Predominance of Isolated Systolic Hypertension Among Middle-Aged and Elderly US Hypertensives

Analysis Based on National Health and Nutrition Examination Survey (NHANES) III

Stanley S. Franklin, Milagros J. Jacobs, Nathan D. Wong, Gilbert J. L’Italien, Pablo Lapuerta

Abstract—The purpose of the present study was to examine patterns of systolic and diastolic hypertension by age in the nationally representative National Health and Nutrition Examination Survey (NHANES) III and to determine when treatment and control efforts should be recommended. Percentage distribution of 3 blood pressure subtypes (isolated systolic hypertension, combined systolic/diastolic hypertension, and isolated diastolic hypertension) was categorized for uncontrolled hypertension (untreated and inadequately treated) in 2 age groups (ages <50 and ≥50 years). Overall, isolated systolic hypertension was the most frequent subtype of uncontrolled hypertension (65%). Most subjects with hypertension (74%) were ≥50 years of age, and of this untreated older group, nearly all (94%) were accurately staged by systolic blood pressure alone, in contrast to subjects in the untreated younger group, who were best staged by diastolic blood pressure. Furthermore, most subjects (80%) in the older untreated and the inadequately treated groups had isolated systolic hypertension and required a greater reduction in systolic blood pressure than in the younger groups (-13.3 and -16.5 mm Hg versus -6.8 and -6.1 mm Hg, respectively; \( P<0.0001 \)) to attain a systolic blood pressure treatment goal of <140 mm Hg. Contrary to previous perceptions, isolated systolic hypertension was the majority subtype of uncontrolled hypertension in subjects of ages 50 to 59 years, comprised 87% frequency for subjects in the sixth decade of life, and required greater reduction in systolic blood pressure in these subjects to reach treatment goal compared with subjects in the younger group. Better awareness of this middle-aged and older high-risk group and more aggressive antihypertensive therapy are necessary to address this treatment gap. (Hypertension. 2001;37:869-874.)

Key Words: hypertension, essential ■ blood pressure ■ clinical trials ■ hypertension, systolic, isolated

Multiple clinical and observational studies in the elderly have demonstrated that elevated systolic blood pressure (SBP) is a more potent predictor of adverse cardiovascular outcomes than is elevated diastolic blood pressure (DBP)\(^1\)–\(^5\) and that treating isolated systolic hypertension (ISH) in the elderly reduces risk of cardiovascular disease events.\(^6\)–\(^7\) Despite the strength of these observational and intervention studies, only about one quarter of hypertensive individuals are being treated to goal.\(^8\) Recently, the Coordinating Committee of the National High Blood Pressure Education Program (NHBPEP), recognizing the magnitude of this public health problem, stated that SBP in general and ISH in particular should become the major criteria for the diagnosis, staging, and therapeutic management of hypertension in the middle-aged and elderly.\(^9\)

ISH is strongly age dependent. Both the Framingham Heart Study and the nationally representative National Health and Nutrition Examination Survey (NHANES) III (conducted in 1988 to 1994) showed that a similar pattern of progressively increasing SBP occurs throughout adult life in untreated individuals.\(^10\),\(^11\) In contrast, DBP was shown to increase in adults until age 50 years and decline from the sixth decade forward.\(^10\),\(^11\) This age-related pattern of increasing rates of ISH for ages ≥50 years was not only observed in the Framingham Heart Study\(^10\) and in NHANES III participants,\(^11\) but also in a meta-analysis of 10 studies that reported the prevalence of ISH.\(^12\) In total, these studies suggest that age 50 years is a useful cutpoint to dichotomize arbitrarily hypertensive individuals into 2 groups for the purpose of classifying hypertension by subtype.

The present study focused on the new NHBPEP advisory guidelines with the expressed purpose of further characterizing subtypes of systolic and diastolic hypertension. By use of the NHANES III national data set, specific attention was directed toward identifying frequency of ISH and other subtypes of hypertension by age\(^1\) and examining hypertension awareness, staging, and treatment target goals across the entire adult age spectrum.\(^2\) We also examined the hypothesis...
that subtypes and staging of hypertension are distinctly different in middle-aged and older individuals versus their younger counterparts.

