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Mechanisms of late stroke after myocardial infarct: the Lausanne Stroke Registry

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Abstract

To assess the potential mechanisms and patterns of late stroke after myocardial infarct, 94 consecutive patients with first ever stroke at least three months after myocardial infarction (anterior 67%; inferior 12%; widespread 12%) were studied. Systematic investigations were those of the Lausanne Stroke Registry and included brain CT, extra/transcranial Doppler ultrasound, 12-lead ECG, three-lead continuous ECG monitoring for at least 24 hours after admission, and transthoracic two dimensional echocardiography. All patients had an akinetic left ventricular segment, but only 11 (12%) had a visible thrombus. Eleven (12%) of the patients had long standing hypertension and a small deep infarct so that lacunar infarction due to small artery disease was as likely to be the cause as cardioembolic stroke. There was severe internal carotid artery disease ($\geqslant$ 50% stenosis or occlusion) ipsilateral to the infarct in 20 (21%) of the patients with anterior circulation stroke. A potential cardiac source of embolism other than akinetic left ventricular segment was found in 14 (15%) patients, atrial fibrillation (12%) being the commonest. Only 13 (14%) patients had no potential cause for stroke other than akinetic left ventricular segment. The study group was compared with 466 patients with first stroke but no akinetic left ventricular segment on two dimensional echocardiography, and with 94 patients with first stroke and a potential cardiac source of embolism but no akinetic left ventricular segment and no history of ischaemic heart disease. Logistic regression analysis showed that older age, male sex, hypercholesterolaemia, and vascular claudication were significantly and independently associated with stroke after myocardial infarction. The findings suggest that late stroke after myocardial infarction may often be a direct consequence of the sequelae of myocardial infarction, but other potential cardiac causes of stroke, large artery disease, and lacunar stroke must also be considered.

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Myocardial wall abnormalities are a recognised cause of embolic cerebral infarction.[1–8] Stroke may follow acute myocardial infarction in 3% of the cases,[1] and left ventricular aneurysm may be a cause of delayed stroke after myocardial infarction.[1 2] However, the most common cardiac abnormality after myocardial infarction is not aneurysm but localised wall akinesia without dilatation. As the role of this abnormality in delayed stroke after myocardial infarction is unclear, the aim of the present work was to study a group of consecutive patients with first stroke at least three months after myocardial infarction to assess the potential mechanism and patterns of stroke in these patients. We assessed coexisting potential causes of stroke and compared the findings with those in patients with stroke but without akinetic left ventricular segment and in patients with another potential cardiac source of embolism.

Methods

Patients with stroke at least three months after myocardial infarction were selected from all patients (n = 1802) consecutively included in the Lausanne Stroke Registry, a hospital based computerised prospective registry of patients with first ever stroke (cerebral infarction or haemorrhage, neurological deficit lasting more than 24 hours). The characteristics of this registry have been presented in detail elsewhere.[9]

All patients were assessed by at least one staff neurologist within six days of stroke. Systematic investigations included brain CT (up to four examinations, the first within seven days of stroke) with and without contrast (except when the patient was known to be allergic to contrast material), Doppler ultrasound with frequency spectral analysis and B-mode echotomography (common, external, and internal carotid arteries, vertebral arteries at the retromastoid level, subclavian arteries, ophthalmic arteries), transcranial Doppler, 12-lead ECC, three-lead continuous ECC monitoring for at least 24 hours after admission, two dimensional echocardiography, and standard blood and urine tests. Cerebral angiography was performed in selected patients.

Akinetic left ventricular segment was diagnosed on the basis of two dimensional echocardiography. The criteria for akinetic left ventricular segment were those of the American Society of Echocardiography.[10] Other potential cardiac sources of embolism included intracardiac thrombus or tumour, rheumatic mitral stenosis, prosthetic aortic

