

Comparison of Risk Factors for Stroke Incidence and Stroke Mortality in 20 Years of Follow-Up in Men and Women in the Renfrew/Paisley Study in Scotland

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Background and Purpose—The aim of this study was to relate risk factors in middle-aged men and women to stroke incidence (defined by having a hospital discharge with a main diagnosis of stroke) and compare this with the associations between risk factors and stroke mortality.

Methods—In the early to mid-1970s, when they were 45 to 64 years of age, 7052 men and 8354 women from the Renfrew/Paisley prospective cohort study in Scotland were screened. Risk factors measured included blood pressure, blood cholesterol and glucose, respiratory function, cardiothoracic ratio, smoking habit, height, body mass index, preexisting coronary heart disease, and diabetes. These were related to stroke incidence over 20 years of follow-up.

Results—Diastolic and systolic blood pressure, smoking, cardiothoracic ratio, preexisting coronary heart disease, and diabetes were positively related to stroke incidence for men and women, whereas adjusted FEV₁ (forced expiratory volume in 1 second) and height were negatively related. Cholesterol was not related to stroke. Glucose for nondiabetic subjects had a U-shaped relationship with stroke. Body mass index was not clearly related to stroke, although participants with the highest body mass index had the highest stroke rate. Former smokers had similar stroke rates to never-smokers. Tests between the associations of risk factors and stroke incidence revealed these were not statistically different from the associations with stroke mortality.

Conclusions—The risk factors had a similar effect on stroke incidence as on stroke mortality. Epidemiological studies with information on stroke mortality are likely to give results applicable to stroke incidence. (*Stroke*. 2000;31:1893-1896.)

Key Words: epidemiology ■ prospective studies ■ risk factors ■ stroke prevention

We have previously presented analyses of the relationship between potential risk factors for stroke and stroke mortality in 20 years of follow-up in men and women in the Renfrew/Paisley study.¹ We now compare those results with similar analyses of risk factors with stroke incidence, as defined by having a hospital discharge with a main diagnosis of stroke. The Renfrew/Paisley data set is unique in having risk factor information on a large cohort of middle-aged men and women, with 20 years of follow-up of both stroke mortality and stroke incidence.

Methods

The Renfrew/Paisley general population study was performed between 1972 and 1976 on 7052 men and 8354 women aged 45 to 64 years. Full study details have been reported previously.^{1,2} A questionnaire was completed, and participants attended a screening examination. Smoking habit was defined as never smoked; pipe or cigar smoker only; 1 to 14, 15 to 24, or ≥ 25 cigarettes per day; and ex-smoker. Participants were asked if they were or had ever been diabetic. Cardiovascular symptoms were assessed by use of the Rose angina questionnaire,³ with angina defined as definite or possible.⁴ Severe chest pain was defined as ever having a severe pain across the

front of the chest lasting half an hour or more.⁴ At the screening examination, blood pressure was recorded as the mean of 2 measurements taken in the seated position with a sphygmomanometer.² Diastolic pressure was recorded at the disappearance of the fifth Korotkoff sound. A nonfasting blood sample was taken for measurement of plasma cholesterol and glucose.² Measurements of height and weight were made, enabling body mass index to be calculated in kg/m². A 70-mm chest radiograph was taken, and heart and thoracic width were measured. The cardiothoracic ratio was calculated as the ratio of the heart width to the thoracic width.

The forced expiratory volume in 1 second (FEV₁) was measured at the screening examination by use of a Vitalograph spirometer with the subject standing. The adjusted FEV₁ was defined as the actual FEV₁ as a percentage of the expected FEV₁ (calculated from linear regression equations of age and height for men and women, derived from a healthy subset of the population⁵). A 6-lead ECG was coded according to the Minnesota system⁶ and used to define ischemia on ECG.⁴ Preexisting coronary heart disease (CHD) was defined as having angina, ECG ischemia, or severe chest pain.

