SHORT REPORT

Recurrent lacunar infarction following a previous lacunar stroke: a clinical study of 122 patients

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Objective: To determine clinical variables related to recurrent lacunar infarction following a previous lacunar stroke.

Methods: A total of 122 out of 733 consecutive patients with lacunar infarction collected from a hospital based registry between 1986 and 2004 were readmitted because of a recurrent lacunar infarction. In a subset of 59 patients, cognition was assessed using the Mini-Mental State Examination (MMSE). Predictors of lacunar infarction recurrence were assessed by logistic regression analysis.

Results: First lacunar infarction recurrence occurred in 101 patients (83%) and multiple recurrences in 21. The mean time between first ever lacunar infarction and recurrent lacunes was 58.3 months (range 2–240). In the subset of 59 patients in whom cognition was studied, cognitive impairment, defined as an MMSE score <24, was detected in 16% (8/49) of patients with first lacunar infarction recurrence and in 40% (4/10) of those with multiple lacunar infarction recurrences. In the multivariate analysis, hypertension (odds ratio 2.01, 95% CI 1.23 to 3.30) and diabetes (odds ratio 1.62, 95% CI 1.07 to 2.46) were significant predictors of lacunar stroke recurrence, whereas hyperlipidaemia was inversely associated (odds ratio 0.52, 95% CI 0.30 to 0.90).

Conclusions: Hypertension and diabetes were significant factors related to recurrent lacunar infarction. Hyperlipidaemia appeared to have a protective role. Cognitive impairment was a frequent finding in patients with multiple lacunar infarction recurrences.

Lacunar stroke accounts for more than 25% of brain infarcts.¹ Despite the frequency of lacunar strokes, clinical data of patients presenting with a recurrent lacunar infarction are scarce, and differential features between recurrent and first ever lacunar infarctions have been poorly studied.² Neurological deficit related to a first lacunar infarction is usually mild. In contrast, recurrent lacunar infarctions may be associated with a more severe clinical picture, including lacunar state and vascular dementia.³

A clinical study was performed to provide further information on the salient features of patients with recurrent lacunes and to identify factors influencing the recurrence of a lacunar infarction. The objectives of the study were: (a) to compare demographic data, vascular risk factors, clinical and topographic characteristics, and prognosis between patients with recurrent lacunar infarction and patients with first ever lacunar infarction and (b) to determine predictors of recurrent lacunes. Moreover, cognitive status was assessed in a subset of patients with recurrent lacunar infarction.

PATIENTS AND METHODS

Since January 1986, the Sagrat Cor-Hospital (an acute care 350 bed hospital in Barcelona) has had an ongoing hospital based

stroke registry.⁴ Data from first ever stroke patients are entered following a standardised protocol with 186 items detailing demographics, risk factors, clinical features, laboratory and neuroimaging data, complications and outcome. This study is based on data included in the registry up to December 2004, a time at which 3840 patients had been entered into the database. Subtypes of stroke were classified according to the Cerebrovascular Study Group of the Spanish Society of Neurology and have been used in previous reports.^{4 5}

For the purpose of the present study, 733 consecutive patients with lacunar infarction were collected. Lacunar infarcts were defined as (a) sudden or gradual onset of a focal neurological deficit lasting >24 h of the type described in the common lacunar syndromes (pure motor hemiparesis, pure sensory stroke, sensorimotor stroke, ataxic hemiparesis, dysarthria-clumsy hand and atypical lacunar syndromes); (b) CT scans or brain MRI were either normal or demonstrated only small, localised brain lesions with diameter smaller than 20 mm that seemed appropriate for the neurological deficits; and (c) absence of cortical ischaemia, cervical carotid stenosis or major source for cardioembolic stroke. Recurrent lacunar stroke was considered when the diagnosis of lacunar infarction was established in a patient with a history of a previous stroke of the lacunar type. Cerebrovascular risk factors were defined as in other studies by our group.^{3 4}

All patients were admitted to hospital within 48 h of the onset of symptoms. On admission, demographic characteristics, salient features of clinical history and neurological examination, results of routine laboratory tests, chest radiography and 12 lead electrocardiography were recorded. In all patients, brain CT scan and/or MRI were performed within the first week of hospital admission. The performance of the Mini-Mental State Examination (MMSE) for patients with recurrent stroke was included in the protocol in 1998. A score of <24 points was considered indicative of low cognitive skills.⁶ Medical complications (respiratory, urinary, cardiac, vascular and infectious) and mortality during the acute phase of the disease were assessed. Causes of death were analysed according to the criteria of Silver and colleagues.⁷ After the first ever lacunar infarction, patients received secondary prevention therapy and treatment of cardiovascular risk factors following the current guidelines.⁸

Prior to conducting the study, approval was obtained from the hospital's Ethics Committee on Clinical Research.

