Association Between Blood Pressure and Survival over 9 Years in a General Population Aged 85 and Older

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OBJECTIVES: To investigate the association between blood pressure and mortality in people aged 85 and older.

DESIGN: Population-based prospective study with 9-year follow-up.

SETTING: Department of Neuroscience and Neurology and Department of Public Health and General Practice, University of Kuopio, and Department of Clinical Neurosciences, Helsinki University Hospital.

PARTICIPANTS: Of all 601 people living in the city of Vantaa born before the April 1, 1906, whether living at home or in institutions and alive on April 1, 1991, 521 were clinically examined and underwent blood pressure measurement.

MEASUREMENTS: Blood pressure was measured using a standardized method in the right arm of the subject after resting for at least 5 minutes. Information on medical history for each participant was verified from a computerized database containing all primary care health records. Death certificates were obtained from the National Register; the collection of death certificates was complete.

RESULTS: After adjusting for age, sex, functional status, and coexisting diseases (earlier-diagnosed myocardial infarction, congestive heart failure, dementia, cancer, stroke, or hypertension), low systolic blood pressure (BP) was associated with risk of death.

CONCLUSION: Low systolic BP may be partially related to poor general health and poor vitality, but the very old may represent a select group of individuals, and the use of BP-lowering medications needs to be evaluated in this group. **J Am Geriatr Soc 54:912–918, 2006.**

Key words: elderly; blood pressure; survival

The association between blood pressure (BP), cardiovascular morbidity, and all-cause mortality has been investigated in several studies in old people.[1–11] In some studies, the mortality rate has been highest in people with the lowest BP (i.e., there is an inverse association).[1,3–5,11–14] Others have found a positive linear[2,9,10] or J- or U-shaped association.[7,15–18] Some studies indicate that systolic and diastolic BP may have different effects as predictors of death,[8–10,18,19] but most studies have included subjects aged 65 and older, and the number of very old subjects ($\geq$85) has been limited. Some studies have shown a modest association between hypertension and cardiovascular disease but not all-cause mortality in subjects aged 75 to 85.[20] The greater mortality in subjects with low BP has been considered to be mainly due to confounding chronic illnesses such as cardiovascular diseases (e.g., cardiac failure and cardiac myopathies) or cancer and other terminal illnesses such as dementia.[6,7,21–23] In these cases, low BP has been interpreted as being a marker of approaching frailty or imminent death.[24]

The proportion of the very old among the elderly population is increasing in Western societies. Clinical trials have shown that treatment of hypertension is beneficial in some older people, particularly in those who are "young old" and those with raw comorbidities,[25] although the number of the very old included in these studies has been limited. From a public health perspective, it is important to know whether high BP is a risk factor for all-cause mortality or cardiovascular mortality also in the very old. If so, it is important to determine whether treatment of high BP is beneficial in the very old. The present population-based study examined the association between BP and all-cause mortality in a general population aged 85 and older during 9 years of follow-up, taking into account several important confounders such as clinically significant diseases and functional status.

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METHODS AND SUBJECTS

The Vantaa 85+ Study[26–28] is a prospective, longitudinal, population-based study including all residents of Vantaa, a typical industrial city in southern Finland, aged 85 and older (N = 601) on April 1, 1991 (Figure 1). The aim of the study was to examine the epidemiology and prognosis of diseases and functional capacity in very elderly people.

The whole population of Finland is approximately five million, and Vantaa is the fourth-largest city in the country, with 155,000 inhabitants. Very old subjects ($\geq$85) represent approximately 0.4% of the total population, somewhat more than the average (0.2%) in Finland. All subjects aged 85 and older, whether living in institutions or at home, were invited to participate. The final cohort included 553 (92%) individuals, 36 persons died before the clinical examination, 11 refused to participate, and one could not be reached. Of these 553 clinically examined subjects, BP measurement was available for 521 (86.7%). The baseline clinical examinations took place between April 1, 1991, and March 12, 1992, and the follow-up evaluations were conducted in 1994, 1996, and 1999. Informed consent was obtained from all participants or from a close relative. The ethics committee of the city of Vantaa approved the study.