Table Number (percentage) of patients with risk factors

	Previous myocardial infarction	*Without previous myocardial infarction*	*Potential cardiac source of embolism/no ischaemic heart disease*
Total	94	466	94
Age			
mean (SD)	64 (10)*†	54 (16)	48 (14)
Sex			
men	84 (89)*†	268 (57)	47 (50)
women	10 (11)	198 (42)	47 (50)
Hypertension	42 (45)*†	137 (57)	13 (14)
Diabetes	17 (18)*†	37 (8)	3 (3)
Smoking	36 (38)	168 (36)	34 (36)
Hypercholesterolaemia	21 (22)*	55 (12)	10 (11)
Haematocrit	25 (27)	104 (22)	14 (15)
Family history	12 (13)	29 (6)	4 (4)
Vascular claudication	12 (13)*	17 (3)	3 (3)
Transient ischaemic attacks	24 (26)	104 (22)	26 (28)

*$p < 0.05$ when comparing patients with and without previous myocardial infarction.
†$p < 0.05$ when comparing patients with previous myocardial infarction with patients with another potential cardiac source of embolism without ischaemic heart disease.

and mitral valve, endocarditis, atrial fibrillation, sick sinus syndrome, and global cardiac hypokinesia or dyskinesia. Risk factors and concomitants (hypertension, diabetes mellitus, current or former oral contraceptive use, cigarette smoking, hypercholesterolaemia, venous haematocrit, history of migraine, ischaemic heart disease, arrhythmia or vascular claudication, and family history of stroke or heart disease), characteristics of the stroke onset, clinical findings, previous transient ischaemic attacks (TIAs), functional disability, type and cause of the stroke were defined and analysed following the guidelines of the registry.[9]

We studied separately the subgroup of patients with no alternative cause of stroke other than myocardial infarction sequelae [without coexisting large artery disease (as detected by Doppler ultrasound and B-mode echotomography) and without evidence for small artery disease (no lacunar infarct, no history of hypertension)], in whom the likely cause of stroke was cardioembolism. The patients with late stroke after myocardial infarction were compared (1) with the patients with first ever stroke who were admitted during the same period but who had no akinetic left ventricular segment on two dimensional echocardiography [466 patients, 268 (57·5%) men and 198 (42·5%) women, with a mean age of 54 (SD 16) years (range, 16 to 95 years)]; (2) with the patients with first ever stroke who were admitted during the same period and who had another potential cardiac source of embolism but no akinetic left ventricular segment and no history of ischaemic heart disease [94 patients, 47 (50 %) men and 47 (50%) women, with a mean age of 48 (14) years (range 17 to 77 years)].

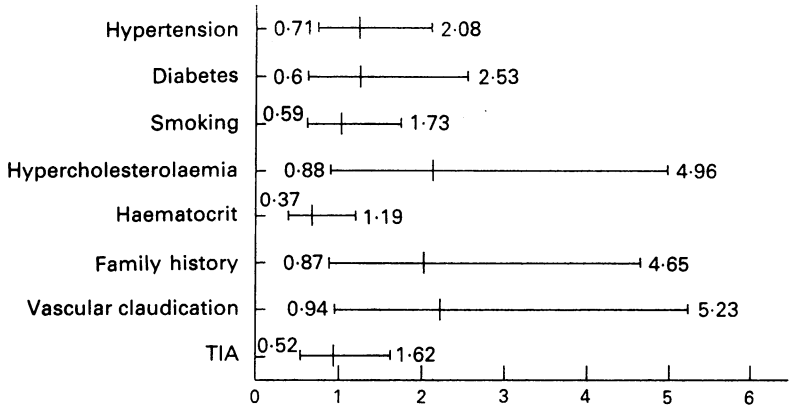

Figure Comparison between patients with and without old myocardial infarction. Odds ratio and 95% confidence interval (adjusted for age and sex) for vascular risk factors.

We performed statistical analysis of 2 × 2 contingency tables using the χ^2 test (on Fisher's two tailed exact test when the expected number in any cell was less than 5). For multiple comparisons, we used the procedure proposed by Hochberg for multiple significance testing.[11] A logistic regression model was fitted using GLIM software[12] to evaluate the presence of risk factors and concomitants as coincidental factors in patients with stroke and akinetic left ventricular segment.