Methods

Study Population
NHANES III, sponsored by the National Center for Health Statistics, was designed to provide estimates of common chronic conditions and associated risk factors for a representative sample of the civilian, noninstitutionalized population of the United States.8,11 The adult BP component of NHANES III was designed to provide estimates of the prevalence, awareness, treatment, and control of hypertension in the general population. A national sample of 19,661 adults ≥18 years of age agreed to be interviewed in their home and have an extensive medical examination at a mobile examination center. Methods of BP measurement have been described previously.8,11

Definitions of Variables
Hypertension was defined as mean SBP ≥140 mm Hg, mean DBP ≥90 mm Hg, or current treatment for hypertension with prescription medication. Awareness of hypertension was determined by interviews only with untreated hypertensive participants. Treatment of hypertension was defined as use of a prescription medication to manage high BP at the time of interview. Treatment success was defined as pharmacological treatment of hypertension associated with SBP <140 and DBP <90 mm Hg, in accordance with the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VI).13 Inadequate treatment was defined as pharmacological treatment of hypertension with SBP ≥140 mm Hg and/or DBP ≥90 mm Hg. Control rates for all participants being treated with antihypertensive medications were calculated separately for SBP, DBP, and individual hypertensive subtypes.

Study Design
NHANES III data were compared by age (<50 or ≥50 years), antihypertensive treatment status (uncontrolled hypertension, divided into untreated and inadequately treated groups), and hypertensive subtype (isolated diastolic hypertension [IDH], SBP <140 and DBP ≥90 mm Hg; combined systolic/diastolic hypertension [SDH], SBP ≥140 and DBP ≥90 mm Hg; and ISH, SBP ≥140 and DBP <90 mm Hg). Distribution of each hypertensive subtype by age was determined and graphed separately for untreated and inadequately treated individuals.

In addition, untreated subjects <50 and ≥50 years of age were compared on the basis of BP staging by SBP and DBP. According to JNC-VI guidelines,7 SBP and DBP stages were divided as follows: optimal and normal (SBP <130 mm Hg and DBP <85 mm Hg); high-normal (SBP 130 to 139 mm Hg or DBP 85 to 89 mm Hg); stage 1 hypertension (SBP 140 to 159 mm Hg or DBP 90 to 99 mm Hg); and stage ≥2 hypertension (SBP ≥160 mm Hg or DBP ≥100 mm Hg). Because so few subjects had stage 3 hypertension, these subjects were collapsed into the stage ≥2 category. When a disparity was seen between SBP and DBP stages, participants were classified into the higher stage (upstaged), in accordance with the JNC-VI guidelines. In the current analysis, participants with high-normal BP or hypertension were classified on the basis of JNC-VI guidelines as having congruent levels of SBP and DBP, upstaged on the basis of SBP alone, or upstaged on the basis of DBP alone.14 BP reductions needed to reach target goals were determined for the 3 hypertensive subtypes in both the untreated and inadequately treated groups, dichotomized at 50 years of age.

Statistical Analysis
NHANES III data were extrapolated to assess the burden of hypertension awareness, treatment, and control among the entire adult civilian, noninstitutionalized population of the United States. These estimates were weighted and adjusted to reduce bias from nonresponses during the interview. Because the design of NHANES III was a multistage probability sample, conventional statistical analyses with underlying distributional assumptions were inappropriate for variance estimation and statistical testing. SUDAAN software (Research Triangle Institute) PROC DESCRIPT was used to compute Taylor series standard errors, t test was used for contrasted means, and χ² and the Cochran-Mantel-Haenszel test were used for survey data.13 Statistical tests were used to compare age grouping and treatment categories.15 All analyses were performed with SAS statistical software (SAS Corp).16

