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Lacunar Infarcts: Clinical and Risk Factors in 864 Patients

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Abstract

Background: To assess the clinical features and incidence rate of lacunar infarcts.

Methods: Hospital-based descriptive study of 864 patients with lacunar infarcts consecutively admitted for stroke during a period of 24 years, and compared to the rest of patients admitted for ischemic non-lacunar stroke (n=2,404).

Results: Lacunar infarcts represented 26.4% of all ischemic strokes. Factors independently associated with lacunar infarcts were arterial hypertension (OR=2.52; 95% CI (2.07-3.06) p<0.001), diabetes mellitus (OR= 1.55; 95% CI (1.26–1.90), p<0.001), female gender (OR= 0.68; 95% CI (0.57-0.82), p<0.001), valvular heart disease (OR=0.61; 95% CI (0.37-0.99), p=0.049), ischemic heart disease (OR=0.68; 95% CI (0.52-0.88), p=0.004), atrial fibrillation (OR=0.124; 95% CI (0.19–0.32), p<0.001), sudden onset (OR=0.74; 95% CI (0.61–0.89), p=0.030), headache (OR=0.26; 95% CI (0.14–0.50), p<0.001), early seizures (OR=0.11; 95% CI (0.02–0.45), p=0.003), nausea/vomiting (OR= 0.44; 95% CI (0.28–0.70), p=<0.001; altered consciousness (OR=0.12; 95% CI (0.08–0.19), p<0.001); sensory disturbances (OR=0.73; 95% CI (0.60-0.91; p=0.010), hemianopia (OR=0.04; 95% CI (0.02–0.08), p<0.001); speech disturbances (OR=0.48; 95% CI (0.39–0.58), p<0.001) and cranial nerve palsy (OR=0.55; 95% CI (0.35–0.85), p=0.005).

Conclusion: Lacunar infarcts represent 26.4% of cerebral infarcts and present their individual and differentiated clinical profile.

Keywords: Lacunar infarcts; Cerebral infarction; Risk factors; Etiology

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Introduction

Lacunar infarctions together with leukoaraiosis, dilatation of perivascular spaces, cerebral microbleeds and cerebral atrophy, are the usual anatomical manifestations of small vessel diseases [1-3]. The onset of small vessel disease may be silent, but will subsequently cause lacunar focal neurological syndromes, cognitive impairment or subcortical type dementia, and mood disturbances [4].

Lacunar infarcts, possibly due to their lower incidence and better short-term recovery, have been less studied in stroke hospital registries in spite of their significant health impact. Thus, there are still many controversial aspects about their natural history when compared to the rest of cerebral infarctions, such as risk factors profile and clinical characteristics.

The present study serves a twofold purpose: on the one hand, analyze the frequency of presentation, cardiovascular risk factors and clinical features of lacunar infarcts; secondly, to perform a comparative analysis between lacunar infarcts and the rest of non-lacunar cerebral infarcts. Toward that end, we analyzed a sample of 864 consecutive patients with lacunar infarctions, and compared it with 2,404 consecutive patients with non-lacunar cerebral infarctions.

Material and Methods

We present a clinical study performed at the Department of Neurology of the Hospital Universitari del Sagrat Cor in Barcelona for 24 years (1986-2009, both inclusive) and based on the analysis of the hospital-based prospective stroke registry. This registry has been previously published and validated [5]. Stroke subtypes, cardiovascular risk factors, and clinical and etiological features were classified according to the recommendations of the Committee of Experts on Cerebral Vascular Diseases of the Catalan Society of Neurology [6] and have been used by our group in other studies [5,7].

Table 1: Results of univariate analysis in patients with cerebral infarction due to lacunar infarct compared with patients with non-lacunar infarct.

