Ten year cerebrovascular morbidity and mortality in 68 year old men with asymptomatic carotid stenosis

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Abstract

Objective—To study the natural course of carotid artery stenosis detected by ultrasonography.

Design—Prospective cohort study. Baseline examination in 1982-3 included ultrasound examination of carotid arteries, measurement of ankle-brachial blood pressure index, and detection of atrial fibrillation by 24 hour ambulatory electrocardiography.

Setting—Malmö, a city in southern Sweden with 230 000 inhabitants.

Subjects—470 men aged 68 years randomly selected from the population.

Main outcome measures—Incidence of stroke and transient ischaemic attack and all cause mortality during 10 years of follow up in relation to carotid stenosis, leg artery disease (ankle-brachial blood pressure index below 0.9), and atrial fibrillation.

Results—Fifty men had a stroke; six of these were haemorrhagic. Another 11 had a transient ischaemic attack. Eighteen of the men with carotid stenosis (21.6 events/1000 person years) and 43 of the men with normal carotid arteries (14.8 events/1000 person years) had a stroke or transient ischaemic attack ($P=0.188$). Men with atrial fibrillation had an increased rate of cerebrovascular events (36.7/1000 person years ($P=0.048$)). The highest rate was found in men with asymptomatic disease of the leg arteries (38.6/1000 person years) ($P<0.001$). The increased risk of stroke or transient ischaemic attack in this group remained after multivariate analysis (relative risk 2.0; 95% confidence interval 1.1 to 3.7).

Conclusions—In this cohort carotid stenosis was not associated with an increased risk of stroke. Part of this lack of association was explained by the high mortality from ischaemic heart disease in men with severe stenosis. Twenty seven of the 61 cerebrovascular events, however, occurred in men who had normal carotid arteries, normal ankle pressure, and no atrial fibrillation.

Introduction

The clinical spectrum of carotid artery disease ranges from an incidentally discovered bruit to a stage with advanced arteriosclerotic lesions and subsequent stroke. Modern ultrasound techniques have extended the range of disease even further, and several studies have published results on the occurrence of asymptomatic carotid stenosis in patients with different arteriosclerotic diseases.¹⁻⁴

We have previously reported on a 25% prevalence of carotid stenosis including a reduction by 30% or more in internal diameter in 68 year old men selected at random from the general population.⁵ This study, which was carried out in 1982-3, showed a relation between history of stroke or transient ischaemic attack and carotid stenosis. The 470 men, who belong to the prospective cohort study of men born in 1914 from Malmö in Sweden, have been followed up since this initial health examination, and it is now possible to describe the 10 year incidence of cerebrovascular disease in relation to prevalence of carotid stenosis at 68 years of age.

Occlusive leg artery disease has been found to be

associated with an increased risk of cerebrovascular disease.⁶ Others have shown a relation between carotid stenosis and non-invasively detected leg artery disease and also that asymptomatic leg artery disease in men with carotid stenosis is associated with an increased risk of future myocardial morbidity.⁷ We compared cerebrovascular morbidity in men with and without an ankle-brachial pressure index <0.9 , which can be regarded as a sign indicating the presence of substantial stenosis of the arteries.^{8,9}

Nineteen (4%) of the 456 men in the original cohort study had atrial fibrillation detected during 24 hour ambulatory electrocardiography in 1982-3.¹⁰ We assessed atrial fibrillation as a risk factor for stroke or transient ischaemic attack¹¹ in the presence of carotid stenosis and leg artery disease.

Subjects and methods

STUDY POPULATION

The cohort study of men born in 1914, which focused on the epidemiology of cardiovascular and pulmonary disease, has been running since 1969.¹² In 1982-3, all men born in even months in 1914 and residing in Malmö were invited to a health examination close to their 68th birthday. Of 621 invited, 500 took part in this examination. Four hundred and seventy (75.7%) of the 621 underwent carotid ultrasound examination and the measurement of arm and ankle blood pressure, and 456 (73.4%) underwent 24 hour ambulatory electrocardiography.