Results

Demographic Characteristics
On the basis of the extrapolated NHANES III data, 42.7 million adult Americans were identified as hypertensive, which represented 24% of the adjusted adult US population. A total of 23.6% of the hypertensive population was treated to target BP goal: the remaining untreated (47.8%) and inadequately treated hypertensive individuals (28.6%) together comprised 64.9% ISH, 21.1% SDH, and 14.0% IDH. More than twice as many individuals (66%) had BP higher than the SBP goal of ≥140 mm Hg than did higher than the DBP goal of ≥90 mm Hg (27%). Participants ≥50 years of age comprised three fourths of all hypertensive subjects. The older group was predominantly female (58%), whereas the younger group was predominantly male (62.5%). The predominant hypertensive subtype was ISH (79.8%) in the older group (75% stage 1 and 25% stage 2 or higher) and IDH (42.8%) in the younger group (98% stage 1 and 2% stage 2 or higher).

Awareness of Hypertension
Among untreated hypertensives in the US, 42% of individuals with DBP ≥90 mm Hg were aware of their condition but only 29% with SBP ≥140 mm Hg knew of their hypertensive status. Similarly, in the age <50 years group, 39% of individuals were aware of their hypertension, whereas only 31% of those age ≥50 years knew of their diagnosis. Hypertension awareness was greatest among subjects with SDH (67.2%), intermediate among those with ISH (58.4%), and least among those with IDH (46.8%; P=0.0008), after adjustment for age and gender. Awareness rates differed significantly between SDH and IDH (P=0.0008) and SDH and ISH (P=0.0004) but not between ISH and IDH (P=0.69), after adjustment for age and gender.

Frequency Distribution of Hypertension Subtypes by Age
The proportion of subjects with ISH was progressively higher and the proportion of subjects with IDH progressively lower with increments in age in the untreated (Figure 1) and inadequately treated groups (Figure 2). ISH was the most common hypertension subtype in participants of age ≥50 years, among both untreated (79.7%) and inadequately treated (80.1%) individuals. Conversely, for the younger hypertensive group, IDH was most common among untreated (46.9%) and SDH was most common among inadequately treated individuals (45.1%). In both the untreated and inadequately treated groups, ISH became the primary hypertensive subtype for subjects in their fifth decade (54%) of life and the overwhelming dominant hypertensive subtype by the sixth decade (87%) of life. Participants ≥50 years of age com-
prised 67% of all untreated and 86% of all inadequately treated individuals with hypertension.

JNC-VI Staging by SBP and DBP
The magnitude of disparity between SBP and DBP in classifying untreated individuals by JNC-VI staging criteria, after participants with congruent normal SBP and DBP were eliminated from study, was compared for the 2 age groups. Figure 3 shows percentages of untreated participants with high-normal BP or hypertension who were classified into each JNC-VI SBP and DBP category for the group of age $\geq 50$ years. Among untreated participants $\geq 50$ years of age with high-normal BP or hypertension, SBP alone correctly classified JNC-VI stage in 94% of subjects (84.8% upstaged on the basis of SBP alone and 9.0% with congruent SBP and DBP), whereas DBP alone correctly classified only 16.3% (7.3% upstaged on the basis of DBP alone and 9.0% with congruent SBP and DBP). In contrast to the older age group, 45.8% of untreated younger NHANES III participants were upstaged by DBP alone, 35.1% were upstaged on the basis of SBP alone, and 19.1% had congruent stages of SBP and DBP (Figure 4).