Variable, n (%)	Lacunar infarcts (n=864)	Non-lacunar infarcts (n = 2,404)	*P* value
Demographic and clinical data			
Sex Male	488 (56.5)	1092 (45.4)	<0.001
Age (years), mean (SD)	74.4 (SD =10.4)	76.7 (SD =11.9)	0.062
Age ≥ 85 year old	140 (16.2)	619 (25.8)	<0.001
Age ≤ 55 year old	51 (5.9)	140 (5.8)	0.495
Hypertension	618 (71.5)	1285 (53.5)	<0.001
Diabetes mellitus	259 (30)	523 (21.8)	<0.001
Valvular heart disease	23 (2.7)	190 (7.9)	<0.001
Ischemic heart disease	113 (13.1)	405 (16.8)	0.005
Atrial fibrillation	85 (9.8)	885 (36.8)	<0.001
Transient ischemic attack	85 (9.8)	280 (11.6)	0.082
Previous cerebral infarction	133 (15.4)	414 (17.2)	0.118
Previous cerebral hemorrhage	12 (1.4)	27 (1.1)	0.324
COPD	72 (8.3)	215 (8.9)	0.321
Obesity	56 (6.5)	100 (4.2)	0.005
Alcohol abuse (>80 g /day)	28 (3.2)	61 (2.5)	0.166
Chronic liver disease	21 (2.4)	57 (2.4)	0.505
Nephropathy	29 (3.4)	100(4.2)	0.175
Smoking (>20 cig./day)	112 (13)	233 (9.7)	0.005
Dyslipidemia	207 (24)	436 (18.1)	<0.001
Peripheral vascular disease	67 (7.8)	199 (8.3)	0.344
Sudden onset	341 (39.5)	1.232 (51.2)	<0.001
Headache	78 (9)	272 (11.3)	0.034
Early seizures	2 (0.2)	856 (2.3)	<0.001
Nausea/vomiting	28 (3.2)	196 (8.2)	<0.001
Decreased consciousness	25 (2.9)	547 (22.8)	0.002
Hemiparesis	650 (75.2)	1.806 (75.1)	0.495
Sensory symptoms	267 (30.9)	882 (36.7)	<0.001
Hemianopsia	11 (1.3)	519 (21.6)	<0.001
Speech disturbances	373 (43.2)	1.324 (55.1)	<0.001
Ataxia	64 (7.4)	151 (6.3)	0.144
Cranial nerves palsy	32 (3.7)	140 (5.8)	0.009
Prognosis and outcomes			
Symptom-free at discharge	182 (21.1)	365 (15.2)	<0.001
Neurologic complications	28 (3.2)	296 (12.3)	<0.001
Respiratory complications	23 (2.7)	293 (12.2)	<0.001
Urinary infections	25 (2.9)	227 (9.4)	<0.001
Cardiac complications	8 (0.9)	137 (5.7)	<0.001
Vascular complications	5 (0.6)	49 (2)	0.002
Infectious complications	37 (4.3)	390 (16.2)	<0.001
In-hospital mortality	5 (0.6)	407 (16.9)	<0.001
Hospital stay (days), mean (SD)	11.6 (7.8)	18.3 (21.5)	<0.001

SD: Standard Deviation; COPD: Chronic Obstructive Pulmonary Disease.

According to the methodology and classification of previous studies [8,9] and to the nomenclature of the study group of cerebral vascular diseases of the Spanish Society of Neurology and the Official Guides of Vascular Cerebral Diseases of the Societat Catalana de Neurologia [5], lacunar infarcts were defined as ischemic strokes characterized by a classical lacunar syndrome (pure motor hemiparesis, pure sensory stroke, sensorimotor stroke, ataxic hemiparesis or dysarthria-clumsy hand), or as an atypical lacunar

Table 2: Variables independently related to lacunar infarction.

Variable	β	SE (β)	OR (95% CI)	p
Statistical model based on demographic, vascular risk factors, and clinical data				
Sex Female	-0.383	0.093	0.68 (0.57-0.82)	<0.001
Hypertension	0.923	0.099	2.52 (2.07-3,06)	<0.001
Diabetes mellitus	0.436	0.105	1.55 (1.26-1.90)	<0.001
Valvular heart disease	-0.496	0.252	0.61 (0.37-0.99)	0.049
Ischemic heart disease	-0.381	0.132	0.68 (0.52-0.88)	0.004
Atrial fibrillation	-1.39	0.134	0.24 (0.19-0.32)	<0.001
Sudden onset	-0.301	0.098	0.74 (0.61-0.89)	0.03
Headache	-1.314	0.317	0.26 (0.14-0.50)	<0.001
Seizures	-2.24	0.744	0.11 (0.02-0.45)	0.003
Nausea/vomiting	-0.809	0.234	0.44 (0.28-0.70)	0.001
Decreased Consciousness	-2.055	0.22	0.12 (0.08-0.19)	<0.001
Sensory symptoms	-0.302	0.104	0.73 (0.60-0.91)	0.01
Hemianopia	-3,071	0.315	0.04 (0.02-0.08)	<0.001
Speech disturbances	-0.73	0.097	0.48 (0.39-0.58)	<0.001
Cranial nerve palsy	-0.589	0.222	0.55 (0.35-0.85)	0.005

CI: Confidence Interval; OR: Odds Ratio.
β = -0.109; SE (β) = 0.117; goodness-of-fit $\chi 2$ = 5,401; *gl* = 8; *P* =0.714

syndrome lasting longer than 24 hours and caused by a cerebral infarct with maximum lesion diameter of 20 mm, visualized or not by neuroimaging and located in the vascular territory of the perforating cerebral arterioles, in the absence of cortical cerebral ischemia, arterial stenosis (> 50%) of the supraaortic trunks, or in the presence of an embolic etiology of cardiac origin.

