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Blood pressure and mortality in elderly people aged 85 and older: community based study

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Abstract

Objective: To determine whether the inverse relation between blood pressure and all cause mortality in elderly people over 85 years of age can be explained by adjusting for health status, and to determine whether high blood pressure is a risk factor for mortality when the effects of poor health are accounted for.

Design: 5 to 7 year follow up of community residents aged 85 years and older.

Setting: Leiden, the Netherlands.

Subjects: 835 subjects whose blood pressure was recorded between 1987 and 1989.

Main outcome measure: All cause mortality.

Results: An inverse relation between blood pressure and all cause mortality was observed. For diastolic blood pressure crude 5 year all cause mortality decreased from 88% (52/59) (95% confidence interval 79% to 95%) in those with diastolic blood pressures < 65 mm Hg to 59% (27/46) (44% to 72%) in those with diastolic pressures > 100 mm Hg. For systolic blood pressure crude 5 year all cause mortality decreased from 85% (95/112) (78% to 91%) in those with systolic pressures < 125 mm Hg to 59% (13/22) (38% to 78%) in those with systolic pressures > 200 mm Hg. This decrease was no longer significant after adjustment for indicators of poor health. No relation existed between blood pressure and mortality from cardiovascular causes or stroke after adjustment for age and sex, but after adjustment for age, sex, and indicators of poor health there was a

positive relation between diastolic blood pressure and mortality from both cardiovascular causes and stroke.

Conclusion: The inverse relation between blood pressure and all cause mortality in elderly people over 85 is associated with health status.

Introduction

In western societies blood pressure rises with age. It is not clear if this is the result of a pathological process that needs treatment or if it is part of the natural ageing process. Treating hypertension helps prevent stroke and coronary heart disease in middle aged and elderly people younger than 80. In two trials, however, no benefit of treatment was observed in subjects aged 80 and older.^{1,2} Treating isolated systolic hypertension does not reduce all cause mortality in this age group, although it prevents stroke and heart failure.^{3,4}

Since the number of subjects aged 80 and older included in these trials is small, evidence from observational studies may help in deciding whether to treat hypertension in patients at this age. Previous observational studies comprised of people aged 80 and older have found no relation between blood pressure and mortality,⁵ and a U shaped relation,⁶ or even an inverse relation in which higher blood pressure was associated with lower mortality.⁷⁻⁹ However, adjustment for confounding factors was made in only one study⁹; in this study only 35 deaths occurred in those aged over 80.

To determine whether the relation between blood pressure and all cause mortality differs in elderly people older than 85 as compared with younger

elderly people and to see whether this relation can be explained by poorer health among those with low blood pressure, we analysed the relation between blood pressure and mortality in a 5 to 7 year study of a cohort of residents of Leiden aged 85 and over; 621 deaths occurred and extensive data on health status at baseline were available.

Subjects and methods

The Leiden 85 plus study is a community based study that was designed to investigate the association between HLA and life expectancy.¹⁰ It contains data on all people aged 85 and over who lived in Leiden on 1 December 1986. There were 1236 cohort members eligible to participate in the study. Of these, 956 agreed to participate, 218 died before they could be visited, 59 declined to cooperate, 2 emigrated, and 1 was not interviewed in error; thus, 94% of all living subjects participated.

Data collection

Subjects were visited at their homes between January 1987 and May 1989 by a doctor. After obtaining verbal informed consent, the doctor recorded their age, sex, the country of origin of their parents and their marital status. The doctor also asked about the subject's medical history, including any drugs they were taking. If the subject was not able to provide the information, it was obtained from a relative or a carer. Medical records were reviewed for patients living in nursing homes. The method of validating a subject's medical history has been reported.¹¹ A minimal state examination¹² was performed, and a venous blood sample was collected after permission was obtained. At the end of the interview, blood pressure was measured once with a mercury sphygmomanometer in 835 participants. Participants were seated while blood pressure was measured or supine in the few cases where the participant was bedridden. The reading was rounded up to the nearest 5 mm Hg as is common clinical practice in the Netherlands. Diastolic pressure was not able to be measured in five subjects.