The evaluation included an interview by a trained nurse and clinical examination performed by a physician. The interview was performed using a structured questionnaire consisting of questions concerning health, health-related behavior, and medication. Cognitive functions were assessed using the Mini-Mental State Examination,[29] depression was assessed using the Zung depression scale,[30] and functional abilities were assessed using the activity of daily living[31] and instrumental activity of daily living[32] scales. Physical examination included cardiac auscultation, BP measurement, and neurological examination. An ambulatory electrocardiogram was also performed. The evaluating neurologist measured BP once using a calibrated mercury sphygmomanometer with a cuff of appropriate size on subjects' right arms. Subjects had rested and remained seated for at least 5 minutes before the measurement. The BP of bedridden subjects was measured in a recumbent position. Korotkoff Phase I was determined as systolic BP (SBP) value and Phase V as diastolic BP (DBP).

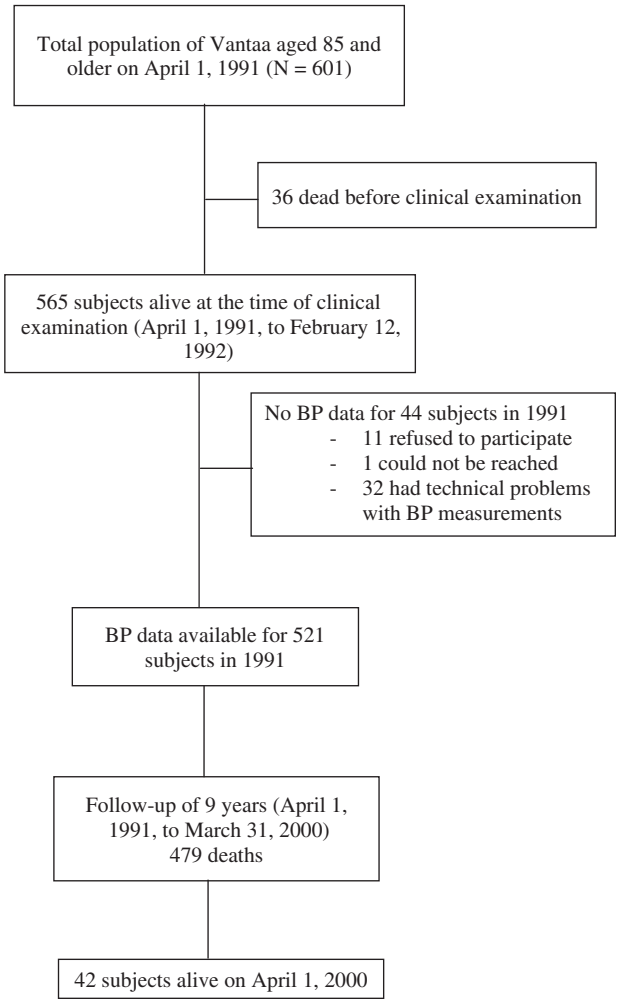

Figure 1. Study flow. BP = blood pressure.

Information on medical history for each participant was verified from a computerized database containing all primary care health records. The use of medications lowering BP was determined based on report from the patient, a relative, or the institution and from an electronic primary healthcare database. These drugs included diuretics, alpha- and beta-blockers, angiotensin-converting enzyme inhibitors, and calcium channel blockers. The history of clinically significant diseases such as hypertension, diabetes mellitus, congestive cardiac failure, myocardial infarction (MI), peripheral arterial disease, and cancer were based on health records. The evaluating neurologist diagnosed dementia clinically according to the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised,* criteria. The presence of stroke was based on clinical neurological findings indicating previous stroke in the health records. Information concerning death, date of death, and cause of death were obtained from the national computerized death certificate register, which contains data on all deaths occurring in Finland. The cause of death was based on the information on the death certificates. The general practitioners or other physicians who had been responsible for treatment of the deceased or the pathologist who had performed an autopsy filled in these forms and sent them to the central registry. The death certificate data used in this article were collected up to March 31, 2000.

