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# Low blood pressure and dementia in elderly people: the Kungsholmen project

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### See editorial and p 801 Abstract

*Objective*—To examine the relation between blood pressure and dementia in elderly people.

Design—Cross sectional, population based study. Setting—Kungsholmen district of Stockholm, Sweden.

Subjects-1642 subjects aged 75-101 years.

Main outcome measures—Prevalence and adjusted odds ratio of dementia by blood pressure.

Results-People with systolic pressure ≤140 mmHg were more often diagnosed as demented than those with systolic pressure >140 mm Hg: odds ratios (95% confidence interval) adjusted for age, sex, and education were 2.98 (2.17 to 4.08) for all dementias, 2.91 (1.93 to 4.38) for Alzheimer's disease, 2.00 (1.09 to 3.65) for vascular dementia, and 5.07 (2.65 to 9.70) for other dementias. Similar results were seen in subjects with diastolic pressure  $\leq 75$  mmHg compared with those with higher diastolic pressure. When severity and duration of dementia were taken into account, only moderate and severe dementia were found to be significantly related to relatively low blood pressure, and the association was stronger in subjects with longer disease duration. Use of hypotensive drugs and comorbidity with cardiovascular disease did not modify the results for all dementias, Alzheimer's disease, and other dementias but slightly reduced the association between vascular dementia and diastolic blood pressure.

*Conclusions*—Both systolic and diastolic blood pressure were inversely related to prevalence of dementia in elderly people. We think that relatively low blood pressure is probably a complication of the dementia process, particularly Alzheimer's disease, although it is possible that low blood pressure may predispose a subpopulation to developing dementia.

Introduction

Blood pressure may be related to dementia in different ways. High blood pressure is recognised as the most powerful risk factor for cerebrovascular disease.<sup>1</sup> Since cerebrovascular disease is the main cause of vascular dementia,<sup>2</sup> it is generally believed that high blood pressure is also the most important risk factor for vascular dementia.<sup>3</sup> But this widely accepted view lacks direct evidence from population studies.<sup>4</sup> On the other hand, clinical observations have shown that episodes of hypotension can result in cerebral hypoperfusion, which may play a causative role in the development of dementia.<sup>56</sup> Furthermore, recent studies have observed that patients with Alzheimer's disease had lower arterial blood pressures than people without dementia,<sup>78</sup> suggesting that blood pressure decreases during the course of Alzheimer's disease.<sup>9</sup> None of these hypotheses for the relation between blood pressure and dementia is supported by strong evidence. Further investigations, especially population studies, are necessary.

The aim of this study was to examine whether blood pressure is a determinant of the prevalence of dementia in a community based population of people aged 75 and over.

#### Subjects and methods

DATA COLLECTION

This report is based on cross sectional data from the Kungsholmen project-a longitudinal study of aging and dementia targeting all the inhabitants of the Kungsholmen district of Stockholm who were aged 75 or more on 1 October 1987.10 Of the eligible subjects, 1810 (77%) participated in the initial survey. Cases of dementia were detected by means of a two phase process: a screening phase and a clinical examination phase. Dementia was defined according to the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, third edition, revised.11 Details of the clinical examination and diagnostic procedure are given elsewhere.<sup>12 13</sup> Severity of dementia was determined according to the clinical dementia rating scale,14 with some modifications.<sup>15</sup> The age when symptoms of dementia first appeared was estimated from information given by an informant, and the duration of the disease was the difference between the date when symptoms started and the date of the screening test.

Arterial blood pressure (systolic Korotkoff phase I and diastolic phase V) was measured with a mercury sphygmomanometer and with the subject sitting after having rested for five minutes. Subjects' educational levels were based on formal schooling and were divided into two categories in the analyses (<8 years and  $\geq$ 8 years). Subjects were considered to be taking a drug if it had been used at any time in the two weeks before the interview. All drugs that potentially could be used for lowering blood pressure (anatomical therapeutic chemical (ATC) classification system,<sup>16</sup> codes C02, C03, and C07) were recorded as hypotensive drugs. If subjects were unable to provide reliable information an informant (relative, carer, or others) was required.

