Relation Between Blood Pressure and Stroke Mortality


The relation between stroke mortality and blood pressure was investigated in 10,186 hypertensive patients followed up in the Department of Health Hypertension Care Computing Project for an average of 9 years. An untreated blood pressure measurement was available in 3,472 men and 3,405 women. The age-adjusted risk of stroke death increased by 1% for every 1 mm Hg increase in untreated systolic blood pressure. The relative hazard rate was 1.014 (95% confidence interval [CI], 1.007, 1.021) in men and 1.009 (1.003, 1.016) in women. The corresponding increases for 1 mm Hg for untreated diastolic blood pressure were almost 3% in men and again 1% in women (relative hazard rate 1.026 [95% CI, 1.014, 1.038] in men and 1.010 [1.000, 1.021] in women). Treated blood pressure measurements were available in 3,073 men and 3,148 women. Stroke mortality increased by 2% for a 1 mm Hg increase in treated systolic pressure and 3% for the corresponding increase in diastolic blood pressure. The relation between stroke mortality and blood pressure was similar over and under the age of 65, although the increase in mortality with pressure was greater for treated diastolic blood pressure in women under the age of 65 than over this age. There was no evidence for a J-shaped relation between stroke mortality and either systolic or diastolic pressure in men. In women there was a suggestion of such a relation, but since this relation was also observed for untreated pressures, any increase in risk at lower pressures is unlikely to be a result of treatment. (Hypertension 1992;20:601-605)

KEY WORDS • blood pressure • cerebrovascular disorders • mortality

Stroke affects mainly the elderly, with about 50% of episodes occurring in patients more than 75 years old. Myocardial infarction is a more common outcome in younger subjects, but only 20% of strokes occur in those less than 65 years old.1 In randomized controlled trials, treatment for hypertension has been shown to reduce stroke events (both fatal and nonfatal) by 40%.2 The relation between blood pressure and stroke mortality needs further investigation in view of the recent controversy concerning the relation between low diastolic blood pressure (DBP) and mortality for ischemic heart disease. Some studies have found that the lower the level of DBP, the lower the risk of death from coronary heart disease.4 In the Systolic Hypertension in the Elderly Program (SHEP), coronary heart disease deaths were significantly reduced in elderly patients with isolated systolic hypertension who were actively treated with antihypertensive therapy and whose average treated DBP was 68 mm Hg.4 In the Hypertension Detection and Follow-Up Program, the trial DBP averaged in the 80s, and the stepped-care group showed a 23% reduction in coronary heart disease mortality compared with the referred-care group.5 Some studies have reported an increase in coronary heart disease mortality for treated DBP below 85 mm Hg.6-8 A recent review article concluded that these relations were unlikely to be treatment related, because they were also observed in patients given placebo.9 Cruickshank, however, has argued that failure of autoregulation, especially likely to occur in subjects with some degree of ischemia already, may lead to further myocardial ischemia. A similar association may exist for stroke, because cerebral blood flow has been found to decrease if the mean systolic blood pressure (SBP) falls below a certain level.10 This may be especially true in the elderly, because cerebral blood flow declines with age.11 Cruickshank and colleagues13 found an increased risk of stroke deaths if the SBP was lowered to below 137 mm Hg in men and women more than 60 years old. It is not clear, however, whether these relations are secondary to some other deterioration in cerebrovascular function, because they also occur for untreated pressures. In subjects screened for the Hypertension in Elderly Patients (HEP) study, death from stroke tended to a J-shaped relation for untreated SBP, with an increasing risk for SBP <120
mm Hg. This was observed only in patients 70–79 years old and in men but not women. In a population survey in Bergen, Norway, the relation between stroke death rates and untreated SBP varied across different age bands with a U-shaped or negative curve found in older people. If the reduction of blood pressure by treatment to below a certain level is associated with an increased risk of stroke, then this will have important implications in the treatment of elderly hypertensive patients. The purpose of the present study was to examine the relation between treated and untreated blood pressure and stroke mortality in hypertensive men and women in the Department of Health Hypertension Care Computing Project (DHCCP) and to test for a differential effect of blood pressure on stroke mortality with age.