Mortality data

Data on mortality were collected from the municipal register or from the nursing home. For this paper subjects were followed until 1 March 1994. Preliminary analysis of data from a longer follow up period showed similar results. The cause of death was obtained by linking the number of the death certificate to the primary cause of death as coded by a physician from the Dutch Bureau of Statistics. Causes of death¹³ were categorised as stroke (ICD-9 codes 430-438), ischaemic heart disease (410-414), all cardiovascular disorders (390-459), cancer (140-239), infection (010-018, 038, 137-137.4, 460-466.1, 475, 480-487.8, 510, 513.0-513.1, 590, 599), and all other causes. In the analyses of specific causes of death follow up information until 1 October 1996 was used.

Statistical analysis

Crude data are presented as 5 year all cause mortality (survival time counted from the time of the home visit) for which 95% confidence intervals were calculated using arc sin transformation. For multivariate analysis the Cox proportional hazards model was used, and age and sex were used as stratifying variables. To examine the shape of the relation between blood pressure and all cause mortality, blood pressure was modelled as a categorical covariate. To test whether a positive or negative linear relation existed between blood pressure and all cause or specific mortality, blood pressure was entered as a continuous covariate. Other covariates were selected either because they are medically important or because they significantly increased the fit of the model.

Continuous variables with a non-linear influence on mortality were modelled by adding quadratic terms. Checking the model showed that the hazard ratios for different blood pressures decreased as the length of time a subject was followed increased. Statistical models that incorporated this time dependency, however, yielded results that were similar to those that assumed a proportional hazard. For simplicity, we present the results of the proportional hazard model. Two covariates with mainly short term effects on

Table 1 Characteristics of 830 participants aged 85 and older by diastolic blood pressure. Values are numbers (percentages) unless indicated otherwise

	Diastolic blood pressure (mm Hg)						P value	All subjects
	50-60	65-70	75-80	85-90	95-100	>100		
Mean (SD) age (years)	90 (3)	90 (3)	90 (3)	89 (2)	90 (3)	89 (3)	0.003	90 (3)
Men	18/59 (31)	44/124 (36)	69/251 (28)	52/224 (23)	32/126 (25)	4/46 (9)	0.002	219/830 (26)
Living independently	22/59 (37)	39/124 (32)	106/251 (42)	94/224 (42)	65/126 (52)	29/46 (63)	0.0001	355/830 (43)
Able to eat, wash, and dress without help	33/57 (58)	83/122 (68)	175/248 (71)	174/222 (78)	101/125 (81)	36/45 (80)	0.0001	602/819 (74)
Mean (SD) score on minimal state examination*	20 (7)	23 (7)	24 (7)	25 (6)	25 (6)	27 (5)	<0.0001	24 (6)
Mean serum albumin (g/l)	39	40	41	41	41	42	<0.0001	41
Medical history								
Heart disease (excluding hypertension)	22/54 (41)	32/122 (26)	74/241 (31)	53/218 (24)	28/122 (23)	6/45 (13)	0.03	215/802 (27)
Stroke	4/54 (7)	18/123 (15)	31/244 (13)	27/220 (12)	19/122 (16)	3/45 (7)	0.90	102/808 (13)
Diabetes mellitus	9/54 (17)	13/122 (11)	30/241 (12)	26/219 (12)	11/122 (9)	4/45 (9)	0.23	93/803 (12)
Cancer	4/54 (7)	12/123 (10)	19/241 (8)	9/219 (4)	2/122 (2)	1/45 (2)	0.002	47/804 (6)
Drug use								
Using diuretics:	29/58 (50)	41/121 (34)	106/245 (43)	90/221 (41)	45/125 (36)	17/46 (37)	0.33	328/816 (40)
Potassium sparing diuretics	8/58 (14)	23/121 (19)	52/245 (21)	51/221 (23)	18/125 (14)	8/46 (17)	0.95	160/816 (20)
Using other antihypertensive drugs	6/58 (10)	16/121 (13)	18/245 (7)	23/221 (10)	20/125 (16)	4/46 (9)	0.51	87/816 (11)
Using glycosides	16/58 (28)	20/121 (17)	42/245 (17)	38/221 (17)	19/125 (15)	2/46 (4)	0.02	137/816 (17)
Using bronchodilators	6/58 (10)	2/121 (2)	12/245 (5)	14/221 (6)	1/125 (1)	3/46 (7)	0.41	38/816 (5)