Results

There were 94 patients with late stroke after myocardial infarction, all with akinetic left ventricular segment on two dimensional echocardiography [84 (89·4%) men and 10 (10·6%) women, with a mean age of 64·5 (10·2) years (range 34 to 39 years)]. Forty two (44·7%) patients had hypertension, 17 (18%) had diabetes mellitus, 36 (38·3%) smoked cigarettes regularly, and 21 (22·3%) had hypercholesterolaemia. Venous haemotocrit on admission was higher than 0·45 in 25 (26·5%) patients, 12 (12·7%) patients had a history of vascular claudication, and 12 (12·7%) had a family history of stroke or heart disease. When compared with the group of patients without myocardial infarction, the patients with old myocardial infarction were significantly older, they were more frequently men, they more often had hypertension, diabetes mellitus, hypercholesterolaemia, or a history of vascular claudication (table). The figure shows the odds ratio with 95% confidence intervals adjusted for age and sex. When compared with patients with another potential cardiac source of embolism, the patients with old myocardial infarction were significantly older, they were more frequently men, and more often had hypertension and diabetes mellitus (table).

After stepwise multiple logistic regression, only age, sex, history of vascular claudication, and hypercholesterolaemia were linked to the presence of old myocardial infarction in stroke patients, according to:

$$P(\text{akinetic left ventricular segment}) = \frac{e^f}{1 + e^f}$$

where: $f = -4{\cdot}43 + 0{\cdot}05x_1 - 1{\cdot}75x_2 + 0{\cdot}81x_3 + 0{\cdot}77x_4$

where: x_1 = age, x_2 = sex, x_3 = history of vascular claudication, x_4 = hypercholesterolaemia. P(old myocardial infarction) = probability of old myocardial infarction in patients with stroke with standard errors of: 0·97 for intercept, 0·01 for age, 0·35 for sex, 0·42 for history of vascular claudication, and 0·31 for hypercholesterolaemia.

Among the 94 patients with old myocardial infarction, only 13 (14%) had no large artery

disease appropriate to the symptoms and no evidence of small artery disease (no lacunar infarct, no hypertension). However, when we compared this subgroup with the remaining patients with old myocardial infarction, there was no significant difference for risk factors and concomitants.

HEART DISEASE

Heart auscultation was abnormal in 33 (35·2 %) patients with akinetic left ventricular segment; 91 (96·8 %) patients with old myocardial infarction had ECG findings of ischaemic heart disease. The topography of akinetic left ventricular segment corresponded with the topography of myocardial infarction on ECG [anterior wall myocardial infarction 63 (67%), inferior wall myocardial infarction 11 (12%), and widespread myocardial infarction 11 (12%)]. Fourteen (14·9%) patients had a history of cardiac dysrhythmias [atrial fibrillation: 11 (12%); sick sinus syndrome: one (1%); supraventricular tachycardia: two (2%)]. On the admission ECG 13 (13·7 %) patients had a cardiac dysrhythmia [atrial fibrillation: nine (10%); ventricular extrasystolia: three (3%); bradycardia: one (1%)], 12 (12·8%) patients had a conduction defect, and five (5·3%) patients had signs of left ventricular hypertrophy. There was no significant difference between the three groups for the frequence of cardiac dysrhythmia and conduction defects. Eleven (11·7%) patients with akinetic left ventricular segment also had a left ventricular thrombus. No patient with akinetic left ventricular segment had coexisting rheumatic mitral stenosis, prosthetic aortic or mitral valve, endocarditis, or intracardiac tumour.

ARTERIAL DISEASE

Thirteen (13·8%) patients with akinetic left ventricular segment had a neck bruit (ipsilateral to the infarct in seven patients, contralateral in one patient, and bilateral in five patients). Twenty (21·3%) patients with old myocardial infarction had $\geqslant$ 50% stenosis or occlusion of the internal carotid artery (ICA) ipsilateral to the cerebral infarct; nine (9·6%) patients had $\geqslant$ 50% stenosis or occlusion of the contralateral ICA. Patients with old myocardial infarction more often had a neck bruit and a significant stenosis or occlusion of precerebral arteries than patients without old myocardial infarction [$\geqslant$ 50% stenosis or occlusion of the ipsilateral ICA: 23 (10%), p = 0·001; $\geqslant$ 50% stenosis or occlusion of the contralateral ICA: eight (2%), p = 0·000] and those with another potential cardiac source of embolism [$\geqslant$ 50% stenosis or occlusion of the ipsilateral ICA: six (6%), p = 0·000; $\geqslant$ 50% stenosis or occlusion of the contralateral ICA: one (1%), p = 0·022]. Eleven (11·70%) patients with old myocardial infarction had coexisting small artery disease. This proportion was similar to that found in the patients without old myocardial infarction and in those with another potential cardiac source of embolism. There was no significant difference between the three groups for the frequency of visible intracranial occlusions suggesting embolism in the patients who had angiography within 48 hours of stroke.

