REVIEW
ΑΝΑΣΚΟΠΗΣΗ

Ultrasonic carotid plaque morphology

The main criterion currently used to assess stroke risk due to atheroma of the carotid bifurcation is the degree of stenosis. Although the benefit of carotid endarterectomy in stroke prevention has been demonstrated by prospective randomised trials, this benefit is moderate. Other risk factors have been suggested, such as ultrasonic carotid plaque characterisation, which may help in the identification of a high risk subgroup which will derive the maximum benefit from carotid endarterectomy. This paper reviews the literature on the clinical importance of carotid plaque characterization on histopathological and ultrasonographic grounds, and underlines the potential of objective quantitative assessment of carotid plaque echodensity in the identification of a high risk group for stroke.

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Υπερηχογραφικά χαρακτηριστικά καρωτιδικής πλάκας

Περίληψη στο τέλος του άρθρου

Key words

Carotid plaque
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Ultrasound

1. INTRODUCTION

The asymptomatic carotid artery stenosis (ACAS) study provided evidence that carotid endarterectomy can reduce the incidence of ipsilateral stroke in patients with asymptomatic carotid stenosis of more than 60%.[1] However it may be necessary to operate on at least 20 patients to prevent one stroke. Factors other than the degree of stenosis may help to identify a subgroup at higher risk of stroke and thus decrease the number of unnecessary operations.

It has recently been shown that the finding of hypoechoic carotid artery plaque at ultrasound is an independent risk factor for ipsilateral ischemic stroke.[2] In addition, the NASCET investigators have reported that the presence of ulceration, as seen on the angiogram, at each level of increasing degree of stenosis, resulted in stroke rates higher than those quoted for lesions not associated with ulceration.[3] It appears that certain specific features of atherosclerotic plaques are associated with an increased risk of stroke, most of which can now be determined non-invasively using ultrasound. Another reason for interest in ultrasonic carotid plaque characterisation was the development of carotid artery angioplasty and stenting. The purpose of this paper is to review the literature on carotid plaque ultrasonic characterisation, with emphasis on its clinical significance. The morphological variables considered are grouped in two categories: (a) plaque surface configuration (smooth or ulcerated) and (b) plaque internal structure.

2. PLAQUE SURFACE CONFIGURATION

It has been suggested that the ultrasonic characteristics of the plaque surface should be classified as smooth or irregular. A plaque is regular when the blood-lesion interface is smooth and unbroken, or irregular where a break in the echo-reflective surface of the lesion is observed or the surface is uneven.[4] The introduction of color in the Duplex assessment of carotid plaques introduced

new refinements in the definition of plaque ulceration. Sitzer defined carotid plaque ulceration using color flow Doppler as a plaque niche filled with reversed flow on longitudinal views, found at the same location on transverse views, without evidence of aliasing phenomena.[5]

The preoperative diagnosis of ulcerated carotid atheroma has attracted the interest of many investigators in the attempt to identify a high risk group for stroke. O'Donnel et al compared B-mode ultrasound and selective arteriography with pathologic specimens obtained from 89 carotid endarterectomies.[6] While arteriography detected only 16 of 27 ulcerations (sensitivity 59%), B-mode ultrasound did better (24/27, sensitivity 89%). The two imaging techniques had comparable specificity (arteriography 73%, B-mode ultrasound 87%).

Most of the studies investigating the ability of B-mode carotid imaging to detect ulceration have failed to address the associated quantitative aspects of carotid plaque. Comerota et al demonstrated that the degree of stenosis significantly affects diagnostic sensitivity.[7] B-mode sensitivity for the presence of ulceration was 77% (10/13) in plaques with less than 50% stenosis and only 41% (26/63) in plaques with greater that 50% stenosis (P= 0.03). The corresponding figures for arteriography were 77% (10/13) and 48% (30/63) respectively. More recently in a study of 43 consecutive patients with greater than 70% internal carotid artery stenosis, plaque surface abnormalities were detected by Duplex imaging evaluation of the corresponding endarterectomy specimens.[5] The sensitivity of Duplex imaging in detecting surface ulceration was only 33%.