We retrospectively analyzed data of the 4,597 patients included in the stroke registry whom were admitted for ischemic stroke, and selected the subgroup of patients with cerebral infarction. For the purposes of this study, we compared the subgroup of patients with lacunar infarct to those with non-lacunar infarcts.

The study population consisted of 3,268 patients, 864 of which were lacunar strokes and 2,404 non-lacunar strokes, with the following distribution: 956 cardioembolic, 944 atherothrombotic, 374 cerebral infarcts of essential cause and 128 cerebral infarcts of unusual etiology.

Demographic characteristics, vascular risk factors and clinical features of patients with lacunar infarct were compared with those with non-lacunar infarct. Univariate analysis for association of individual variables with lacunar infarcts was analyzed with the Student's t test for continuous variables and the chi-square (χ^2) test (with Yate's correction when necessary) for categorical data. Statistical significance was set at p<0.05. The degree of association was estimated by the odds ratio (OR) and the 95% confidence interval (CI). Significant variables related to lacunar infarcts were subjected to multivariate analysis with a logistic regression procedure and forward stepwise selection. The study was approved by the Clinical Research Ethics Committee of our hospital.

Results

Of the initial 3,268 patients with cerebral infarctions, 864 (26.4%) were lacunar infarcts. Mean age (SD) was 74.4 (10.4) years. Overall, 16.2% was older than 85 years and 5.9% younger than 55 years. Men made up 56.5% of patients (n=488) and women 43.5% (n=376). The main cardiovascular risk factors recorded –in order of decreasing frequency- were: hypertension 71.5%, diabetes mellitus 30%, dyslipidemia 24%, previous cerebral ischemia 15.4%, ischemic heart disease 13.1%, and heavy smoking 13%.

Major neurological symptoms were motor disorders in 75.2% of cases, speech disturbances in 43.2%, sensory disturbances in 30.9%, headache in 9%, ataxia in 7.4%, and cranial nerves alteration in 3.7%. The most frequent topographies were internal capsule (32.4%), thalamus (15%), pons (11%), basal ganglia (9.3%), centrum semiovale (5.8%) and mesencephalus (0.7%). Lacunar syndromes included pure motor hemiparesis in 48% of patients, pure sensory syndrome in 17.3%, pure sensorimotor in 11.3%, ataxic hemiparesis in 3.3%, dysarthria clumsy hand in 8%, and atypical lacunar syndrome in 12%.

In-hospital mortality was 0.6% (n=5). The causes of death were sepsis in 1 patient, respiratory infection in 1 patient, sudden death in 1 patient and unknown causes in 2 patients. There was no neurological deficit at discharge in 21.1% of patients. The average length of hospital stay (SD) was 11.6 (7.8) days, with 29.3% of patients staying longer than 12 days.

When the groups of lacunar and non-lacunar infarctions were compared (Table 1), male sex, hypertension, diabetes, obesity, smoking and dyslipidemia were more frequent in the lacunar group. There were less frequent: female sex, ischemic heart disease, valvular heart disease, atrial fibrillation, sudden onset, headache, early seizures, decreased consciousness, nausea or vomiting, sensory disturbances, hemianopia, speech disturbances, cranial nerve palsy, and neurological, respiratory, urinary, cardiac, vascular and infectious complications at admittance, and in-hospital mortality.

In the multivariate analysis (Table 2), significant independent variables related to lacunar infarcts were hypertension (OR=2.52; 95% CI (2.07-3,06); p<0.001), diabetes mellitus (OR= 1.55; 95% CI (1.26–1.90; p<0.001), female sex (OR= 0.68; 95% CI (0.57-0.82); p<0.001), valvular heart disease (OR=0.61; 95% CI (0.37-0.99; p=0.049), ischemic heart disease (OR=0.68; 95% CI (0.52-0.88);