Information on the subjects' medical history was obtained from the computerised inpatient register, which covers all hospitals in the area of Stockholm. Cardiovascular disease (coronary heart disease, cardiac dysrythmia, heart failure, and stroke) was treated as a possible confounder.

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#### STATISTICAL METHODS

In our primary analysis we compared the mean blood pressures of demented subjects and those who were not demented by means of Student's t test and calculated the prevalence of dementia according to blood pressure. We estimated odds ratios from three multiple logistic regression models, all of which included adjustments for age, sex, and education. In the first model blood pressure was continuous variable (in increments of 10 mm Hg); in the second it was a dichotomous variable (systolic blood pressure  $\leq 140$  mm Hg v > 140 mm Hg, diastolic  $\leq 75$  mm Hg v

 Table 1—Mean (SD) systolic and diastolic blood pressure
 in elderly subjects by presence of dementia

	Blood pressure (mm Hg)		
	Systolic	Diastolic	
All dementias (n=202):	143 (25)**	76 (13)**	
Alzheimer's disease (n=112)	144 (23)**	77 (12)**	
Vascular dementia (n=45)	147 (28)*	76 (13)*	
Other dementias (n=45)†	138 (26)**	75 (14)**	
Not demented (n=1440)	156 (22)	81 (11)	
Total (n=1642)	154 (23)	81 (11)	

\*P<0.05; \*\*P<0.01 compared with those not demented. †Includes mixed dementia (3), unspecified type of dementia (11), secondary dementia (19), and questionable dementia (12).

 Table 2—Number (percentage) of elderly subjects with dementia by blood pressure

Blood pressure (mm Hg)	All dementias	Alzheimer's disease	Vascular dementia	Other dementias*	
Systolic:					
≤ 120 (n=142)	46 (32-4)	25 (17.6)	9 (6.3)	12 (8.5)	
121-140 (n=418)	69 (16-5)	38 (9-1)	12 (2.9)	19 (4-5)	
141-160 (n=531)	40 (7.5)	24 (4.5)	11 (2.1)	5 (0.9)	
161-180 (n=416)	37 (8.9)	20 (4-8)	10 (2.4)	7 (1.7)	
>180 (n=135)	10 (7-4)	5 (3.7)	3 (2.2)	2 (1.5)	
Diastolic:					
≤65 (n=186)	43 (23-1)	19 (10-2)	9 (4.8)	15 (8-1)	
66-75 (n=380)	62 (16-3)	36 (9-5)	14 (3.7)	12 (3.2)	
76-85 (n=623)	60 (9-6)	39 (6-3)	13 (2.1)	8 (1.3)	
86-95 (n=346)	27 (7.8)	13 (3-8)	7 (2.0)	7 (2.0)	
>95 (n=107)	10 (9.3)	5 (4-7)	2 (1.9)	3 (2-8)	

\*Includes mixed dementia (3), unspecified type of dementia (11), secondary dementia (19), and questionable dementia (12).

>75 mm Hg); and in the third it was an indicator variable, with four categories compared with the reference group (141-160 mm Hg and 86-95 mm Hg for systolic and diastolic pressure, respectively). We also used models 1 and 2 to examine the relation of blood pressure with severity of dementia (questionable or mild dementia v moderate or severe dementia) and its duration ( $\leq 5$  years v > 5 years). We used the spss statistical package for all calculations.<sup>17</sup>

## Results

Of the 1810 subjects who were screened, 1642 (91%) were included in this study—392 men and 1250 women with a mean (SD) age of 82.3 (5.1) years. The rest were excluded because of non-participation in the clinical examination (110) or because their blood pressure was not recorded (58). The 110 who did not participate in the examination included more people aged 85 or more than did the study population (47.3% v 29.1%), but there were no differences with regard to the sex ratio or systolic or diastolic blood pressure. The 58 subjects with a missing record of blood pressure were slightly older than the study population (proportion of those aged 85 or more, 37.9% v 28.7%) but had a similar sex ratio. Among them, there were nine people with Alzheimer's disease, seven with vascular dementia, and seven with other types of dementia. The study population included 202 subjects with dementia, giving an overall prevalence of 12.3% (202/1642). These subjects were affected by Alzheimer's disease (112), vascular dementia (45), mixed dementia (3), unspecified type of dementia (11), secondary dementia (19), and questionable dementia (12).

