Carotid Atherosclerosis and Lacunar Stroke a Possible Association

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Abstract

Stroke remain the third cause of death and a major cause of disability worldwide. Our modern time enemy, atherosclerosis, with his many faces, is strongly related with stroke and its major subtypes. Ischemic stroke account up to 80 % of all stroke. As a subtype of ischemic stroke, lacunar infarcts remain an important concern. Aim of this study is to correlate carotid disease findings with lacunar stroke. We studied a group of 129 patients with carotid disease, and we established a possible relationship with lacunar stroke. Ultrasonography findings were correlated with the presence of lacunar stroke, confirmed by CT scan. Our study demonstrate that carotid plaques number could be a good predictor for lacunar stroke risk. External carotid plaques number is strongly correlate with lacunar stroke presence.

Keywords: atherosclerosis, plaques, carotid tree, lacunar stroke.

1. Introduction

In 1960, Miller Fisher redefined lacunas as "small, deep cerebral infarcts" due to occlusion of a single perforating vessel [1]. He coined the term "lipohyalinosis" for the segmental arterial pathology that affects small penetrating arteries and causes lacunar infarcts. He also showed that atherosclerosis of the origins of penetrating

arteries, "micro atheroma," is a frequent cause of lacunar infarcts [1]. However, is known that lacunar infarcts may be due to other causes like large arteries disease or even cardio embolic disease. Lacunar infarcts has an incidence comparable with the incidence of large vessel atherosclerotic stroke (25/100.000). Lacunar strokes, and more often so called lacunar state is strongly relying with dementia and poor quality of life. Lacunar strokes account up to 15 -20 % for all strokes [2].

2. Material and Method

We investigated the relation between carotid disease pattern and lacunar stroke for 129 patients in our department. The study was a prospective one, with a follow-up time of one year. All patients signed an informed consent when enrolled.

Carotid ultrasound was performed at the initial visit. The assessment of carotid disease was done by ultrasound and Duplex examinations according to the protocol, with high resolution B mode, color Doppler and pulse Doppler. We measured IMT index (mean after three points examination at 1 cm below bifurcation of both coon carotid arteries) and we assessed the presence and the number of plaques. There were designated as focal intima-media thickening greater than 1.3 mm.

We performed ultrasonography examinations with an ultrasound scanner (Philips HD 15) equipped with a 7.5MHz linear array transducer.

The assessment by CT scan was done by using native craniocerebral examination, performed with multislice CT scanner. Lacunar stroke confirmed by CT scan was mandatory for a patient to be included in the lacunar stroke group.

AS exclusion criteria, we excluded other causes of ischemic stroke as dissections, vasculopathy, Takayasu disease, cardio-embolic strokes and TIA, due to heterogeneity of symptoms and causes. We excluded a priori all intracerebral hemorrhages and large strokes.

According to the number of plaques at each evaluated level, we divided patients into two groups. First group consisted of patients with maximum two plaques and the second group patients with three or more plaques.

For the evaluation of the Intima-Media Thickness (IMT) we considered values higher than 0.9 as being abnormal.

To test the association between plaques number and lacunar stroke we used Fisher's Exact Test. For comparing continuous variables, we tested the normality of the distribution using Shapiro-Wilk test. If the distribution didn't differ significantly from a normal one we continued by using parametric tests and in the case the distribution differed in a significant way, we used non-parametric alternatives

3. Results and Discussions

From the total of 129 patients included in this study, 17 of them were diagnosed with lacunar stroke