The data were analyzed using SPSS for Windows, Release 10.0.7 (SPSS Inc., Chicago, IL). Risk of death was assessed using relative risk or hazard ratios (HRs) and 95% confidence intervals (CIs). SBP was divided into three groups: below 140 mmHg (low SBP), 140 to 159 mmHg (reference group), and 160 mmHg or over (high SBP). The categories for DBP were less than 80 mmHg, 80 to 89 mmHg (reference group), and 90 mmHg or over, respectively. For the analysis of risk, all deaths that occurred during the 9-year follow-up period were analyzed. The association between death and BP was analyzed using Cox proportional hazards model adjusted for age, sex, education, underlying concomitant diseases (hypertension, MI, congestive heart failure, arteriosclerosis, diabetes mellitus, cancer, dementia, stroke, depression) and other confounding factors such as smoking, alcohol consumption, BP-lowering medication, functional status (independent in daily living or not), and their interactions. All terms were inserted in the model, and the terms of lowest statistical

significance were manually stepwise rejected. If a major term was to be removed but was a member of an interaction term, it was left in the model. Kaplan-Meier life-table analysis was also performed.

RESULTS

Table 1 gives sociodemographic data of the study population. At baseline, the mean age of the participants was 88.8 (range 85–103.5); 411 (79%) were female. There were no differences in average age or of sex distribution between the participants and the nonparticipants. Although the nonparticipants were more often living in an institution, there was no significant difference in the need for help in daily living between the groups. This may be due to the fact that service housing and living in nursing homes were considered to be institutional living. Women needed more help in daily living and were more likely to be living in an institution than men, probably because they were older (Table 1).

Figure 2 shows the distribution of participants into different SBP categories. The mean SBP ± standard deviation and DBP values were 149 ± 27.7 mmHg (range 90–230 mmHg) and 82 ± 12.7 mmHg (range 45–125 mmHg), respectively (Table 1). There were no significant differences in SBP or DBP between those who used BP-lowering medication (n = 263) and those who did not (n = 258). Most subjects (n = 205) were using only one BP-lowering medication, but 58 were taking two or more such medications. Two hundred ten (40.3%) subjects were taking a diuretic, 55 (10.6%) a calcium channel blocker, 49 (9.4%) a beta-blocker, and 13 (2.5%) an angiotensin-converting enzyme inhibitor.

SBP was higher in women than in men ($P = .02$), but there was no difference in DBP between the sexes. Women were more likely to have previously diagnosed hypertension (27.7%) than men (18.2%) ($P = .04$) and more often used BP lowering medication (52.6%) than men (42.7%).

The mean length of follow-up was 3.5 years before death, the longest being 9 years; the survey accounted for 1,817.9 person-years. Four hundred seventy-nine (86.6%) participants died during follow-up; the mean mortality rate was 263.5 deaths per 1,000 person-years.

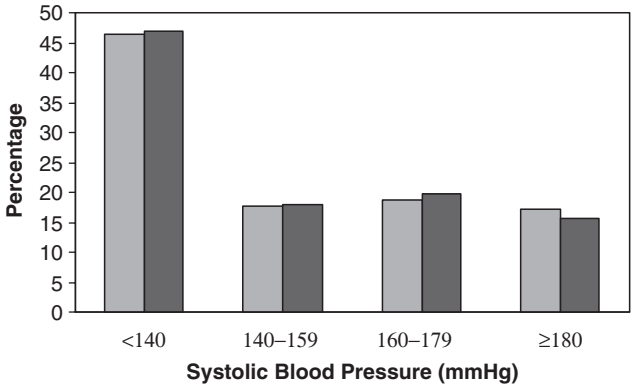

Figure 2. Distribution of the participants into different systolic blood pressure (BP) categories. Left column represent subjects not using BP-lowering medication, and right column represents subjects using BP-lowering medication.

