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Systolic and diastolic blood pressures as predictors of coronary heart disease in middle aged Norwegian men

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Abstract

Systolic and diastolic blood pressures were compared as predictors of mortality from coronary heart disease in Norwegian men aged 35-49. A total of 39 207 men were followed up for an average of 8·9 years; 385 died of coronary heart disease. Diastolic blood pressure seemed to be the better predictor, the difference being most pronounced in the age group 35-39. At this age 26% more deaths from coronary heart disease were found in the upper quintile of diastolic blood pressure compared with the upper quintile of systolic blood pressure. At ages 45-49 there were almost the same numbers of deaths from coronary heart disease in the upper quintiles of systolic and diastolic pressures.

These findings suggest that the relative predictive strength of systolic and diastolic blood pressure may be dependent on age. Furthermore, for very obese men the association between blood pressure and death from coronary heart disease is much weaker.

Introduction

The Whitehall study compared systolic and diastolic blood pressures as predictors of death from coronary heart disease.[1] The findings suggested that clinicians should pay more attention to systolic pressure as a criterion for making decisions. In the youngest age group (40-44), however, the pattern was reversed, diastolic pressure coming out (non-significantly) as the better predictor.

The Oslo and Tromsø cardiovascular studies combined with the study in Norwegian counties[2-4] provided a large body of data for men aged 35-49. This paper therefore examines the possible interaction of age with the relative strengths of systolic and diastolic pressures as predictors of death from coronary heart disease. In addition, the possible interaction between blood pressure and body mass index is examined in relation to death from coronary heart disease.

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Subjects and methods

In the Oslo heart study (1972-3)[2] all men aged 40-49 and a 7% random sample of the age group 20-39 were invited to attend for a health examination. In the Tromsø study (1973-4)[3] all men aged 20-49 were invited, and in the study of the counties of Finnmark, Sogn og Fjordane, and Oppland (1974-8)[4] all men and women aged 35-49 and a 10% random sample of the age group 20-34 were invited. All these people, with the exception of a few who had emigrated, were followed up till 31 December 1983. This report concerns men aged 35-49 who gave negative answers to questions about myocardial infarction, angina pectoris, "other heart disease," arteriosclerosis of the legs, cerebral stroke, diabetes, treatment for hypertension, and symptoms suggesting angina pectoris or atherosclerosis obliterans or both ("healthy" men). The proportion of subjects who were not "healthy" was 9·8%, ranging from 5·6% in the age group 35-39 to 12·6% in the age group 45-49. The attendance rate among men aged 35-49 was 78%, ranging from 65% in Oslo to 90% in Sogn og Fjordane and Oppland.

Systolic and diastolic blood pressures were measured twice with a mercury sphygmomanometer. The Oslo and Norwegian counties studies used the second measurement, whereas the Tromsø study recorded only the lowest measurement. In the Oslo and Norwegian counties studies the interval between the first and second measurements was one minute, and in the Tromsø study it was four to five minutes. Diastolic pressure was recorded at the disappearance of Korotkoff sounds (phase V). When phase V was absent phase IV was used. Standard size cuffs were used throughout.

In the Tromsø study serum cholesterol concentrations were determined at Tromsø University Hospital, using a manual Lieberman-Burchard procedure.[3] Serum cholesterol concentrations in the other studies were determined at the Central Laboratory, Ullevaal Hospital, Oslo, also by a Lieberman-Burchard procedure but using a Technicon autoanalyser. The methods have been described.[5]

Altogether the study population consisted of 39 207 men followed up for an average of 8·9 years, of whom 385 died of coronary heart disease (four of these did not have height and weight measured). Coronary heart disease was defined as codes 410-411, 412.0-412.3, and 413 in the Norwegian version of the ICD (8th revision).[6] The officially coded underlying cause of death was used. The criteria for coronary heart disease may have varied from one part of the country to another, but any bias introduced by knowledge of the risk factors was thought to be of little relevance in this analysis.

As in the Whitehall study, the analysis was carried out on the standardised normal deviate (z score), as follows: z score=(observed value−age specific value)/age specific standard deviation. Each of the three five year age groups was considered separately.

Comparing the importance of the two blood pressures in relation to other risk factors was done by Cox multiple regression analysis.[7] Other independent variables (covariates) were serum cholesterol, number of cigarettes smoked daily, body mass index, and age at examination. Standardised relative risks with corresponding 95% confidence intervals are presented. Standardised relative risk is the exponential of the actual regression coefficient multiplied with the standard deviation of the variable. The standard deviation of diastolic blood pressure varied between 9·9 and 10·9 and of systolic blood pressure between 14·9 and 17·2 in the different subgroups where Cox regressions were run. Hence with minor inaccuracy the standardised relative risks for systolic and diastolic blood pressures may also be interpreted as the relative risks between two groups 15 and 10 mm Hg apart, respectively.