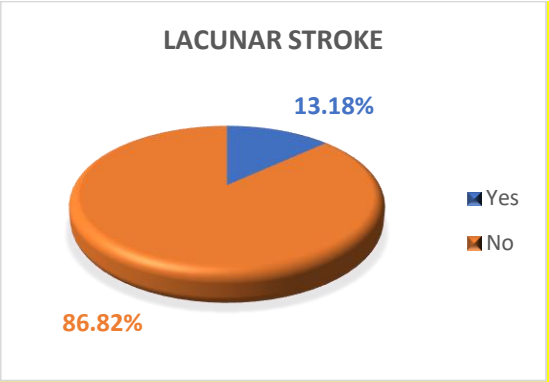

Fig. 1 Proportion of patients with lacunar stroke

According to the sex of the patients, 72 (55.8%) were women and 57 (44.2%) males

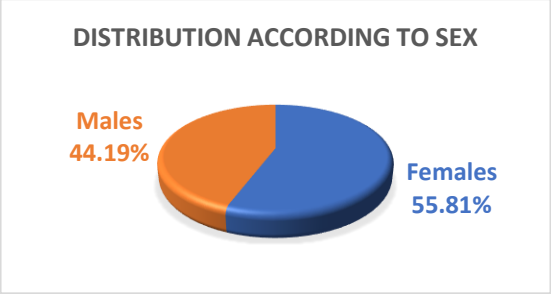

Fig. 2 Distribution according to sex

The percentage of men with lacunar stroke is statistically significant (p=0.034) higher compared to the females (19% vs 7.5%). The odds ratio is 3.573 (95% CI 1.178 – 10.838), the risk being higher for men (see Figure 3).

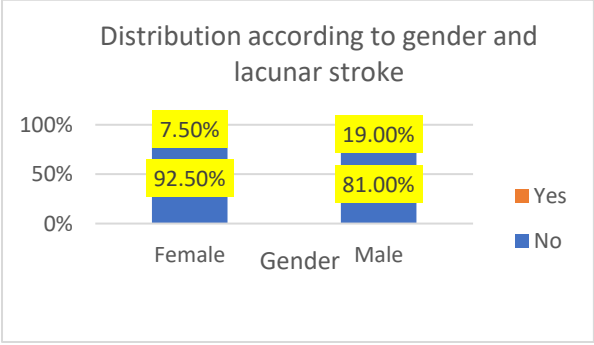

Fig.3 Distribution according to sex

The average age for the patients without lacunar stroke is 62.53 years (SD 11.90) and a median of 63 years. For the group of patients with lacunar stroke, the average and the median age are higher, with values of 69.41 years (SD 8) and a median of 70. The difference is statistically significant (U=604, z=-2.425, p=0.015).

Table 1 Descriptive analysis for the age

Lacunar Stroke	No.	Mean	Std. Deviation	Median	Minimum	Maximum
No	112	62.53	11.903	63.00	24	86
Yes	17	69.41	8.000	70.00	51	79
Total	129	63.43	11.677	64.00	24	86

3.1. Intima-Media Thickness

In the group of patients without lacunar stroke, 65.2% have normal IMT, while in the group of patients with lacunar stroke the percentage is 70.6% . The difference is not statistically significant (p=0.787).

Table 2 IMT distribution for the two groups

IMT Group * Lacunar Stroke Cross tabulation					
			Lacunar Stroke		
			No.	Yes	Total
IMT Group	Normal	Count	73	12	85
		% within Lacunar Stroke	65.2%	70.6%	65.9%
	Abnormal	Count	39	5	44
		% within Lacunar Stroke	34.8%	29.4%	34.1%
Total		Count	112	17	129
		% within Lacunar Stroke	100.0%	100.0%	100.0%

Further, we analyzed the IMT values, comparing them among the two groups. The purpose is to see if patients with lacunar stroke have higher values of IMT compared to patients without lacunar stroke, even though as proportion of normal/abnormal values there are no differences. In this case we also found no statistically significant difference (U=930, z—0.181, p=0.856).

Table 3 IMT Descriptive statistics

Lacunar Stroke	No.	Mean	Std. Deviation	Median	Minimum	Maximum
No	112	1.264	.6412	.900	.9	4.0
Yes	17	1.306	.7537	.900	.9	3.5
Total	129	1.270	.6540	.900	.9	4.0

3.2 The Presence of Atheroma Plaques or Atheromatosis Modifications

The presence of atheroma plaques or atheromatosis modification have a higher percentage in the lacunar stroke group. Almost 95% of the patients with lacunar stroke have this modification, while for the no-lacunar stroke group these appear in 71.4% of the investigated patients. The difference is not statistically significant (p=0.07).