Table 1 shows that the subjects with dementia had lower mean systolic and diastolic blood pressures than those who were not demented. Table 2 shows the prevalence of dementia by blood pressure: a similar pattern occurred with both systolic and diastolic blood pressure, with the two groups with the lowest blood pressure having a higher prevalence of dementia.

Table 3 shows the adjusted odds ratios for dementia according to systolic and diastolic pressure derived from the three multiple logistic regression models. A significant linear trend existed between increase in systolic or diastolic blood pressure and decrease in odds ratio for any type of dementia. The odds ratio for any type of dementia was significantly higher among subjects with systolic blood pressure  $\leq 140 \text{ mm Hg or}$  diastolic pressure  $\leq 75 \text{ mm Hg than among those with higher blood pressures. Furthermore, the largest odds$ 

Table 3—Association between blood pressure and dementia among 1642 elderly people. Values are odds ratios (95% confidence interval) adjusted for age, sex, and education based on three multiple logistic regression models

	All dementias	Alzheimer's disease	Vascular dementia	Other dementias*
Systolic blood pressure				
Model 1 (continuous variable, per 10 mm Hg increment)	0·78 (0·72 to 0·84)	0.78 (0.71 to 0.86)	0.83 (0.73 to 0.96)	0.68 (0.59 to 0.79)
Model 2 (dichotomous variable, $\leq$ 140 v > 140 mm Hg)	2.98 (2.17 to 4.08)	2.91 (1.93 to 4.38)	2.00 (1.09 to 3.65)	5.07 (2.65 to 9.70)
Model 3 (indicator variable):				
≤ 120 mm Hg	5-26 (3-17 to 8-74)	4-59 (2-40 to 8-78)	3.66 (1.45 to 9.22)	10-82 (3-67 to 31-92)
121-140 mm Hg	2.45 (1.59 to 3.76)	2.35 (1.35 to 4.09)	1.53 (0.66 to 3.52)	5.31 (1.95 to 14.47)
141-160 mm Hg	1.00	1.00	1.00	1.00
161-180 mm Hg	1.14 (0.70 to 1.85)	1.04 (0.55 to 1.97)	1.08 (0.45 to 2.59)	1.69 (0.53 to 5.41)
>180 mm Hg	0.85 (0.41 to 1.79)	0.76 (0.28 to 2.08)	0.90 (0.24 to 3.30)	1.25 (0.24 to 6.57)
Diastolic blood pressure				
Model 1 (continuous variable, per 10 mm Hg increment)	0.72 (0.63 to 0.83)	0.76 (0.63 to 0.91)	0.70 (0.54 to 0.92)	0.62 (0.47 to 0.81)
Model 2 (dichotomous variable, $\leq 75 v 75 \text{ mm Hg}$ )	2.05 (1.50 to 2.80)	1.79 (1.19 to 2.69)	2.03(1.11  to  3.71)	3.01 (1.63 to 5.58)
Model 3 (indicator variable):	,		(	
≤65 mm Hg	3.17 (1.84 to 5.48)	3.05 (1.42 to 6.56)	2.46 (0.89 to 6.85)	4.05 (1.59 to 10.32)
66-75 mm Hg	2.16 (1.31 to 3.56)	2.51 (1.26 to 5.01)	1.96 (0.77 to 4.96)	1.80 (0.69 to 4.67)
76-85 mm Hg	1.31 (0.80 to 2.15)	1-80 (0-92 to 3-53)	1.09 (0.43 to 2.77)	0.67 (0.24 to 1.88)
86-95 mm Hg	1.00	1.00	1.00	1.00
>95 mm Hg	1.37 (0.63 to 2.98)	1.41 (0.48 to 4.17)	0.97 (0.20 to 4.81)	1.50 (0.38 to 5.97)

\*Includes mixed dementia (3), unspecified type of dementia (11), secondary dementia (19), and questionable dementia (12).