*Scores range from 0 to 30.¹²

Table 2 Crude 5 year all cause mortality among 835 participants aged 85 and older by systolic blood pressure and among 830 participants aged 85 and older by diastolic blood pressure. Diastolic pressure could not be measured in five participants. Values are numbers (percentages; 95% confidence intervals)

Blood pressure (mm Hg)	All participants		Participants not using antihypertensive drugs	
	No	5 year mortality	No	5 year mortality
Systolic:				
90-120	112	95 (85; 78 to 91)	57	46 (81; 70 to 90)
125-140	222	166 (75; 69 to 80)	121	84 (69; 61 to 77)
145-160	241	147 (61; 55 to 67)	134	78 (58; 50 to 66)
165-180	153	98 (64; 56 to 71)	88	51 (58; 48 to 68)
185-200	85	59 (69; 59 to 79)	43	28 (65; 50 to 78)
>200	22	13 (59; 38 to 78)	12	7 (58; 31 to 83)
Diastolic:				
50-60	59	52 (88; 79 to 95)	27	23 (85; 70 to 96)
65-70	124	92 (74; 66 to 81)	72	53 (74; 63 to 83)
75-80	251	172 (69; 63 to 74)	132	86 (65; 57 to 73)
85-90	224	148 (66; 60 to 72)	124	76 (61; 53 to 70)
95-100	126	82 (65; 57 to 73)	72	42 (58; 47 to 69)
105-140	46	27 (59; 44 to 72)	26	12 (46; 28 to 65)

mortality (current infections and fractures) were entered as time dependent covariates.

The final model contained the following variables: type of residence (nursing home, home for the elderly, independent); score on the minimal state examination; health status according to the senior European (SENIEUR) criteria¹⁴ (that is, whether considered immunologically healthy based both on clinical information and laboratory data according to the SENIEUR protocol); presence of cachexia; dependence in activities of daily living (defined as not being able to eat, dress, or wash without help); history of cancer, diabetes mellitus, coronary heart disease, or heart failure; presence of oedema of the lower extremities, other circulatory diseases, chronic obstructive pulmonary disease, current infectious disease, or current fracture; use of potassium sparing diuretics or other diuretics, antihypertensive drugs, glycosides, antiarrhythmic drugs, or nitrates; packed cell volume; lymphocyte fraction; monocyte fraction; and serum concentrations of glucose, lactate dehydrogenase, sodium, chloride, urea, creatinine, and albumin. Using multiple imputation, we showed that possible bias caused by the missing measurements of blood pressure in 121 (13%) participants was negligible (unpublished data).

Results

Most of the risk factors for mortality—such as a low score on the minimal state examination, dependency in activities of daily living (being unable to eat, wash, or dress without help), low serum concentrations of albumin, heart disease, and cancer—occurred more frequently in subjects with low diastolic blood pressure (table 1). Similar results were found when population characteristics were compared with systolic blood pressure. No differences between groups with different blood pressures were seen in the use of antihypertensive drugs.

For diastolic blood pressure crude 5 year all cause mortality decreased from 88% (52/59) (95% confidence interval 79% to 95%) in those with diastolic blood pressures < 65 mm Hg to 59% (27/46) (44% to 72%) in those with diastolic blood pressures > 100 mm Hg. For systolic blood pressure, it decreased

from 85% (95/112) (78% to 91%) in those with systolic blood pressures < 125 mm Hg to 59% (13/22) (38% to 78%) in those with systolic blood pressures > 200 mm Hg. The results were similar when subjects using antihypertensive drugs were excluded (table 2).