Study participants were flagged at the National Health Service Central Register in Edinburgh, UK, which enabled the study team to be notified of dates and causes of death. These methods had been assessed previously, and notification was found to be virtually complete, with no important discrepancies regarding causes of death.⁷ In addition, recent computerized linkage of the cohort with

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TABLE 1. 20-Year Age-Adjusted Stroke Rate per 10 000 Person-Years in Renfrew/Paisley Men (n=7052) and Women (n=8354) by Quintile of Risk Factor

Risk Factor	Quintile*					Trend (P)
	1	2	3	4	5	
SBP						
Men	33.9	36.3	48.8	59.2	79.7	<0.0001
Women	30.4	29.7	39.0	47.1	68.8	<0.0001
DBP						
Men	37.9	40.2	48.7	61.4	75.4	<0.0001
Women	33.6	32.6	40.7	40.5	70.0	<0.0001
Cholesterol						
Men	45.8	59.8	46.6	50.0	63.8	0.40
Women	46.1	44.5	41.6	42.6	43.4	0.63
Glucose†						
Men	59.2	51.6	45.8	46.3	54.2	0.13
Women	49.9	35.5	42.7	36.4	45.8	0.017
Adjusted FEV ₁						
Men	61.0	60.7	52.5	47.1	39.7	<0.0001
Women	53.3	48.9	48.5	34.9	30.9	<0.0001
Cardiothoracic ratio						
Men	42.0	54.6	51.1	61.4	55.4	0.0005
Women	35.9	37.8	36.9	49.4	56.9	<0.0001
Body mass index						
Men	55.4	45.2	50.4	46.2	63.4	0.038
Women	43.6	37.2	47.6	32.3	55.2	0.017
Height						
Men	63.0	52.4	55.1	51.1	41.3	0.002
Women	48.3	52.4	38.8	39.4	38.8	0.002

SBP indicates systolic blood pressure; DBP, diastolic blood pressure.

Stroke was defined as hospital discharge with main diagnosis of stroke.

*Quintiles are given in a previously published article.¹

†Excluding diabetic subjects.

the Scottish Morbidity Records for acute hospital discharges (SMR1) provided information on main diagnoses of stroke (International Classification of Diseases, 8th and 9th revisions [ICD-8, ICD-9] codes 430 to 438).⁸ This computerized method enabled 86% of the cohort to be linked to an SMR record (acute, mental health, or cancer admission) or death record.⁸ The first hospital admission with a main diagnosis of stroke was taken in a 20-year follow-up period. Age-adjusted stroke incidence rates per 10 000 per year were calculated by a life table approach and standardized by 5-year age groups, with the age distribution of the Renfrew/Paisley cohort used as the standard. Cox proportional hazards regression models were used to calculate trends for each continuous variable and to calculate relative rates for a 1-SD increase or decrease for each continuous variable. The difference between relative rates for stroke incidence and stroke mortality was tested by standardized normal deviate tests.

Results

In the 20-year follow-up period, 472 men and 557 women had a hospital discharge for stroke. Clear positive relationships were seen between both systolic and diastolic blood pressure and stroke in men and women (Table 1). Men and women in the highest blood pressure quintiles (systolic: ≥ 167 mm Hg for men, ≥ 172 mm Hg for women; diastolic: ≥ 97 mm Hg for men and women) had more than double the stroke incidence

TABLE 2. 20-Year Age-Adjusted Stroke Rate per 10 000 Person-Years in Renfrew/Paisley Men and Women by Smoking Habit

	Number	Strokes	Age-Adjusted Rate
Men			
Never	1184	78	45.8
Ex	1735	95	39.5
Pipe, cigar	141	9	36.9
1–14 cigarettes/day	839	56	51.7
15–24 cigarettes/day	2058	152	63.4
≥ 25 cigarettes/day	1095	82	69.0
Trend*			P=0.05
Women			
Never	3827	235	35.4
Ex	623	35	34.3
1–14 cigarettes/day and pipe, cigar	1572	120	53.1
15–24 cigarettes/day	2018	147	54.4
≥ 25 cigarettes/day	314	20	52.4
Trend*			P=0.20

