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CLINICAL RESEARCH STUDY

Orthostatic Hypotension-Related Hospitalizations in the United States

Cyndya Shibus, MD,^a Carlos G. Grijalva, MD, MPH,^b Satish R. Raj, MD, MSCI,^a Italo Biaggioni, MD,^a Marie R. Griffin, MD, MPH^{b,c,d}

^aDepartment of Medicine, Division of Clinical Pharmacology, Vanderbilt University, Nashville, Tenn; ^bDepartment of Preventive Medicine and ^cDepartment of Medicine, Vanderbilt University, Nashville, Tenn; ^dClinical Research Center of Excellence and Geriatric Research and Education Center, Tennessee Valley VA, Nashville, Tenn.

ABSTRACT

BACKGROUND: Orthostatic hypotension has been commonly described in elderly persons and is associated with an increased risk of falls, syncope, and cerebrovascular events. Nevertheless, the precise burden of this condition in the US is currently unknown.

METHODS: We analyzed discharge data from the Nationwide Inpatient Sample to identify orthostatic hypotension-related hospitalizations and associated comorbidities after excluding acute causes of this condition. National hospitalization rates were estimated using US census population estimates, and the medical conditions most frequently associated with orthostatic hypotension were assessed.

RESULTS: In 2004, there were an estimated 80,095 orthostatic hypotension-related hospitalizations, yielding an overall rate of 36 (95% confidence interval, 34 to 38) hospitalizations per 100,000 US adults. Orthostatic hypotension was the primary diagnosis in 35% of these hospitalizations. The number of orthostatic hypotension-related hospitalizations increased steadily with age, and patients aged 75 years or older had the highest annual hospitalization rate, 233 per 100,000 (95% confidence interval, 217 to 249). The median length of hospital stay was 3 days (IQR 2-6) and the overall in-hospital mortality was 0.9%. Caucasian males were most likely to be hospitalized with orthostatic hypotension. Syncope was the most common comorbid condition reported among orthostatic hypotension patients.

CONCLUSIONS: Orthostatic hypotension is a relatively common condition among hospitalized US elderly patients. In light of the progressive aging of the US population, the contribution of orthostatic hypotension to morbidity and mortality is likely to increase, and deserves further scrutiny. © 2007 Elsevier Inc. All rights reserved.

KEYWORDS: Epidemiology; Orthostatic hypotension; Syncope

Orthostatic hypotension is defined as a fall in systolic blood pressure of at least 20 mm Hg or diastolic blood pressure of at least 10 mm Hg within 3 minutes upon standing.¹ Affected patients commonly experience lightheadedness or syncope that predisposes them to falls and impaired quality of life.^{2,3}

In normal individuals, postural changes do not result in major fluctuations in blood pressure because of physiological mechanisms that compensate for the gravitational blood pooling in lower limbs while standing.⁴ However, in subjects with autonomic nervous system impairment or in those taking medications that alter their response to stimuli these compensatory mechanisms fail and orthostatic hypotension results.

Although orthostatic hypotension is the cardinal manifestation of primary autonomic dysfunctions such as multiple system atrophy or pure autonomic failure,^{5,6} these conditions are rare. More common diseases associated with orthostatic hypotension include diabetes mellitus and neu-

Requests for reprints should be addressed to Marie R. Griffin, MD, MPH, Department of Preventive Medicine, Vanderbilt University School of Medicine, 1500 The Village at Vanderbilt, Suite # 2600, Nashville, TN 37212.

E-mail address: marie.griffin@vanderbilt.edu

rodenerative conditions such as Parkinson's disease.⁷⁻⁹ Orthostatic hypotension also has been associated with myocardial infarction and stroke.^{10,11} Furthermore, it has been identified as an independent predictor of mortality in elderly^{12,13} and end-stage renal disease patients.^{14,15} In addition, medications such as antihypertensives and antidepressants¹⁶ can induce de novo orthostatic hypotension or further complicate underlying autonomic dysfunction.

