suggestions for inpatient BP management for stroke patients.⁷ Patients with ischemic stroke were more likely to have received beta-blockers in our cohort. Evidence supporting beta-blockers' efficacy and safety profile in acute stroke suggests it is neuroprotective by mitigating glutamate excitotoxicity and decreasing focal cerebral ischemia by inhibiting apoptosis and the inflammatory response,^{21–23} whereas patients with hemorrhagic stroke in our cohort preferentially received calcium-channel blockers. Calcium-channel blockers' safety and efficacy in time to goal BP and mitigation of vascular spasm makes them suitable agents for acute BP lowering in the setting of hemorrhagic stroke.^{24,25}

The management of hypertension associated with stroke begins in the ED. Recommendations by the AHA/ASA can guide BP treatment for patients presenting with acute stroke. Adherence to the guidelines and recommendations to treat hypertension remains suboptimal in the

setting of stroke. More research is needed to identify ways for improved adherence to guidelines of antihypertensive use and the choice of antihypertensive agents in the acute management of stroke.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

GN, KTX, JS, TB, and JCDT contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript. GN take the final responsibility of the manuscript.

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