Table 4—Association between blood pressure and dementia among 1642 elderly people according to severity and duration of disease. Values are odds ratios (95% confidence interval) adjusted for age, sex, and education based on two multiple logistic regression models

	Severity of dementia*		Duration of dementia†	
	Questionable and mild (n=79)	Moderate and severe (n=117)	≤5 years (n=73)	>5 years (n=79)
Systolic blood pressure				
Model 1 (continuous variable, per 10 mm Hg increment)	0.92 (0.83 to 1.02)	0.68 (0.62 to 0.75)	0.83 (0.74 to 0.92)	0.69 (0.61 to 0.78)
Model 2 (dichotomous variable, $\leq$ 140 v > 140 mm Hg)	1.55 (0.97 to 2.47)	4·94 (3·42 to 7·54)	2.25 (1.39 to 3.62)	4-06 (2-50 to 6-59)
Diastolic blood pressure				
Model 1 (continuous variable, per 10 mm Hg increment)	1.02 (0.83 to 1.25)	0.56 (0.37 to 0.83)	0.80 (0.65 to 0.99)	0.65 (0.53 to 0.81)
Model 2 (dichotomous variable, $\leq$ 75 v > 75 mm Hg)	1.20 (0.75 to 1.93)	3.05 (2.04 to 4.58)	1.75 (1.08 to 2.83)	2-40 (1-50 to 3-82)
*Information missing for six patients.				

†Information missing for 50 patients.

ratios for dementia occurred in the two groups with lowest blood pressure when systolic and diastolic pressure were entered as indictor variables (model 3). High blood pressure (systolic > 160 mm Hg or diastolic >95 mm Hg) was not related to dementia.

Table 4 shows the relation between dementia and blood pressure according to the severity and duration of the disease. A significant inverse relation existed between blood pressure and dementia in moderate and severe cases but not in questionable and mild cases. With regard to the duration of dementia, a significant relation was found among the subjects with dementia for  $\leq 5$  years as well those with dementia for >5 years, but the association was stronger in the second group.

We repeated all the logistic regression analyses after including use of hypotensive drugs and presence of cardiovascular disease in the models to control for potential confounding effects. The adjustment had no substantial effect on the odds ratios for all dementias, Alzheimer's disease, and other dementias, but the association of vascular dementia with diastolic pressure was somewhat reduced.

### Discussion

In this large population based study we found a strong inverse association between both systolic and diastolic blood pressure and dementia. Relatively low blood pressure was related to higher prevalence of dementia. Significantly elevated odds ratio for dementia was seen among those with systolic pressure  $\leq$  140 mm Hg or diastolic pressure  $\leq$  75 mm Hg, who comprised 34.1% (560/1642) and 34.5% (566/1642) of all subjects in the study respectively. Use of hypotensive drugs and presence of cardiovascular disease could not account for the results. Because of the cross sectional design of the study, however, this association does not necessarily mean that low blood pressure is a risk factor for dementia. As the relation was stronger in those with a longer duration of disease and those with more severe dementia, the results may support the alternative explanation that relatively low blood pressure is caused by dementia. This may be true especially for Alzheimer's disease.

The observation that blood pressure is lower in people with Alzheimer's disease than in people without dementia has been reported previously,<sup>78</sup> but no mechanism for this reduction is known. Burke *et al* observed three patients with Alzheimer's disease over a long period and found that blood pressure decreased in all three patients; they postulated that blood pressure changes in Alzheimer's disease as the neurones which regulate it degenerate.<sup>9</sup> In addition, deficit in neurotransmitters which regulate blood pressure may also reduce blood pressure in Alzheimer's disease.<sup>18</sup> Reduced blood pressure may also be a consequence of some of the characteristics of Alzheimer's disease, such as lower blood glucose concentration,<sup>7 19</sup> weight loss,<sup>20</sup> and lower prevalence of history of smoking.<sup>21</sup>

BLOOD PRESSURE AS RISK FACTOR FOR DEMENTIA

Our results also show that low blood pressure was related to vascular dementia and other dementias. This may mean that blood pressure decreases during the course of vascular and other dementias. More importantly, however, it raises the possibility that low blood pressure may predispose a subpopulation to developing dementia since relatively low blood pressure was significantly associated with dementia even when it was of shorter duration (five years or less).