When age and sex were adjusted for a significant inverse relation between blood pressure and mortality was observed, mainly due to an increase in the risk of mortality among those subjects with low diastolic pressure (diastolic blood pressure ≤ 60 mm Hg) or low systolic pressure (≤ 140 mm Hg) (figs 1 and 2). The risk of dying for a subject with low diastolic pressure was slightly diminished if an adjustment was made for the systolic blood pressure. The same was true if the risk of dying for a subject with low systolic pressure was adjusted for the diastolic pressure. None the less, the risk of dying among subjects with low blood pressure remained highly significant (highest P value = 0.006).

The effect of high blood pressure was insignificant when all information that predicts mortality was adjusted for, including relevant comorbidity and the use of antihypertensive drugs, and the effect of low blood pressure on all cause mortality was reduced and no longer significant.

Similar results were seen when the mortality risks of men and women were analysed separately. However, because of the smaller numbers in each subgroup, for men the negative relation between blood pressure and

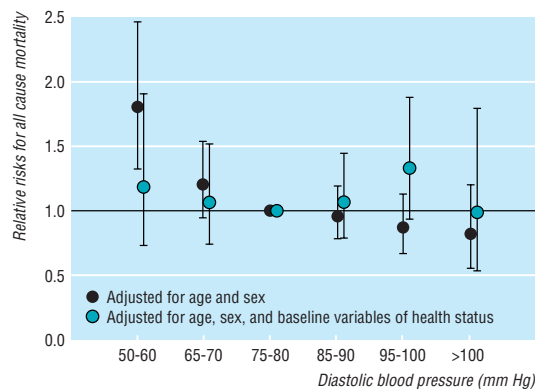


Fig 1 Relative risks for all cause mortality by diastolic blood pressure among 830 participants aged 85 and older

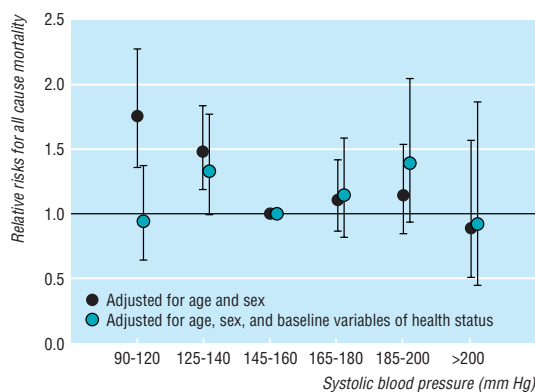


Fig 2 Relative risks for all cause mortality by systolic blood pressure among 835 participants aged 85 and older

mortality from all causes adjusted for age remained strong only with diastolic blood pressure ($P=0.0004$) and was not significant for systolic blood pressure. For women the relation remained strong for systolic blood pressure ($P=0.0002$), and was only of borderline significance for diastolic blood pressure.

The fully adjusted relative risks in figure 1 are from a model that contains a large number of often related variables. The disappearance of a significant effect of low blood pressure, however, had already been seen in models containing only a few strong predictors of mortality, such as age, sex, type of residence, and concentrations of serum albumin. When the score on the minimal state examination was included in the model the relative risks of dying associated with low blood pressure decreased; this finding is similar to the results of a study done in a younger population.¹⁵ The disappearance of a significant effect was not due to the exclusion of subjects with missing data on the additional variables.

When data were analysed by cause of death and only age and sex were adjusted for, a significant inverse relation was observed between systolic blood pressure and death from other causes (that is, not cardiovascular causes, cancer, or infection). When health status was also adjusted for, this relation was no longer significant. However, a significant positive relation between higher diastolic blood pressure and an increased risk of dying from stroke and all cardiovascular causes was observed when adjusting for age, sex, and health status.

