BLOOD PRESSURE COMPONENTS AS PREDICTORS OF STROKE MORTALITY IN WEST SCOTLAND

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ABSTRACT

The relative importance of systolic (SBP) versus diastolic blood pressure (DBP) and other combinations of SBP and DBP in the prediction of stroke have been re-examined in a long term cohort study of 10,541 men and women aged 45-64 in West Scotland.

During a mean follow-up of 11.6 years 1,616 deaths occurred, among which 160 (9.9%; 80 male, 80 female) were due to stroke.

In a multiple logistic regression (MLR) model the predictive values of SBP, DBP, mean arterial pressure (MAP), mean arterial index (MAI) and pulse pressure (PP) were examined in relation to stroke mortality after adjustment for age, body mass index (BMI), casual blood glucose, serum cholesterol, and cigarette smoking at entry. All blood pressure measures were associated with stroke mortality; in females the risk of stroke mortality was more strongly associated with DBP; in males SSP and DBP have the same predictive influence on stroke mortality and the MAP and MAI have stronger associations with it than either SBP and DBP. PP is associated with the least excess risk in both genders.

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INTRODUCTION

Blood pressure is the most potent risk factor for the development of stroke.[1-5] Although both the systolic and diastolic components of blood pressure are recognized predictors of stroke risk,[6-8] whether SBP or DBP is the more important risk indicator still remains controversial.

The assumption that DBP is the most important predictor of cardiovascular morbidity from hypertension is supported by the fact that essential hypertension is associated with an increase in peripheral resistance which is manifested chiefly by a rise in DBP.[9,10] This viewpoint however, has been questioned[8,11-17] and for cerebrovascular disease two epidemiological investigations[17,18] have favoured SBP as the strongest predictor.

In the follow-up study of a cohort healthy population of 10,451 middle aged men and women for eleven years we have re-examined the predictive value of several combinations of SBP and DBP measurements, made at entry to the study, for stroke mortality.

MATERIALS AND METHODS

Subjects

The population sampling frame and methods of the midspan study have been described in detail by Hawthorne, et al.[19,20] The population of this cohort study comprised 10,541 (78% response rate) men and women in the towns of Renfrew and Paisley, Scotland,

Table I. Systolic and diastolic blood pressure, mean aterial pressure, mean arterial index, pulse pressure and standard normal deviate by age group, for men who survived and who died of stroke after 10-14 years of follow-up.

Age (yr)	Alive at the End of Study			Died of stroke		
	No. of Cases	Mean (SD)	Standardized Normal Devi. (SD)	No. of cases	Mean (SD)	standardized Normal Devi. (SD)
Systolic Blood Pressure						
45-49	1084	142.0(19.9)	-0.01(0.99)	3	145.7(40.1)	0.17(1.99)
50-54	1063	144.8(21.2)	-0.03(0.98)	15	154.9(25.8)	0.44(1.20)
55-59	904	147.1(21.8)	-0.08(1.01)	33	166.9(28.5)***	0.82(1.32)***
60-64	748	151.9(22.5)	-0.09(0.92)	29	166.3(29.4)*	0.52(1.24)*
Diastolic Blood Pressure						
45-49	1084	85.2(19.9)	-0.01(0.99)	3	95.3(18.5)	0.78(1.43)
50-54	1063	85.0(12.2)	-0.05(0.97)	15	90.4(15.5)	0.38(1.23)
55-59	904	84.9(12.9)	-0.06(0.98)	33	96.0(17.5)***	0.78(1.33)***
60-64	748	84.6(13.3)	-0.05(0.98)	29	90.0(16.4)*	0.35(1.22)*
Mean Arterial Pressure						
45-49	1084	104.1(14.1)	-0.01(0.99)	3	112.1(25.4)	0.55(1.79)
50-54	1063	104.9(13.8)	-0.04(0.97)	15	111.9(18.5)	0.45(1.30)
55-59	904	105.6(14.6)	-0.07(0.97)	33	119.0(20.0)***	0.85(1.33)***
60-64	748	107.0(14.8)	-0.07(0.97)	29	115.4(19.5)*	0.47(1.28)*
Mean Arterial Index						
45-49	1084	123.1(16.6)	-0.01(0.99)	3	128.9(32.7)	0.34(1.95)
50-54	1063	124.9(17.1)	-0.04(0.98)	15	133.4(22.0)	0.45(1.27)
55-59	904	126.4(17.8)	-0.08(0.97)	33	143.0(23.8)***	0.83(1.30)***
60-64	748	129.5(18.1)	-0.08(0.95)	29	140.9(24.1)***	0.51(1.27)***
Pulse Pressure						
45-49	1084	56.7(14.1)	-0.00(0.99)	3	50.3(23.0)	-0.45(1.62)
50-54	1063	59.8(16.3)	-0.00(0.99)	15	64.5(13.5)	0.28(1.22)
55-59	904	62.2(16.1)	-0.06(0.96)	33	70.5(18.7)*	0.43(1.11)*
60-64	748	97.3(17.4)	-0.07(0.95)	29	76.2(19.7)*	0.41(1.08)*

