In a prospective study of 72 patients with stroke and atrial fibrillation, we classified strokes as cardioembolic or noncardioembolic based on arterial assessment using Doppler sonography and angiography. We analyzed and cross-tabulated 18 clinical characteristics and found four to be significantly associated with a cardioembolic mechanism: stroke with onset during activity and peak deficit at onset ($p<0.008$), previous infarct in a different vascular territory ($p<0.01$), previous transient ischemic attack in a different vascular territory ($p<0.01$), and transient ischemic attack lasting >1 hour ($p<0.02$). Starting with these four characteristics, we used a step-down procedure to select variables for a logistic regression model. Only previous infarct in a different vascular territory (odds ratio=7.38) and transient ischemic attack lasting >1 hour (odds ratio=7.89) were selected by the model. Using M-mode and two-dimensional echocardiography, we compared left atrial size in 46 patients with that in 78 controls who had atrial fibrillation without stroke. Left atrial size in patients and controls with mitral valvulopathy was significantly larger than that in patients and controls without mitral valve disease. There was, however, no difference in left atrial size between patients with nonvalvar atrial fibrillation and cardioembolic stroke and controls or patients with nonvalvular atrial fibrillation and noncardioembolic stroke. We concluded that some clinical characteristics are closely related to cardioembolic stroke and that left atrial enlargement reflects underlying cardiopathy rather than atrial emboli-forming capability. 

(Stroke 1989;20:1648–1652)
iation showed blood flow alterations suggesting tributary vessel stenosis within the affected area or an angiogram revealed one or more of the following features: stenosis of >50% in the tributary vessel, ulcerated atheromatous plaque(s), or intracranial vessel stenosis.

In Groups A and B patients, we assessed the following clinical characteristics to compare their independent occurrence in both groups: onset of stroke during sleep, with peak deficit at onset or with fluctuating initial deficit; onset of stroke during activity, with peak deficit at onset or with fluctuating initial deficit; carotid murmur; seizures at onset; history of lacunar syndrome or CT images suggesting old lacunar infarcts; angina simultaneous with stroke; syncope; transient monocular blindness (TMB); previous systemic embolisms; history of TIA in the same vascular territory; history of TIA in a different vascular territory; previous infarcts in the same vascular territory; previous infarcts in other vascular territories; TIA lasting >1 hour; TIA lasting <1 hour; and hemorrhagic infarct on CT scan.

For controls we included persons with chronic NVAF (Group C) and persons with MS and AF (Group D). No control had a history of embolism nor did any control receive anticoagulants.

Using a Toshiba Echograph (Nasu, Japan) with a 3.5-Hz transducer phased array, both M-mode and two-dimensional (2D) echocardiograms were taken in both patients and controls. Three atrial diameters were measured, one of them in both M-mode and 2D. With the subject in the left lateral decubitus position, the anteroposterior (AP) diameter was measured with 2D by means of a left ventricular longitudinal projection and a projection through the left parasternal window. The same diameter was measured in M-mode, with the ultrasonic beam placed at the level of the aortic valve. The supero-inferior (SI) and transverse diameters were measured using a four-chamber projection through the apical window. The diameter analyzed was the average of those measured in five consecutive heart beats.

Student's t test was used to study the association between two-category qualitative variables and a quantitative variable; the χ² test was used to study the relation between two qualitative variables. To study the association between a qualitative variable with more than two categories and a quantitative variable, analysis of variance (ANOVA) with one factor was used. When the results of ANOVA were significant, differences between categories were established using Scheffé's method. Those characteristics deemed to be clinically important or found to be significant at the 0.05 level were candidates for inclusion in a multiple logistic regression model. This model allowed us to estimate for a given patient the probability of having had a cardioembolic stroke. We assigned the "one" value (Y=1) to cardioembolic stroke and the "zero" value (Y=0) to noncardioembolic stroke. All the above techniques were calculated by means of the SPSS-X statistical package used by the Barcelona Instituto Municipal de Investigación Médica VAX computer systems. The data are presented as mean±SD. Significance was set at p<0.05.