Comparison of BP Reduction Needed to Reach Treatment Goals
In the inadequately treated group age $\geq 50$ years, 82% had SBP in excess of the target goal versus 17% with DBP in excess of the target goal; in contrast, 50% of the younger group had BPs that exceeded both SBP and DBP target goals. Comparisons of BP reductions needed to reach treatment goals in the untreated individuals and those categorized as inadequately treated are shown for hypertension subtypes by age categories in the Table. A significantly greater reduction in SBP was required to reach treatment goal in the ISH subtype for the older versus the younger age group among untreated people with hypertension (-13.3 versus -6.8 mm Hg, respectively; $P = 0.0001$) and among inade-
Mean Levels of DBP and SBP With Reductions Required To Reach Targeted Goal in Untreated and Inadequately Treated Subjects

<table>
<thead>
<tr>
<th>Hypertension Subtype/Blood Pressure Component</th>
<th>Untreated Individuals, t Test Category Differences by Age (&lt;50 y vs ≥50 y)</th>
<th>Inadequate Treatment, t Test Category Differences by Age (&lt;50 y vs ≥50 y)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age&lt;50 y</td>
<td>Age≥50 y</td>
</tr>
<tr>
<td>IDH, mm Hg (mean±SE)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>130.6±0.55*</td>
<td>132.8±0.93†</td>
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<tr>
<td>DBP</td>
<td>93.1±0.26</td>
<td>93.0±0.59</td>
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<tr>
<td>DBP required reductions for goal</td>
<td>−4.1</td>
<td>−4.0</td>
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<tr>
<td>SDH, mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>148.6±0.77</td>
<td>161.9±1.29#</td>
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<tr>
<td>DBP</td>
<td>96.5±0.55</td>
<td>95.3±0.52</td>
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<tr>
<td>DBP required reductions for goal</td>
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<td>−6.3</td>
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<tr>
<td>SBP required reductions for goal</td>
<td>−9.6</td>
<td>−22.9</td>
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<tr>
<td>ISH, mm Hg</td>
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<tr>
<td>SBP</td>
<td>145.8±0.94</td>
<td>152.3±0.54#</td>
</tr>
<tr>
<td>DBP</td>
<td>81.7±1.10</td>
<td>76.6±0.32#</td>
</tr>
<tr>
<td>SBP required reductions for goal</td>
<td>−6.8</td>
<td>−13.3</td>
</tr>
</tbody>
</table>

*Standard error of the mean.
†Reduction in DBP to reach JNC-VI minimum treatment goal, <90 mm Hg.
‡Reduction in SBP to reach JNC-VI minimum treatment goal, <140 mm Hg.
§Reduction in SBP to reach JNC-VI minimum treatment goal, <90 mm Hg.
#P<0.05; $P<0.01; †P<0.001.

Discussion

The present study demonstrated that ISH in both untreated and inadequately treated individuals is the most frequent form of uncontrolled hypertension in the United States (65%), that ISH is the most common hypertension subtype (54%) for persons between the ages of 50 and 59 years, and that ISH is the overwhelmingly dominant hypertensive subtype (87%) by the sixth decade of life. In contrast, the small group of individuals with hypertension who are <50 years of age predominantly have diastolic hypertension that consists largely of IDH and SDH. More than 4 times as many inadequately treated individuals of age ≥50 years had SBP (82%) versus DBP (17%) that was higher than target goals, whereas an equal number (50%) had both SBP and DBP higher than target goals in the younger group. Furthermore, individuals of age ≥50 years with ISH who were either untreated or inadequately treated required more than a 2-fold greater reduction in SBP to attain JNC-VI treatment goals versus their younger counterparts.

Earlier studies in the elderly that defined ISH as SBP <160 mm Hg and DBP <90 or <95 mm Hg understandably found a lower frequency of ISH of 5% to 22%. More recently, the community-based Framingham Heart Study, which defined ISH as SBP <140 mm Hg and DBP <90 mm Hg, reported a higher frequency of ISH in untreated individuals of 35% to 40% in the age group of 50 to 59 years and values of 65% to 70% in the age group of ≥60 years. In contrast, the present NHANES III study, which examined combined untreated and inadequately treated individuals, observed a considerably larger ISH frequency of 54% in the age group of 50 to 59 years and values of 87% in the age group of ≥60 years.

