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Sonographic evaluation of plaque morphology in haemodynamic and non-haemodynamic symptomatic carotid artery stenoses.

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Summary

A prospective duplex ultrasound and Colour Doppler imaging studies were performed on 52 consecutive patients with 63 carotid arteries (11 patients with bilateral carotid interrogation). The cases were classified into two study groups — non-haemodynamically (< 50 %) and haemodynamically (=50 %) significant stenoses in relation to clinical events and carotid plaque echomorphology. Of the 63 carotid arteries that were evaluated, 36 (57.1 %) revealed non-haemodynamic and 27 (42.9 %) haemodynamic stenoses. Our study confirmed that more than half of the cases with hemispheric symptoms (stroke and TIA) were related to nonhaemodynamic stenosis accounting for 53.7%. While heterogeneous and homogeneous plaques were seen in both study groups with hemispheric symptoms, no heterogeneous plaque was seen in haemodynamic stenosis with non-hemispheric symptoms. No statistically significant differences were seen between heterogeneous and homogeneous plaques in non-haemodynamic and haemodynamic cases. Predominantly hypoechoic stenoses, representing thrombotic materials are more common in haemodynamic cases of stroke accounting for 64.3% and in 76.9 % of non-haemodynamic cases in TIA. Plaque surface irregularity and ulceration did not seem to be related to the severity of stenosis as there was no statistically significant difference in the frequencies. However, while irregularly surfaced plaques are of equal frequency in non-haemodynamic and haemodynamic cases in stroke, there was no ulceration in non-haemodynamic cases. There was preponderance of irregular surfaced plaques in non-haemodynamic and ulceration in haemodynamic cases in TIA. Our study showed higher frequency of smooth plaque in relation to hemispheric and non-hemispheric symptoms in non-haemodynamic stenosis and mainly ulceration/ irregular plaques in haemodynamic stenosis. The trend of plaque echomorphology and surface characteristics in the study groups were highlighted. The pathogenesis of the symptoms was discussed. In conclusion, there is more to the occurrence hemispheric symptoms than the severity of the stenosis. While flow-limiting effects of stenosis in conjunction with or without embolic potentials are causes of symptoms in haemodynamic, embolic potentials are the main factors in non-haemodynamic cases.

Keywords: *Atherosclerosis, carotid stenosis, ultrasound, cardiovascular disease*

Résume

Des études de l'ultrasound duplex propective et la radiographie coleur de Doppler étaient faite sur 52 patients consécutifs avec 63 artéres carotique (11 patients ayant la carotide bilatérale interrogation). Ces patients étaient classifiés en 2 groupes de sténose non-hémodynamique (<50%) et de hémodynamiques (>50%) significative en relation avec les symptomes cliniques et l'échomorphologie du nœud de la carotide. Sur 63 artéres carotiques evalues, 36(57%) montraient des sténoses non hémodynamique et 27 (42.9%) de sténose hémodynamique avec plus de la moitié des cas ayant des symptomes hémipheriques (Stroke , TIA) liés a la sténose non-hémodynamique. Cependant les plaques héterogéne et homogene étaient observés dans chez les 2 groupes ayant des symptomes hémodynamique. La sténose hypoéchoique representant les matériels thrombotique sont plus commun en stroke de cas hémipherique de 64.3% et 76.9% en TIA de cas non-hémispherique ayant une ulcération.Une fréquence égale des plaques irréguliére en surface était observé. Cette étude a montré une fréquence elevée des plaques douce en relation aux symptomes de la sténose hémispherique et non-hémispherique et essentiellement l'ulcération/la sténose hémisppherique a plaque irrégulier. Les tendences des plaques échomorphologiques et les charactéristriques des surfaces chez ces groupes étaient élucidées et la pathogénese des symptomes discutée. En conlusion, il y a plus de symptomes hémispheriques que le séverité de la sténose. Cependant, les effects de la sténose en conjonction avec ou sans des potential emboliques sont les causes des symptomes d'hémodynamiques et qui sont des facteur principal des cas non-hemodynamique.

