Cross-classification of JNC VI Blood Pressure Stages and Risk Groups in the Framingham Heart Study

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Background: The recently published Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI) includes a classification of blood pressure stages and a new risk stratification component. Patients with high-normal blood pressure or hypertension are stratified into risk group A (no associated cardiovascular disease risk factors, no target organ damage or cardiovascular disease); group B ($\geq 1$ associated cardiovascular disease risk factor excluding diabetes, no target organ damage or cardiovascular disease); or group C (diabetes or target organ damage or cardiovascular disease).

Objective: To examine the prevalence of risk groups and blood pressure stages in a community-based sample.

Methods: We evaluated 4962 subjects from the Framingham Heart Study and Framingham Offspring Study examined between 1990 and 1995. We cross-classified men and women separately according to their JNC VI blood pressure stages and risk groups.

Results: In the whole sample, 43.7% had optimal or normal blood pressure and 13.4% had high-normal blood pressure; 12.9% had stage 1 hypertension and 30.0% had stage 2 or greater hypertension or were receiving medication. As blood pressure stage increased, the proportion of subjects in group A decreased, whereas the proportion in group C increased. Among those with high-normal blood pressure or hypertension, only 2.4% (all women) were in risk group A, 59.3% were in group B, and 38.2% were in group C. In the high-normal or hypertensive group, 39.4% qualified for lifestyle modification as the initial intervention according to JNC VI recommendations, whereas 60.6% were eligible for initial drug therapy or were already receiving drug therapy. Nearly one third of high-normal subjects were in risk group C, in which early drug therapy may be needed. Among those in stage 1, only 4.0% were in group A, in which prolonged lifestyle modification is recommended.

Conclusions: These results provide a foundation for estimating the number of individuals with hypertension who fall into different risk groups that require different treatment approaches. With nearly 50 million individuals with hypertension in the United States, there are important implications for clinicians and policymakers if JNC VI recommendations are widely adopted in clinical practice.

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METHODS

STUDY SAMPLE

The Framingham Heart Study was established in 1948, when 5,209 residents of Framingham, Mass, aged 28 to 62 years, were enrolled in a prospective epidemiologic cohort study to evaluate potential risk factors for coronary heart disease. Members of this cohort have received follow-up evaluations every 2 years with medical histories, physical examinations, and selected laboratory tests, including fasting lipid levels and 12-lead electrocardiograms. In 1971, 5,124 additional subjects (offspring of original cohort subjects and their spouses) were enrolled into the Framingham Offspring Study. These participants have received follow-up evaluations every 4 years. Study design and entry criteria for both cohorts have been detailed elsewhere.10–14 The current study sample included 11,64 subjects from the original Framingham Heart Study cohort who participated in examination cycle 22 (1990-1994), and 3,798 participants from the Framingham Offspring Study who participated in examination cycle 5 (1991-1995).

BLOOD PRESSURE MEASUREMENT

At each examination, resting blood pressure was measured in the left arm twice in the seated position by an examining physician using a mercury column sphygmomanometer. Means of the 2 separate systolic and diastolic blood pressure measurements were then calculated to derive the reported blood pressure for that examination. Subjects were classified according to the JNC VI criteria: normal (<130/<85 mm Hg); high-normal (130-139/85-89 mm Hg); stage 1 hypertension (140-159/90-99 mm Hg); or stage 2 or greater hypertension (≥160/≥100 mm Hg). Blood pressure stages 2 and 3 were combined for the purposes of all analyses because of the low prevalence of stage 3 hypertension. When the systolic and diastolic blood pressures fell into different stages, the higher stage was selected to classify the subject’s blood pressure, as per JNC VI recommendations.1 Patients already receiving medical therapy for hypertension were classified as having stage 2 or greater hypertension.