PREVIOUS TIAS AND STROKE ONSET

Twenty four (25·5%) patients with old myocardial infarction reported TIAs before the stroke. There was no significant difference when compared with the patients without old myocardial infarction [104 (22%)], but compared with patients with another potential cardiac source of embolism, patients with old myocardial infarction less frequently had TIAs ipsilateral to the cerebral infarct [13 (14%) vs 22 (23%), p = 0·041]. There was no significant difference between the three groups for the number and duration of the TIAs or for the TIA stroke interval. In the old myocardial infarction patient group, stroke was immediately complete in 79 (84%) patients, progressed smoothly in six (6·4%) patients (< 24 hours in four patients > 24 < 36 hours in two patients), and fluctuated in nine (9·6%) patients (< 24 hours in one patient, > 24 < 30 hours in eight patients). Stroke was more often immediately complete in patients with than without old myocardial infarction (84% vs 74%, p = 0·010). Stroke was as often immediately complete in patients with old myocardial infarction as in patients with another potential cardiac source of embolism. Two (2·1%) patients with old myocardial infarction had a syncope (sudden transient loss of consciousness) as the first cerebral symptom.

CEREBRAL INFARCT

The stroke was seen on CT in 85 (87·2%) patients with old myocardial infarction, in 393 (84·3%) patients without old myocardial infarction, and in 84 (89·36%) patients with another potential cardiac source of embolism. Ninety three (98·9%) patients with old myocardial infarction had a cerebral infarction and one (1·1%) patient apparently had a primary cerebral haemorrhage. This proportion was similar to that found in patients without old myocardial infarction [cerebral infarct: 450 (96·6%); primary cerebral haemorrhage: 16 (3·4%)]. Patients with old myocardial infarction had a lower proportion of cerebral haemorrhage than patients with another potential cardiac source of embolism (cerebral infarction 84 (89·36%); cerebral haemorrhage 10 (10·63%). Fifty one (54%) patients with old myocardial infarction had a left cerebral infarction, 34 (36%) patients had a right cerebral infarction, and nine (10%) had a bilateral cerebral infarction. In 21 (22%) with old myocardial infarction, the cerebral infarction was vertebrobasilar and in 64 (68%) patients it was in the carotid territory [inferior division of the middle cerebral artery (MCA):19 (20%); deep ICA:16 (17%); superior division MCA:20 (21%); superficial + deep MCA:seven (7%); watershed infarct: two (25)]. There was no significant difference between patients with old myocardial infarction, patients without old myocardial infarction, and patients with

another potential cardiac source of embolism for the topography of the cerebral infarcts.

NEUROLOGICAL DEFICIT

Patients with old myocardial infarction more often had headache at onset than patients without old myocardial infarction (11 (11·7%) vs 109 (23·4%, p = 0·049)), and as often as patients with another potential cardiac source of embolism. Eleven (11·7%) patients with old myocardial infarction had decreased consciousness (somnolence or coma) on admission similar to the patients without old myocardial infarction or the patients with another potential cardiac source of embolism. Fifty three (56%) patients with old myocardial infarction had speech disturbances (dysarthia or aphasia). The clinical findings of patients with old myocardial infarction were: motor only: 30 (32%); sensory only: four (4%); visual field only: 10 (11%); motor + sensory: 19 (20%); motor + visual field: one (1%); motor + sensory + visual field: 11 (12%); sensory + visual field: three (3%); other deficit: 16 (17%). There was no significant difference between the three groups for the clinical findings.