Student's *t* test and the χ^2 test (with Yates' correction when necessary) were used to compare features of patients with recurrent lacunar infarction with those with first ever lacunar stroke. Variables related to recurrent lacunar infarction in the univariate analysis in addition to age and sex were studied in a multiple regression model based on demographics, vascular risk factors and clinical and neuroimaging variables, in which lacunar infarction recurrence was the dependent variable.

Abbreviation: MMSE, Mini-Mental State Examination

Table 1 Comparison between patients with recurrent lacunar stroke and patients with first ever lacunar infarction

	Lacunar infarction		p Value
	First ever	Recurrent	
Total No of patients	573	122	
Sex			
Male	322 (76.1)	78 (19.5)	0.116
Female	251 (81.0)	44 (14.9)	
Age (y) (mean (SD))	73.8 (10.5)	75.1 (9.1)	0.206
Age $\geq$ 85 y	84 (14.7)	19 (15.6)	0.796
Vascular risk factors			
Hypertension	399 (69.6)	99 (81.1)	0.010
Diabetes	163 (28.4)	45 (36.9)	0.065
Valvular heart disease	17 (3.0)	4 (3.3)	1.000
Ischaemic heart disease	77 (13.4)	19 (15.6)	0.535
Atrial fibrillation	61 (10.6)	13 (10.7)	0.997
Congestive heart failure	17 (3.0)	5 (4.1)	0.716
TIA	56 (9.8)	16 (13.1)	0.271
Chronic obstructive pulmonary disease	45 (7.9)	14 (11.5)	0.192
Peripheral vascular disease	44 (7.7)	11 (9.0)	0.619
Alcohol abuse (>80 g/day)	18 (3.1)	2 (1.6)	0.547
Smoking (>20 cigarettes/day)	66 (12.5)	17 (13.9)	0.455
Hyperlipidaemia	138 (24.1)	18 (14.8)	0.025
Clinical findings			
Sudden onset	237 (41.4)	46 (45.9)	0.356
Headache	54 (9.4)	12 (9.8)	0.888
Nausea/vomiting	23 (4.0)	2 (1.6)	0.312
Limb weakness	432 (75.4)	88 (72.1)	0.451
Sensory symptoms	188 (32.8)	33 (27.0)	0.215
Speech disturbances	243 (42.4)	51 (41.8)	0.902
Ataxia	38 (6.6)	10 (8.2)	0.536
Cranial nerve palsy	19 (3.3)	1 (0.8)	0.230
Topography			
Internal capsule	189 (33.0)	36 (29.5)	0.456
Thalamus	84 (14.7)	14 (11.5)	0.359
Basal ganglia	35 (6.1)	14 (11.5)	0.035
Mesencephalus	3 (0.5)	1 (0.8)	1.000
Pons	65 (11.3)	14 (11.5)	0.967
Corona radiata	33 (5.8)	5 (4.1)	0.464
Outcome			
Symptom free at discharge	130 (22.7)	31 (25.4)	0.518
Respiratory complications	15 (2.6)	2 (1.6)	0.755
Urinary infections	15 (2.6)	3 (2.5)	1.000
Cardiac complications	6 (1.0)	1 (0.8)	1.000
Vascular complications	4 (0.7)	0	0.790
Infectious complications	25 (4.4)	2 (1.6)	0.248
Duration of stay (days) (mean (SD))	11.8 (7.6)	11.7 (7.9)	0.913
Inhospital mortality	2 (0.3)	2 (1.6)	0.293

TIA, transient ischaemic attack.

Data are n (%) unless otherwise indicated.

RESULTS

Of the 733 patients with radiologically proven lacunar infarction, 573 had a first ever lacunar infarction and 160 presented with recurrent lacunar stroke. However, 38 patients with recurrent lacunes were excluded because the first ever stroke was of the non-lacunar type (atherothrombotic infarction in 36, cardioembolic infarction in two). Therefore, recurrent lacunar infarction accounted for 17.5% (122/695) of all patients with lacunar stroke diagnosed during the study period.