Another explanation for the association might be that, if we had misclassified subjects with high blood pressure as having a middle blood pressure level because of our single recording of blood pressure, people with high blood pressure or hypertension had a lower risk of developing dementia or Alzheimer's disease while those with low or middle level of blood pressure had the same higher risk. In fact, we did find that high blood pressure was unrelated to any type of dementia.

High blood pressure or hypertension may be no longer a risk factor for cerebrovascular events, and therefore for dementia, after the age of 75. It has been suggested that survival selection should be taken into account when interpreting results about the effect of high blood pressure in elderly people since many hypertensive people will have died before reaching old age.<sup>22</sup> It is also likely that people with cerebrovascular events due to hypertension may have lower risk of dementia that those with cerebrovascular events from other causes, even in other age groups. As stated above, our single reading of blood pressure should be considered when interpreting the results for high blood pressure.

Decreased cerebral blood flow is known to occur in both Alzheimer's disease and vascular dementia, and the degree of reduction generally correlates with the severity of dementia.<sup>23-25</sup> It seems possible that low blood pressure might accelerate the process of dementia by lowering cerebral blood flow. This mechanism could be reinforced by the dysfunction in autonomic nervous system observed in patients with Alzheimer's disease.<sup>8</sup> It is not known whether a reduction in blood pressure is correlated with the reduced cerebral blood flow found in dementia.

### POSSIBLE SHORTCOMINGS OF STUDY

There are three possible limitations in this report. First, the prevalence of dementia might have been underestimated because of people dropping out of the study in the screening and clinical examination phases. There is, however, no reason to think that such an underestimation would apply differently to the subjects with higher and lower blood pressure. Second, • Both dementia and disorders of blood pressure (high or low) are common in elderly people, and it has been suggested that they may be linked

We studied prevalence of dementia in 1642 subjects aged 75-101 and found that those with relatively low blood pressure (≤140 mmHg systolic, ≤75 mmHg diastolic) were significantly more likely to have dementia

• When severity and duration of dementia were taken into account, only moderate and severe dementia were found to be significantly related to low blood pressure, and the association was stronger in subjects with longer duration of disease

• Use of hypotensive drugs and comorbidity with cardiovascular disease could not account for the association

• We think that relatively low blood pressure is probably a complication of the dementia process, particularly Alzheimer's disease, but it is possible that low pressure may predispose some people to developing dementia

in spite of the high sensitivity of the mini-mental state examination<sup>26</sup> as a screening test for dementia, we estimated that 26 subjects were wrongly included in the group without dementia. But such a number of false negatives could not substantially change our results even if they all had relatively high blood pressure. Finally, the single measurement of blood pressure may diminish the accuracy of the data. Since such imprecision would bias the odds ratio towards unity, we may have underestimated the association between low blood pressure and dementia.

#### CONCLUSION

Our study shows that both systolic and diastolic blood pressure were inversely related to the prevalence of dementia in a population of elderly people. Although our results can be interpreted in different ways, we think that the most likely explanation is that blood pressure decreases during the course of Alzheimer's disease and that this may also be true for vascular and other dementias. Our results emphasise the need for further studies, particularly on the role of blood pressure in the actiology of dementia.

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# ONE HUNDRED YEARS AGO

THE GENERAL MEDICAL COUNCIL AND THE BRITISH MEDICAL ASSOCIATION.

We have noticed of late with much interest the revival of a healthy energy in the profession for the protection of the public against unqualified practitioners, and for the defence of its own individual and collective interests. Quite recently our columns contained a report of the hearing of the summons against Ferdinand, the self-styled "first physician in the world," and the important decision obtained in that case by the action of the Medical Defence Union. We have also reported two cases, in which fees and damages were recovered in the Manchester County Court from a "hernia specialist" and a "cancer curer." All these

three cases illustrate very effectively methods by which the public and the profession may be safeguarded by the wisely directed efforts of a voluntary medical organisation. The most noteworthy fact, however, is that the feeling which is stirring medical men has penetrated the hitherto inaccessible mind of the General Medical Council...

We congratulate the Council on the fact that, after thirty-six years of timid impotence, it has determined to use its powers. The Act of 1858 is likely to prove at length what its able authors meant it to be, a statute valuable not only for the improvement of medical education, but also, as its preamble states, for enabling "the public to distinguish between qualified and unqualified persons."