The Long-term Prognostic Significance of Repeated Blood Pressure Measurements in the Elderly

SPAA (Studio sulla Pressione Arteriosa nell’Anziano) 10-Year Follow-up

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Background: In young and middle-aged people, both systolic (SBP) and diastolic (DBP) blood pressure have a continuous, strong, and independent relationship with subsequent cardiovascular morbidity and mortality. These relationships are not well documented in older people and, until now, studies in the elderly do not provide homogeneous results on the importance of DBP compared with SBP as a cardiovascular risk factor.

Objective: To determine whether SBP and DBP are independent indicators of mortality risk in the elderly.

Design: An observational prospective cohort study to analyze the long-term prognostic significance of repeated SBP and DBP measurements in the elderly.

Patients and Methods: A total of 3858 outpatients 65 years or older (mean age [SD], 72.9 [4.9] years, 43.5% men) were selected randomly by 444 Italian National Health Service general practitioners in 1983. The population was followed up for 10 years. Crude and adjusted incidence rates of total and cardiovascular mortality were analyzed for classes of SBP and DBP based on the values recorded at the 2 initial visits 1 week apart and those measured during the first 12 months of follow-up.

Results: During the 10-year follow-up, 74 patients (1.9%) were lost to follow-up and 1561 (41.3%) died, 709 (45.4% of all deaths) from cardiovascular causes. A positive continuous, graded, strong, and independent association was observed with both total (P<.001) and cardiovascular (P<.001) mortality for SBP but not for DBP. The pattern was similar in both sexes, in persons younger and older than 75 years, regardless of preexisting cardiovascular diseases, and whether they had been receiving antihypertensive treatment at baseline. There was no J-shaped mortality curve in the subjects with the lowest SBP and DBP.

Conclusions: These findings suggest that SBP, but not DBP, is a strong, positive, continuous, independent indicator of mortality risk in the elderly and should be stressed much more than DBP in the diagnosis and treatment of hypertension in this age group.

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METHODS

STUDY DESIGN

SPAA was designed as an observational study on the prevalence and natural history of hypertension in the elderly, started in 1983 with the participation of 444 Italian GPs from the National Health Service.

The organization conducting the study, the characteristics of the participating physicians, and the quality of collected data have been reported in detail elsewhere. All the physicians who agreed to participate attended preliminary meetings, under the supervision of central and local coordinators, during which they checked their sphygmomanometers and were trained in the standard methods of blood pressure (BP) and anamnestic recording. Each GP agreed to enroll a random sample of 10 patients older than 64 years who had presented to his or her clinic for any reason: the first eligible patient was chosen each day until recruitment was completed. A list of all outpatients attending the surgery during the recruitment period was used to verify accuracy of the admission process.

The initial assessment of each patient consisted of an examination at recruitment and a further visit 1 week later. The purpose of the study was explained to the patient and consent was obtained. Body weight and height of all patients were measured during the initial visit; information was obtained about the patients' physical activity and smoking and alcohol-drinking habits; and their medical and pharmacological history was recorded, with specific attention to features or events related to the cardiovascular and cerebrovascular system and other noteworthy diseases.

The patient's BP and heart rate were recorded at both visits, first with the subject sitting, then after lying down for 5 minutes, then again after 30 seconds standing. One BP measurement was taken on each arm, while the patient was sitting; subsequent measurements were taken on the arm that initially had the higher values. Systolic BP and DBP were recorded at Korotkoff phases I and V (rounding the reading to the nearest even-numbered measurement).

Subjects enrolled were assessed at 4 further visits at quarterly intervals during the first follow-up year. Average BP in the supine position at the 2 initial visits (baseline BP) and at all 6 visits during the first year (first-year BP) were used to define the patient's BP status.

In 1993, 10 years after the initial assessment, the vital status of the population was ascertained through the census offices or by the GPs. Causes of death were coded blindly with respect to BP and other characteristics, according to the underlying cause of death (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]) by a single nosologist (C.A.). Cardiovascular disease deaths were those assigned ICD-9-CM codes 400 through 438.