SHORT TERM EVOLUTION

Short term evolution was similar in patients with old myocardial infarction, those without old myocardial infarction, and those with another potential cardiac source of embolism. In the old myocardial infarction group, three (3·2%) patients died and 56 (59·6%) were able to return to all or most previous activities.

Discussion

The frequency and potential role of the sequelae of myocardial infarction in patients with stroke have not been extensively studied and when mentioned it is usually without special analysis.[13–22] The frequency of old myocardial infarction in our series of first stroke patients (17%) was between the 5·2% (three of 76 patients studied by two dimensional echocardiography) reported by Caplan *et al*[14] and the 24·5% (14 of 57 patients studied by two dimensional echocardiography) reported by Franco *et al.*[18] Our study is the first in which systematic CT, Doppler ultrasound, and echocardiography were performed in patients with late stroke after myocardial infarction, providing an evaluation of the coexistence of other potential causes of stroke than akinetic left ventricular segment in these patients. When compared with patients with stroke but no old myocardial infarction, or with patients with another potential cardiac source of embolism, the main characteristics of the patients with old myocardial infarction were older age, male gender, history of vascular claudication, and hypercholesterolaemia. Most of our patients had an anterior wall myocardial infarction and akinetic left ventricular segment, which is more often associated with left ventricular thrombi than inferior wall myocardial infarction.[23 24]

Follow up studies have suggested that patients with myocardial infarction had a significant increase in risk of stroke during the first two to three months after myocardial infarction, but the subsequent risk was poorly assessed.[25 26] Clinical trials with a long term follow up suggested that the risk of ischaemic stroke during the first three years after myocardial infarction is about 3%.[27 28] Jones, *et al.*[29] found that 10 of 34 patients with myocardial infarction at least three months before stroke had no possible cause of stroke other than an akinetic left ventricular segment. Fourteen per cent of our patients had no potential cause for stroke other than akinetic left ventricular segment, and we assume that at least in that subgroup of patients, akinetic left ventricular segment was a likely source of cerebral embolism, even without visible thrombi.

Many of the patients with ischaemic stroke may have a coexisting potential cardiac source of embolism and arterial disease.[15 19] A previous study from this centre[30] showed that approximately one quarter of the patients with cerebral hemispheric infarcts and a potential cardiac source of embolism also had appropriate carotid disease. In our series, more than a fifth of the patients with old myocardial infarction had $\geqslant$ 50% stenosis or occlusion of the ICA ipsilateral to the stroke, this proportion being higher than that found in patients without old myocardial infarction and in patients with another potential cardiac source of embolism. Also, 12% of the patients with old myocardial infarction had long standing hypertension and a small infarct limited to the territory of deep perforators, an association which has been considered to be very suggestive of small artery disease.[31 32] This proportion was not different from that found in patients without old myocardial infarction and in patients with another potential cardiac source of embolism, and is also similar to the 13% reported in patients with nonvalvular atrial fibrillation.[33] Conversely, 17% of patients with infarct in the territory of deep perforators may have a potential cardiac source of embolism.[34] Coexisting potential cardiac sources of embolism may also confuse the exact role of each potential source. These facts make it difficult to determine the exact mechanism of stroke in many patients, in whom small artery disease, artery to artery embolism and cardioembolism may be equally likely.

Although it seems impossible to establish a predictive clinical profile of cardioembolic stroke, there are some features which may suggest an embolic mechanism.[30 35–37] Actually, in 84% of our patients with old myocardial infarction, stroke was immediately complete, a fact which has been associated with the presence of a potential cardiac source of embolism.[14 30 37 38] Also, only 14% of the patients with old myocardial infarction reported prior TIAs ipsilateral to the cerebral infarction, which have usually been linked to an atherothrombotic mechanism, though they may also occur in cardioembolic stroke.[30 37 38]

Finally, cerebral infarct involved the superficial MCA territory in nearly half of our patients with old myocardial infarction, a location which suggests an embolic mechanism,[39 40] but which may not allow distinction of an arterial from a cardiac source of embolism, though the proportion of cardioembolism is higher in posterior MCA territory infarcts and lower in anterior MCA territory infarcts.[30]

Though many patients with old myocardial infarction have coexisting small and large artery disease, there is a subgroup of patients in whom we were unable to find another potential cause of stroke. These data suggest that myocardial infarction and its direct cardiac consequences may be a cause of stroke not only acutely but also thereafter.