Existing estimates of orthostatic hypotension prevalence range from 6% among otherwise healthy elderly persons¹⁷ to 68% among patients hospitalized in a geriatric ward.¹⁸ Nevertheless, national estimates of the orthostatic hypotension disease burden are lacking. The objectives of our cross-sectional study using data from the Nationwide Inpatient Sample were to examine the magnitude of orthostatic hypotension-related hospitalizations in the US and to identify patient demographic and clinical characteristics associated with the occurrence of symptomatic orthostatic hypotension.

METHODS

The Nationwide Inpatient Sample

The Nationwide Inpatient Sample (NIS), sponsored by the Agency for Healthcare Research and Quality, annually collects discharge-level information about clinical characteristics and resource utilization from a sample that approximates 20% of admissions to community hospitals in the US. Discharge diagnoses are recorded in up to 15 diagnosis fields using the *International Classification of Diseases 9th revision, Clinical Modification* (ICD9-CM). The first listed diagnosis (primary) is considered the main reason for admission and its original position is preserved in NIS records. The NIS is the largest source of inpatient data publicly available in the US, and its sampling design allows the calculation of national estimates and the examination of relatively uncommon conditions. The present study analyzed NIS data for 2004, the most recent data available. NIS data are devoid of identification elements, and this study was considered exempt from review by the Institutional Review Board of Vanderbilt University.

Definition of Orthostatic Hypotension and Medical Conditions

We first identified all hospitalization discharge records that contained a compatible ICD9-CM code 458.0 ("Orthostatic

hypotension") in any listed diagnosis field. We aimed to assess orthostatic hypotension-related hospitalizations associated with conditions that resulted in an impaired autonomic response, rather than acute or transitory events. These nonacute causes of orthostatic hypotension are more likely to have a neurogenic origin. Acute or transitory events encompassed: blood volume depletion, including dehydration and hemorrhage; intravascular volume contraction associated with pheochromocytoma, Addison's disease, islet of Langerhans neoplasm, renovascular hypertension, and eating disorders; insufficiency of intravascular volume resulting from pregnancy, hyperthyroidism, or beriberi; and circulating vasodilators associated with carcinoid syndrome, mastocytosis, or status post-gastric-bypass.⁵ These conditions were identified using ICD9-CM codes (Appendix) and excluded from further analyses. Because orthostatic hypotension is uncommon in children we also excluded subjects younger than 18 years of age.

We assessed the primary diagnoses among those records with orthostatic hypotension listed in any diagnosis field. Similarly, we assessed the secondary diagnoses among those records whose primary diagnosis was orthostatic hypotension. In addition, we identified common chronic comorbidities known to result in orthostatic hypotension, including Parkinson's disease, abnormal degenerative diseases of the basal ganglia (multiple system atrophy, progressive supranuclear palsy, and oligopontocerebellar atrophy), and autonomic neuropathy, regardless of its cause, ie, diabetes mellitus, amyloidosis.

Statistical Analyses

All analyses were stratified by age (18-34, 35-44, 45-54, 55-64, 65-74, and 75 years or older). Orthostatic hypotension-related hospitalization rates were estimated by dividing the weighted number of hospitalizations obtained from the NIS by the estimated population figures obtained from the US Census Bureau.¹⁹ All rates and their respective 95% confidence intervals were expressed as hospitalizations per 100,000 people, and all estimates used the weight, strata, and cluster variables to account for the NIS complex sampling design. Census data were assumed to be derived from complete enumeration of the US population and thus were considered free of sampling error. All analyses were performed using SAS 9.1 (SAS Institute Inc., Cary, NC) and Sudaan 9.0.1 (Research Triangle Institute, Research Triangle Park, NC).

CLINICAL SIGNIFICANCE

- The rate of nonacute orthostatic hypotension-related hospitalization of US adults increases substantially with age, up to 233 per 100,000 adults aged 75 years or older.
- The changing demographics and health characteristics of the US population are expected to increase the rate of orthostatic hypotension-related hospitalization, increasing the burden on health services.
- Whether standard therapies for orthostatic hypotension can reduce this burden has not been determined.