### Results

During the study period, 76 patients (51 women and 25 men, aged 50–93 [mean±SD 72.8±9.6] years) were admitted with AF-related stroke. Four patients were later excluded (two with thrombocytopenia and two with valvular prostheses).

Group A comprised 36 patients (28 women and 8 men, mean±SD age 70.8±9.8 years). There were 21 patients (17 women and 4 men) in Subgroup AI (mean±SD age 73.3±9.3 years) and 15 patients (11 women and 4 men) in Subgroup AII (mean±SD age 67.4±9.7 years). In Subgroup AII 15 patients showed isolated AF, three had AF with mitral ring calcification, and the other three had dilated cardiomyopathy, hypertrophic cardiomyopathy, or ventricular dyskinesia with intraventricular thrombus. In Subgroup AII 12 patients had MS and the other three had a double mitral lesion. In the 36 patients in Group A, Doppler examination was normal in 35; the remaining patient had a normal angiogram 7 days after the stroke, without previous Doppler examination.

Group B comprised 36 patients (20 women and 16 men, mean±SD age 74.7±9.2 years). Two patients had MS associated with >50% stenosis of the tributary vessel and three had mitral ring calcification. Doppler examination was carried out in all 36 patients and showed blood flow alterations suggesting stenosis in 35. Transfemoral angiograms in six patients revealed ulcerated lesions at the beginning of the internal carotid artery in two and 50% stenosis of the tributary carotid artery lumen in three (bilateral in one patient and as a result of stenosing kinking in another); although the angiogram of the extracranial vessels was normal in the remaining patient, signs of diffuse arteriosclerosis in the intracranial vessels were apparent.

Nosologic and topographic data of the 72 patients are shown in Table 1.

**Table 1. Topography of Lesions by Nosologic Groups**

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Group A (cardioembolic stroke)</th>
<th>Group B (noncardioembolic stroke)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid TIA</td>
<td>4 (17%)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Vertebrobasilar TIA</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Carotid RIND</td>
<td>6 (21%)</td>
<td>7 (20%)</td>
</tr>
<tr>
<td>Vertebrobasilar RIND</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Carotid infarct</td>
<td>24 (83%)</td>
<td>20 (56%)</td>
</tr>
<tr>
<td>Vertebrobasilar infarct</td>
<td>0 (0%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Missed data</td>
<td>2 (7%)</td>
<td>4 (11%)</td>
</tr>
</tbody>
</table>

TIA, transient ischemic attack; RIND, reversible ischemic neurologic deficit.
The clinical characteristics of Groups A and B are shown in Table 2. Onset of stroke during activity with peak deficit at onset, history of TIA in a different vascular territory, previous infarcts in other vascular territories, and TIA lasting >1 hour were significantly related to a cardioembolic stroke. The following variables were selected as candidates for the multiple logistic regression model: time of onset (diurnal vs. nocturnal), history of TIA in the same vascular territory, history of TIA in a different vascular territory, previous infarcts in the same vascular territory, previous infarcts in other vascular territories, TIA lasting >1 hour, TIA lasting <1 hour, and history of lacunar syndrome. Of these, only previous infarct(s) in other vascular territories and TIA lasting >1 hour were selected by the model (Table 3).

Group C comprised 68 persons (31 women and 37 men, mean±SD age 68.2±8.4 years). Group D comprised 10 persons (seven women and three men, mean±SD age 67.1±11 years).

An M-mode and a 2D echocardiogram were taken in 46 of the 72 patients and in all 78 controls. Only two of the four diameters were measured in three of the 46 patients. SI and AP were significantly larger in Subgroup AII and Group D than in Subgroup AI and Groups B and C (Table 4). The other two diameters showed a tendency to a larger atrial size in Subgroup AII and Group D.

### Discussion

The incidence of cardioembolic stroke in our study is lower than that in most series (Table 5). This may be explained partly by the coexistence of cardiac and arterial sources of emboli in many (50%) of our patients (double the figure reported by Weinberger et al23) and partly by our classification criteria. These criteria were based on the importance of an extracranial source of emboli in the pathogenesis of stroke, and their aim was to be as conservative as possible in elderly patients. It seems reasonable to assume that some patients in Group A could have had relevant arterial intracranial lesions that would have remained undetected unless intracranial Doppler sonography or angiography had been carried out. Although some Group B patients had emboligenic cardiopathies in addition to AF, carotid stenosis of >50% was found in the two Group B patients with MS who underwent angiography.