Participants were classified in 4 groups for SBP and 3 groups for DBP, based on baseline and first-year BP, as suggested by the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure43: for SBP, “below 140 mm Hg,” “from 140 to 159 mm Hg,” “from 160 to 179 mm Hg,” and “180 mm Hg or more”; and for DBP, “below 90 mm Hg,” “from 90 to 99 mm Hg,” and “100 mm Hg or more.” To ensure an equal number of patients in each BP group, analysis by tertiles of baseline and first-year SBP and DBP also were made.

To test the hypothesis of a J-shaped association between BP and mortality (higher death rates in the subgroups with the lowest BP), 4 other subgroups of DBP were defined: (1) “below 75 mm Hg,” (2) “75 to 79 mm Hg,” (3) “80 to 84 mm Hg,” and (4) “85 to 89 mm Hg.” Accordingly, for SBP, 3 other subgroups were identified: (1) “below 120 mm Hg,” (2) “120 to 129 mm Hg,” and (3) “130 to 139 mm Hg.”

STATISTICAL ANALYSIS

In the univariate analysis, mortality differences between SBP and DBP groups were assessed using the $\chi^2$ test for trend. Multivariate analysis was done using the Cox proportional hazards model to assess the independent prognostic contribution of SBP and DBP adjusted for the different distribution of cardiovascular risk factors, diseases, and antihypertensive drug treatment at baseline (listed in Table 1) and for heart rate. The statistical package used was the SAS.45 As suggested by Harrell and colleagues,46 the candidates’ prognostic factors included in the multivariate analyses were less than 10 times the events considered. The proportional hazards assumption in Cox regression was assessed using the graphic methods suggested by Hess.46 The results are expressed in terms of relative risk and 95% confidence intervals. Differences and trends were considered statistically significant if $P$ values were less than .05.

The aim of this study was to assess the prognostic significance of repeated SBP and DBP measurements in one of the largest databases of elderly people, a cohort of 3858 subjects 65 years or older enrolled by their GPs in SPAA (Studio sulla Pressione Arteriosa nell’Anziano [Study on Blood Pressure in the Elderly]) and followed up for 10 years.

The vital status at 10 years was obtained for 3784 (98.1%) of the 3858 subjects enrolled in the study. Seventy-four persons (1.9% of the total population) were lost to follow-up. Since their mean follow-up was...
less than 1 year and their baseline characteristics were not significantly different from those of the population followed up for 10 years, they were excluded from the mortality analyses.

The baseline characteristics of the population are summarized in Table 1. In 1082 patients (28.6%), the reasons for the initial visit were the appearance of new symptoms or difficulties with current health problems; other reasons included a checkup for a chronic disease, 1379 (36.5%), and a BP checkup, 1322 (34.9%).

At baseline, 3025 (79.9%) of the 3784 participants had SBP of 140 mm Hg or higher, and 1356 (35.8%), DBP of...
90 mm Hg or higher. Of the 2074 patients (54.8%) with a history of hypertension, 1831 (88.3% of patients with hypertension) were receiving antihypertensive treatment.

During the 10 years from recruitment, 1561 deaths occurred (41.3% of the total population), 709 (45.4% of all deaths) due to cardiovascular diseases. Noncardiovascular causes accounted for 597 deaths (38.3%), while for 255 deaths (16.3%) the cause was unknown or undefined (Table 2). The distribution of known and unknown deaths was similar at different ages and BP values and in both sexes.

The rates of total and cardiovascular mortality by mean SBP and DBP at the 2 initial visits are shown in Figure 1. A positive significant association was observed between baseline SBP and both total (P < .001) and cardiovascular (P < .001) mortality, but no association was found with baseline DBP.