* p<0.05,   ** p<0.01,   *** p<0.001   (Comparing "deceased" with "survive").

aged 54-64 years old. They accepted a single general health examination between 1972 and 1976; in this study their mortality experience has been followed to January, 1986.

Examination

The baseline examination in 1972-76, included measurement of height and weight with the subject in indoor clothing and without shoes. Adiposity was expressed as BMI which was calculated as weight (kg) divided by square height (m). Blood samples were collected in the afternoon and evening. A 10 ml. causal sample of venous blood was taken without venous stasis and glucose was determined (using whole blood) by the measurement of oxygen consumption.[21] Serum cholesterol was determined by autoanalyser.[22] SBP and DBP were measured seated using the London School of Hygiene and Tropical Medicine sphygmomanometer[23] with a bladder of 12×22 cm. DBP was taken as the disappearance of the fifth Korotkoff sound. Observers had been trained to measure blood pressure, using a special tape recording, in order to reduce bias and observer variation.[24] Monthly mean blood pressures in each observer were compared with group means to ensure quality control. Cigarette smoking status was assessed by a standard questionnaire.[25]

Mortality and Follow-up

The population was flagged at the National Health Service Central Registry and deaths have been reported monthly. Causes of death have been classified using the Eighth Revision (1972 to 1978) and the Ninth Revision (after 1979) of the International Statistical Classification of Disease, Injuries and Cause of Death (ICD).[26] The ICD codes for stroke are the same in the 8th and 9th revision. The comparability ratio, for the change of classification from the Eighth to Ninth Revision used in this analysis, was estimated as 1.043 for cerebrovascular mortality by the Registrar General

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Table II. Systolic and   pressure and   diastolic blood
standard normal deviate by age group, for women who survived and who died of stroke after 10-14 years of follow-up.

Age (yr)	Alive at the End of Study			Died of stroke		
	No. of Cases	Mean (SD)	Standardized Normal Devi. (SD)	No. of Cases	Mean (SD)	Standardized Normal Devi. (SD)
Systolic Blood Pressure						
45-49	1303	139.3(21.3)	0.00(1.00)	7	141.3(21.2)	0.09(1.01)
50-54	1420	144.9(22.9)	0.00(1.00)	10	147.8(25.2)	0.13(1.11)
55-59	1263	151.0(25.0)	-0.05(0.97)	18	163.0(25.4)*	0.42(0.99)*
60-64	1140	157.0(24.7)	-0.04(0.98)	45	163.7(25.1)	0.23(1.00)
Diastolic Blood Pressure						
45-49	1303	81.7(12.3)	0.01(1.00)	7	82.6(16.2)	0.08(1.31)
50-54	1420	83.6(12.5)	0.00(1.00)	10	84.2(11.6)	0.04(0.92)
55-59	1263	85.1(13.2)	-0.02(0.97)	18	88.9(14.3)	0.26(1.05)
60-64	1140	86.5(13.2)	-0.03(0.97)	45	95.9(15.5)***	0.64(1.11)***
Mean Arterial Pressure						
45-49	1303	100.9(14.0)	0.00(1.00)	7	102.1(16.5)	0.09(1.65)
50-54	1420	104.1(14.6)	0.00(0.99)	10	105.4(15.2)	0.09(1.03)
55-59	1263	107.1(15.7)	-0.04(0.98)	18	113.6(16.6)	0.37(1.03)
60-64	1140	110.0(15.7)	-0.04(0.98)	45	118.5(16.9)***	0.49(1.06)***
Mean Arterial Index						
45-49	1303	120.1(17.3)	0.00(1.00)	7	121.7(18.3)	0.09(1.06)
50-54	1420	124.5(18.3)	0.00(1.00)	10	126.6(19.9)	0.11(1.09)
55-59	1263	129.0(19.9)	-0.05(0.97)	18	138.3(20.0)	0.41(1.02)
60-64	1140	133.5(19.2)	-0.04(0.98)	45	141.1(20.4)*	0.34(1.01)*
Pulse Pressure						
45-49	1303	57.6(15.7)	0.00(0.99)	7	58.7(15.2)	0.58(1.47)
50-54	1420	61.3(17.1)	-0.01(1.01)	10	63.6(17.9)	0.14(1.06)
55-59	1263	65.8(18.7)	-0.05(0.96)	18	74.0(20.1)	0.37(1.03)
60-64	1140	70.4(19.0)	-0.02(0.96)	45	67.8(19.6)	-0.16(0.99)