RISK FACTOR, TARGET ORGAN DAMAGE, AND CARDIOVASCULAR DISEASE STATUS

The major cardiovascular disease risk factors considered for classification of subjects into risk group B included the following: regular smoking within the past year; dyslipidemia (defined as a total cholesterol level greater than 6.21 mmol/L [240 mg/dL]), high-density lipoprotein cholesterol level ≤0.90 mmol/L [35 mg/dL], or currently receiving antihyperlipidemic therapy; age older than 60 years; male sex; or postmenopausal status in women. Family history of coronary artery disease was not collected routinely in all participants; therefore, this variable was not considered. Conditions considered for the classification of subjects into risk group C included the following: diabetes mellitus (defined as a previous diagnosis of diabetes, casual blood glucose level ≥11.1 mmol/L [200 mg/dL] in the original cohort, fasting blood glucose ≥7.8 mmol/L [140 mg/dL] in the offspring cohort, or receiving therapy); concurrent electrocardiographic evidence of left ventricular hypertrophy (defined as increased voltage in the presence of a strain pattern or ST-segment abnormality); presence of definite angina or prior myocardial infarction; prior coronary revascularization (percutaneous transluminal coronary angioplasty or coronary artery bypass surgery); congestive heart failure; stroke or transient ischemic attack; and peripheral arterial disease (defined by the presence of intermittent claudication, abdominal aortic aneurysm, any peripheral arterial bruit, or absent pulse). Although the JNC VI definition of target organ damage includes nephropathy and retinopathy, we did not collect data regarding these diagnoses. Diagnoses of angina, myocardial infarction, congestive heart failure, stroke or transient ischemic attack, and peripheral arterial disease were established by a panel of 3 physicians in accordance with published criteria.9 After review of records from the Framingham Heart Study, interim hospitalizations, and visits to personal physicians.

STATISTICAL ANALYSIS

Sex-specific prevalences of each hypertension stage and risk group were calculated. The prevalence of each risk factor and disease diagnosis was also calculated and was stratified by sex, blood pressure stage, and risk group. Comparisons between groups of subjects across blood pressure stages or risk groups were performed using the Pearson χ² test for discrete variables and the t and Wilcoxon rank sum tests for continuous variables, as appropriate. Two-tailed P values less than .05 were considered statistically significant. All analyses were performed using the Statistical Analysis System.15

RESULTS

STUDY SAMPLE CHARACTERISTICS

Of 4,962 subjects examined during the study period, 2,195 (44.2%) were men (mean ± SD age, 59.6 ± 13.1 years) and 2,767 (55.8%) were women (mean ± SD age, 61.8 ± 14.6
years). Mean systolic and diastolic blood pressures, respectively, were 131 and 76 mm Hg for men and 129 and 72 mm Hg for women (Figure 1). A total of 25.8% of men and 27.1% of women were receiving antihypertensive medications. Overall, 43.7% of subjects fell into the optimal or normal blood pressure range (\(\leq 130/\leq 85\) mm Hg), 13.4% had high-normal blood pressure (130-139/85-89 mm Hg), 12.9% had stage 1 hypertension (140-159/90-99 mm Hg), and 30.0% had stage 2 or greater hypertension (\(\geq 160/\geq 100\) mm Hg) or were receiving antihypertensive medications. Mean age of subjects increased with increasing blood pressure stage (\(P<.001\)).

Prevalence of each cardiovascular disease risk factor is shown in Table 1, stratified by sex and blood pressure stage. Mean (±SD) number of risk factors (excluding hypertension) present in subjects in risk group B was 1.9 ± 0.8, which increased in a stepwise fashion, from 1.8 ± 0.7 for those with normal blood pressure up to 2.2 ± 0.7 for those with stage 2 or greater hypertension. There were significantly fewer current smokers among subjects with stage 2 or greater hypertension compared with other blood pressure stages (\(P<.001\)). Prevalence of dyslipidemia increased with increasing blood pressure stage in men and women. The proportion of subjects with diabetes was uniformly distributed across blood pressure stages in men and women.

Table 2 shows the prevalence of specific clinical cardiovascular diseases or target organ damage in the study sample, stratified by sex and blood pressure stages. Mean (±SD) number of clinical cardiovascular disease or target organ damage diagnoses was 1.8 ± 1.1 for all subjects in group C. Among men and women, there were higher prevalences of electrocardiographic left ventricular hypertrophy, coronary revascularization, cerebrovascular events, and peripheral arterial disease for those with stage 2 or greater hypertension compared with those in lower stages (all \(P<.01\)). In addition, women with stage 2 or greater hypertension had a higher prevalence of coronary heart disease (\(P<.01\)).

CROSS-CLASSIFICATION OF BLOOD PRESSURE STAGES AND RISK GROUPS

Table 3 displays the number of individuals with high-normal blood pressure and hypertension who fell into each risk group. The proportion of subjects in each risk group is shown in Figure 2, stratified by sex and blood pressure stage. As blood pressure stage increased, the proportion of subjects in risk group A decreased, and the proportion in group C increased. Overall, 40.7% of subjects with hypertension were in risk group C.