Introduction

Several studies have related the extent of atherosclerotic lesions and the severity of the attendant stenosis to the presence of clinically manifest cerebrovascular disease (CVD) such as stroke and transient ischaemic attack (TIA) [1, 2]. While some studies showed that haemodynamically significant stenoses are more often associated with stroke and TIA, pathologic studies have suggested that certain types of atherosclerotic plaques are more likely to cause cerebrovascular symptoms [1].

Doppler ultrasound (US) of the carotid arteries is a well recognized diagnostic modality used for screening haemodynamically significant (= 50% lumen diameter narrowing) internal carotid stenosis. This has shown that differences in the texture of the atherosclerotic plaque are related to the likelihood of disease progression [2] and clinical event [3, 4]

Since less than 50% of patients with hemispheric symptoms have haemodynamically significant stenoses [5], it is important to evaluate the nonhaemodynamically significant stenoses, which even though do not produce flow-limiting effects, yet produce CVD.

The present study, evaluates the sonographic morphology of carotid plaques between the haemodynamically and non-haemodynamically significant stenoses in relation to clinically manifest hemispheric symptoms.

Patients and methods

A 1*-year (June 1999 - - December 2000) prospective duplex ultrasound and color Doppler imaging studies were performed with 5 & 7MHz linear array transducers of Aloka machine on 52

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consecutive patients (40 men and 12 women) with 63 carotids (11 patients with bilateral carotid interrogation) at the King Khalid University Hospital, Riyadh, Saudi Arabia. Patients were examined after a suspected clinical impression of acute CVD related events and confirmation by computed tomography. The age ranged from 47— 87 years (mean ± SD = 75.3 + 3.3 years).

The systolic velocities (PSV) measured in the internal carotid arteries were the primary diagnostic criteria for determining diameter stenosis. Velocities less than 1.5m/sec were categorized into <24%, 25% - 49% stenoses, 1.5 — 2.5m/sec were considered to represent 50% - 74% stenoses, 2.5m/sec corresponded to 75% - 99% [1].

Occlusion was determined by absence of spectral signal. Colour Doppler was used to confirm such occlusions. The cases were further classified into two study groups viz — non-haemodynamic (stenosis <50 %) or haemodynamically (stenosis = 50 %) significant. Clinical events as occurred in these groups were recorded. The echotexture of each carotid arterial lesion of focal wall thickness of at least 1.5mm were categorized. These were classified into homogeneous plaques when the echogenicity is uniform or heterogeneous when mixed, respectively. The dominant echopatterns as well as the surface characteristics of the plaques were also noted.

Clinical data documented from the patients record included presence or absence of bruit in the neck, blood pressure (BP), history of diabetes, laboratory measurements of low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol levels and serum glucose level. Patients with vertebrobasilar and cardiac symptoms were excluded from the study. All data were analysed on a microcomputer using the SPSS statistical programme (SPSS Incorp. 1999). All differences were taken as significant at $P < 0.05$.

Results

Of the 63 carotid arteries that were evaluated, 36 (57.1 %) revealed non-haemodynamic (< 50 %) and 27 (42.9 %) haemodynamic (= 50 %) stenosis. Thirty (47.6 %) carotid arteries were investigated for stroke, 24 (38.1 %) for TIA and 9 (14.3 %) for non-hemispheric symptoms (loss of vision 3, ptosis 3, intermittent claudication 2 and Takayasu arteritis 1).

Table 1: Distribution of clinical events in relation to the severity of stenosis

Clinical Events	Severity of stenosis on US <24 %	25 – 49 %	50 – 74 %	75 – 99 %	Total
Strok	6	10	8	6	30 (47.6)
Tia	4	9	6	5	24 (38.1)
Others	4	3	2	-	9 (14.3)
Total	14	22	16	11	63 (100)

Others - Non-hemispheric symptoms

Table 1 shows the distribution of the clinical events in relation to the severity of stenosis and Fig.1, the frequency of echotexture to clinical event. Twenty nine (53.7%) out of 54cases with hemispheric symptoms (Stroke and TIA) and seven (77.8 %) out of nine cases with non-hemispheric, were related to <50% stenosis. No significant differences were found in the frequency of risk factors such as hypertension, hypercholesterolemia and diabetes in the groups. Three patients with carotid bruit were seen with > 75 % stenoses.