TABLE III—*Mortality from coronary heart disease in upper age specific quintile of systolic and diastolic blood pressures. Men reporting neither cardiovascular disease nor symptoms of angina pectoris or intermittent claudication*

Age group	No at risk (upper quintile)	Coronary heart disease mortality (8·9 years) per 10 000 at risk: Systolic	Diastolic	Ratio diastolic:systolic
35-39	1748	65	82	1·26
40-44	2940	141	161	1·14
45-49	3153	254	257	1·01
35-49	7841	181	189	1·04

Results

Table I shows the variable means and z scores for the blood pressures and for two other important risk factors—namely, serum cholesterol concentration and cigarette consumption. For all four variables the means were higher for men who died of coronary heart disease than for the others. At age 35-39 the difference was not significant for either systolic or diastolic pressure. The z scores showed a similar pattern. Among men who died of coronary heart disease the mean z score for cholesterol was larger than the z scores for the other variables at ages 35-39 and 40-44. At ages 45-49 the mean z scores for all variables were about equal.

pressure, representing 26% more deaths from coronary heart disease in the upper quintile of diastolic pressure compared with the upper quintile of systolic pressure. At ages 40-44 the ratio was 1·14 and at ages 45-49 the rates were almost equal.

The Whitehall study included both initially diseased and initially healthy men but entered ischaemic electrocardiographic findings and angina pectoris as independent variables. In addition to the data in tables I to III, which deal with "healthy" men only, we also ran Cox multiple regressions

TABLE I—*Risk factors and z scores. Men reporting neither recognised disease nor symptoms of angina pectoris or intermittent claudication*

	Died of coronary heart disease			Alive at end of study		
Age at entry:	35-39	40-44	45-49	35-39	40-44	45-49
No of men:	37	123	225	8469	14 522	15 288
Systolic blood pressure (mm Hg):						
Mean pressure (SD)	136·6 (19·1)	143·2 (20·2)	144·0 (19·8)	133·4 (14·4)	134·3 (15·2)	136·1 (16·6)
Mean z score (SD)	0·22 (1·33)	0·57 (1·32)	0·46 (1·19)	−0·01 (1·00)	−0·01 (1·00)	−0·01 (1·00)
Diastolic blood pressure (mm Hg):						
Mean pressure (SD)	86·8 (13·6)	90·7 (12·4)	91·4 (12·0)	82·4 (10·4)	84·8 (10·5)	85·9 (10·5)
Mean z score (SD)	0·41 (1·30)	0·54 (1·18)	0·50 (1·14)	−0·01 (1·00)	−0·01 (1·00)	−0·01 (1·00)
Serum cholesterol concentration (mmol/l):						
Mean concentration (SD)	7·80 (1·69)	7·97 (1·97)	7·68 (1·42)	6·67 (1·35)	6·90 (1·32)	7·04 (1·31)
Mean z score (SD)	0·82 (1·25)	0·80 (1·48)	0·48 (1·08)	−0·01 (1·00)	−0·01 (1·00)	−0·01 (1·00)
No of cigarettes smoked daily						
Mean No (SD)	11·0 (9·2)	11·9 (9·3)	9·7 (7·7)	6·4 (8·1)	6·3 (8·1)	6·0 (7·8)
Mean z score (SD)	0·55 (1·13)	0·67 (1·15)	0·46 (0·98)	−0·01 (1·00)	−0·01 (1·00)	−0·02 (1·00)

Table II shows the standardised relative risks for systolic and diastolic blood pressures adjusted and unadjusted for other variables and stratified by age at examination. Systematically diastolic pressure turned out to be the stronger predictor, the difference being most pronounced in the youngest age group. As another way of expressing this result, the relative risk between two groups with diastolic pressures 10 mm Hg apart corresponded to the relative risk of two groups with systolic pressures 37, 17, and 18 mm Hg apart in the age groups 35-39, 40-44, and 45-49, respectively, when adjusting for serum cholesterol, number of cigarettes a day, and body mass index in the Cox regression analysis.