*For current cigarette smokers only, using Cox's proportional hazards models, with number of cigarettes smoked as a continuous variable.

rate of those in the lowest quintiles. No relationship was seen between cholesterol and stroke in men and women. The relationship between glucose (excluding diabetic subjects) and stroke appeared U shaped in both men and women, with the highest rate seen in the lowest quintile. Adjusted FEV₁ was inversely related to stroke for men and women, with strong significant trends. Cardiothoracic ratio was positively related to stroke for both men and women. The relationship of body mass index with stroke was less clear, but men and women with the highest body mass index had the highest stroke rate. Height was negatively associated with stroke.

There was a dose-response relationship between cigarette smoking and stroke for men (Table 2). Ex-smokers had stroke rates similar to never-smokers.

The relative rates of stroke for a 1-SD change in each risk factor are shown in Table 3 and compared with previously published relative rates of stroke mortality for a 1-SD change in each risk factor.¹ Tests between the associations were all nonsignificant. The relative rates of stroke incidence and stroke mortality are also shown for diabetes and preexisting CHD. For diabetic subjects, the relative rate for stroke mortality was higher than that for stroke incidence for both men and women, but tests between them were also nonsignificant.

Discussion

The Renfrew/Paisley study is unique in the United Kingdom in having a large general population cohort of both men and women with comprehensive information on risk factors in middle age and 20 years of follow-up for both stroke mortality and incidence. Sufficiently large numbers of participants had hospital stays due to stroke to enable relationships between risk factors and stroke incidence to be investigated. If participants had nonfatal strokes at home and were not

TABLE 3. Comparison of Relationships of Risk Factors With Stroke Incidence and Stroke Mortality

	Men			Women		
	Incidence	Mortality*	Test for Difference† (P)	Incidence	Mortality*	Test for Difference† (P)
Relative rate for 1-SD increase						
SBP	1.45 (1.33–1.58)	1.50 (1.35–1.66)	0.62	1.43 (1.32–1.55)	1.37 (1.25–1.51)	0.52
DBP	1.37 (1.26–1.48)	1.44 (1.30–1.59)	0.45	1.40 (1.29–1.51)	1.42 (1.29–1.55)	0.81
Cholesterol	1.04 (0.95–1.15)	0.94 (0.83–1.05)	0.16	0.98 (0.90–1.06)	0.91 (0.82–1.02)	0.33
Glucose	1.07 (0.98–1.18)	1.10 (0.99–1.23)	0.71	1.12 (1.02–1.24)	1.21 (1.11–1.33)	0.24
Cardiothoracic ratio	1.18 (1.07–1.29)	1.20 (1.07–1.34)	0.82	1.20 (1.10–1.31)	1.15 (1.04–1.28)	0.54
Body mass index	1.10 (1.01–1.21)	1.01 (0.90–1.14)	0.25	1.10 (1.02–1.19)	1.07 (0.97–1.18)	0.67
Relative rate for 1-SD decrease						
Adjusted FEV ₁	1.23 (1.12–1.34)	1.27 (1.14–1.41)	0.66	1.22 (1.12–1.32)	1.24 (1.31–1.37)	0.75
Height	1.16 (1.06–1.27)	1.21 (1.08–1.35)	0.60	1.14 (1.05–1.24)	1.13 (1.03–1.25)	0.88
Relative rate associated with 20 more cigarettes/day	1.28 (1.00–1.64)	1.47 (1.08–2.00)	0.49	1.25 (0.89–1.76)	1.64 (1.10–2.45)	0.31
Relative rate associated with having						
Diabetes	1.52 (0.72–3.21)	2.89 (1.49–5.62)	0.21	2.83 (1.63–4.90)	3.98 (2.29–6.91)	0.39
Preexisting CHD	1.63 (1.34–1.97)	1.63 (1.28–2.06)	0.99	1.52 (1.28–1.81)	1.74 (1.42–2.14)	0.32

SBP indicates systolic blood pressure; DBP, diastolic blood pressure.