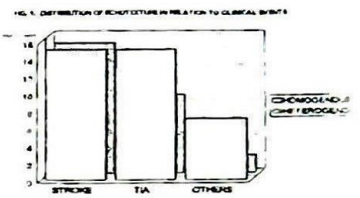

Fig. 1: Distribution of echotexture in relation to clinical events

Stroke

Of the 30 cases with stroke, 53.3 % (n = 16/30) were related to < 50% stenosis and 46.7 % (n = 14/30) to = 50% stenosis (Fig. 2). Homogeneous plaques were more common in < 50% lesions, accounting for 56.3 % while heterogeneous plaques were more in> 50% accounting for 57.1 %. Although, there was no statistical difference, the trend was that the frequency of the homogeneous plaque decreased from 9 in < 50% to 6 in = 50% and that of heterogeneous slightly increased from 7 to 8.

There was more of hyperechoic plaques in < 50% cases [56.3 % (n 9/16)] than = 50% cases [35.7 % (n = 5/14)] (Table 2). Calcified hypoechoic plaques were seen in 4 out of 9 cases in = 50% cases. The trend was that the frequency of hyperechoic plaque decreased from 9 in < 50% to 5 in = 50% and that of hypoechoic increases from 7 in < 50% to 9 in = 50% cases.

Table 2: Frequency distribution of echomorphology in relation to clinical events and severity of stenosis

Plaque echomorphology	Stroke <50 %	Stroke ≥50 %	Tia <50 %	Tia ≥50 %	Others <50 %	Others ≥50 %	Total
Heterogeneous Hyperechoic	4	3	2	2	1	-	12
Heterogeneous Hypoechoic	3	5	3	2	1	-	14
Homogeneous Hyperechoic	5	2	1	1	3	1	15
Homogeneous Hypoechoic	4	4	7	4	2	1	22
Total	16	14	13	11	7	2	63

<50 % = Non-haemodynamic Stenosis
≥50 % = Haemodynamic Stenosis
Others = Non-hemispheric Symptoms

While there was no difference in the frequency of the irregularly surfaced plaque (dominant feature) between the two groups (9 cases each), it was clear that the smooth surfaced lesions were predominant in the <50% (7/8) cases. Four ulcerated lesions were seen in the = 50% cases and none in the < 50% cases.

Although, there was no difference in the frequency of irregular surfaced plaques in = 50% and < 50% groups, heterogeneous plaques showed more irregular surface characteristics in both groups.

TIA

Thirteen of the 24 cases (54.2 %) were related to < 50% stenosis and 45.8 % (n 11/24) to = 50% stenosis (fig 2).

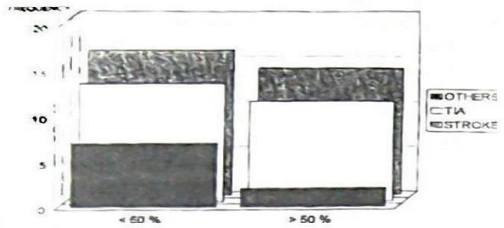

Fig. 2 Frequency distribution of clinical events in relation to severity of stenosis.

Homogeneous plaques were more common in both groups accounting for 61.5 % (n = 8/13) and 63.6 % (n = 7/11) in < 50% and = 50% stenosis respectively. There was significant preponderance of hypoechoic plaques in < 50% stenosis cases accounting for 76.9% (n = 10/13) but slight in = 50% stenosis cases accounting for 54.5 % (n = 6/11) (Table 2). The trend was a significant decrease in the frequency of hypoechoic plaques from the <50% to = 50% cases. Irregularly surfaced plaques were more in < 50% stenosis cases accounting for 7 cases while ulceration was more in = 50% cases with a frequency of 4. No difference was seen in the frequency of the smooth plaques between the two groups (Table 3).