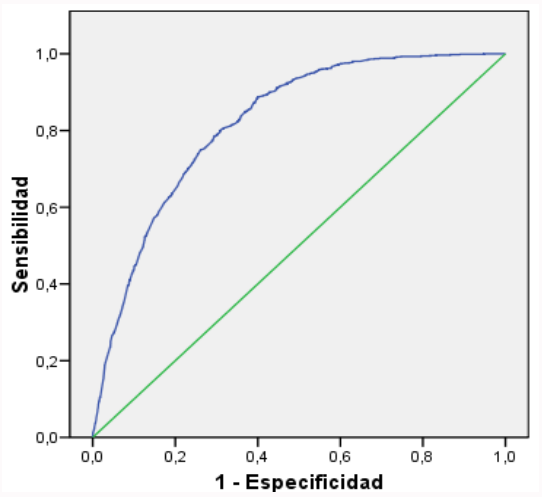

Figure 1: Area under the ROC curve=0.820; sensitivity 81.6%, specificity 65.9%, positive predictive value =46.2%, negative predictive value =90.9%, correct classification: 70.06%.

p=0.004), atrial fibrillation (OR=0.124; 95% CI (0.19–0.32); p<0.001), sudden onset (OR=0.74; 95% CI (0.61–0.89); p=0.030), headache (OR=0.26; 95% CI (0.14–0.50); p<0.001), early seizures (OR=0.11; 95% CI (0.02–0.45); p=0.003), nausea and vomiting (OR= 0.44; 95% CI (0.28–0.70); p<0.001; decreased consciousness (OR=0.12; 95% CI (0.08–0.19); p<0.001); sensory disturbances (OR=0.73; 95% CI (0.60-0.91); p=0.010), hemianopia (OR=0.04; 95% CI (0.02–0.08); p<0.001); speech disturbances (OR=0.48; 95% CI (0.39–0.58; p<0.001) and cranial nerve palsy (OR=0.55; 95% CI (0.35–0.85); p=0.005). Results from the area under the ROC curve are shown in Figure 1.

Discussion

In our study, lacunar infarcts accounted for 26.4% of cerebral infarctions, and these findings are similar to those reported by other studies ranging from 28.6% [10] to 19.2% [11]. The most common vascular risk factors independently associated with lacunar infarcts were hypertension in 71.5% of cases and diabetes in 30%. These findings are similar to those obtained by Lv "et al." [10], in which hypertension and white matter hyperintensities were variables independently related to lacunar infarction compared with cerebral ischemia of large vessels. By contrast, in the study of Ntaios "et al." [11] performed in a sample of diabetic patients, it was noteworthy that small and large vessel diseases showed a similar incidence, despite prognosis was worse in patients with non-lacunar infarcts.

It is remarkable the reduced incidence of ischemic heart disease, valvular heart disease and atrial fibrillation in lacunar infarcts, which could be explained by being the main vascular risk factors of cardioembolic infarcts [12], which constitute, in turn, the subtype of cerebral infarction with a worse functional prognosis.

The lower frequency of sudden onset of neurological deficit, the presence of headache, early seizures, decreased level of consciousness, nausea and vomiting, sensory symptoms, visual and speech disturbances, and cranial nerves alterations could also be explained by the fact that these clinical variables are mainly related to atherothrombotic, cardioembolic or unusual cause strokes [13]. Neurological semiology characteristic of lacunar infarcts, instead, occurs in the form of classical lacunar syndromes and, less frequently, atypical lacunar syndromes [14,15] as observed in the present clinical series, thus fulfilling the lacunar hypothesis initially described by Miller Fisher, which states that lacunar syndromes are mainly due to cerebral infarctions of the lacunar type [2].

Our study also revealed the significant good short-term prognosis of lacunar infarcts, as neurological, respiratory, urinary, cardiac, vascular and infectious complications were uncommon during in hospital stay, and mortality rate was only 0.6%, with a total recovery of neurological deficit at discharge in 21% of patients. These findings are consistent with the results of other studies [10,11,16,17]. However, it should be noted that this good short-term prognosis is totally misleading since it has been shown that lacunar infarcts present a higher risk of cerebral vascular relapse, of silent progression of small vessel disease, mainly related to an increase in white matter hyperintensities, of cerebral atrophy, and are the most common cause of subcortical vascular dementia [18-20].

It is therefore necessary an adequate control of cerebrovascular risk factors, hypertension and diabetes mellitus in this case, together with a correct antiplatelet therapy [3] as an optimal secondary prevention of relapse of cerebral ischemia and progression of small cerebral vessel disease.

In summary, approximately one in four patients admitted for cerebral infarction suffers a lacunar infarct, which shows a differentiated clinical profile compared to the rest of cerebral infarctions.

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