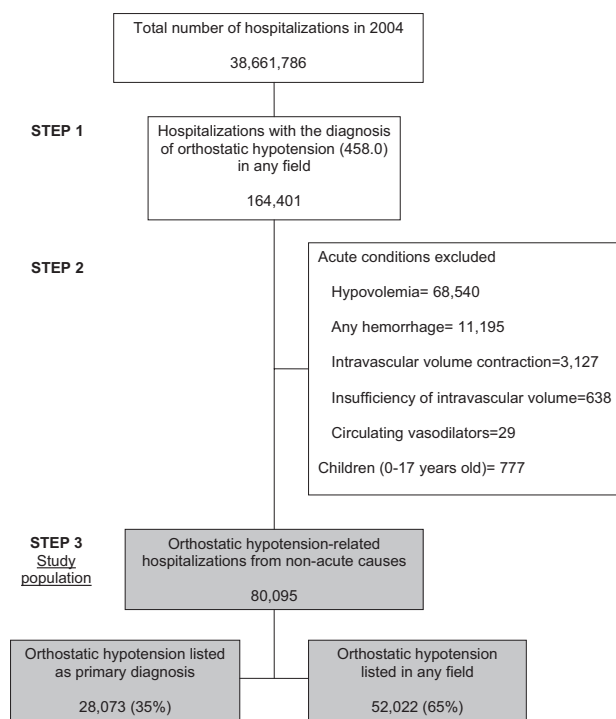


Figure 1 Stepwise definition of the population studied.

RESULTS

During 2004, there were an estimated 38,661,786 total hospitalizations in the US. Among these, a total of 164,401 (0.43%) orthostatic hypotension-related hospitalizations were identified. Within this group, 84,306 (51%) orthostatic hypotension-related hospitalizations met our criteria for acute or transitory conditions and were excluded. Excluded patients encompassed 777 children aged 0-17 years. The 2 major reasons for exclusion were: hypovolemia/dehydration (68,540 hospitalizations) and hemorrhage (11,195 hospitalizations), representing about 98% of all excluded observations (Figure 1). The remaining 80,095 orthostatic hypotension-related hospitalizations are the subjects of this study. Orthostatic hypotension was listed as the primary diagnosis in 28,073 (35%) hospitalizations. Other conditions commonly listed as a primary diagnosis in this group were syncope and collapse (8.5%), cardiac arrhythmias, primarily atrial fibrillation (5.0%), physical therapy and rehabilitation (3.3%), acute pulmonary syndromes (3.0%), coronary atherosclerosis disease (2.9%), cerebrovascular disease (2.8%), congestive heart failure (2.6%), unspecified chest pain (1.7%), and acute infectious diseases (urinary tract infection and gastroenteritis) (1.1%).

Similarly, among those whose primary diagnosis was orthostatic hypotension, the most frequent secondary diagnoses were cardiac arrhythmias, particularly atrial fibrillation (10.7%), hypertension (8.9%), syncope (8.2%), chronic obstructive pulmonary disease (7.7%), congestive heart failure (6.7%), urinary tract infection (4.6%), cardiac valve disease, particularly aortic valve disease (4.1%), diabetes mellitus (3.2%), and chest pain (1.8%).

The overall annual rate for orthostatic hypotension-related hospitalizations listed in any field was 36 per 100,000 (95% confidence interval, 34 to 38) US adults. Rates increased steadily with age when the diagnosis of orthostatic hypotension was listed as primary discharge diagnosis (Figure 2A) or in any diagnostic field (Figure 2B). Orthostatic hypotension-related hospitalization rates were consistently higher in males than in females (Figure 2A and 2B).