* $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$ (Comparing "deceased" with "survive")

for Scotland.[27]

During a mean follow-up of 11.6 years (range 10-14), 1,616 (961 male and 655 female) deaths occurred, among which 160 (9.9%; 80 male and 80 female) were caused by cerebrovascular accident (ICD-9 codes 430-438). Deaths from causes other than stroke have been excluded from this analysis.

Analysis

The blood pressure variables examined in relation to stroke mortality in this study included: SBP, DBP, PP (SBP-DBP), MAP (2/3 DBP + 1/3 SBP) and MAI (1/3 DBP + 2/3 SBP).

As SBP and DBP and derived combinations of them differ in both range and variance and also depend upon age and gender, they were transformed to give an age-gender-adjusted standardised normal deviation (SND) for each individual. This was done by subtracting the age-gender-specific mean and dividing by the age-gender-specific standard deviation, as in the

Whitehall Study.[28] For example, for a male in the 45-49 age group the SND for SBP is calculated as follows:

SND for SBP =

$$\frac{\text{Observed SBP-mean SBP for males aged 45-49}}{\text{Standard deviation of SBP for males aged 45-49}}$$

The SND indicates the degree to which an individual's pressure (whether SBP, DBP, MAP, MAI or PP) deviates from an age-specific mean in standard deviation units. These differences provide a direct method for comparing the power of these five measures of blood pressure to predict stroke mortality. If the hypothesis that no difference between the DBP and SBP and derived combinations of them in individuals dying of stroke is true, we would expect the average difference in those subjects to be close to zero. Significance was assessed by a paired T-test for the difference between each component of blood pressure and DBP

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Table III. Mean (SD) standard normal deviates adjusted for age for systolic (SBP) and diastolic pressure (DBP), mean arterial pressure (MAP), mean arterial index (MAI) and pluse pressure (PP) and their difference with DBP by 10-14 year mortality outcome, in men and women.

Blood Pressure Components	Male		Female	
	Alive at the End of Study	Died of Stroke	Alive at the End of Study	Died of Stroke
No.	of cases 3799	80	5126	80
SBP	-0.05(0.96)	0.49(1.28)***	-0.02(0.98)	0.22(1.00)***
DBP	-0.04(0.98)	0.57(1.29)***	-0.01(0.98)	0.25(1.17)***
MAP	-0.05(0.97)	0.58(1.33)***	-0.02(0.98)	0.26(1.11)***
MAI	-0.05(0.96)	0.53(1.31)***	-0.02(0.98)	0.24(1.06)***
PP	-0.03(0.96)	0.17(1.12)**	-0.02(0.97)	0.23(1.00)*
SBP-DBP	-0.01(0.80)	-0.08(0.86)	-0.01(0.79)	-0.03(0.91)
MAP-DBP	-0.01(0.38)	0.01(0.41)	-0.01(0.39)	0.01(0.43)
MAI-DBP	-0.01(0.64)	-0.04(0.69)	-0.01(0.64)	-0.01(0.73)
PP-DBP	0.01(1.31)	-0.40(1.43)**	-0.01(1.25)	-0.02(1.49)