This different impact of baseline SBP and DBP on mortality was confirmed by the multivariate analysis, taking into account other cardiovascular risk factors, diseases, and antihypertensive drug treatment at baseline: a significant trend for risk of total (P = .001) and cardiovascular (P < .001) death was observed only for SBP, and no excess of risk was found with DBP at baseline (Figure 2). The pattern was similar in both sexes, younger or older than 75 years, with and without preexisting cardiovascular diseases, and with and without antihypertensive treatment at baseline (Figure 3). A significant positive association was found between baseline SBP and total and cardiovascular mortality, both in patients with baseline DBP lower than 90 mm Hg (P = .007 and P = .003, respectively) and in those with baseline DBP of 90 mm Hg or higher (P = .01 and P = .03, respectively), whereas no association was found between baseline DBP and mortality in patients with baseline SBP lower than 140 mm Hg and in those with baseline SBP of 140 mm Hg or higher.

Because of the variability in BP, average supine BP at all the 6 visits during the first year was also used to define the patient’s BP status. Again, a significant association was seen between first-year BP and total (P < .001) and cardiovascular mortality (P < .001) for SBP. For first-year DBP, no association was found with total or with cardiovascular mortality (Figure 4).

To compare our results more closely with others, the data were reanalyzed using tertiles of BP values, instead of predefined clinical BP categories, and sitting BP values instead of supine ones. The results were similar, showing a significant positive association between SBP (both baseline and first-year values) and total and cardiovascular mortality but no association between DBP and mortality.

To exclude the possibility that the lack of positive association between DBP and mortality was due to higher death rates in groups with the lowest BP, as observed in

Figure 2. Ten-year total and cardiovascular mortality according to baseline systolic blood pressure (SBP) (top) and diastolic blood pressure (bottom) (average SBP and DBP at the 2 initial visits): multivariate analysis. Parameters in the model are all the baseline characteristics listed in Table 1 plus baseline heart rate. The vertical lines denote 95% confidence intervals.

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some studies\textsuperscript{21,22,30,31} of elderly populations and attributed to frailty and comorbidity in people near death: (1) the data were reanalyzed after excluding the deaths within the first 3 years of follow-up, according to the criterion used by Glynn and colleagues.\textsuperscript{31} A significant trend toward increased total and cardiovascular mortality was confirmed in the multivariate analysis for baseline (P < .001 and P < .006, respectively) and first-year (both P < .001) SBP, but no excess of deaths associated with high DBP was observed, using the average BP either at the 2 initial visits (P = .86 for total and P = .89 for cardiovascular mortality) or for all 6 visits in the first year (P = .76 and P = .37, respectively); and (2) a multivariate analysis was done considering the subgroups with DBPs and SBPs lower than 90 and 140 mm Hg, respectively, at the 2 initial visits or at all 6 visits in the first year. No significant increase in total and cardiovascular mortality was associated with low DBPs and SBPs.

It is unlikely that our findings are artifacts or due to chance or to a more aggressive treatment of DBP than SBP during the follow-up, since the results did not change after adjustment for confounding variables, including the presence of antihypertensive drug treatment. This was prescribed to half the population at baseline and during the follow-up, with similar control of SBP and DBP at the start of the study and during follow-up.\textsuperscript{46}

The results also did not change when deaths within the first 3 years of follow-up were excluded, to avoid the possible confounding effect of short-term mortality due to comorbidity in patients with low BPs. A significant risk of cardiovascular and total mortality was associated with SBP but not with DBP by sex, age, and presence or absence of cardiovascular comorbidity and of antihypertensive treatment at baseline.

Given the high prevalence of patients with ISH, it could be argued that the predictive power of DBP might be obscured by SBP because of the association between high SBP and low DBP in these subjects; however, the analyses in the subgroups of subjects with normal or high DBP, or with normal or high SBP, confirmed the results of the whole population.