Discussion

In a population of 85 year olds we found an inverse relation between blood pressure and all cause mortality; this was consistent with the findings of a study of 85 year olds in Finland.^{7,8} Our data show, as have other studies,^{8,16} that poor health was more common in those with low blood pressure. It is unclear how much of this relation may be a result of poor health causing lower blood pressure (for example, by impairing cardiac function), or if it may have occurred because those who live to age 85 despite having high blood pressure are a highly selected group of healthy individuals. However, the inverse relation between blood pressure and all cause mortality disappeared after adjustment for health status.

No clear relation between blood pressure and all cause mortality was observed after frailty and poor health were adjusted for; this is in contrast to a study in a younger population with a mean age of 74 years.¹⁶ We found a positive relation between diastolic blood pressure and mortality from all cardiovascular causes and mortality from stroke after adjusting for poor health. One possible explanation for this discrepancy between our study and others¹⁶ is the older age of our subjects. The little evidence that is available from clinical trials on hypertension in very elderly people^{1,2} indicates that there is a reduced effect of treatment as patients get older, possibly because the survival gained by treating hypertension becomes negligible when compared to the high overall mortality among very elderly people.

All cause mortality as a measure of outcome is not specific enough to detect the effect of differences in blood pressure. This would be consistent with our finding that after adjusting for health status there was a positive relation between diastolic blood pressure and

Key messages

- Among community residents aged 85 and older there was a paradoxical inverse relation between blood pressure and all cause mortality: higher blood pressure was associated with lower mortality
- This inverse relation seems mainly to be due to higher mortality in those with low blood pressure; low blood pressure seems to be caused by poor health
- There was no longer a significant relation between blood pressure and all cause mortality after adjusting for health status. However, there was a positive relation between diastolic blood pressure and mortality from both cardiovascular causes and stroke
- Treating hypertension does not shorten life expectancy among elderly people aged 85 and older, and it might prevent disability from stroke

mortality from both cardiovascular causes and stroke. Another explanation might be that the variables measured in this study do not completely account for all aspects of poor health. For instance, many elderly people have had silent myocardial infarctions or have tumours that are undiagnosed and thus these types of diseases would not have been registered in this study. The last possible explanation is the inaccuracy caused by using a single, unstandardised measurement of blood pressure. This might bias the observed relative risks in the direction of unity. However, the fact that we observed a clear effect of low blood pressure on mortality indicates that the measurements are accurate enough to detect some effects.

In this study data were available on mortality, but not on the incidence of functional impairment or disability during the follow up period (for example, from non-lethal strokes or heart failure). We observed that—health status being equal—mortality from stroke was associated with high blood pressure. Therefore, it is likely that the incidence of functional impairment and disability from stroke will be similarly associated with high blood pressure. Thus, people aged 85 or older may benefit from treatment for hypertension even if it is not useful in prolonging life, because it might prevent disability.

Whether it is wise to prescribe antihypertensive treatment to mildly hypertensive people older than 80 can only be determined by randomised clinical trials. In the meantime this epidemiological study indicates that treating hypertension does not decrease life expectancy and it might prevent functional impairment.

Contributors: HCB reviewed the literature, analysed the data, interpreted results, wrote the paper, and is guarantor for the paper. GJI discussed core ideas, provided technical assistance with the Leiden 85 plus database, participated in the interpretation of the results and in writing the paper. SvB helped analyse the data (particularly the multiple imputations), interpreted the results, and participated in writing the paper. GJL supervised activities, discussed core ideas, participated in the interpretation of the results and in writing the paper. AM Lagaay was responsible for the baseline population survey of the Leiden 85 plus study and together with WCA van Beek she collected the baseline data. RGJ Westendorp provided assistance with the analysis of the data on the causes of death and commented on the manuscript.

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Conflict of interest: None.