Two sample t-test values for persons who died compared to persons alive at the end of the study and paired t-test to compare the difference between the mean of each component of blood pressure and diastolic pressure from zero: * p<0.05, **p<0.01, ***p<0.001. Age-adjusted mean standard normal deviation by averaging five year age-group.

and by a two sample T-test for the difference between blood pressure in persons who died compared to subjects who were still alive after 10-14 years.

In order to examine the contributions of SBP and DBP and derived combinations of them, as well as calculating adjusted estimates of relative risk as the standardised odds ratio (SDR) of stroke mortality, MLR analysis (BMDP PLR[29]) was used, to allow for potential confounding factors.[30]

The possible interaction of cardiovascular risk factors with SBP, DBP, and various combinations of SBP and DBP as predictors of death from stroke was also examined in males and females separately.

SBP, DBP, and the derived MAP, MAI and PP, age, BMI, serum cholesterol and casual blood glucose were entered as continuous independent variables. Current cigarette smoking habits were entered as a dichotomous variable.

Because of differences in the usual range of values for SBP, DBP, MAP, MAI, and PP and since the magnitude of the coefficients is affected by the variance of the characteristic, a direct comparison of the logistic function coefficients is not appropriate to determine the relative predictive strength of each blood pressure. In order to put all the coefficients on the same scale, the coefficient is multiplied by the standard deviation of

Table IV. Univariate logistic regression coefficients and odds ratio of cerebrovascular disease mortality on various components of blood pressure in 10-14 years follow-up by gender.

Blood Pressure Component	Male			Female		
	coefficient	Odds Rutio	Z-Test	Logistic Coefficient	Odds Ratio	Z-Test
Systolic BP	0.030	1.93	6.9***	0.019	1.59	4.7***
Diastolic BP	0.042	1.71	5.7***	0.039	1.67	5.1***
Mean Arterial Pressure (DBP+PP/3)	0.043	1.85	6.8***	0.034	1.69	5.3***
Mean Arterial Index (2*SBP+DBP/3)	0.037	1.92	7.0***	0.025	1.63	5.0***
Pulse Pressure (SBP-DBP)	0.030	1.64	4.9***	0.015	1.32	2.6**

Walker-Duncan evaluation of logistic parameters (139). The approximate relative risk (standardized odds ratio) for a change in the risk factor by an amount equal to its standard deviation.
* P<0.5, ** p<0.01, *** p<0.001

the variable, and then exponentiated. This gives the odds ratio associated with a change of one standard deviation in the continuous variables of interest.[31]

RESULTS

Table I and II and Figure 1 indicate the relationship of age and gender to blood pressure measurements. In survivors at follow-up the expected age related gradients of SBP, MAP, MAI and PP, at entry, is seen in each category for both males and females. This relationship is stronger for females than males. In persons who died from stroke the mean SBP, MAP and MAI levels, at entry, were widely separated and approximately parallel in males and females in the younger age groups and closer, or overlapped at lower levels, in older males. Males who died from stroke at follow-up showed higher pressure levels at entry, except for PP which was higher in females in age groups 50-59. In survivors, entry DBP was lower in females than males up to the 55-59 age group. In males who died from stroke, there was no consistent relationship between the DBP level and age, while in females higher levels were associated with advancing age. Overall the mean values for SBP, DBP, MAP, MAI and PP at entry, were significantly greater for those dying of stroke than for survivors after 10-14 years. The most marked age-specific differences were for males aged 55-59 and 60-64. But for MAP and DBP the mean values were very high for younger ages also.