3. PLAQUE INTERNAL STRUCTURE

High resolution ultrasound has the major advantage over arteriography of anabling the investigator to visualise not only the lumen of the vessel, but also the size and consistency of atherosclerotic plaques.

One of the early systems of classification of carotid plaques was introduced by Johnson et al in 1985 in a study on the natural history of patients with asymptomatic carotid stenosis followed up for 3 years.[8] Three types of plaques were defined: calcified, dense (high level echoes) and soft (low level echoes).

Another classification system allowing a closer study of the character and behavior of plaques was introduced by Reilly et al[9] in 1982 and subsequently used by others.[10] Two distinct types of plaque were recognised of which the first was termed homogenous and was defined as plaque with uniformly high or medium level echoes. Homogenous plaques were histologically fibrous lesions. The second type was termed heterogeneous and was defined as plaque with high, medium and low level echoes. Histologically heterogenous plaques contained variable amounts of intraplaque hemorrhage, lipids, cholesterol crystal and a loose stroma.[5]

In a refinement of this classification system introduced by Gray-Weale et al[11] in 1988, four plaque types were defined based on the degree of echolucency visualised on B-mode scan:

- *Type 1:* Predominantly echolucent with a thin echogenic cap
- *Type 2:* Intermediate echolucent lesions with small areas of echogenicity
- *Type 3:* Intermediate echogenic lesions with small areas of echolucency (<25%)
- *Type 4:* Uniformly echogenic lesions (equivalent to homogenous).

The authors' group[12] has added a further type 5 for plaques which cannot be classified due to acoustic shadowing artifact and a good interobserver agreement has been reported (k=0.79). Furthermore it has been realised that in patients with carotid stenosis of greater than 70%, 69% of type I plaques do not have a thin echogenic cap and can be missed unless velocity measurements (or color flow imaging) are made.[13]

Studies correlating B-mode ultrasound imaging of carotid plaques histological characteristics have shown that echogenic plaques are fibrous. The echogenicity increases with increasing amounts of collagen. Echolucent plaques contain lipid and/or hemorrhage, with relatively little fibrous tissue. The presence of calcification results in high echoes in corresponding areas with extensive acoustic shadowing.[6,14,15] Pathological studies have demonstrated that increased lipid concentration makes carotid plaques unstable and prone to embolism.[16,17]

The association between intraplaque hemorrhage in endarterectomy specimens and ipsilateral symptoms has been reported by several groups.[18–20] There is general agreement that intraplaque hemorrhage is common in all plaques but its incidence is increased in plaques associated with ipsilateral symptoms. Attempts to distinguish between intraplaque hemorrhage and lipid using ultrasound have so far been unsuccessful, but clinically this may not be so critical as both types of content make the plaque potentially unstable.[21]

Steffen et al[22] reported that in symptomatic arteries, for all degrees of stenosis, there was a preponderance of echolucent type 1 and 2 lesions (67%), whereas in pa-

tients without symptoms there was a preponderance of echogenic plaques, type 3 and 4 (86%). Geroulakos et al[12] confirmed that these findings also apply to patients with stenosis of greater than 70%, in which group an increased incidence of cerebral infarction has been demonstrated on CT ipsilateral to type 1 plaques (36%) compared with a low incidence (14%) ispilateral to all the other types (2–4) combined ($P<0.03$).[23] The European Carotid Plaque Study Group reported that patients with recent symptoms had plaques with more soft tissue than patients with earlier symptoms ($P=0.0004$).[24] These findings imply that carotid plaques are not static, but dynamic structures which change in composition over a period of time. Further work is needed to test this hypothesis.