Table 1. Prevalence of Cardiovascular Risk Factors in the Framingham Heart Study Population, Stratified by Sex and JNC VI Blood Pressure Stages*  

<table>
<thead>
<tr>
<th>Blood Pressure Stage (mm Hg)</th>
<th>Smoking</th>
<th>Dyslipidemia</th>
<th>Diabetes</th>
<th>Age &gt;60 y</th>
<th>Male Sex or Postmenopausal Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (n = 2195)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optimal or normal ((\leq 130/\leq 85))</td>
<td>19.9</td>
<td>36.7</td>
<td>11.1</td>
<td>27.1</td>
<td>100</td>
</tr>
<tr>
<td>High-normal (130-139/85-89)</td>
<td>20.0</td>
<td>40.4</td>
<td>12.3</td>
<td>38.6</td>
<td>100</td>
</tr>
<tr>
<td>Stage 1 (140-159/90-99)</td>
<td>18.0</td>
<td>40.4</td>
<td>9.9</td>
<td>51.3</td>
<td>100</td>
</tr>
<tr>
<td>Stages 2 and 3 ((\geq 160/\geq 100) or treated)</td>
<td>11.4</td>
<td>52.8</td>
<td>8.4</td>
<td>70.0</td>
<td>100</td>
</tr>
<tr>
<td>Total (men)</td>
<td>17.2</td>
<td>42.4</td>
<td>10.4</td>
<td>44.9</td>
<td>100</td>
</tr>
<tr>
<td>Women (n = 2767)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optimal or normal ((\leq 130/\leq 85))</td>
<td>21.0</td>
<td>19.7</td>
<td>8.9</td>
<td>26.8</td>
<td>59.2</td>
</tr>
<tr>
<td>High-normal (130-139/85-89)</td>
<td>15.5</td>
<td>31.2</td>
<td>10.4</td>
<td>54.3</td>
<td>81.7</td>
</tr>
<tr>
<td>Stage 1 (140-159/90-99)</td>
<td>15.7</td>
<td>33.2</td>
<td>7.6</td>
<td>59.9</td>
<td>85.8</td>
</tr>
<tr>
<td>Stages 2 and 3 ((\geq 160/\geq 100) or treated)</td>
<td>11.0</td>
<td>43.2</td>
<td>8.5</td>
<td>79.8</td>
<td>93.4</td>
</tr>
<tr>
<td>Total (women)</td>
<td>16.7</td>
<td>29.4</td>
<td>8.8</td>
<td>50.1</td>
<td>75.4</td>
</tr>
<tr>
<td>Total (both sexes)</td>
<td>16.9</td>
<td>35.3</td>
<td>9.5</td>
<td>47.8</td>
<td>86.3</td>
</tr>
</tbody>
</table>

* Data are percentages of patients. Percentages as displayed may not sum exactly because of rounding. JNC VI indicates Sixth Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.
TREATMENT-ELIGIBLE SUBJECTS

According to JNC VI recommendations, all individuals with high-normal blood pressure or frank hypertension should attempt lifestyle modification. Initial drug therapy is recommended for those with stage 2 or greater hypertension or stage 1 hypertension in risk group C. In addition, individuals with high-normal blood pressure in risk group C who also have diabetes, congestive heart failure, or nephropathy are also candidates for initial drug therapy. Among the 2794 subjects with high-normal blood pressure or hypertension, 1306 were men and 1488 were women. Because male sex is considered a cardiovascular risk factor, precluding classification of any males into risk group A.

Among subjects in our sample with high-normal blood pressure or hypertension, the proportion eligible for initial drug therapy or already receiving drug therapy were 30.9% in group A, 48.7% in group B, and at least 81.0% in group C. (Data were not available regarding nephropathy, so the proportion of subjects in group C who would be recommended for initial drug therapy may be even higher.) Therefore, among subjects with high-normal blood pressure or hypertension, 39.4% at most qualified for lifestyle modification as the sole initial intervention, whereas at least 60.6% were eligible for initial drug therapy or were already receiving it. Among subjects with stage 1 or greater hypertension, these proportions were 20.4% and 79.6%, respectively.