Univariate analyses suggested that age, cancer (HR = 1.49, 95% CI = 1.10–2.02), diabetes mellitus (HR = 1.34, 95% CI = 1.08–1.67), dementia (HR = 2.17, 95% CI = 1.80–2.62), cardiovascular disease (MI, cardiac insufficiency, or stroke), SBP less than 140 mmHg (HR = 1.52, 95% CI = 1.22–1.90), DBP less than 80 mmHg (HR = 1.18, 95% CI = 0.94–1.48), and low functional status (HR = 0.47, 95% CI = 0.38–0.57) were associated significantly with risk of death (Table 2). In multivariate analysis, only smoking (HR = 1.97, 95% CI = 1.09–3.52), functional status (HR = 0.56, 95% CI = 0.42–0.76), cancer (HR = 1.42, 95% CI = 1.00–2.03), dementia (HR = 1.47, 95% CI = 1.15–1.88), stroke (HR = 1.80, 95% CI = 1.37–2.37), and SBP less than 140 mmHg remained significantly associated with mortality. The risk of death was highest in the group of subjects with SBP less than 140 mmHg (HR = 1.35, 95% CI = 1.04–

Table 1. Sociodemographic Characteristics of Participants and Nonparticipants

	Participants				Nonparticipants	
Characteristic	Men (n = 110)	Women (n = 411)	Total (N = 521)	*P*-value	Total (n = 80)	*P*-value
Age, mean ± SD	88.5 ± 2.6	88.9 ± 2.9	88.8 ± 2.8	.2	88.6 ± 3.2	.5
Age, %						
85–89	80.9	76.6	77.5	.6	75.0	.8
90–94	16.4	19.0	18.5		21.2	
≥95	2.7	4.4	4.0		3.8	
Education						
Years, mean ± SD	4.8 ± 3.7	4.0 ± 2.7	4.2 ± 3.0	.02	3.4 ± 1.5	.4
<Primary school, %	20.8	23.9	23.2	.3	28.6	.4
Living at home, %	69.1	56.2	58.9	.02	32.5	<.001
Fully independent, %	22.7	14.6	16.3	.04	12.5	.4
Blood pressure, mmHg, mean ± SD						
Systolic	144.0 ± 23.6	150.0 ± 28.6	149 ± 27.7	.02	—	
Diastolic	80.0 ± 10.7	82.0 ± 13.2	82 ± 12.7	.2	—	

SD = standard deviation.

Table 2. Relative Risk of Death Calculated Using Univariate and Multivariate Cox Proportional Hazards Models

Risk Factor	Univariate	Multivariate
	Hazard Ratio (95% Confidence Interval)	
Age		
85–89	1	1
90–94	1.10 (0.87–1.38)	1.24 (0.96–1.61)
≥95	1.21 (0.78–1.88)	1.44 (0.87–2.40)
Male	0.95 (0.76–1.18)	0.78 (0.60–1.01)
Education > 6 years	1.08 (0.77–1.50)	0.95 (0.66–1.34)
No alcohol use	0.64 (0.51–0.80)	0.82 (0.64–1.05)
Smoking	1.13 (0.65–1.96)	1.97 (1.09–3.52)
Fully independent	0.47 (0.38–0.57)	0.56 (0.42–0.76)
Cancer	1.49 (1.10–2.02)	1.42 (1.00–2.03)
Dementia	2.17 (1.80–2.62)	1.47 (1.15–1.88)
Stroke	2.26 (1.80–2.83)	1.80 (1.37–2.37)
Myocardial infarction	1.30 (1.01–1.68)	1.22 (0.91–1.64)
Arteriosclerosis	1.16 (0.85–1.58)	0.92 (0.63–1.33)
Hypertension	0.97 (0.79–1.19)	1.06 (0.83–1.34)
Congestive heart failure	1.56 (1.30–1.88)	1.23 (0.91–1.64)
Diabetes mellitus	1.34 (1.08–1.67)	1.27 (0.98–1.63)
Blood pressure, mmHg		
Systolic		
<140	1.52 (1.22–1.90)	1.35 (1.04–1.74)
140–159	1	1
≥160	0.85 (0.68–1.05)	0.97 (0.76–1.24)
Diastolic		
<80	1.18 (0.94–1.48)	1.11 (0.86–1.42)
80–89	1	1
≥90	0.81 (0.65–1.02)	0.75 (0.59–0.96)