*From Reference 1.

†Difference between incidence and mortality.

admitted to hospital, then no information was available to the study team. Contemporary estimates suggest that 70% of stroke patients are admitted to hospital,⁹ with younger stroke sufferers being more likely to be admitted.¹⁰ The median age of stroke admission in our study was 70.6 years, and given the age at entry of our participants, no strokes could have occurred over the age of 85, after which admission rates become low. Therefore, most nonfatal strokes are likely to have been ascertained through stroke discharge data. It is also unlikely that risk factors for strokes leading to hospital admission are different in any considerable way from risk factors for strokes that are not admitted.

It is important to know whether risk factors have the same effect on stroke incidence as on stroke mortality. If the risk is similar for incidence and mortality, then measures that have been shown to reduce risk will prevent nonfatal stroke and consequent disability, which has quality-of-life implications and health service resource implications. We have demonstrated that in this cohort, risk factors for stroke had a similar effect on stroke incidence as on stroke mortality. When all the risk factors were simultaneously entered into a multivariate model, most retained a statistically significant association with stroke incidence in a similar way to multivariate analysis of stroke mortality in this cohort¹ (results not shown).

Raised blood pressure is an established risk factor for both stroke incidence^{11,12} and mortality.^{13,14} The 12-year follow-up of the Oslo study of men found blood pressure to be significantly related to stroke mortality and incidence, with mortality being predicted better than incidence.¹⁵ Cholesterol was not found to be related to stroke incidence or mortality, but this may mask a relationship of cholesterol with some

stroke subtypes.¹⁶ Glucose in nondiabetic subjects was significantly related to stroke incidence and mortality in women but not men. However, glucose was not measured for all sectors of the Paisley cohort and was missing for 4703 people. The Oslo study failed to find significant relationships between glucose and stroke incidence or mortality.¹⁵ Cardiothoracic ratio and FEV₁ have not generally been measured in other studies, but here both were related to stroke incidence in the same way as mortality. Body mass index was not clearly related to stroke incidence or mortality in the present study. The Oslo study found no relationship between body mass index and stroke mortality or incidence.¹⁵ Generally, there is less evidence of obesity being related to stroke, although it could be acting through its association with other risk factors for stroke, such as elevated blood pressure, blood glucose, and obstructive sleep apnea.^{11,17} Height was inversely associated with stroke incidence and mortality. In the British Regional Heart Study of men, an inverse association was seen with fatal but not nonfatal stroke.¹⁸ Height was inversely associated with stroke events for men but not women in a study in southeastern New England.¹⁹ In the Oslo study, there was a suggested inverse association between height and stroke incidence and mortality.¹⁵

Smoking has been seen as a risk factor for stroke incidence in other studies.^{11,15,20,21} In the Oslo study of men, smoking was found to be a stronger predictor of stroke mortality than incidence.¹⁵ A dose response was seen with cigarette smoking, and smoking cessation reduced the stroke incidence risk. This was also seen for stroke mortality in the present cohort.¹ Other studies have shown this effect,¹² which suggests that a real way to reduce both stroke occurrence and mortality is to

encourage smoking cessation. Diabetes has been recognized as a risk factor for stroke incidence^{11,20} and mortality.^{22,23} Preexisting CHD was significantly related to stroke, confirming other studies.^{11,20}

To conclude, we have found that the risk factors considered had similar relationships for stroke incidence as stroke mortality, and control of some risk factors could be expected to reduce stroke incidence and any resulting disability, in addition to reducing stroke mortality. Epidemiological studies with only mortality outcomes are likely to give results that are also applicable to stroke incidence.

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