Methods

The DHCCP is a multicenter computer-based study of the survival and treatment of 10,186 hypertensive patients who attended hospital hypertension clinics or general practices between 1971 and 1986. Ninety-five percent entered the study on presentation at one of five hospital clinics (King’s College Hospital, London; Hammersmith Hospital, London; John Radcliffe Hospital, Oxford; Dudley Road Hospital, Birmingham; Aberdeen Royal Infirmary). The remainder were recruited from four general practices (Kentish Town [London], Harlow, Oxford, and Norwich). The study was set up to use the clinical data of patients referred by their general practitioners to one of the hospital hypertension clinics. A diagnosis of hypertension was made on a clinical basis and not on the basis of a cutoff point and did use Phase V Korotkoff sounds. All patients who were referred to the five hospital clinics were automatically included in the study. Blood pressure, diagnoses, and other clinical data were recorded at presentation and at subsequent visits by specialized staff. Because this was a longitudinal, multicenter study, it was not possible to standardize blood pressure measurements. Patients were registered for mortality follow-up with the Office of Population Censuses and Surveys. Death certificates were coded by trained staff according to the Eighth Revision of the International Classification of Diseases (ICD). At coding, every effort was made to follow the same conventions as those who code death certificates for the country as a whole. By March 31, 1990, 1,762 patients had died. The average length of follow-up was 9 years (maximum, 19 years). Sex and age at presentation were not recorded for six and seven patients, respectively. The data were analyzed separately for men and women for any mention on the death certificate of stroke (ICD codes 430.0-438.9). Death rates, age-adjusted by the direct method, were calculated for fifths of the blood pressure distribution. Untreated blood pressure analyses were based on measurements taken no later than 3 months after presentation if the patient was known not to be on antihypertensive therapy. If no such reading was available, the most recent untreated blood pressure reading taken within 1 year before presentation was used. Treated blood pressure was the average of readings taken between 3 and 12 months after presentation. Patients who died within the first year were not included in the treated blood pressure analyses, because mortality was predicted from the first year. The Cox proportional hazards model was used to examine the effect on mortality of blood pressure and age. The exponentials of the regression coefficients are reported, giving the relative hazard rate (RHR) for a unit increase in age or pressure. The RHR is the estimated ratio of hazard rate with a unit increment in age or blood pressure compared with the hazard rate of a given value of these variables. For example, an RHR of 1.03 for DBP indicates that a 1 mm Hg increase will be associated with an increase in mortality rate of 3%.

A differential effect of blood pressure on stroke mortality with age was examined with patients being grouped according to whether their age at presentation was <65 or ≥65.

Results

Untreated Blood Pressure

The characteristics of patients included in the untreated blood pressure analyses are shown in Table 1. Untreated blood pressure readings were available for 3,472 men and 3,405 women (3,148 men and 2,875 women were <65 years old). The average untreated blood pressure was 174±106 mm Hg. A positive history of stroke, defined as a positive mention of cerebrovascular accident, cerebral hemorrhage, cerebral infarction or thrombosis, or a subarachnoid hemorrhage at or before presentation, was present in only 6% of men and 4% of women. Eighty-five men and 96 women had a mention of stroke on their death certificates. There was a significant positive relation between untreated blood pressure and stroke mortality with age.
TABLE 2. Change in Risk for an Increase of 1 mm Hg in Pressure for Any Mention of Stroke

<table>
<thead>
<tr>
<th>Untreated pressure</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure</td>
<td>1.014</td>
<td>1.009</td>
</tr>
<tr>
<td>95% CI</td>
<td>(1.007, 1.021)</td>
<td>(1.003, 1.016)</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>1.026</td>
<td>1.010</td>
</tr>
<tr>
<td>95% CI</td>
<td>(1.014, 1.038)</td>
<td>(1.000, 1.021)</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.0001</td>
<td>&lt;0.01</td>
</tr>
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<table>
<thead>
<tr>
<th>Treated pressure</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure</td>
<td>1.018</td>
<td>1.021</td>
</tr>
<tr>
<td>95% CI</td>
<td>(1.011, 1.026)</td>
<td>(1.013, 1.029)</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>1.035</td>
<td>1.028</td>
</tr>
<tr>
<td>95% CI</td>
<td>(1.020, 1.051)</td>
<td>(1.012, 1.044)</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.0001</td>
<td>&lt;0.001</td>
</tr>
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</table>

CI, confidence interval. Relative hazard rates and their statistical significance are given. The same patients may occur in both the treated and untreated analyses.

pressure (both SBP and DBP) and any mention of stroke in men (p<0.0001) (Table 2). In women, the RHRs were smaller and either of borderline significance (DBP, p<0.07) or significant at the 1% level (SBP). There was no evidence of an interaction between age and untreated blood pressure for either men or women (0.1<p<0.3). Nor was there any definite evidence of a difference between men and women in the association between untreated blood pressure and stroke mortality (p=0.2 for SBP and 0.06 for DBP difference). Figures 1 and 2 illustrate the increase in death rate from stroke (any mention) according to fifths of the untreated SBP in men and women, respectively. The increase in death rate for stroke with increasing SBP can be seen for both men and women over and under the age of 65, although the death rate in men under the age of 65 appears constant between 120 and 175 mm Hg.