With regard to the topography of the lesions, the lowest incidence of stroke was found among patients with vertebralbasilar territory lesions (three of 72 patients). All three had noncardioembolic stroke. This agrees with other reports4,8,20,21,24,25 From a nosologic point of view, 67% of TIAs were cardioembolic. Although the importance of emboliforming cardiopathies as a cause of TIA26 has been questioned, several studies12,14,27 have shown emboliforming cardiopathies in a significant proportion of TIA cases.

Among the variables that have been suggested as markers of cardioembolic or noncardioembolic stroke,2–6,10,13 we found the following to be significantly associated with cardioembolic stroke: onset during activity, with peak deficit at onset; history of TIA in a different territory; previous infarct(s) in different vascular territories; and TIA lasting >1 hour.

As far as TIA duration is concerned, some reports28–30 have established a strong association between TIA's of long duration and a cardiac origin of emboli, but others13 have not. An interesting finding was the association between infarcts in several vascular territories and a cardiac source of emboli. Recently, Kempster et al31 found a 13%
incidence of multiple cerebral infarcts in patients with AF compared with a 4% incidence in patients with sinus rhythm. Indeed, previous infarct(s) in different vascular territories and TIA lasting >1 hour were the only variables selected by the logistic regression model.

We found a significant correlation between a cardiac origin of emboli and onset during activity, with peak deficit at onset (72.2%). However, non-cardioembolic strokes had the same onset in 41.7% of the cases. Onset during sleep was more common in non-cardioembolic than in cardioembolic stroke, although the difference was not significant by the two-tailed χ² test. We tested diurnal vs. nocturnal onset in the logistic regression model. Time of onset did not contribute to a differentiation of noncardioembolic from cardioembolic stroke. Although some authors have suggested that the nocturnal onset of stroke is a predictor of hemodynamic origin, two studies specifically addressing this point were unable to prove such a hypothesis.

Fluctuating deficit after onset during activity appeared in 30.6% of non-cardioembolic strokes and 13.9% of cardioembolic strokes. Some characteristics associated with cardioembolic stroke such as seizures, syncope, or angina pectoris or with non-cardioembolic stroke such as TMB or carotid murmur were absent. It seems that the mode and time of stroke onset are of little value in the diagnosis of etiology in a given patient.

In 1986, Caplan et al compared left atrial size in 20 patients with AF and stroke with that in 20 patients with AF without stroke. These authors reported significant left atrial enlargement in the group with stroke. This group included five patients with valvular AF. In spite of the few persons with valvular AF in our study, we found that atrial size was significantly larger in patients with cardioembolic stroke and valvular AF and controls with valvular AF than in patients with cardioembolic stroke and NVAF, patients with noncardioembolic stroke, or controls with NVAF. No difference in left atrial size was found among these latter three groups. This agrees with other series that have studied left atrial size in NVAF. Some authors have related left atrial enlargement in AF to the type of cardiopathy and to duration of AF. Our results favor the first hypothesis. Halperin and Hart have raised the question of the intermittency of stroke in chronic AF. As small atria in AF are less stable, it is possible to assume that they have a great emboli-forming capability.

Our results do not contribute to a definition of the clinical profile of cardioembolic stroke because the logistic regression model selected only two clinical characteristics that contributed to a differentiation between cardioembolic and noncardioembolic stroke. Therefore, it is not surprising that 45% of the infarcts found in the Pilot Stroke Data Bank were of unknown cause. Left atrial enlargement reflects mitral valvulopathy but is not in itself a reliable predictor of emboli-forming atria in NVAF. Since more than one third of our patients suffering cardioembolic stroke had had previous infarcts, it is evident that AF-related stroke carries a serious prognosis. Further studies are needed both to resolve the clinical conundrum of the etiologic diagnosis of AF-related stroke and to find a reliable marker of embolic NVAF.

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