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1 Cerebral Embolism Task Force. Cardiogenic brain embolism. *Arch Neurol* 1986;**43**:71–84.
2 Cerebral Embolism Task Force. Cardiogenic brain embolism. The second report of the Cerebral Embolism Task Force. *Arch Neurol* 1989;**46**:727–43.
3 Komrad MS, Coffey CE, Coffey KS, McKinnis R, Massey EW, Califf RM. Myocardial infarction and stroke. *Neurology* 1984;**34**:1403–9.
4 Left ventricular thrombosis and stroke following myocardial infarction. Editorial. *Lancet* 1990;**335**:759–60.
5 Fuster V, Halperin JL. Left ventricular thrombi and cerebral embolism. *N Engl J Med* 1989;**320**:392–4.
6 Stratton JR, Nemanich JW, Johannessen KA, Resnick AD. Fate of left ventricular thrombi in patients with remote myocardial infarction or idiopathic cardiomyopathy. *Circulation* 1988;**78**:1388–93.
7 Fuster V, Gersh BJ, Giuliani ER, Tajik AJ, Brandenburg RO, Frye RL. The natural history of idiopathic dilated cardiomyopathy. *Am J Cardiol* 1981;**47**:525–31.
8 Gottdiener JS, Gay JA, VanVoorhees L, DiBianco R, Fletcher RD. Frequency and embolic potential of left ventricular thrombus in dilated cardiomyopathy: assessment by two-dimensional echocardiography. *Am J Cardiol* 1983;**52**:1281–5.
9 Bogousslavsky J, Van Melle G, Regli F. The Lausanne Stroke Registry: analysis of 1000 consecutive patients with first stroke. *Stroke* 1988;**19**:1083–92.
10 Henry WLA, DeMaria A, Feigenbaum H, *et al.* Report of the American Society of Echocardiography Committee on Nomenclature and Standards: identification of myocardial wall segments. *J Am Soc Ech* 1982;**3**:1–15.
11 Hochberg Y, Benjamini Y. More powerful procedures for multiple significance testing. *Statistics in Medicine* 1990;**9**:811–8.
12 GLIM 3·77. London, Royal Statistical Society, 1985.
13 Greenland P, Knopman DS, Mikell FI, Asinger RW, Anderson DC, Good DC. Echocardiography in diagnostic assessment of stroke. *Ann Intern Med* 1981;**95**: 51–3.
14 Caplan LR, Hier DB, D'Cruz I. Cerebral embolism in the Michael Reese Stroke Registry. *Stroke* 1983;**14**: 530–6.
15 Gagliardi R, Benvenuti L, Frosini F, Ammannati F, Barletta GA, Fantini F. Frequency of echocardiographic abnormalities in patients with ischemia of the carotid territory—a preliminary report. *Stroke* 1985;**16**:118–20.
16 Rosa A, Masmoudi K, Barbieux D, Cartz L, Mizon JP, Lesbre JPH. Echocardiographie bidimensionnelle dans 100 cas d'accidents ischemiques cérébraux inexpliqués. *Press Méd* 1990;**19**:73–5.
17 Kittner SJ, Sharkness CM, Price TR, *et al.* Infarcts with a cardiac source of embolism in the NINCDS Stroke Data Bank: historical features. *Neurology* 1990;**40**: 281–4.
18 Franco R, Alam M, Ausman J, Pickard SD, Goldstein S. Echocardiography in cerebrovascular accidents and cerebral transient ischemic attacks. *Circulation* 1980; **62**(supp III):22.
19 Rem JA, Hachinski VC, Boughner DR, Barnett HJM. Value of cardiac monitoring and echocardiography in TIA and stroke patients. *Stroke* 1985;**16**:950–6.
20 Bogousslavsky J, Hachinski VC, Boughner DR, Fox AJ, Viñuela F, Barnett HJM. Cardiac and arterial lesions in carotid transient ischemic attacks. *Arch Neurol* 1986; **43**:223–8.
21 Good DC, Frank S, Verhulst S, Sharma B. Cardiac abnormalities in stroke patients with negative arteriograms. *Stroke* 1986;**17**:6–11.