Table III shows the mortality from coronary heart disease in the age specific upper quintiles of systolic and diastolic pressures and the ratios of these death rates. At ages 35-39 the ratio was 1·26 in favour of diastolic

TABLE II—*Standardised relative risks (95% confidence intervals in parentheses) of systolic and diastolic blood pressures for coronary heart disease from Cox regression analysis. Men reporting neither cardiovascular disease nor symptoms of angina pectoris or intermittent claudication*

	Age at examination: 33-39	40-44	45-49
	Relative risks not adjusted for other variables		
Diastolic	1·46 (1·10-1·92)	1·62 (1·38-1·90)	1·56 (1·39-1·75)
Systolic	1·23 (0·92-1·65)	1·60 (1·39-1·84)	1·48 (1·33-1·65)
	Relative risks adjusted for serum cholesterol, number of cigarettes a day, and body mass index		
Diastolic	1·32 (0·96-1·81)	1·51 (1·28-1·79)	1·54 (1·36-1·75)
Systolic	1·11 (0·81-1·51)	1·42 (1·23-1·64)	1·45 (1·30-1·62)
	Relative risks adjusted for serum cholesterol, number of cigarettes a day, body mass index, and systolic (respectively diastolic) pressure		
Diastolic	1·40 (0·92-2·13)	1·31 (1·03-1·66)	1·34 (1·12-1·60)
Systolic	0·91 (0·62-1·35)	1·20 (0·97-1·48)	1·20 (1·02-1·41)

with all men examined, including a dichotomous healthy-not healthy variable in addition to serum cholesterol, number of cigarettes smoked, and body mass index. As might be expected, the standardised relative risk for this dichotomous variable increased strongly with age, being non-significant at ages 35-39. The standardised relative risks in table II for systolic and diastolic blood pressures changed little and the relative importance of the two blood pressures was unchanged.

Holme and Waaler introduced a second order polynomial of blood pressures in their five and a quarter year mortality follow up study.[8] When we included systolic pressure squared in our Cox regressions for the age group 35-39 the χ^2 with one degree of freedom for the difference between the models with and without this squared term was not statistically significant. The same applied to diastolic blood pressure.

Table IV shows the standardised relative risks for systolic and diastolic pressures for three strata of body mass index. Diastolic blood pressure came out as the better predictor in all three strata. Both systolic and diastolic pressures were slightly stronger predictors when body mass index was less than 2·4 compared with 2·8 or more, but the middle range of body mass index (2·4 to 2·7) was associated with the lowest relative risk; hence there was no consistent trend. Cox regression analysis for a body mass index of 3·1 or higher (1052 men; 17 deaths from coronary heart disease) gave non-significant standardised relative risks of 1·10 for diastolic and 1·03 for systolic pressure. Hence the association between blood pressure and death from coronary heart disease seemed to disappear when the body mass index was particularly high; and in this connection there are two important points. Firstly, the absolute risk of death from coronary heart disease was 16·2/1000 (17 out of 1052) among men with a body mass index of 3·1 or higher compared with 9·5/1000 (364 out of 38 155) among those with a body mass index below 3·1. The mean ages of these groups were 42·9 and 43·1 years, respectively. Secondly, the mean systolic and diastolic pressures were 131·8 and 82·0 mm Hg, respectively, in men with a body mass index below 2·3 and 147·7 and 94·9 mm Hg in men with a body mass index of 3·1 or higher. The mean ages were 42·8 and 43·1 in these strata.

When Cox analysis was done with cholesterol concentrations stratified as <6·5 mmol/l (74 deaths from coronary heart disease) and ≥ 8·0 mmol/l (157 deaths) and adjusting (separately) for systolic and diastolic pressures and for serum cholesterol, age at examination, number of cigarettes a day, and body mass index, diastolic blood pressure came out as the better predictor in both strata, though both blood pressures were statistically significant. There was a very slight tendency for both systolic and diastolic pressures to be stronger predictors in the lower stratum of cholesterol values.

Though not relevant to the main theme, it should be noted that a serum cholesterol concentration below 6·5 mmol/l was not a significant predictor of death from coronary heart disease when adjusting for age, number of cigarettes smoked, body mass index, and either systolic or diastolic blood pressure. (An increase in cholesterol concentration of 1·3 mmol/l was associated with a relative risk of 1·14 (0·59-1·80) when the values were below 6·5 mmol/l compared with a relative risk of 1·22 (1·08-1·38) when values were 8·0 mmol/l or higher.

An interaction between body mass index, cholesterol concentration, and death from coronary heart disease was also apparent. When adjusting for age, number of cigarettes smoked, body mass index, and either systolic or diastolic pressure the relative risk associated with an increase in cholesterol of 1·3 mmol/l was 1·49 (1·35-1·65) for a body mass index below 2·4, 1·35 (1·23-1·48) for a body mass index of 2·4 to 2·7, and 1·21 (1·00-1·46) for a body mass index of 2·8 or greater.