CAROTID ARTERY EXAMINATION

A reduction of the internal diameter of the carotid artery of 30% or more in one or both arteries was used for the definition of carotid stenosis.⁵ A quarter of the men fulfilled this criterion. Forty seven (10%) had a reduction in diameter exceeding 45%. In men with bilateral stenosis the most severely affected side was used for classification of the degree of lumen reduction.

The ultrasound examination of the carotid arteries was made with a continuous wave Doppler with a 5 MHz transducer (Dopscan 1050, Carolina Medical Electronics, King, North Carolina). With Dopscan 1050 it is possible to detect stenoses which reduce the internal carotid artery diameter by 30% or more with a sensitivity of 97% and a specificity of almost 100%. A reduction in diameter of 30% corresponds to a maximum frequency shift of 3.1 kHz, and a stenosis of $>45\%$ corresponds to a cut off point of 4.3 kHz.¹³ The examination was made with the subject in the supine position after 10 minutes of rest. Measurements were made in the common carotid artery 2 cm beneath the bifurcation; in the proximal internal carotid artery from the point of the vessel where the most abnormal Doppler signals were found; and 2 cm distally of the obstruction. If no Doppler signals could be obtained in the proximal and distal part of the internal carotid artery the vessel was diagnosed as totally occluded.

History of stroke at the baseline examination was based on the results of a questionnaire, clinical examination, and hospital records. The final judgment was made by a neurologist who was unaware of the result from the ultrasound examination.⁵

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The recording system consisted of pulse sensors (mercury in Silastic strain gauges) placed on the big toes and thumbs; two Wheatstone bridges with amplifiers to record changes in the resistance of the strain gauges; blood pressure cuffs (18×60 cm to measure systolic ankle pressure and 12×35 cm to measure the systolic upper arm pressure); a pressure transducer (Siemens-Elema EMT 746 with amplifier EMT 311) to record cuff pressures; and a six channel ink jet recorder (Siemens-Elema; Mingograph).^{14 15} Duplicate recordings were made with the subject in the supine position and the arithmetic average used. For each leg, an ankle-brachial blood pressure index was calculated by dividing the systolic pressure in the ankle by the highest systolic pressure in the upper arm.

Leg artery disease was defined as an ankle-brachial pressure index <0.90 in one or both legs.^{8 9} Subjects with a pressure index ≥0.90 in both legs were considered free from leg artery disease.

RISK FACTORS FOR ARTERIOSCLEROTIC DISEASE

Systolic and diastolic (phase V) blood pressures were measured in the right arm with the subject in the sitting position after 15 minutes of rest. Blood pressure was recorded to the nearest 5 mm Hg. Smoking habits were assessed by means of a structured questionnaire. The men were divided into never smokers (less than 1 g of tobacco a day for less than one year); former smokers (those who had stopped smoking at least a month before investigation); and current smokers. Plasma cholesterol concentrations were analysed by standard methods and expressed as mmol/l. Diagnosis of atrial fibrillation was based on the findings of 24 hour ambulatory electrocardiography.¹⁰

FOLLOW UP DATA

Mortality—The men were followed up from the baseline study in 1982-3 until their death or 31 March 1993. Mean (range) follow up time was 102.9 (3.2-128.4) months. Data on mortality were obtained from the mortality register of the Swedish National Bureau of Statistics. In 65% of the deaths necropsy was performed. Mortality was expressed as deaths per 1000 person years of observation. Cases coded 430.0-438.9 according to the *International Classification of Diseases*, eighth revision (ICD-8) were counted as deaths from cerebrovascular disease and cases coded 410.0-412.9 as deaths from ischaemic heart disease.

Rate of cerebrovascular events—The follow up period was from the cross sectional study in 1982-3 until the first cerebrovascular event, death, or 31 March 1993. Status was updated on each subject until this date. Mean (range) follow up was 97.0 (2.8-128.4) months. Cerebrovascular events were traced through the local patient administrative system, to which both of the two hospitals in the city are linked. End points were validated by study of the hospital records, results from computed tomography, and necropsy reports. A cerebrovascular event was defined as stroke by using the WHO definition¹⁶ (ICD-8 codes 430.0-434.9 and 436.0-438.9) or as transitory ischaemic attack¹⁷ (codes 435.0-435.9). Rates of cerebrovascular events were expressed as events per 1000 person years of observation.