Although race information was missing in 27% of records, the analyses of those with race data available indicated that patients hospitalized with orthostatic hypotension were predominantly Caucasians (60%) and African-Americans (7.4%). The remaining race/ethnic groups (Hispanic, Asians, Native Americans) represented 5.6% of the total number of admissions. This race distribution was consistent across all age groups (Table).

Most orthostatic hypotension patients were admitted through emergency departments; the median length of hospitalization was 3 days (interquartile range: 2-6 days) and similar among all age groups. The overall in-hospital mortality was 0.2% when the orthostatic hypotension was listed as primary diagnosis and 0.9% when listed in any field. Overall, 4% of orthostatic hypotension-related hospitaliza-

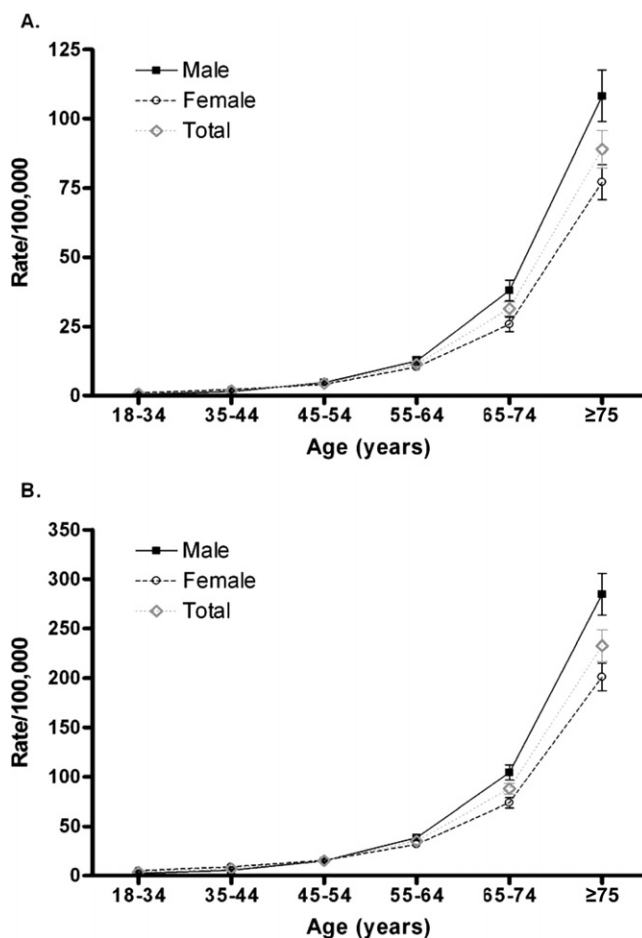


Figure 2 Hospitalization rates for orthostatic hypotension listed as primary discharge diagnosis (A) or in any diagnosis field (B) according to age and sex, NIS 2004.

Table Characteristics of Orthostatic Hypotension-Related Hospitalizations, United States, 2004*