TABLE IV—*Standardised relative risks of systolic and diastolic blood pressures for coronary heart disease from Cox regression analysis. Men reporting neither cardiovascular disease nor symptoms of angina pectoris or intermittent claudication*

	Standardised relative risk*	95% Confidence interval
	Body mass index <2·4 (144 coronary heart disease deaths)	
Diastolic	1·58	1·37-1·83
Systolic	1·52	1·35-1·73
	Body mass index 2·4-2·7 (172 coronary heart disease deaths)	
Diastolic	1·40	1·21-1·61
Systolic	1·29	1·15-1·46
	Body mass index ≥2·8 (65 coronary heart disease deaths)	
Diastolic	1·49	1·19-1·86
Systolic	1·35	1·09-1·68

* Adjusted for serum cholesterol, number of cigarettes a day, age at examination, and body mass index.

TABLE V—*Summary of z scores separating survivors from men who died of coronary heart disease in present study and Whitehall study*

	Present study		Whitehall study	
Age group	Systolic	Diastolic	Systolic	Diastolic
35-39	0·22	0·41		
40-44	0·57	0·54	0·01	0·54
45-49	0·46	0·50	0·54	0·50

Discussion

Table V summarises the z scores separating survivors from men who died of coronary heart disease in this and the Whitehall study. On the whole, diastolic blood pressure appeared to be the better predictor at ages below 50. This was supported by Cox regression analysis and the comparison of mortality from coronary heart disease in the upper quintiles of blood pressure. Possibly diastolic blood pressure is a relatively stronger predictor the younger the men. By contrast, the Whitehall study gave preference to systolic blood pressure at ages 50-64.

In their seminal paper from the Framingham study on predicting coronary heart disease Truett *et al* did not include diastolic pressure in the discriminant function.[9] A later paper,[10] however, compared systolic and diastolic pressures in a 14 year follow up of men and women aged 30-69 and free of coronary heart disease at their initial examination. "For men under the age of 45 at entry, diastolic blood pressure is clearly a better discriminator. For men in age group 45 to 59 at entry, there is no distinction between the two measurements as predictor of coronary heart disease. At older ages systolic pressure tends to be the better predictor."[10] Hence both the Whitehall and Framingham studies gave preference to systolic pressure at age 60 and above. At ages 45-59 the results were not clear cut, and below the age of 50 all three studies (including this one) by and large found diastolic pressure to be the stronger predictor.

In this and the Whitehall study angina pectoris was handled differently as an independent variable, but, as shown above, this was unlikely to have much effect on the conclusions. It is more difficult to assess the effect of the inclusion of angina pectoris in the Framingham study as part of the dependent variable, though Halperin *et al* showed no clear effect of including angina pectoris on the relative importance of the predictors.[11]

An interaction between diastolic blood pressure, body mass index, and death from cardiovascular disease was reported by Cambien *et al*.[12] Our study supports their finding but, conversely, showed that the association between blood pressure and death from coronary heart disease disappeared only in very obese people, who accounted for only a very small proportion of the population at risk. Hence this interaction may not readily be found. For instance, when we, like Cambien *et al*, introduced an interaction term between diastolic pressure and body mass index in addition to diastolic pressure, serum cholesterol concentration, number of cigarettes smoked, and body mass index in the Cox model, running the analysis separately for the three age groups 35-39, 40-44, and 45-49, the interaction term was non-significant in all three age groups. Similar analysis for systolic pressure gave a similar result, except that in the age group 40-44 the interaction term came out significantly.

Systolic and diastolic pressures may be combined as one variable —for example, by using diastolic pressure plus one third of the difference between systolic and diastolic pressures. Such a variable is likely to have only part of the predictive power of the simultaneous entry of systolic and diastolic pressures in the Cox regression. Moreover, the optimal formula is likely to vary, not only with age but also with the disease to be predicted. The enthusiasm for pursuing this problem is dampened by the growing use of electronic devices for measuring blood pressure in epidemiological studies. These devices record diastolic pressure unbiased by the prior reading of systolic. The relative power of the two pressures may well be affected in such a way as to make obsolete the findings based on sphygmomanometer readings.

When selecting screened subjects for further examination and possible treatment we should do better than "systolic pressure >160 and/or diastolic >90." The main difficulty, however, is the doubtful relevance of epidemiological follow up findings based on blood pressure measured on a single occasion to a clinical setting that requires repeated measurements over weeks or months.

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