Figures 3 and 4 illustrate the corresponding increases with untreated DBP. In men and women under the age of 65, the relation was flat under an untreated DBP of 110 mm Hg (men) and 106 mm Hg (women).

Treated Blood Pressure

The characteristics of patients included in the treated blood pressure analyses are shown in Table 1. Treated blood pressure analyses were based on 3,073 men and 3,148 women who had been followed up for at least 1 year and for whom blood pressure readings were available. Of these, 2,658 men and 2,535 women were aged <65 years. A positive history of stroke was present in 4% of men and 2% of women. Stroke was mentioned on the death certificates of 120 men and 106 women. The average treated blood pressure was 155/93 mm Hg. Both SBP and DBP were significant positive predictors of mortality in both men and women, with RHRs greater than with untreated pressure (Table 2). There was a statistically significant interaction between age and DBP for women. The risk of stroke death from a unit increase in treated DBP was 1.017, 95% CI (0.996, 1.038), p=0.11 in women more than 65 years old and 1.044, 95% CI (1.019, 1.069), p<0.001 in the younger age group. There was no evidence of a difference between the sexes in the relation between treated blood pressure and stroke mortality (0.5<p<0.9). Figures 1 and 2 illustrate the increase in death rate from stroke (any
Discussion

For the blood pressure range studied, there was a strong positive relation between death from stroke and both treated and untreated blood pressure. In all cases, the RHRs were higher for the treated pressure than for the untreated, suggesting that the pressure acquired on treatment is a better predictor than the untreated pressure. This has been reported previously.12 Scrutiny of the plots of quintiles of blood pressure against death rates per thousand patient years from stroke showed the anticipated much higher stroke rate in the older men and women. The increase in stroke with quintile of blood pressure was not linear, with generally much higher rates in the upper two quintiles of pressure. There was no real indication of any increase of deaths from stroke in the lowest quintile of blood pressure.

The evidence in the literature for a J-shaped relation between blood pressure and stroke is conflicting, partly because of different ranges of blood pressure studied. A community-based study in Bergen, Norway, reported on the mortality of 70,000 subjects more than 15 years old followed up over a 5-year period.13 The results showed that stroke mortality tended to increase exponentially in both men and women for untreated SBP and DBP. There was, however, some indication of an increased risk in women whose SBP was below 115 mm Hg. A similar result was also observed in women for DBP <65 mm Hg. When nine prospective, observational studies were pooled, however, data on the 420,000 subjects (average follow-up of 10 years) showed that there was no evidence of a threshold level of "usual DBP" below which there was an increase in the risk of stroke.14 Study participants had no known history of stroke, most were under 70 years of age at baseline, and the usual DBP ranged from 70 to 110 mm Hg. No data were presented for SBP. Although this provides strong evidence of a continuous, positive relation between risk of stroke and DBP >70 mm Hg, this may not be the case in elderly patients. In a study in Finland of 561 people (minimum age, 85 years), SBP levels below 140-159 mm Hg or DBP below 80-89 mm Hg were associated with decreased survival.15 In 10,732 patients 60-79 years old screened for hypertension in the HEP study, increased stroke mortality was observed for untreated SBP below 120 mm Hg only in older men. No such relation was found for DBP.16 In the Bergen study, a U-shaped relation was found for untreated SBP in people more than 70 years old for stroke mortality.17 The observations of J-shaped relations with untreated SBP strongly suggests confounding variables, such as poor health, associated with a fall in blood pressure rather than an adverse effect of a low pressure per se. In the Clatterbridge study, a U-shaped relation for treated SBP in 939 patients with moderate-to-severe hypertension was observed.18 This U-shaped relation applied to subjects more than 60 years old; patients with a treated SBP <136 mm Hg (six deaths) had a stroke rate three times that of subjects with a SBP of 137-148 mm Hg (one death). Our results, based on 226 deaths, show that for treated hypertensive patients, increasing blood pressure
was associated with increasing risk of stroke death for the blood pressure range studied. Nevertheless, because most patients in the DHCCP study had no history of stroke, it is possible that preexisting cerebrovascular disease may result in a different relation between blood pressure and stroke mortality from that observed here.

There was no evidence that, in hypertensive patients, the effect of untreated blood pressure on the risk of stroke was different between the young and the old. There was a significant interaction between age and treated DBP in women, indicating that the risk of increased diastolic pressure on stroke was less pronounced in older women on treatment than in the young, but nonetheless, increased DBP remained a potent risk factor.

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