Age Groups, Years	18-34		35-44		45-54		55-64		65-74		≥75	
	Primary	Any	Primary	Any	Primary	Any	Primary	Any	Primary	Any	Primary	Any
No. of hospitalizations	472	2599	805	3211	1829	6354	3312	10,186	5786	16,230	15,868	41,517
Female (%)	69.3	66.5	59.6	62.5	46.8	51.4	47	46.8	44.7	45.6	54	53.8
Race (%)												
White	56	51.2	52	48.3	48.6	50.7	54	54.2	56.5	58.9	63.2	65.3
Black	11.2	10.9	12.3	13.3	15	13	10.4	9.9	8.4	7.9	5.6	4.9
Hispanic	6	7.1	6.5	5.3	4.7	5.4	2.7	3.5	3	3.2	2	1.9
Asian	0	0.9	0	0.6	1.4	0.8	1.6	1.5	0.9	1.2	1.1	1.2
Native American	0	0.2	1.2	1.3	0	0.2	0.3	0.4	0.2	0.3	0.2	0.1
Other	1.9	1.9	1.3	1.8	2.1	2	0.9	1.3	1	1.1	0.7	0.8
Missing	24.8	27.8	26.7	29.4	28.2	27.9	30.1	29.2	30	27.3	27.2	25.8
Admission (%)												
Emergency	61.6	53.6	65.4	57.7	69.3	59.3	69.1	57.6	68	58.3	68.8	61.8
Urgent	12.7	19	19.2	19.5	16.4	18.9	18	18.4	17.6	18.6	17.3	18.5
Elective	20.5	19.2	10.1	15.3	10.2	15.3	7.7	17.1	9.2	15.8	7.9	12.3
Trauma Center	0	0.8	0	0.3	0.3	0.4	0.1	0.1	0.1	0	0	0
Other	0	0.4	0	0	0	0.1	0	0.2	0	0	0	0
Missing	5.3	7	5.2	7.2	3.9	6.1	5	6.6	5.2	7.2	6	7.4
In-hospital fatality (%)	0	0	0.6	0.6	0	0.6	0	0.6	0.3	0.8	0.2	1.1
LOS (mean)	3	6	3.3	5	2.9	5	3.3	5	3.4	4.8	3.8	4.9
IQR	(1-3)	(2-6)	(1-4)	(2-6)	(1-4)	(2-6)	(2-4)	(2-6)	(2-4)	(2-6)	(2-5)	(2-6)
Comorbidities (%)												
Abnormal degeneration of basal ganglia	2.1	0.4	0	0.2	0.5	0.6	0.4	1	0.5	0.8	0.9	1
Parkinson's disease	0	0.2	0	0	0.3	0.3	2.3	2	3.8	4.9	5.2	5.8
Autonomic neuropathy	2	3.4	7.1	6.1	2.3	5.5	4.8	5.6	2.3	4.6	1.7	2.8

LOS = length of stay; IQR = interquartile range.

*Data are from the Nationwide Inpatient Sample.

tions were associated with Parkinson's disease, 4% with autonomic neuropathy, and 0.9% with abnormal degeneration of basal ganglia. There were no material differences in the prevalence of these conditions between those who had orthostatic hypotension as primary diagnosis compared with those who had it in any diagnosis field (Table).

DISCUSSION

To the best of our knowledge, this is the first study that examined the epidemiology of orthostatic hypotension among hospitalized patients in the US. We found that orthostatic hypotension-related hospitalization rates increased exponentially with age, and they were consistently higher in elderly males compared with females.

Previous assessments of the burden of orthostatic hypotension focused on geriatric wards, nursing homes, and elderly community dwellers, with estimated prevalence of 68%,¹⁸ 54%,² and 6%,¹⁷ respectively. The high prevalence of orthostatic hypotension among institutionalized patients likely reflects the presence of multiple risk factors such as neurodegenerative diseases known to cause orthostatic hypotension and the utilization of vasoactive medications that may impair a proper response to postural changes.^{18,20} Our findings are consistent with these reports and suggest that symptomatic orthostatic hypotension is a relatively common condition among the hospitalized elderly, and its incidence increases substantially with age. Aging is associated with physiological changes that may predispose to orthostatic problems. For instance, there is a loss of baroreflex responsiveness,^{21,22} reduced cardiac compliance,²³ and attenuation of the vestibular sympathetic reflex.²⁴ Therefore, the association between age and orthostatic hypotension has plausible physiological mechanisms.

We found that orthostatic hypotension-related hospitalizations occurred more frequently among Caucasians than in other racial groups. This is in agreement with previous studies that reported racial differences in the development of orthostatic hypotension particularly between Caucasians and African Americans.²⁵ Differences in orthostatic hypotension prevalence may be due to differences in definitions of orthostatic hypotension in these studies. Furthermore, the differences observed in our study could also be due to differential recognition or recording of orthostatic hypotension as a contributory cause to the hospitalization.