Table 4 Cross tabulation Lacunar Stroke – Presence of atheroma plaques/atheromatosis modifications

			Lacunar Stroke		
			No	Yes	Total
Presence of atheroma plaques/atheromatosis modifications	No	Count	32	1	33
		% within Lacunar Stroke	28.6%	5.9%	25.6%
	Yes	Count	80	16	96
		% within Lacunar Stroke	71.4%	94.1%	74.4%
Total		Count	112	17	129
		% within Lacunar Stroke	100.0%	100.0%	100.0%

3.3. Plaques Number Pre Bulbar Level

Analyzing the number of plaques at pre bulbar level, 17.6% of the patients with lacunar stroke presented three or more plaques, while in the group of patients without lacunar stroke the percentage was 12.5%. The difference is not statistically significant, p=0.669, thus we concluded that the presence of three or more plaques is not associated with an increased risk of lacunar stroke.

Table 5 Cross tabulation Lacunar Stroke – Plaques number at pre bulbar segment level

			Lacunar Stroke		
			No	Yes	Total
Plaques number at pre bulbar segment level	<=2	Count	98	14	112
		% within Lacunar Stroke	87.5%	82.4%	86.8%
	3+	Count	14	3	17
		% within Lacunar Stroke	12.5%	17.6%	13.2%
Total		Count	112	17	129
		% within Lacunar Stroke	100.0%	100.0%	100.0%

3.4. Plaques Number Carotidal Bulb Level

More than 70% of the patients present three or more plaques at carotidal bulb level, compared with a significantly lower percentage for the patients without lacunar stroke (38.4%). The difference is statistically significant (p=0.017), fact that sustains the idea that a higher number of atheroma plaques at bulbar level is associated with an increased risk of lacunar stroke. The odds ratio is 3.85 (95% CI 1.27 – 11.69).

Table 6 Cross tabulation Lacunar Stroke – Plaques number at carotidal bulb level

			Lacunar Stroke		
			No	Yes	Total
Plaques number at carotid bulb level	<=2	Count	69	5	74
		% within Lacunar Stroke	61.6%	29.4%	57.4%
	3+	Count	43	12	55
		% within Lacunar Stroke	38.4%	70.6%	42.6%
Total		Count	112	17	129
		% within Lacunar Stroke	100.0%	100.0%	100.0%

3.5. Plaques Number at External Carotid Artery Level

Further we examined the influence of atheroma plaques at external carotid artery level. Almost 60% of the patients with lacunar stroke had three or more plaques at ECA level. For the group of patients without lacunar stroke, the percentage of patients with three or more plaques is significantly lower (22.3%). This result sustains the idea that there is a statistically significant (0.003) association between number of plaques at ECA level and the development of lacunar stroke. The odds ratio is 4.97 (CI 95% 1.72 – 14.39).

Table 7 Cross tabulation Lacunar Stroke – Plaques number at

External Carotid Artery level

			Lacunar Stroke		
			No	Yes	Total
ECA	<=2	Count	87	7	94
		% within Lacunar Stroke	77.7%	41.2%	72.9%
	3+	Count	25	10	35
		% within Lacunar Stroke	22.3%	58.8%	27.1%
Total		Count	112	17	129
		% within Lacunar Stroke	100.0%	100.0%	100.0%

3.6. Plaques Number at Internal Carotid Artery Level

In the case of atheroma plaques identified at the internal carotid artery level, almost two thirds of the patients with lacunar stroke (64,7 %) present three or more plaques. By comparison, in the group of patients without lacunar stroke the percentage of patients with three or more plaques is 37.5%. Using the Fisher Exact test, the result is not statistically significant (p=0.06), thus the number of plaques at ICA level can be considered not to be associated with lacunar stroke. This p value obtained is, at the same time, very close to the point of rejecting the null hypothesis and it is known that Fisher exact test is more conservative.