The mean SND values showed a similar pattern to the blood pressure component but no consistent increase with increasing age. The mean SND for SBP, DBP, MAP and MAI were all significantly greater for those dying of stroke than for those still living at the time of follow-up. In women who died from stroke the overall age-standardised normal deviations for DBP were slightly greater than SBP, MAI, MAP, and PP (Table III). In men who died from stroke the overall SND for SBP were slightly greater than DBP and PP but there is nothing to suggest SBP was a better predictor of stroke death than MAP or MAI. Women dying of stroke have a DBP that deviates from the mean for their age-adjusted group to a small and not significantly greater extent than does their SBP, MAP, and MAI. In women DBP was significantly better than PP. Men dying of stroke have a SBP, MAP and MAI that deviates from the mean for their age-adjusted group to a small and not significantly greater extent than does their DBP.

Tables IV and V show the results of using the logistic model to predict IHD mortality. First the SBP, DBP, MAP, MAI and PP were studied separately as predictors of stroke mortality, without adjustment for other main cardiovascular risk factors (Table IV). The logis-
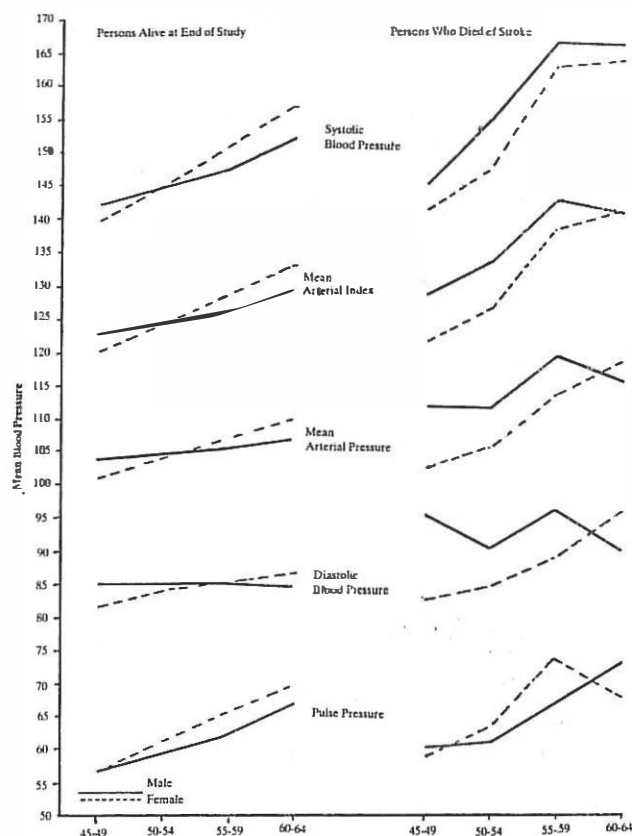

Figure 1. Average of systolic, diastolic, mean arterial pressure, mean arterial index and pulse pressure at initial examination by gender.

tic coefficients for SBP, DBP, MAP, MAI and PP each showed a strong relationship with stroke in both genders. The odds ratios are largest for SBP and MAI in men followed by MAP and DBP. In women the odds ratio is highest for MAP followed by DBP and MAI, whereas PP is associated with the least associated risk in both genders.

It is conceivable, although unlikely because of the strength of the relationship, that the association of elevated blood pressure with increased risk of stroke mortality derives at least in part from factors related both to blood pressure and to the risk of stroke mortality. This was assessed by including age, serum cholesterol, blood glucose, BMI and cigarette smoking habits in the logistic regression. The results (Table V) indicate that SBP, DBP, MAP, MAI and PP are all potent independent predictors of stroke mortality, after allowing for the effects of other risk factors.

The SBP provides an indication of the relative contribution of each component. The fact that all components of pressure contribute to the risk of stroke mortality is very likely due to the high correlation between SBP and DBP. Thus, although each of the five blood pressure measures was found to show a strong relationship to the risk of stroke after adjustment for

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Table V. Multiple logistic coefficients and standardised odds rutio of systolic (SBP) and diastolic blood pressure (DBP). mean arterial pressure (MAP), mean arterial index (MAI), and pulse pressure (PP) for 10-14 years mortality from stroke by gender and single SBP, DBP, MAP, MAI or PP and both SBP and DBP.