Syncope was the most frequent diagnosis associated with orthostatic hypotension, and the majority of the orthostatic hypotension-related hospitalizations were admitted as emergencies. Previous studies have recognized syncope as a frequent cause of emergency department visits,²⁶ and orthostatic hypotension has been previously documented in 24%-31% of patients presenting to emergency departments with syncope.^{20,27}

Several neurodegenerative conditions can cause orthostatic hypotension. Abnormal degeneration of basal ganglia, autonomic neuropathy, and Parkinson's disease can damage central or peripheral autonomic pathways, causing inability to engage

the sympathetic nervous system upon standing, resulting in orthostatic hypotension.^{28,29} It is noteworthy that we found a high prevalence of these conditions in orthostatic hypotension-related hospitalizations, indicating that orthostatic hypotension is a common cause of hospitalization in these patients. Parkinson's disease was reported in 4% of orthostatic hypotension-related hospitalizations, that is, 13 times higher than the estimated prevalence of this condition in the general US population (0.3%).³⁰ Considering the growing burden of this neurological condition in the US, it is expected that orthostatic hypotension-related hospitalization will increase, challenging health policy planners to anticipate the need for health services.³¹ In this context, future studies should be directed to determine if the standard therapy available for orthostatic hypotension that increases blood volume (fludrocortisone) or blood pressure (midodrine) effectively prevents orthostatic hypotension-related hospitalizations.

In conclusion, orthostatic hypotension is a relatively common condition among US hospitalized elderly. Considering the dynamics of the US population and the increasing incidence of neurological conditions associated with orthostatic hypotension, the burden of orthostatic hypotension-related hospitalizations is likely to increase over time and certainly deserves further scrutiny.

Strengths and Limitations

The interpretation of our results requires the consideration of several caveats. First, the identification of orthostatic hypotension-related hospitalizations relied on discharge diagnosis codes and, although we designed an algorithm to improve our disease ascertainment, it was not possible to validate orthostatic hypotension diagnoses. In addition, there are no procedure codes to identify the tests required to establish an orthostatic hypotension diagnosis (eg, tilt table). Second, data on additional factors potentially related to orthostatic hypotension, such as medication use, were not available. Third, missing data on race/ethnicity precluded further analysis of this information. However, our study likely identified the most severe episodes of orthostatic hypotension that required hospital admission and provides an estimation of the orthostatic hypotension disease burden without regard to specific etiologic conditions.

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APPENDIX

ICD9-CM codes to define the following excluded sets:

Reduced blood volume:

Volume depletion (276.5), persistent vomiting (536.2), diabetes insipidus (253.5, 588.1), burns (948.x), diarrhea (558.9, 787.91), hemorrhage (hemorrhagic abortion: 640, 634.1, 635.1, 636.1, 637.1, 638.1, 639.1, 666; Gastrointestinal hemorrhage: 456.0, 456.20, 530.21, 530.7, 530.82, 531.0, 531.2, 531.4, 531.41, 531.6, 532.0, 532.2, 532.4, 532.6, 533.0, 533.2, 533.4, 533.6, 534.0, 534.2, 534.4, 534.6, 535.01, 535.11, 535.21, 535.31, 535.41, 535.51, 535.61, 537.83, 562.02, 562.03, 562.12, 562.13, 569.85, 578, 578.0, 578.1, 578.9; hemoptysis: 786.3, hemorrhagic complications: 958.2, 998.1, 998.11, 998.12, 998.13; Other hemorrhage: 285.1, 459.0).

Intravascular volume contraction:

Pheochromocytoma (194.0, 227.0, 255.6), Addison's disease (255.4, 255.5, 017.6), malignant/benign neoplasm of islet of Langerhans (157.4, 159.0, 211.7, 211.9), renovascular hypertension (584.x), eating disorders (307.1, 307.5).

Insufficiency of intravascular volume:

Pregnancy (641, 642, 643, 644, 645, 646, 647, 648, 633, V22), hyperthyroidism (242.x), beriberi (265.0).

Vasodilators:

Carcinoid syndrome (259.2), mastocytosis (202.6), post-gastric surgery syndrome (564.2).