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Lone atrial fibrillation in vigorously exercising middle aged men: case-control study

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Introduction

Regular physical exercise reduces cardiovascular morbidity.^{1,2} However, our clinical impression is that atrial fibrillation is quite common in otherwise healthy middle aged men engaged in long term vigorous

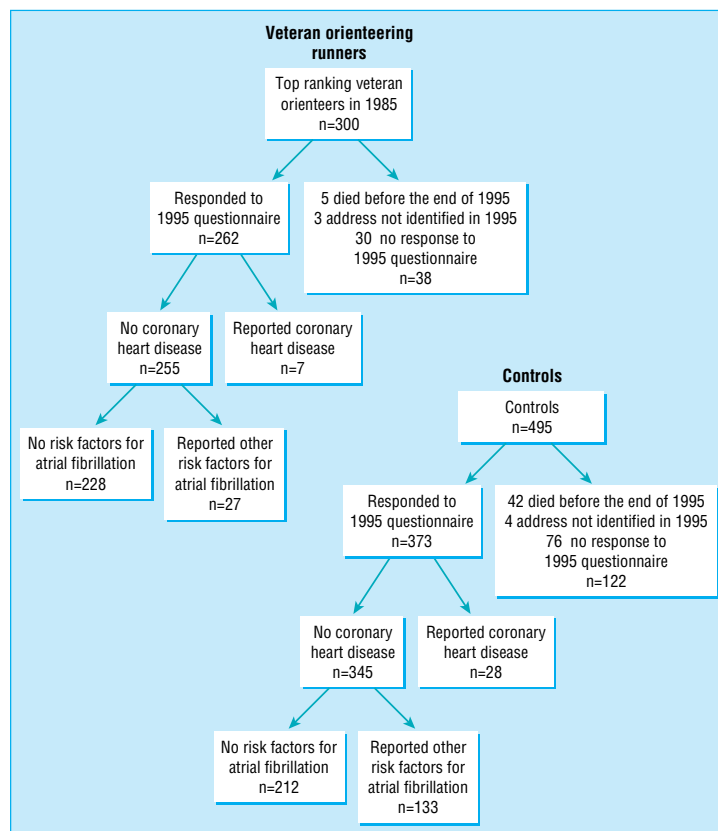
endurance sports. We therefore compared the prevalence of atrial fibrillation in middle aged men doing intense endurance training and men from the general population.

Subjects, methods, and results

We chose top level veteran orienteers to represent subjects doing long term vigorous exercise. A high position in the veteran ranking list is an indicator of years of intense training. We enrolled the 60 top ranked orienteers in 1984 from the race classes age 35-39 years, 40-44 years, 45-49 years, and 55-59 years, a total of 300 runners. The 495 controls comprised all men aged 35-59 enrolled for an earlier study.² At 20 years old these subjects had been completely healthy (fully fit for military service). Mean (SD) age at baseline was 47.5 (7.0) years in orienteers and 49.6 (5.3) years in controls. Controls had responded in 1985 to a questionnaire which included items on physical activity and occurrence of various diseases.²

In 1995 we sent a similar questionnaire to the orienteers and controls but which contained an additional question on cardiac arrhythmias: "Has a doctor ever told you that you have atrial fibrillation or atrial flutter?" Those who answered "yes" completed another detailed questionnaire on atrial fibrillation, and electrocardiograms and other data were obtained from their medical records to confirm the diagnosis. We excluded all subjects who reported known risk factors for atrial fibrillation.³

Ninety per cent (262) of the orienteers and 83% (373) of the controls responded to the questionnaire (figure). Compared with the general population orienteers had much lower mortality (1.7% (95% confidence interval 0.5 to 3.8%) v 8.5% (6.2% to 11.3%)), lower reported coronary heart disease since 1985 (2.7% (1.1 to 5.4%) v 7.5% (5.1% to 10.7%)), and fewer risk factors for atrial fibrillation (figure). However, in men without known risk factors, lone atrial fibrillation had been



Flow chart of study. Other risk factors for atrial fibrillation were hypertension, myocardial or valve disease, diabetes, thyroid disorder, and severe obesity