STATISTICAL METHODS

Mortality and rate of cerebrovascular events in men with signs of carotid stenosis and in men with signs of leg artery disease were compared with rates in men without corresponding signs of disease. Computations were made by using the Kaplan-Meier method with the generalised Wilcoxon test.¹⁸ Risk factors at baseline were compared in men with and without carotid

stenosis who did and who did not suffer a cerebrovascular event during follow up by using analysis of variance comparison of means and χ^2 tests for comparison of proportions. Cox's proportional hazards model was used to study mortality and rate of cerebrovascular events in relation to carotid stenosis and arm-ankle pressure index, systolic blood pressure, smoking, and presence of atrial fibrillation, when previous stroke was controlled for.¹⁹

Results

ALL CAUSE MORTALITY AND RATE OF CEREBROVASCULAR EVENTS

Of the 470 men who were examined at 68 years of age, 26 (5.5%) had a history of stroke. Sixty one (13.0%) had at least one cerebrovascular event during follow up (table I). Of these, 54 (88.5%) had no previous episode of cerebrovascular disease. The cerebrovascular event was classified as stroke in 50 (82.0%) of the 61 cases. Ten of these had a transient ischaemic attack before their stroke. Eleven (18%) of the 61 men had a transient ischaemic attack only. Six men had haemorrhagic stroke. Seven men died within two weeks after the onset of stroke. The diagnosis of stroke was confirmed by computed tomography or by findings at necropsy in 38 (76.0%) of the 50 cases.

During follow up 158 men (33.6%) died. Of these, 16 died from focal cerebrovascular disease and 51 from ischaemic heart disease. Of the 121 men who were invited to participate in the health examination at 68 years of age but who declined to participate, 73 (60.3%) died during the follow up period. Three of these died from stroke and 17 from ischaemic heart disease.

INCIDENCE OF CEREBROVASCULAR DISEASE AND ALL CAUSE MORTALITY IN RELATION TO CAROTID STENOSIS

Fifteen of the 113 men with carotid stenosis involving a reduction of >30% in internal diameter had a stroke and three had a transient ischaemic attack, corresponding to a cerebrovascular event rate of 21.6/1000 person years. This rate was not significantly different from the rate in men with normal carotid arteries (14.8/1000 person years) ($P=0.188$) (table II; fig 1). Six out of 43 events (14%) were of the

FIG 1—Ten year survival rate free of cerebrovascular disease in 68 year old men with both carotid stenosis and low ankle-brachial pressure index (—○—); in men with low ankle-brachial pressure index only (---○---); in men with carotid stenosis only (—△—); and in men with no signs of disease (—□—)

vertebrobasilar type in men who had normal carotid arteries. In men with carotid stenosis no such events occurred. The rate of cerebrovascular events in men with a stenosis >45%—that is, the top 10% of the distribution—was 20.7/1000 person years (7/48).

The mortality in men with carotid stenosis >30% was 52.2/1000 person years. Men with normal carotid arteries had a mortality of 36.1/1000 person years ($P=0.030$) (table II; fig 2). Of the 47 men with carotid stenosis who died during follow up, five died from cerebrovascular disease and 22 from ischaemic heart disease. Of the 48 men who had carotid stenosis

exceeding 45%, 21 died during follow up, 14 of them from ischaemic heart disease.

INCIDENCE OF IPSILATERAL STROKE AND TRANSIENT ISCHAEMIC ATTACK

In the 65 men who had right carotid artery stenosis, 11 cerebrovascular events occurred. Of these, four were localised to the ipsilateral cerebral hemisphere, five affected the contralateral hemisphere, and two affected both hemispheres (table I). Among the 65 men with left sided carotid stenosis eight events occurred: five ipsilateral, two contralateral, and one bilateral (table I).