The study population consisted of 122 patients (78 men, 44 women), with a mean (SD) age of 75.1 (9.1) years. Fifteen per cent of patients were older than 85 years. First lacunar infarction recurrence occurred in 101 patients (83%) and multiple recurrences in 21. Lacunar stroke recurrence occurred after a mean (SD) of 58.3 (56.1) months (range 2–240) of the index event. Hypertension was the most frequent risk factor followed by type 2 diabetes mellitus, ischaemic heart disease, hyperlipidaemia, heavy smoking (>20 cigarettes/day) and history of transient ischaemic attack. Salient clinical features were sudden onset of symptoms in 45.9% of patients, limb weakness in 72.1%, speech disturbances in 41.8% and sensory symptoms in 27%. Lacunar stroke included pure motor stroke

in 70 patients, pure sensory stroke in 18, atypical lacunar syndromes in 16, sensorimotor stroke in eight, dysarthria-clumsy hand in seven and ataxic hemiparesis in four.

In the subset of 59 patients with recurrent lacunar infarction diagnosed between 1998 and 2004, data on MMSE were available. Cognitive impairment, defined as an MMSE score <24 , was detected in 16% (8/49) of patients with first lacunar infarction recurrence and in 40% (4/10) of those with multiple lacunar infarction recurrences.

Two patients died (inhospital mortality rate 1.6%). Causes of death included pulmonary thromboembolism and sudden death of unknown cause. Absence of neurological disability at discharge was recorded in 25.4% of patients.

Differences between the groups of patients with recurrent lacunar stroke and first ever lacunar infarction are shown in table 1. Patients with recurrent lacunar stroke showed a higher frequency of hypertension, type 2 diabetes and basal ganglia topography than patients with first ever lacunar infarction, whereas hyperlipidaemia was significantly less frequent.

In the multivariate analysis, only hypertension (odds ratio 2.01; 95% CI 1.23 to 3.30) and diabetes (odds ratio 1.62; 95% CI 1.07 to 2.46) were significant variables related to recurrent

lacunar infarction. Hyperlipidaemia was inversely associated with recurrent lacunes (odds ratio 0.52; 95% CI 0.30 to 0.90).

DISCUSSION

In this hospital based study, we found that one in every five patients admitted with a lacunar stroke had a previous history of lacunar infarction. Prospective studies reported a stroke recurrence rate of 4–11% per year in patients with lacunar stroke.^{2 3 9 10} In agreement with other studies, recurrent strokes were more likely to be lacunar if the index event was lacunar.¹¹ In a systematic review of cohort studies with ischaemic stroke subtype specific follow-up data on death and recurrent stroke,¹¹ the risk of a lacunar recurrence following a lacunar event at baseline was twice as great as the risk of lacunar recurrence following a non-lacunar event at baseline.

In contrast, in a previous study by our group, mild cognitive impairment of the vascular type was diagnosed in 55% (22/40) of patients with lacunar infarction studied within 1 month after stroke.¹² Lacunar infarct is the most common stroke subtype that predisposes to vascular dementia,^{2 3 13} and it has been shown that recurrent stroke is one of the factors involved in producing dementia.¹⁴ In the present study, cognitive impairment was observed in 40% of patients with multiple recurrent lacunes and in 16% of those with first lacunar infarction recurrence. Therefore, identification of factors associated with recurrent lacunes in patients with first ever lacunar infarction is particularly relevant from a clinical perspective. Hypertension and diabetes were the only significant variables independently associated with recurrent lacunar infarction. There is a large body of evidence for treating hypertension in stroke prevention. Optimal treatment of hypertension has a direct impact in reducing the incidence of first ever stroke and stroke recurrence,^{15 16} but it is also likely that adequate blood pressure control may exert a beneficial effect in the prevention of cognitive decline. It is well known that diabetes accelerates the clinical course of atherosclerosis and contributes to cerebrovascular recurrence and to increased cardiovascular morbidity and mortality.¹⁷

In addition to the high frequency of cognitive impairment in patients with multiple recurrent lacunes, an interesting finding of the study was the protective role of hyperlipidaemia. This observation is consistent with results of previous studies in which higher levels of cholesterol are associated with a better outcome in the early phase after ischaemic stroke.^{18 19} In addition, clinical trials have demonstrated that cholesterol lowering statin therapy reduces the risk of ischaemic stroke. Statin drugs are effective and safe in preventing initial and recurrent stroke.^{20 21}

In summary, one in every five patients admitted with a lacunar stroke was a recurrent lacunar infarction. Hypertension and diabetes were significant factors associated with recurrent lacunes, whereas hyperlipidaemia had a protective role. Recurrent lacunar infarction, especially in the case of multiple episodes of recurrent lacunes, may alert to the presence of cognitive impairment.

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