1.74; $P = .02$). There was a tendency toward lower mortality in those with SBP of 160 mmHg or greater (HR = 0.97, 95% CI = 0.76–1.05). There was no significant association between mortality and DBP less than 80 mmHg (HR = 1.11, 95% CI = 0.86–1.42) or DBP of 90 mmHg or greater (HR = 0.75, 95% CI = 0.59–0.96) (Table 2). A history of hypertension (HR = 1.06, 95% CI = 0.83–1.34) and use of BP-lowering medication (HR = 1.16, 95% CI = 0.92–1.45) were not related to mortality.

SBP less than 140 mmHg was associated with the risk of death in men and women. The effect of SBP less than 140 mmHg was most obvious during the first 2 follow-up years (Figure 3). Subjects with SBP less than 140 mmHg did not survive as long as subjects with higher SBP. The association was particularly strong in subjects who did not have dementia, cancer, or a history of stroke (Table 3).

DISCUSSION

In this large cohort of very old people (≥85), there was an association between all-cause mortality and SBP less than 140 mmHg even after adjusting for age sex, functional status (activities of daily living), dementia, cancer, and cardiovascular diseases. In contrast to some previous studies,[11,13] this association was found for both sexes. The association was statistically significant in the youngest age group (85–89), but the trends were similar in the older age groups. The lack of significance was probably due to the small number of subjects aged 90 and older.

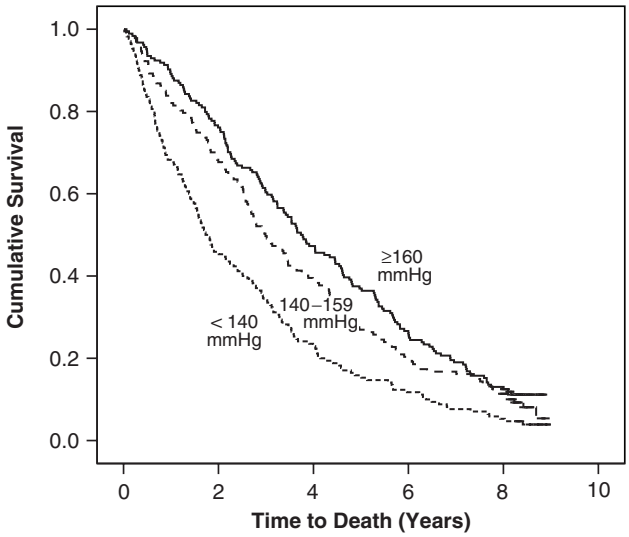

Figure 3. Systolic blood pressure and time to death analyzed using Kaplan-Meier life-table analysis.

Previous studies reporting the association between BP and mortality have shown inconsistent results,[25] but subjects aged 85 and older have seldom been the target of prospective studies. Some studies such as the Kungsholmen project[13] and the Framingham Study[6] have included participants aged 75 and older and have reported a greater relative risk of death in subjects with low SBP and DBP. Previous Finnish studies[1,3] have detected the highest mortality in those subjects with low SBP and DBP, although one study[1] did not analyze the possible confounders for this relationship, and the number of very old subjects in the other study was small.[3] Several strengths of the present study allow reliable conclusions to be drawn. The participation rate was exceptionally high (92%), institutionalized and home-dwelling people were included, the follow-up time was long (up to 9 years), and collection of information of deaths was complete. No corrections were used to reduce the possibility of a type 1 error from multiple comparisons, and it is possible that some associations occurred by chance. However, the association between low SBP and mortality is likely to be a true relationship, because it was consistently found in all tested subgroups, even after controlling for biologically relevant confounders.