INCIDENCE OF CEREBROVASCULAR DISEASE AND ALL CAUSE MORTALITY IN MEN WITH LOW ANKLE-BRACHIAL PRESSURE INDEX

Thirty six per cent (24/66) of the men with leg artery disease had carotid stenosis >30%. The rate of cere-

brovascular events in men who had an ankle-brachial pressure index below 0.9 in either leg (38.6/1000 person years) was almost three times as high as it was in men with normal arm-ankle indices (13.5/1000 person years) ($P < 0.001$) (table II). Of the men with leg artery disease, the rate of cerebrovascular events in men without carotid stenosis was 40.7/1000 person years, and in men with carotid stenosis it was 34.8/1000 person years (fig 1).

Men with asymptomatic leg artery disease had an all cause mortality of 82.2/1000 person years, which was 2.5 times higher than that in men with normal pressure indices (34.2/1000 person years) ($P < 0.001$) (fig 2).

ATRIAL FIBRILLATION IN RELATION TO INCIDENCE OF CEREBROVASCULAR DISEASE AND ALL CAUSE MORTALITY

Of the 456 men participating in ambulatory electrocardiography, 19 (4.2%) had atrial fibrillation. Of these, 17 had chronic and two had intermittent atrial

TABLE I—Clinical characteristics of men with cerebrovascular disease (stroke and transient ischaemic attack) during 10 year follow up study of cohort of men born in 1914

Baseline data					Follow up event								
Case No	History of stroke	Atrial fibrillation	Left carotid stenosis (%)	Right carotid stenosis (%)	Transient ischaemic attack		Stroke				Death		
					Follow up time (months)	Type of transient ischaemic attack	Follow up time (months)	Type of stroke	Outcome	Verification by computed tomography	Verification by necropsy	Follow up time (months)	Cause of death
1			—	—	52	Left hemisphere	42	Cerebellar		Positive	NA		
2			—	—			36	Left hemisphere		NA	Positive	62	Biliary carcinoma
3			—	—			117	Brainstem		Negative	NA		
4			—	—	51	Vertebrobasilar	41	Cerebellar		Positive	NA		
5			—	—	16	Left hemisphere	35	Right hemisphere		Positive	NA	81	Cerebrovascular disease
6			—	—			110	Left plus brain stem		NA	NA		
7			—	—	99	Amaurosis fugax (right)				NA	NA		
8			—	—			5	Left hemisphere		Positive	NA		
9			—	—	3	Left hemisphere				Negative	NA		
10			—	—			110	Right hemisphere		Positive	NA		
11			—	—			24	Left hemisphere		NA	Positive	39	Pulmonary embolism
12			—	—			111	Right hemisphere		Positive	NA		
13			—	—	122	Amaurosis fugax (right)				Negative	NA		
14			—	—			50	Right hemisphere†		Positive	NA	97	Cerebrovascular disease
15			—	—			30	Both hemispheres		Positive	NA	82	Ischaemic heart disease
16	Yes	Yes	—	—	4	Right hemisphere	58	Right hemisphere	Fatal	Positive	Positive	58	Cerebrovascular disease
17			—	—	115	Right hemisphere				NA	NA		
18	Yes		—	—	46	Left hemisphere	32	Left hemisphere		Positive	NA	116	Cerebrovascular disease
19	Yes		—	—			13	Left hemisphere		Positive	Positive	13	Cerebrovascular disease
20	Yes		—	—	41	Left hemisphere*				NA	NA	115	Ischaemic heart disease
21			—	—			58	Right hemisphere	Fatal	Positive	NA	59	Cerebrovascular disease
22			—	—			39	Right hemisphere	Fatal	NA	Positive	39	Cerebrovascular disease
23		Yes	—	—			24	Cerebellar		Positive	Positive	69	Ischaemic heart disease
24			—	—	102	Left hemisphere				Positive	NA		
25		Yes	—	—			90	Right hemisphere		Positive	NA	106	Cerebrovascular disease
26			—	—	59	Left hemisphere	60	Left hemisphere		Positive	NA		
27			—	—			57	Left hemisphere		NA	NA		
28			—	—			92	Left hemisphere		Positive	NA		
29			—	—	34	Unclear	83	Right hemisphere†		Positive	NA		
30			—	—			104	Right hemisphere		NA	NA		
31			—	—			71	Right hemisphere		Positive	NA		
32			—	—				Right hemisphere plus cerebellum		Positive	NA		
33			—	—			111			Positive	NA		
34			—	—	28	Right hemisphere	79	Both hemispheres		Positive	NA	84	Cerebrovascular disease
35			—	—						NA	NA		
36			—	—			11	Paraphasia		NA	NA		
37			—	—			16	Right hemisphere		NA	NA	71	Cerebrovascular disease
38			—	—			19	Left hemisphere		NA	Positive	31	Ischaemic heart disease
39		Yes	—	—	58	Left hemisphere	59	Left hemisphere		NA	NA		
40	Yes		—	—			53	Right hemisphere		Positive	NA	98	Cerebrovascular disease
41			—	—			9	Left hemisphere		NA	NA	99	Cerebrovascular disease
42			—	—			48	Brain stem		Positive	NA		
43			—	—	31	Amaurosis fugax (left)				NA	NA		
			—	—			50	Both hemispheres		Positive	NA		
44			>30	—			63	Right hemisphere		Positive	NA		
45			>30	—			16	Left hemisphere		NA	NA		
46			>30	—	62	Right hemisphere				Negative	NA		
47			—	>30			82	Left hemisphere		NA	Positive	95	Endocarditis
48			—	>30			124	Left hemisphere		Positive	NA		
49			—	>30			7	Left hemisphere†		NA	Positive	8	Cerebrovascular disease
50			—	>30			36	Left hemisphere†	Fatal	Positive	NA	101	Cerebrovascular disease
51	Yes		—	>30			15	Right hemisphere†		Positive	NA	30	Accident
52			—	>30	69	Amaurosis fugax (bilateral)*				NA	NA		
53			—	>30			31	Right hemisphere†	Fatal	NA	Positive	31	Cerebrovascular disease
54			—	>30			23	Left hemisphere		Positive	NA		
55			>45	—	51	Left hemisphere	54	Left hemisphere		NA	NA		
56			>45	—	58	Left hemisphere				NA	NA		
57		Yes	>45	—			28	Left hemisphere		Positive	NA	45	Duodenal ulcer
58			—	>45	30	Left hemisphere*	74	Right hemisphere		NA	NA		
59			—	>45			30	Right hemisphere		Positive	NA	60	Cerebrovascular disease
60			>45	>45			103	Both hemispheres		Positive	NA		
61	Yes	Occluded					41	Left hemisphere		NA	NA	81	Ischaemic heart disease

