

Short reports

The relation between cholesterol and haemorrhagic or ischaemic stroke in the Renfrew/Paisley study

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Studies have found little association between cholesterol and overall stroke risk, but this could be attributable to different relations for haemorrhagic and ischaemic stroke. Stroke mortality data from prospective studies cannot usually be divided into stroke subtypes. We have therefore analysed stroke based on hospital admissions, obtained by computerised linkage with acute hospital discharges in Scotland for a large prospective cohort study.

Methods and Results

The Renfrew/Paisley study was carried out between 1972 and 1976 involving 15 406 residents aged 45-64 from the towns of Renfrew and Paisley.¹ The linkage provided records of all main diagnoses of stroke in a 20 year follow up period. There was no information on participants having strokes and not being admitted to hospital, but with this relatively young age group, most would be admitted. Blood samples were taken for the measurement of plasma cholesterol, measured in mg/dl and converted to mmol/l by multiplication by 0.0259. After excluding participants with missing cholesterol readings, there were 6997 men and 8270 women. Cholesterol

quintiles were calculated separately for men and women, as women have higher concentrations of cholesterol than men.² Cholesterol groups were formed by taking each fifth as the corresponding fifth for men and for women.

Stroke was defined as ICD8 and ICD9 codes 430-438. Haemorrhagic stroke was defined as ICD8 codes 430 and 431, and ICD9 codes 430-432. It included subarachnoid haemorrhage and cerebral haemorrhage. Ischaemic stroke was defined as ICD8 codes 432-435 and 437, and ICD9 codes 433-435. Age adjusted stroke rates per 10 000 per year were calculated using a life table approach and standardised by five year age groups using the age distribution of the cohort. Cox's proportional hazards models were used to calculate trends using cholesterol as a continuous variable and for calculating relative rates with the lowest fifth as the baseline, and also for calculating the relative rates associated with one standard deviation increase in cholesterol. There were no significant interactions between cholesterol and sex for each type of stroke, so data for the men and women were analysed together.

Table 1 Haemorrhagic and ischaemic stroke rates by cholesterol in men and women aged 45-64 from the Renfrew/Paisley study in 20 years of follow up

	Cholesterol quintile (mmol/l)						
	≤5.08	5.09-5.59	5.60-6.09	6.10-6.68	≥6.69	Trend*	Relative rate associated with 1 standard deviation increase in cholesterol
For men	≤5.08	5.09-5.59	5.60-6.09	6.10-6.68	≥6.69		
For women	≤5.57	5.58-6.09	6.10-6.60	6.61-7.28	≥7.29		
Number of participants	3276	3070	3038	3116	2767		
<i>All stroke</i>							
Number of strokes	199	216	195	209	200		
Age adjusted rate	45.7	51.1	43.9	45.7	49.4		
Relative rate†	1	1.10	0.95	0.98	1.07	0.71	0.99
(95% CI)		(0.90, 1.33)	(0.78, 1.16)	(0.81, 1.19)	(0.88, 1.30)		(0.93, 1.05)
Relative rate‡	1	1.05	0.93	0.96	1.01	0.84	0.99
(95% CI)		(0.86, 1.27)	(0.76, 1.13)	(0.79, 1.17)	(0.83, 1.23)		(0.93, 1.06)
<i>Haemorrhagic</i>							
Number of strokes	23	22	17	23	5		
Age adjusted rate	4.6	4.9	3.2	4.5	1.1		
Relative rate†	1	0.97	0.73	0.95	0.23	0.017	0.76
(95% CI)		(0.54, 1.74)	(0.39, 1.36)	(0.53, 1.69)	(0.09, 0.61)		(0.61, 0.95)
Relative rate‡	1	0.92	0.71	0.92	0.22	0.011	0.74
(95% CI)		(0.51, 1.65)	(0.38, 1.34)	(0.52, 1.65)	(0.08, 0.57)		(0.59, 0.94)
<i>Ischaemic</i>							
Number of strokes	50	41	35	50	60		
Age adjusted rate	11.5	9.3	7.6	11.8	14.5		
Relative rate†	1	0.85	0.70	0.98	1.35	0.08	1.12
(95% CI)		(0.56, 1.28)	(0.46, 1.08)	(0.66, 1.45)	(0.93, 1.96)		(0.99, 1.28)
Relative rate‡	1	0.82	0.70	0.97	1.30	0.12	1.11
(95% CI)		(0.54, 1.24)	(0.45, 1.07)	(0.66, 1.44)	(0.89, 1.89)		(0.97, 1.26)

*Using cholesterol as a continuous variable. †Adjusted for age and sex. ‡Adjusted for age, sex, diastolic blood pressure, height, smoking (cigarettes per day and a 0/1 term for ex-smokers) and pre-existing coronary heart disease (angina, severe chest pain lasting half an hour or more, or ischaemia on electrocardiogram).

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Accepted for publication 14 July 2000

There were 1019 participants who had a hospital discharge with a main diagnosis of stroke, 90 of which were classified as haemorrhagic and 236 as ischaemic. The majority of strokes (693) were thus ill defined. Those with ill defined strokes were on average two years older than those with haemorrhagic or ischaemic strokes but there was no difference between the sexes. Although there was no apparent relation between cholesterol and overall stroke, there was a statistically significant inverse relation between cholesterol and haemorrhagic stroke (table 1). In contrast, the relation between cholesterol and ischaemic stroke was J shaped with participants in the middle fifth having the lowest stroke rate and participants in the highest fifth having the highest stroke rate. The difference between the relative rates for haemorrhagic and for ischaemic stroke adjusting for age and sex was statistically significant ($p=0.004$). Relative rates of stroke were calculated with additional adjustment for other risk factors for stroke but this did not account for the different associations with haemorrhagic and ischaemic stroke and had very little effect on the relative rates.

Comment

There have been few studies examining the association between cholesterol and stroke subtype, although the limited data available suggest cholesterol is positively related to ischaemic stroke and inversely related to

haemorrhagic stroke.^{3,4} This is particularly clear in eastern Asia where haemorrhagic stroke is more common than in western Europe and North America.⁴ Cholesterol concentrations are lower in eastern Asia than in this study. Randomised trials of cholesterol lowering with statins show reductions in overall stroke incidence and no increase in haemorrhagic stroke, although power to detect the latter is limited in studies completed to date.⁵ The observational inverse association of cholesterol and haemorrhagic stroke risk may be non-causal and in populations where ischaemic stroke is considerably more common than haemorrhagic stroke the overall benefits of cholesterol lowering are clear.

Funding: this study was provided with grants from Chest, Heart and Stroke Scotland, and the Stroke Association.

Conflicts of interest: none.

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