Frequency of ISH, also defined with a cutoff of <140/90 mm Hg, was reported in a previous NHANES III (1988 to 1991) analysis as 64.8% in a group of age ≥60 years. These results are consistent with those presented in the present analysis. A key difference is that the present analysis focused on the uncontrolled hypertensive population rather than on all individuals with hypertension. The intent was to examine more closely how SBP and DBP play different roles in defining the problem of uncontrolled hypertension.

In addition to age-related differences in subtype analysis, the 2 hypertensive age groupings were strikingly dissimilar with respect to JNC-VI staging and eligibility for therapy in untreated individuals. This dissimilarity was evidenced by the pronounced difference with respect to upstaging, which was almost entirely related to SBP in people ≥50 years of age, whereas the reverse was observed in individuals <50 years of age, among whom upstaging was mostly related to DBP. But because most of the individuals with hypertension in the NHANES III population were ≥50 years of age (74%) with a predominance of ISH (80%), SBP was by far the most...
important overall determinant of JNC-VI upstaging and, hence, eligibility for therapy. These results in the NHANES III age group of ≥50 years reinforce the findings of SBP upstaging in the middle-aged and older community-based Framingham Heart Study and introduce the new concept of DBP upstaging in the younger age group.

Poor levels of awareness, treatment, and control of hypertension were a problem in all age groups. Although hypertension was less likely to be treated in younger than older people, the absolute number of untreated individuals was more than twice as high in older individuals. Furthermore, awareness of ISH was significantly lower than awareness of SDH, after correcting for the confounding effects of age and gender.

Clinical Implications

Many factors may contribute to the inadequate treatment of hypertension, as recent reviews have emphasized. Both physician bias toward focusing primarily on a DBP treatment goal and physician fear of excessive lowering of DBP, have contributed to poor SBP control. Furthermore, as noted in the present study, among patients with hypertension, a greater number of older persons have high levels of SBP compared with younger patients. Most older patients with ISH may be resistant to therapy as a result of increased left ventricular hypertrophy, vascular hypertrophy and remodeling, high levels of sympathetic tone, and nonmodulation of the renin-angiotensin-aldosterone system.

Millions of people with untreated or inadequately treated hypertension would benefit from full implementation of JNC-VI guidelines, which recommend initiating lifestyle and pharmacological intervention, controlling both SBP and DBP, and simultaneously treating other major cardiovascular risk factors. The potential value of dietary management should not be underestimated, as recent investigations have demonstrated. However, a significant percentage of untreated and inadequately treated older individuals with high and resistant ISH or SDH require a more innovative strategy that includes a multiple drug regimen for adequate control of BP. An alternative or supplemental strategy that holds some promise is the development of more potent antihypertensive agents that have minimal side effects and are specifically targeted to reduce SBP.

Strengths and Limitations

The present study, which uses a national population database, reinforces and expands the conclusions of the new NHBEPEP guidelines by demonstrating that individuals with hypertension generally fall into 1 of 2 distinct categories: (1) a smaller, younger population presenting primarily with diastolic hypertension and requiring a small reduction in both SBP and DBP to reach treatment goal and (2) a much larger, middle-aged and older population presenting primarily with ISH as the major cause of uncontrolled hypertension and requiring a large reduction in SBP to reach treatment goal. Because of the cross-sectional nature of NHANES III, the effect of treatment on hypertensive subtypes and control rates cannot be determined. However, it is probable that a significant percentage of individuals with inadequately treated ISH may have had SDH before beginning therapy but did not reach SBP goal because of a treatment bias or because they had a more difficult to treat form of hypertension. Exploring these trends will be an important subject for future clinical research.

In conclusion, the present study demonstrates that ISH is the overwhelmingly dominant subtype of hypertension in the middle-aged and elderly population, that ISH requires a large reduction in SBP to reach treatment goal and, that ISH is the predominant subtype among persons with untreated and inadequately treated hypertension. Successful treatment of systolic hypertension in general, and ISH in particular, represents an important public health challenge that will require more aggressive efforts at management.

References


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_Hypertension_. 2001;37:869-874
doi: 10.1161/01.HYP.37.3.869

_Hypertension_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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