22 Bergeron GA, Shah PM. Echocardiography in patients with acute cerebral events. *Clin Cardiol* 1982;**5**:637–9.
23 Asinger RW, Mikell FL, Elsperger J, Hodges M. Incidence of left-ventricular thrombus after acute transmural myocardial infarction. Serial evaluation by two-dimensional echocardiography. *N Engl J Med* 1981; **305**:297–302)
24 Keren A, Goldberg S, Gottlieb S, *et al.* Natural history of left ventricular thrombi: their appearance and resolution in the posthospitalization period of acute myocardial infarction. *JACC* 1990;**15**:790–800.
25 McAllen PM, Marshall J. Cerebrovascular incidents after myocardial infarction. *J Neurol Neurosurg Psychiatry* 1977;**40**:951–5.
26 Dexter DD, Whisnant JP, Connolly DC, O'Fallon WM. The association of stroke and coronary heart disease: a population study. *Mayo Clin Proc* 1987;**62**:1077–83.
27 Report of the 60-Reinfarction Study Research Group. A double-blind trial to assess long-term anticoagulant therapy in elderly patients after myocardial infarction. *Lancet* 1980;**ii**:989–94.
28 Resnekov L, Chediak J, Hirsh S. Antothrombotic agents in coronary artery disease. *Chest* 1986;**89**(supp):54s-67s.
29 Jones RD, Breslin DR, Naggar CZ, Burlington MA. Cerebrovascular disease associated with echocardiographic documented focal segmental hypokinesia and remote myocardial infarction: does a causal relation exist? *Ann Neurol* 1986;**20**:159.
30 Bogousslavsky J, Cachin C, Regli F, Despland PA, Van Melle G, Kappenberger L (for the Lausanne Stroke Registry Group). Cardiac sources of embolism and cerebral infarction—clinical consequences and vascular concomitants: The Lausanne Stroke Registry. *Neurology* 1991;**41**:855–9.
31 Fisher CM. Lacunes: small, deep cerebral infarcts. *Neurology* 1965;**15**:774–84.
32 Fisher CM. Lacunar infarcts: a review. *Cerebrovasc Dis* 1991;**1**:311–20.
33 Bogousslavsky J, Van Melle G, Regli F, Kappenberger L. Pathogenesis of anterior circulation stroke in patients with nonvalvular atrial fibrillation: the Lausanne Stroke Registry. *Neurology* 1990;**40**:1046–50.
34 Ghika JA, Bogousslavsky J, Regli F. Infarcts in the territory of the deep perforators from the carotid system. *Neurology* 1989;**39**:507–12.
35 Ramirez-Lassepas M, Cipolle RJ, Bjork RJ, Kowitz J, Snyder BD, Weber JC, Stein SD. Can embolic stroke be diagnosed on the basis of neurologic clinical criteria? *Arch Neurol* 1987;**44**:87–9.
36 Kittner SY, Sharkness C, Price TR, Sloan MA, Wolf PA, Mohr JP, Hier DB. Infarcts with a cardiac source of embolism: cortical versus subcortical deficits. *Ann Neurol* 1989;**26**:156.
37 Kittner SJ, Sharkness CM, Sloan MA, *et al.* Infarcts with a cardiac source of embolism in the NINDS Stroke Data Bank: neurologic examination. *Neurology* 1992;**42**: 299–302.
38 Chambers BR, Donnan GA, Bladin PF. Patterns of stroke. An analysis of the first 700 consecutive admissions to the Austin hospital stroke unit. *Aust NZ J Med* 1983;**13**:57–64.
39 Damasio H. A computed tomographic guide to the identification of cerebral vascular territories. *Arch Neurol* 1983;**40**:138–42.
40 Blackwood W, Hallpike JF, Kocen RS, Mair WGP. Atheromatous disease of the carotid arterial system and embolism from the heart in cerebral infarction: a morbid anatomical study. *Brain* 1969;**92**:897–910.