Non-hemispheric (other) symptoms

These were cases that were initially thought to be due to CVD but ruled out on CT. The presence of the plaques was not related to the presenting complaints especially in the 2 cases with = 50% stenosis who presented with ptosts.

Table 3: Frequency distribution of surface characteristic in relation to clinical events and severity of stenosis

Plaque surface characteristic	Stroke <50 %	Stroke ≥50 %	TIA <50 %	TIA ≥50 %	Others <50 %	Others ≥50 %	Total
Smooth	7	1	4	4	5	2	23
Irregular	9	9	7	3	2	-	30
Ulcerated	-	4	2	4	-	-	10
Total	16	14	13	11	7	2	63

< 50 % = Non-haemodynamic Stenosis
≥50 % = Haemodynamic Stenosis
Others = Non-hemispheric Symptoms

Out of the 9 cases, 2 (22.2 %) were related to = 50% stenosis and 7 (77.8 %), < 50% stenosis (fig 2).

The two = 50% cases were homogeneous in echotexture with small calcifications. 5 of the <50% cases were homogeneous and 2, heterogeneous. Preponderance of hyperechoic and hypoechoic plaques were noted in < 50% than in = 50% cases (Table 2). Two of the < 50% cases were associated with mildly irregular surfaced plaques with < 24 % stenosis. These were the cases of Takayasu arteritis and one intermittent claudication. The remaining five cases with < 50% stenosis and the two with = 50% stenosis showed smooth plaques (Table 3).

Discussion

Our study confirmed that more than half of the cases with hemispheric symptoms were related to < 50% stenosis accounting for 53.7 %. This is similar to the finding in the study by Carroll [5].

The atherosclerotic plaque texture is shown to be related to clinical events in both study groups. Previous studies have shown that heterogeneous echogenenicity was indicative of plaque haemorrhage [6, 7] and attempt had also been made to investigate association between plaque haemorrhage, heterogeneous and hemispheric symptoms [8]. Inspite of all these, no studies have isolated plaque features peculiar to patients with a symptom type [9]. Associations of risk factors to hemispeheric symptoms have been made with echotextures. Echogenic plaques were found to be more common in men, coronary artery disease and smokers while echo lucent plaques were more in women and diabetics [10]. Such associations were not significant or related to the degree of stenosis in our study.

Hypoechoic homogeneous plaques which are regarded as newly formed plaques [11] have been shown to herald an increased risk of development of TIA or stroke [12]. These previous studies however, did not separately analyse the echogenicity in different degrees of stenosis as we have done in this study in relation to clinical events.

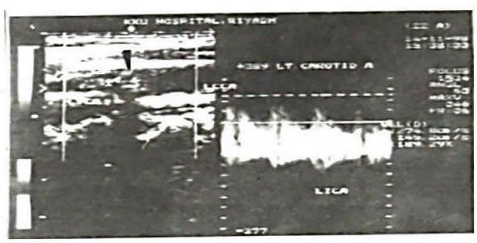

Fig. 3: Sonogram of the left internal carotid artery, showing a heterogeneous hyperechoic plaque (black arrow head) causing 80%-90% stenosis. Note the filling of the spectral window (spectral broadening) and aliasing from post-stenosis turbulence

In our study, heterogeneous plaques (Fig. 3) were found in high frequency in both <50% and = 50% stenoses, in cases presenting with hemispheric symptoms - stroke and TIA, while no heterogeneous plaque was seen in = 50% stenosis with non-hemispheric symptoms (Table 2). Since there were no statistically significant differences between heterogeneous and homogeneous plaques in < 50% and = 50% stenosis cases, these have not distinguished the occurrence of symptoms in both groups. However, heterogeneous plaques have been found to be more responsible for the occurrence of hemispheric symptoms in general [1,4,11,13].