*Patient in whom transient ischaemic attack led to carotid thromboendarterectomy.

†Haemorrhagic stroke.

NA=not applicable.

TABLE II—Ten year mortality and rate of cerebrovascular events (stroke and transient ischaemic attack) in relation to carotid stenosis, low ankle-brachial blood pressure index, and atrial fibrillation at 68 years of age

Presence of disease	Total mortality					Cerebrovascular event rate			
	No of subjects	No of deaths (%)	Total follow up time (years)	Deaths/1000 person years (95% confidence interval)	P value	No of events (%)	Total follow up time (years)	Events/1000 person years (95% confidence interval)	P value
Carotid stenosis > 30% one or both sides:									
No	357	111 (31.1)	3074.2	36.1 (24.3 to 79.9)	0.030	43 (12.0)	2910.0	14.8 (7.2 to 22.3)	0.188
Yes	113	47 (41.6)	900.7	52.2 (38.0 to 66.3)		18 (15.9)	835.4	21.6 (12.5 to 30.6)	
Ankle-brachial blood pressure index < 0.9 one or both ankles:									
No	404	120 (29.7)	3512.4	34.2 (22.7 to 45.6)	< 0.001	45 (11.1)	3331.3	13.5 (6.3 to 20.7)	< 0.001
Yes	66	38 (57.6)	462.6	82.2 (64.4 to 99.9)		16 (24.2)	414.0	38.6 (26.5 to 50.8)	
Atrial fibrillation:									
No	437	133 (30.4)	3762.9	35.3 (23.7 to 47.0)	0.005	53 (12.1)	3557.8	14.9 (7.3 to 22.5)	0.048
Yes	19	12 (63.2)	151.2	79.4 (61.9 to 96.9)		5 (26.3)	136.4	36.7 (24.8 to 48.5)	