For the purposes of this study, we combined all subjects receiving antihypertensive medications with untreated subjects in the stage 2 or greater hypertension group. To explore the implications of our assumption, we compared untreated subjects with stage 2 or greater hypertension (n = 173) with treated subjects (n = 1306). Mean blood pressures of untreated and treated subjects were 171/86 and 142/75 mm Hg, respectively. The pro-
portion of subjects in risk groups A, B, and C, respectively, were 2.3%, 64.7%, and 33.0% in untreated subjects and 1.3%, 53.0%, and 45.7% in treated subjects. The distributions were significantly different between the 2 groups ($P = .001$). These results demonstrate that a higher proportion of treated subjects were in risk group C; therefore, even if treated subjects’ pretreatment blood pressure only qualified them for stage 1 hypertension, JNC VI guidelines would still recommend that they receive initial drug therapy or were already receiving medications; the remainder (39.4%) qualified for lifestyle modification with subsequent drug therapy, if necessary. Among those with high-normal blood pressure, nearly one third were in risk group C, in which early drug treatment may be needed. In subjects with stage 1 hypertension, few (4.0%) were in risk group A, in which prolonged lifestyle modification may be appropriate, and one third were in risk group C and were eligible for initial drug therapy.

An increased burden of cardiovascular disease risk factors confers increased risk for coronary events and cardiovascular death. Our results bear out the assertion by the Joint National Committee that most individuals with hypertension will have at least 1 other associated risk factor and fall into risk group B. In our study sample, high-normal and hypertensive subjects in group B had, on average, 2 other cardiovascular disease risk factors (other than diabetes) in addition to hypertension. Similarly, subjects in group C had, on average, 2 comorbid diseases (including diabetes, target organ damage, or clinical cardiovascular disease) in addition to hypertension.

The age of our sample had a significant impact on blood pressure stages and risk group classification. Approximately 45% of men and 50% of women in our sample were older than 60 years, qualifying them for risk group B. However, age was not the sole criterion for classification in these subjects. All subjects older than 60 years had at least 1 additional cardiovascular disease risk factor: either male sex or postmenopausal status. Older individuals also have an increasing prevalence of dyslipidemia and diabetes, so the effect of the older age of our study sample may have manifested itself both indirectly and directly in determining risk group. Even among our younger subjects (≤60 years) with high-normal blood pressure or hypertension, only 7.3% fell into risk group A. Examination of the cross-classification of risk groups and blood pressure stages in other populations with different age distributions would be useful. It is expected that fewer subjects would fall into risk group B or C in populations younger than ours.

The overall prevalence of hypertension was 42.9% in our study sample, which is higher than the estimated prevalence of hypertension for the entire US adult population (24.0%) from the Third National Health and Nutrition Examination Survey (NHANES III, phase 1). This discrepancy reflects the older age of our study sample, which had a mean age of 61 years compared with a mean age of approximately 49 years for NHANES III screenes. These results provide insight into the potential impact of the newly established JNC VI risk groups and blood pressure stages on eligibility for treatment of hypertension. In our middle-aged and older community-based sample, 56.3% of subjects had high-normal blood pressure or hypertension. In this subset, only 2.4% (all women) fell into risk group A, whereas 59.3% had at least 1 associated risk factor (group B), and 38.2% already had target organ damage, clinical cardiovascular disease, or diabetes (group C). At least 60.6% of the subjects with hypertension or high-normal blood pressure met JNC VI recommendations for initial drug therapy or were already receiving medications; the remainder (39.4%) qualified for lifestyle modification with subsequent drug therapy, if necessary. Among those with high-normal blood pressure, nearly one third were in risk group C, in which early drug treatment may be needed. In subjects with stage 1 hypertension, few (4.0%) were in risk group A, in which prolonged lifestyle modification may be appropriate, and one third were in risk group C and were eligible for initial drug therapy.

**Figure 2.** Proportion of subjects in each risk group according to blood pressure stage, as defined by Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, for men (top) and women (bottom). Stage ≥2 indicates subjects with stage 2 or 3 hypertension or treated. Black section of column indicates risk group C; gray, risk group B; white, risk group A.
was 67 years, whereas the average age of a white individual with hypertension in the United States is approximately 60 years. Since hypertension is predominantly a disease of older persons, our data may have particular relevance for clinicians and policymakers to estimate the proportion of patients in clinical practice who will require therapy for elevated blood pressure, based on JNC VI recommendations.