The pathogenesis of these symptoms has been related to the presence of inflammation in the plaques as demonstrated by the increase numbers of macrophages and T lymphocytes, causing thinning of fibrous cap and eventual plaque rupture [14,15] or ulceration. Plaque rupture depends on the balance between the tensile strength of the plaque and the stress exerted on it [9]. Such stress could be triggered by sudden increase in

blood pressure or pulse rate [16], vasospasm forcing plaque contents through a weakened cap [17] and intra-plaque hemorrhage [18]. Such rupture exposes necrotic core of the plaque to circulation and promotes thrombosis, plaque progression and embolisation [9]. The possible predisposing factors to these symptoms are similar in both groups of cases in our study and therefore could not have greatly influenced the final outcome of our analysis.

As opined by Belcaro [4], high-grade stenoses with heavy calcifications do not only result in stenosis but are prone to dis-aggregation and microembolism. Calcifcations in plaques resulting from ageing process, are associated with stroke [4] but O'Holleran [13] encountered no stroke in such cases in their study. Stroke was found in heavily calcified plaques in cases with = 50% stenoses in our study. Incidentally minor calcifications were encountered in the 2 cases with proptosis (Fig. 4).

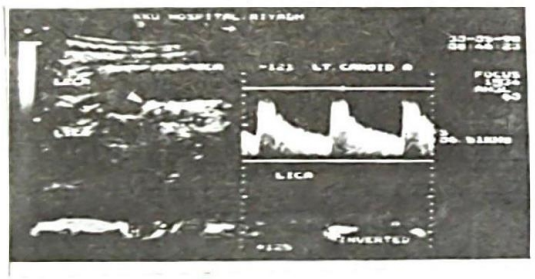

Fig. 4: Sonogram of the left internal carotid artery, showing a heterogeneous plaque with surface calcifications (white arrow) and posterior acoustic shadowing. Note the clear spectral window from non-haemodynamically significant stenosis

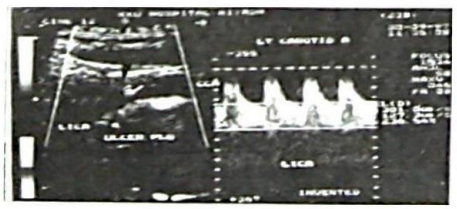

Fig. 5: Sonogram of the left internal carotid artery, showing a heterogeneous hypoechoic circumferential plaque (black arrow head) with a small ulcer on the posterior wall (small arrow)

Predominantly hypoechoic stenoses, representing thrombotic materials adjacent to plaques are potentially embolic, and are more frequent among symptomatics [19]. These echolucent plaques have been found to be rich in lipids and also been shown to herald an increase of subsequent development of TIA and stroke [12]. This is more common in = 50% stenosis cases of stroke accounting for 64.3% and in 76.9 % of < 50% cases in TIA (Fig. 5). Plaque surface irregularity and ulceration which are other potential sources of emboli, did not seem to be related to the severity of stenosis as there was no statistically significant difference in the frequencies. However, while irregularly surfaced plaques are of equal frequency in < 50% and = 50% stenosis cases in stroke, there was no ulceration in < 50% cases. There was preponderance of irregular surfaced plaques in < 50% and ulceration in = 50% stenosis cases in TIA.

Moore *et al* [20] showed that ulcerated lesions are more likely to cause stroke than smooth. Our study showed higher frequency of smooth plaque in relation to hemispheric and nonhemispheric symptoms in < 50% stenosis and mainly ulceration/irregular plaques in = 50% stenosis. The observation of more ulceration in = 50% stenosis is similar to the findings in the series by Bassiouny *et al* [21], in which ulcerations were more frequent in symptomatic high-grade stenosis. This is true in stroke but the difference is not statistically significant in TIA in this study. On plaque irregularity and ulceration, it must be stated that these characteristics are not always a reliable predictor of hemispheric symptoms. They are regarded as markers of instability of the plaques [9]. Therefore, the presence of symptoms in < 50% stenosis cases with irregular plaque surface or ulcerations are due to the possible disintegration and microembolism of the plaques, rather than flow-limiting consequences.

In conclusion, there is more to the occurrence of hemispheric symptoms than the severity of the stenosis. While flow-limiting effects of stenosis in conjunction with or without embolic potentials are causes of symptoms in haemodynamic, embolic potentials are the main factors in nonhaemodynamic cases.

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