TABLE III—Distribution of arteriosclerotic risk factors (mean (SD) 95% confidence interval) in relation to presence of carotid stenosis at baseline at 68 years of age

Follow up event	Risk factors at 68 years of age							
	Total No of subjects	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)	Plasma cholesterol (mmol/l)	No (%) who never smoked	No (%) of former smokers	No (%) of current smokers	No (%) with atrial fibrillation
No carotid stenosis:								
No disease	314	152 (20; 150 to 154)	92 (10; 91 to 93)	5.9 (1.0; 5.8 to 6.1)	63 (20)	144 (46)	107 (34)	12 (3.7)
Stroke or transient ischaemic attack	43	161 (26; 153 to 169)	97 (11; 93 to 100)	6.3 (1.0; 5.9 to 6.6)	9 (21)	17 (39)	17 (39)	4 (9.8)
Carotid stenosis:								
No disease	95	154 (22; 150 to 159)	92 (12; 89 to 94)	6.1 (1.2; 5.9 to 6.3)	15 (16)	47 (49)	33 (35)	3 (3.4)
Stroke or transient ischaemic attack	18	156 (26; 142 to 169)	93 (12; 87 to 99)	6.0 (1.0; 5.6 to 6.5)	0	12 (67)	6 (33)	1 (6.3)
P value when comparing groups		0.052	0.066	0.225	0.352			0.314

TABLE IV—Multivariate analysis (Cox's proportional hazards model) of rate of cerebrovascular events (stroke and transient ischaemic attack) and mortality in relation to carotid stenosis, leg artery disease, and risk factors at 68 years of age, when previous stroke is controlled for

Risk	Rate of cerebrovascular events		Mortality	
	Relative risk (95% confidence interval)	P value	Relative risk (95% confidence interval)	P value
Carotid stenosis (yes v no)	1.2 (0.7 to 2.2)	0.547	1.2 (0.8 to 1.8)	0.342
Leg artery disease (yes v no)	2.0 (1.1 to 3.7)	0.041	2.0 (1.3 to 3.0)	0.001
Atrial fibrillation (yes v no)	1.8 (0.7 to 4.6)	0.248	1.6 (0.9 to 3.0)	0.114
Systolic blood pressure (per 5 mm Hg)	1.082 (1.017 to 1.150)	0.013	1.030 (0.990 to 1.073)	0.147
History of smoking (yes v no)	1.2 (0.6 to 2.5)	0.618	1.8 (1.1 to 3.1)	0.036

fibrillation. Men with atrial fibrillation had a higher rate of cerebrovascular events (36.7/1000 person years) ($P=0.048$) and higher total mortality (79.4/1000 person years) ($P=0.005$) than men without fibrillation (corresponding rates 14.9/1000 and 35.3/1000, respectively; table II).

RATE OF CEREBROVASCULAR EVENTS IN RELATION TO ARTERIOSCLEROTIC RISK FACTORS

In the risk factor analysis men who did and who did not develop cerebrovascular disease during follow up were compared after stratification according to presence and absence of carotid stenosis at 68 years of age (table III). In men who had no signs of carotid stenosis at 68, mean systolic blood pressure at that age was significantly higher in men who during follow up suffered a stroke or a transient ischaemic attack (161 mm Hg; 95% confidence interval 153 to

169 mm Hg) than it was in the men who remained free from cerebrovascular disease (152 mm Hg; 150 to 154 mm Hg).

MULTIVARIATE ANALYSIS

Multivariate analysis of mortality and cerebrovascular morbidity in relation to carotid stenosis, arm-ankle pressure index, previous stroke, and risk factors showed that the presence of a pressure index < 0.9 in one or both legs at 68 years of age was independently associated both with an increased mortality (relative risk 2.0; 95% confidence interval 1.3 to 3.0) and with an increased rate of cerebrovascular events 2.0; 1.1 to 3.7 during 10 years of follow up (table IV). The association between carotid stenosis and mortality that was found in the univariate analysis did not remain in the Cox's proportional hazards model (1.2; 0.8 to 1.8). No significant association was found between carotid stenosis and rate of cerebrovascular events (1.2; 0.7 to 2.2). Systolic blood pressure was found to be independently associated with an increased rate of cerebrovascular events, with an 8.2% rise of relative risk per 5 mm Hg increment of systolic blood pressure.