The explanation for the association between low SBP and mortality remains unclear. Aging is associated with many functional and structural alterations to the cardiovascular system that may affect BP. The association with mortality in subjects with low BP has been considered to be mainly due to concomitant underlying diseases, particularly cardiovascular disease (e.g., cardiac failure and cardiac myopathies).[6,7,22,23] In these cases, low BP is interpreted as a marker of approaching frailty or imminent death.[24] In the present study, cardiac failure was more common in subjects with SBP less than 140 mmHg (68.3%) than in those with higher SBP (58.5%). Also, mean SBP was lower in subjects with a history of MI or stroke than in those without cardiovascular disease (data not shown), although the effect

Table 3. Mortality of Subjects with Concomitant Diseases Subdivided According to Blood Pressure Categories

Systolic Blood Pressure, mmHg	n	Deceased, n	Length of Follow-Up Py	Mortality/1,000 Py	Odds Ratio (95% Confidence Interval)	
History of hypertension						
Total	134	124	478.4	259.2		
<140	26	26	51.9	500.7	1.87	(1.13–3.08)
140–159	39	37	137.9	268.3	ref	
≥160	69	61	288.6	211.4	0.79	(0.52–1.18)
Stroke						
Total	102	102	221.0	461.5		
<140	42	42	77.9	539.2	1.27	(0.79–2.03)
140–159	30	30	70.6	425.2	ref	
≥160	30	30	72.5	413.8	0.97	(0.59–1.61)
Myocardial infarction						
Total	77	72	218.5	329.5		
<140	31	31	65.2	475.4	1.84	(1.06–3.21)
140–159	23	21	81.5	257.8	ref	
≥160	23	20	71.9	278.2	1.08	(0.58–1.99)
Cardiac failure						
Total	321	287				
<140	41	40	29.8		0.22	(0.15–0.30)
140–159	176	160	138.6		ref	
≥160	104	87	204.0		1.47	(1.13–1.91)
Dementia						
Total	188	185	442.2	418.4		
<140	92	90	182.7	492.5	1.28	(0.92–1.78)
140–159	57	57	147.6	386.3	ref	
≥160	39	38	111.9	339.7	0.89	(0.59–1.34)
Cancer						
Total	49	47	126.5	371.5		
<140	17	17	35.5	479.0	1.01	(0.51–1.97)
140–159	17	17	35.7	475.8	ref	
≥160	15	13	55.3	234.9	0.49	(0.24–1.02)
No hypertension						
Total	387	355	1,339.5	265.0		
<140	144	137	391.3	350.1	1.42	(1.11–1.82)
140–159	128	116	472.1	245.7	ref	
≥160	115	102	476.1	214.1	0.87	(0.67–1.14)
No stroke						
Total	419	377	1,596.9	236.1		
<140	128	121	365.3	331.2	1.45	(1.13–1.87)
140–159	137	123	539.4	228.0	ref	
≥160	154	133	692.2	192.1	0.84	(0.66–1.08)
No infarction						
Total	438	401	1,585.4	252.9		
<140	138	131	377.1	347.4	1.41	(1.10–1.79)
140–159	141	129	522.3	247.0	ref	
≥160	159	141	685.9	205.6	0.83	(0.66–1.06)
No cardiac failure						
Total	200	152				
<140	15	14	38	368.9	2.00	(1.13–3.52)
140–159	104	80	433.1	184.7	ref	
≥160	81	58	361.3	160.5	0.87	(0.62–1.22)
No dementia						
Total	333	294	1,375.8	213.7		
<140	78	73	260.5	280.2	1.35	(1.00–1.83)
140–159	110	96	462.4	207.6	ref	
≥160	145	125	652.9	191.5	0.92	(0.71–1.20)
No cancer						
Total	472	432	1,691.4	255.4		
<140	153	146	407.8	358.1	1.51	(1.20–1.91)
140–159	150	136	574.2	236.8	ref	
≥160	169	150	709.4	211.5	0.89	(0.71–1.13)