The odds ratio is 3.06 (CI 95% 1.05 – 8.87), identifying a higher risk of lacunar stroke for patients with three or more plaques at the ICA level.

Table 8 Cross tabulation Lacunar Stroke – Plaques number at internal carotid artery level

			Lacunar Stroke		
			No	Yes	Total
ICA	<=2	Count	70	6	76
		% within Lacunar Stroke	62.5%	35.3%	58.9%
	3+	Count	42	11	53
		% within Lacunar Stroke	37.5%	64.7%	41.1%
Total		Count	112	17	129
		% within Lacunar Stroke	100.0%	100.0%	100.0%

4. Conclusions

In our study, we found that men are at higher risk for lacunar infarcts than women, and this was the same in literature [3]. Stroke are the fourth leading cause of death in men, so we have to take care about it. After all, stroke remains the major cause of disability in the worldwide [4]. Women and men with stroke also differ in their risk factor profiles, and they respond differently to primary-prevention and acute stroke treatment. Women experience variations in endogenous estrogens throughout their life cycle and might also be exposed to exogenous estrogens, both of which markedly affect the brain.

Measurement of intima-media thickness is a marker of atherosclerosis. Increases in IMT thickness have been associated with involvement of other arterial beds with atherosclerosis and an increased risk of stroke in adults. However, there is only a little knowledge concerning the relationship between IMT and subtypes of brain infarction. Recently, it has been observed that an increased IMT was associated with brain infarctions both overall and in the main subtypes [5].

Our study found no statistical correlation between IMT thickness and lacunar stroke risk, whereas Touboul et al observed a slight but significantly higher IMT even in lacunar infarcts compared with control subjects. The difference of our population study is coming from the fact that our patients were patients with first stroke or stroke like suspicion.

Unlike other types of ischemia such as cortical infarctions in which the relationship with atherosclerotic extracranial lesions is well established, the question of whether the occlusion of a perforating artery by mechanisms related to atherosclerotic extracranial lesions can result in a lacunar stroke is controversial.

Fisher, the creator of the “lacunar hypothesis,” observed in some postmortem examinations that it was not possible to explain all lacunar stroke as secondary to specific disease of the perforating vessel and assumed that the cases in which no histological abnormality was identified in the perforating artery could indicate that the occlusion depended on embolic mechanisms [6].

Carotid plaques increase the risk of stroke, and this is a statement. However, in our study, athematosis changes are not significant statistically associated with lacunar ictus.

As for presence of the plaques in common carotid artery level, we found out that more than three plaques are more likely to be associated with lacunar stroke but it was not statistically significant. Carotid plaques increase the risk of stroke and cerebral infarction, irrespective of their location (Hollander and all). It is likely that carotid plaques in neurologically asymptomatic subjects are both markers of generalized atherosclerosis and sources of thromboembolic.

As for carotidal bulb level, we found out that higher number of plaques at this level, is strongly associated with lacunar stroke risk, independently of carotid stenosis or aspects of plaques. Also more than 3 plaques in distal carotid arteries are strongly related with lacunar stroke.

A big surprise in our study was the correlations between number of plaques in external carotid arteries are strongly related with lacunar stroke risk. Few articles are about external carotid arteries disease importance in stroke relationship. In fact, many clinicians paid no attention for external carotid arteries disease, and the real importance is not established. We found out that major's studies were no taken into account this Cinderella arteries of carotid tree.

The ECA is an important collateral pathway in patients with ipsilateral ICA occlusion and recurrent symptoms; this may influence the surgical decisions involving revascularization of the stenotic ECA. ECA stenosis may not be clinically significant, with no need to change patient care [7]. However, the external carotid arteries disease is an important predictor for lacunar stroke in our study, and perhaps of generalized atherosclerosis.

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