POTENTIAL PUBLIC HEALTH IMPACT OF JNC VI

Applying NHANES III, phase 1 data, there are currently an estimated 47.9 million individuals with hypertension in the United States. Although there have been substantial improvements in the prevalence, awareness, treatment, and control of hypertension since the 1960s; only 55% of adults with hypertension who were younger than 74 years were receiving treatment in the NHANES III, phase 1 sample. Furthermore, only 29% were controlled to a goal blood pressure of less than 140/90 mm Hg. Our data suggest that a large percentage of individuals with hypertension nationwide will fall into risk strata that make them eligible for initial drug therapy. Therefore, universal adoption of the JNC VI recommendations in clinical practice may result in a large additional burden of health care costs initially. However, by shifting therapy toward higher-risk and away from lower-risk patients, the adoption of JNC VI should be cost-effective across the spectrum of patients treated because of the prevention of death, future strokes, and other cardiovascular disease.

POTENTIAL CLINICAL IMPACT OF JNC VI

Whether JNC VI recommendations will affect clinical practice by increasing the number of patients treated remains to be seen. Some data are available regarding changes in hypertension classification and practice patterns following the publication of earlier reports from the JNC. Pogue et al studied 1158 patients with hypertension who participated in the High Blood Pressure Program at Harlem Hospital, New York, NY. Using JNC IV criteria, which classified hypertension based principally on diastolic blood pressure stages, the proportions of patients with mild, moderate, or severe hypertension were 48.2%, 28.9%, and 18.9%, respectively. In the same patients, applying JNC V criteria, which classified hypertension on the basis of systolic and diastolic blood pressure, resulted in a large number of patients being shifted into a more severe category. The proportions with equivalent levels of hypertension using JNC V criteria were 20.7%, 34.9%, and 44.4%, respectively. Furthermore, subjects who were shifted into a more severe category with the newer classification were more likely to have renal disease or other target organ damage. Two similar analyses have found a considerable increase in the prevalence of hypertension using JNC V as opposed to older World Health Organization criteria, among patients with diabetes in Denmark and residents of a municipality in India.

Other than merging hypertension stages 3 and 4, the classification of blood pressure stages in JNC VI is unchanged from JNC V. The only significant difference in classification between JNC VI and JNC V that affects initial drug therapy decisions involves patients with high-normal blood pressure or stage 1 hypertension in risk group C. Without information on nephropathy, it is difficult to estimate the absolute number of individuals in our study sample who would be affected by the new risk group classification and who would be treated differently based on the new JNC VI recommendations.

LIMITATIONS

There are several limitations to this study. First, the sample consisted almost exclusively of white individuals, limiting the generalizability of our findings to other ethnicities in whom the prevalence of hypertension, target organ damage, and cardiovascular disease may be different. For example, the prevalence of hypertension is higher in African Americans. Our data, therefore, may underestimate the population prevalence of treatment-eligible individuals. Second, we were unable to ascertain in our sample the prevalence of all the risk factor, target organ damage, and cardiovascular disease diagnoses used by JNC VI for risk-based stratification. For example, we did not routinely collect data on the prevalence of nephropathy, retinopathy, or family history of premature cardiovascular disease. Knowledge of the status of these risk factors and diseases would increase the proportion of subjects classified into risk group B or C. This may also have led to an underestimate of treatment-eligible individuals. However, our ascertainment of other diseases and risk factors relied on objective data rather than self-report of the participants, allowing confidence in our prevalence estimates for diagnoses such as congestive heart failure, angina, and myocardial infarction. Finally, for purposes of the study, we classified patients receiving antihypertensive therapy into stage 2 or greater hypertension, although some of them may have been treated for milder blood pressure elevation. The immediate pretreatment blood pressures of these individuals were not routinely available, and in many cases, they had been treated for years before the study period.

CONCLUSIONS

Hypertension is a highly prevalent risk factor for cardiovascular disease, and it is widely undiagnosed and undertreated. The high prevalence of coexisting cardiovascular disease risk factors, target organ damage, and clinical cardiovascular disease in our middle-aged and elderly sample highlights the importance of risk stratification for individuals with hypertension. These results provide a foundation for estimating the number of individuals with hypertension who fall into different risk groups that require different treatment approaches according to JNC VI recommendations. With nearly 50 million individuals with hypertension in the United States, there are important implications for clinicians and policymakers if JNC VI recommendations are widely adopted in clinical practice.

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REFERENCES


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