Py = person-years, ref = reference.

of low SBP remained significant after adjusting for these diseases as confounders. Low BP may also be considered to be a sign of poor general health and decreased vitality, and it may be associated with deaths from noncardiovascular causes such as cancer or dementia.[7,13] The inverse correlation between low BP and mortality has disappeared in some studies after adjustment for indicators of poor health.[25] The association between BP and mortality in the present study was not independent of coexisting diseases, but in contrast to some studies,[13] the effect of low SBP on mortality was more evident in those subjects without cancer, dementia, or a history of stroke than in those with these disorders. One previous study including a large community cohort aged 65 and older found that low BP was related to excess deaths within the first 3 years of follow-up.[2] These results agree with the results of the current study showing that greater mortality was particularly evident during the first 2 years of follow-up.

In addition to mortality, BP is a significant contributor to cardiovascular morbidity and has also been associated with cognitive decline. Isolated systolic hypertension is an established risk factor for stroke at least in younger old subjects.[25] The present study focused on the association between BP and mortality. The complex relationship between BP, stroke and cognition is currently being analyzed in this population. Clinical trials have demonstrated that treatment of hypertension in some categories of older people (relatively young old and those with little comorbidity) decreases total and cardiovascular mortality,[25] but the numbers of the very old in these trials have been small. With increasing age, there are generalized structural and functional changes in arterial circulation that contribute to alterations in regional blood flow and progression of atherogenesis and may lead to microvascular abnormalities.[33,34] Sufficiently high BP may be necessary to guarantee adequate cardiac and cerebral perfusion. Two large trials (the European Working Party on High Blood Pressure in the Elderly Study and the European Trial on Isolated Systolic Hypertension in the Elderly) showed that the benefit of treatment for high SBP with regard to mortality was lost in very old ($\geq$80) subjects and that mortality was actually higher in the treatment group.[35–37] However, antihypertensive treatment was able to prevent cardiovascular complications, stroke, and cardiac events (e.g., MI).[36] Preliminary results from the Hypertension in the Very Elderly Trial suggest that excess all-cause mortality in the active treatment group may have outweighed the benefit from reduction in stroke events.[38] The current study is an observational epidemiological study, and thus it is not possible to draw conclusions about the benefits of treatment of hypertension. Approximately 15% of all participants had SBP of 180 mmHg and higher, but the risk of death was even lower in these subjects than in those with SBP of 160 to 179 mmHg (data not shown). Mean SBP was lower in subjects with a history of MI or stroke than in those without these comorbidities. One explanation for this may be that BP was more intensely treated in the subjects with cerebrovascular complications than in those without. The use of BP-lowering medication in these subjects was not associated with mortality.

The results of the present epidemiological study showed that risk of death in subjects aged 85 and older was associated with low SBP. The focus of the study was on mortality, and conclusions cannot be drawn about the treatment of BP and cardiovascular morbidity. It is possible that the very old represent a select group of individuals, and the results from clinical trials including younger participants should be applied cautiously and individually in the very old.

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Author Contributions: Sari Rastas: study design, acquisition of subjects, interpretation of data, preparation of manuscript. Tuula Pirttilä: study concept and design, preparation of manuscript, interpretation of data. Petteri Viramo: acquisition of subjects, preparation of manuscript. Auli Verkkoniemi: study concept and design, acquisition of subjects, preparation of manuscript. Pirjo Halonen: analysis and interpretation of data. Kati Juva: interpretation of data, preparation of manuscript. Leena Niinistö, Esko Länsimies, Raimo Sulkava: study concept and design, preparation of manuscript. Kimmo Mattila: study design, preparation of manuscript.

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