Blood Pressure Variables	Male			Female		
	Logistic Coefficient	Odds Ratio	Z-Test	Logistic Coefficient	Odds Ratio	Z-Test
Single Component of Blood Pressure						
SBP	0.027	1.81	5.91***	0.015	1.44	3.40***
DBP	0.045	1.78	6.03***	0.044	1.78	5.25***
MAP	0.043	1.86	6.50***	0.035	1.72	4.90***
MAI	0.035	1.85	6.30***	0.023	1.57	4.12***
PP	0.020	1.39	3.20**	0.005	1.10	0.77
Both Systolic and Diastolic Blood Pressure						
SBP	0.015	1.39	2.42*	0.001	1.02	0.24
DBP	0.027	1.41	2.58*	0.044	1.78	5.25***

The approximate relative risk (odds ratio) for a change in the risk factor by an amount equal to its standard deviation.
* $p<0.05$, ** $p<0.01$,
*** $P<0.001$
80 deaths in 5,232 females and 79 death in 3,900 males.

other risk factors, further joint analysis of the SBP and DBP measures is required to determine which measure has the most influence. Interpretation of the results at the foot of Table V is focused on the analysis which includes both SBP and DBP. Although major changes were noted in the predictive strength of these adjusted factors compared to the results shown for only SBP and DBP analysis, the overall results are the same. In females SBP was not a statistically significant predictor of stroke death and there was an interaction between DBP and age. However, DBP in males, (SOR 1.41; $p<0.001$), shows the same predictive risk for stroke death as SBP, (SOR 1.39; $p<0.001$). For females, DBP (SOR 1.78; $p<0.001$) is a better predictor of stroke deaths than SBP (SOR 1.02; $p=0.78$).

DISCUSSION

Both SBP an
stroke risk[6,7] but many authors have considered the diastolic component to be the most important. Recently this view has been questioned. The purpose of the present analysis was to examine the comparative predictive strength of each component of blood pressure in males and females separately. The results, as in most other studies,[1-7,32,33] suggest that the risk of stroke death is significantly and independently related to the level of antecedent casual blood pressure and is proportional to the blood pressure level. The risk of increased stroke mortality appeared to be related even to a single causal blood pressure determination made during the initial health examination, despite the effect of lability, diurnal variaton, artifacts of measurements

(obese arm, technical errors, digit preference and other sources of variation[34]) and the response to therapy.[1]

The SNDs, calculated according to the Whitehall Criteria[28] provide an estimate of the capacity of each component of the blood pressure to predict those who were at high risk of stroke death in the total population under study. On the whole, there was no significant difference in predictors of stroke mortality between DBP and SBP, MAP or MAI for both genders and PP in men. Generally, an examination of the mean SND for all blood pressure variables in men reveals a larger deviation for SBP, MAP and PP than for DBP. MAP and MAI did not predict stroke deaths any better than the SBP, although they were generally better than DBP or PP. The observation that MAP and DBP and MAI and SBP as single measures predict stroke mortality to the same extent may derive from the fact that MAP and MAI are combinations of both SBP and DBP and reflect the effect of DBP and SBP respectively.

There is nothing to suggest MAP is a better predictor than MAI in both genders. It is also consistent with the hypothesis that a combination of the blood pressure components do not make a greater contribution than either alone.

Multivariate analyses indicated that in females, when SBP and DBP are analysed either separately or together, DBP was found to be a stronger predictor of stroke mortality than SBP. In males, when SBP and DBP were analysed separately and simultaneously the SBP and DBP showed essentially the same predictive accuracy for stroke.

Another way to examine the possibility that both components of the arterial pressure contribute inde-

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pendently to the risk is to determine if prediction of stroke mortality is better achieved by employing a combination of both SBP and DBP values rather than either alone. The logistic regression analysis revealed that in males both MAP and MAI are better predictors than SBP or DBP alone; there was no significant difference between MAP and MAI. In women, MAP and MAI were not better than DBP alone but achieved more than SBP alone, and MAP achieved more than MAI.

We conclude that the general concept that DBP is more important than SBP as a predictor of stroke death is supported by data in women, while in men SBP and DBP predict stroke mortality to a similar extent.

The results of this study provide no support that SBP should be given more consideration than DBP when used as an epidemiological tool or in ordinary practice for predicting stroke mortality.

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