A similar scenario was obtained using all the measurements during the first year of the study, with the aim

**COMMENT**

Our study indicates that in the elderly high SBP but not high DBP, measured by a GP, is associated with a significant excess of total and cardiovascular mortality and should be taken into account when diagnosing and treating hypertension in this age group.
of overcoming the dilution effect of regression to the mean (arising both from imprecision in BP measurements on 2 occasions 1 week apart and from temporary fluctuations in an individual’s usual BP). This may be especially important in studies on the elderly because of the wide BP variability in this age group.34-40 No other study had the opportunity to verify the prognostic significance of BP based on repeated measurements during such a long period. As expected, BP measurements taken during a long period—1 year—are more predictive than a few measurements taken 1 week apart (see relative risks in Figure 4 in comparison with Figure 2). The better prognostic value of first-year SBPs than baseline SBPs was not paralleled by a similar behavior for DBP, which was never significantly and independently associated with total or cardiovascular mortality.

This different pattern of associations was confirmed using sitting BP instead of supine BP values, which are used less in clinical trials and everyday practice, or analyzing data using tertiles of BP values instead of the usual clinical categories.

Finally, there is no evidence that an excess of mortality at lower levels of DBP obscured the risk of death at higher DBP; there was no excess of deaths in the subgroups with lower DBPs, in accordance with recent studies that U-shaped or J-shaped associations of BP with mortality in elderly people7,11,12,15,16,22,30,31 are probably artifacts of short-term follow-up, comorbidity, or low BPs in people near death.21,22,30,31

Therefore our results, based on one of the largest databases of elderly people, followed prospectively to investigate the prognostic significance of BP in old age, confirm the positive relationship between SBP and total and cardiovascular mortality in the elderly reported by the majority of previous studies.1,16,20-32,47,48 However, the association between DBP and mortality is not uniformly reported in the literature. Some authors26-29 observed a similar prognostic significance for high DBP and SBP in the elderly, but the majority of prospective population studies suggest that DBP is a weaker indicator of cardiovascular risk than SBP, particularly with increasing age.1,4,16,23-25,31,32,49-51 This behavior, unlike that observed in the young-adult population, might be the result of people who had diastolic hypertension in their young or adult life (especially if untreated or undertreated) not surviving to become elderly, while systolic hypertension, particularly ISH, is a condition (and a risk factor) more common only in old age.

The 2 largest cohort studies20,30 of elderly people so far assessed mortality risk factors in about 6000 subjects aged 60 to 79 years and 10 000 aged 65 to 79 years who were followed up for 5 years. Both found an association between risk of cardiovascular death and increas-

![Figure 4. Ten-year total and cardiovascular mortality according to first-year systolic blood pressure (SBP) (top) and diastolic blood pressure (DBP) (bottom) (average SBP and DBP at all 6 visits during the first follow-up year): multivariate analysis. Parameters in the model are all the baseline characteristics listed in Table 1 plus baseline heart rate. The vertical lines denote 95% confidence intervals.](http://archinte.jamanetwork.com/pdfaccess.ashx?url=/data/journals/intemed/11945/)
benefits found in trials that admitted elderly patients on and treatment of hypertension in older age groups. The results and current practice, suggests that DBP has not DBP, viewed in relation to randomized, clinical trial and independent association in our elderly population different ages, BP groups, and both sexes, suggesting that the relationship between BP and cardiovascular mortality is not an artifact. This study was conducted in general practice by the physicians usually responsible for the patients' care, making our findings more reliably generalizable.

In conclusion, the strong, positive, continuous, and independent association in our elderly population between total and cardiovascular mortality and SBP, but not DBP, viewed in relation to randomized, clinical trial results and current practice, suggests that DBP has been, and, perhaps still is, overstressed in the diagnosis and treatment of hypertension in older age groups. The benefits found in trials that admitted elderly patients on the basis of their high DBP and SBP might be attributable more to the lowering of SBP than to the lowering of DBP.  

Our findings in any case highlight the importance of treating all elderly subjects with high SBP more aggressively than has been done recently, as the efficacy of antihypertensive therapy in systolic hypertension, isolated or not, is well documented by the results of several trials.  

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