Discussion

This cohort study was designed to describe the natural course of carotid stenosis. In agreement with the ethics committee at Lund University we decided that the probands and their doctors should not be informed about the results from the carotid artery examination. The lack of an association between carotid stenosis and cerebrovascular disease should therefore not have been confounded by selective treatment of men with carotid stenosis to prevent stroke. Only four of the men with carotid stenosis were subject to carotid endarterectomy during follow up. Three of these had their cerebrovascular end point before surgery.

The relatively narrow 95% confidence interval around the point estimate of the relative risk does not indicate that the lack of association is explained by low power. A more plausible explanation is a concomitant higher mortality from other arteriosclerotic diseases in men with carotid stenosis, which agrees with conclusions of other studies.²⁰⁻²² The mortality from

FIG 2—Ten year survival rate in 68 year old men with both carotid stenosis and low ankle-brachial pressure index (—); in men with low ankle-brachial pressure index only (---); in men with carotid stenosis only (....); and in men with no signs of disease (- - -)

Key messages

- New technologies have made it possible to assess non-invasively the presence of asymptomatic atherosclerosis in different parts of the arterial tree
- Asymptomatic atherosclerosis in carotid and leg arteries is a common occurrence among elderly people
- Both conditions were found to be associated with an excess cardiovascular mortality
- Compared with leg artery disease, asymptomatic carotid stenosis was not found to be associated with an increased risk of stroke
- Assessment of peripheral atherosclerotic disease by measurement of arm and ankle blood pressure is a useful method for identifying patients with an increased risk of stroke

ischaemic heart disease increased with the severity of carotid stenosis. Of the 34 men who had a carotid stenosis exceeding 50%, 17 died during follow up, 13 of them from ischaemic heart disease. Three of these had had a stroke. None of the 17 men with severe stenosis who survived during follow up, however, had a stroke.

The incidence of cerebrovascular events in relation to carotid artery disease must take into account the validity of the method used for detection of carotid stenosis. Dopscan 1050 has in comparison with angiograms been shown to have a sensitivity of 97% and a specificity of almost 100% for the detection of a reduction in the diameter of the carotid artery lumen 30% or more.¹³ Hence we could not explain the high proportion of cerebrovascular events in men with normal results of carotid ultrasound examination on the basis of an inadequate sensitivity.

Carotid stenosis is associated with an increased prevalence of leg arteriosclerosis.⁷ Non-invasively detected leg artery disease has previously been reported to be associated with stroke.⁶ In this study, a low ankle-brachial pressure index was found to be the strongest marker for cerebrovascular disease. These men had no clinical signs or symptoms of leg artery disease. The high incidence of myocardial infarction⁷ and stroke associated with a low arm-ankle index illustrates that leg artery disease is a sign indicating generalised arteriosclerosis. As the increased mortality associated with carotid stenosis disappeared in the multivariate analysis we cannot consider carotid stenosis to be a similar marker. The risk of stroke or transient ischaemic attack associated with leg artery disease was independent of carotid stenosis. Prediction of risk of future stroke or transient ischaemic attack can therefore be improved by measurement of the arm-ankle pressure gradient.

We have confirmed the well known risk of stroke associated with high systolic blood pressure and presence of atrial fibrillation.^{11,23} The association between stroke and high blood pressure, however, was not observed in men with carotid stenosis. This is probably because of selection bias—that is, hypertensive men with carotid stenosis had died from ischaemic heart disease.

An important finding in our study is the much

increased risk of cerebrovascular disease in subjects with a reduced arm-ankle pressure index. The risk associated with a certain marker should not be assessed in relative numbers only. Seventy four per cent (45/61) of the cerebrovascular events occurred in men with normal ankle-brachial index, 70% (43/61) in men without carotid artery stenosis, and 44% (27/61) in men who had normal carotid arteries, normal arm-ankle index, and no atrial fibrillation. This suggests that in a non-selected group of men the event leading to stroke in several cases is triggered within the intracerebral vascular area. This observation should be considered in the clinical evaluation of patients with asymptomatic carotid artery stenosis.

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