In a prospective series of 242 patients, Bock et al[25] found that vessels with echolucent carotid plaques were associated with a 5.7% annual rate of transient ischemic attacks (TIA) and stroke, significantly greater than the 2.4% rate found among vessels with echogenic plaques. These findings were recently confirmed by the Cardiovascular Health Study, which enrolled 5,201 individuals aged over 65 years, without cerebrovascular symptoms, who were followed for an average of 3.3 years. The incidence of stroke in this study was significantly increased in individuals who had echolucent plaques (odds ratio 2.53).[2]

Asymptomatic echolucent plaques are associated with an increased number of asymptomatic embolic events in the middle cerebral artery observed on transcranial Doppler.[26] Further work is needed to determine whether the number of asymptomatic emboli detected can predict the development of cerebrovascular events.

A recent consensus on carotid plaque characterisation has suggested that echodensity measurements should be used to reflect the brightness of the plaque with the term hyperechoic referring to echogenic and the term hypoechoic referring to echolucent plaques.[27] The consensus suggested that measurements of texture should not be confused with measurements of echodensity. The term homogenous should refer to plaques of uniform consistency irrespective of whether they are predominantly hypoechoic or hyperechoic. The term heterogenous should be used for plaques of non-uniform consistency, i.e. having both hypoechoic and hyperechoic areas. Although this is a relatively simplistic view it is the foundation for the classification and measurements which may eventually result in the development of international standards.

The echographic assessment of plaque structure in all the studies is based on reviewed subjective, qualitative evaluation of the carotid plaques. Because ultrasound scanning is operator dependent, ultrasonic carotid plaque characterisation is subject to significant interobserver variability. In an attempt to overcome this subjectivity and improve the comparability of the ultrasonic features of the plaques the authors' group has introduced a new technique for the quantitative and objective assessment of these features using computer assisted digital image processing[28] (figures 1, 2).

B-mode ultrasonic images of 96 carotid plaques were captured transferred to magneto-optic disc and normalised using linear scaling so that the adventitia would have a grey scale median (GSM) value of 185–195 and blood 0–5. The GSM and the percentage of echolucent pixels (PEP) in the normalised images of the carotid plaques

Figure 1. Hypoechoic plaque (GSM=6) with the histogram of the frequency distribution of the grey tones of the pixels included in the outlined area of interest (plaque). The median of this distribution is the grey scale median (GSM). The x axis is the grey scale (ranges from 0= black to 255=white) and the y axis is the number of pixels belonging to a particular grey scale value.

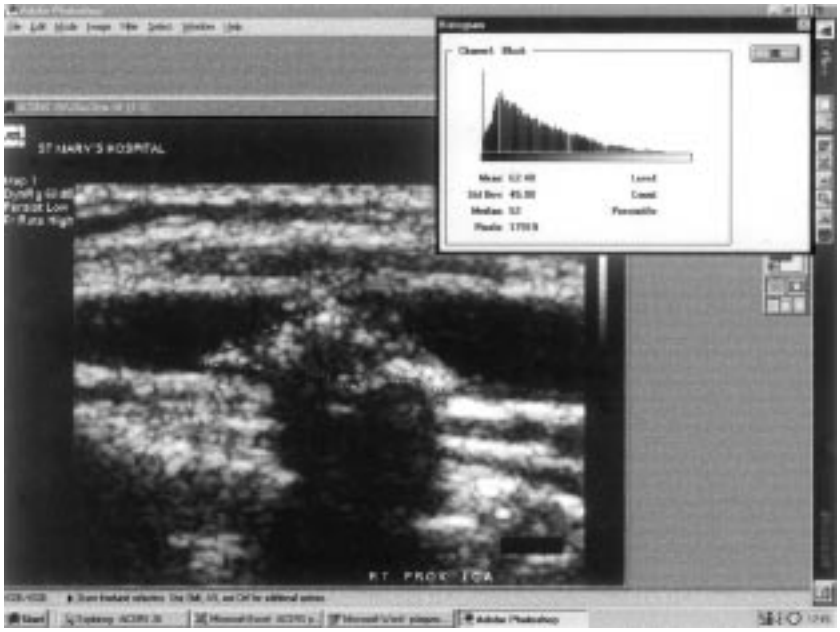

Figure 2. Hyperechoic plaque (GSM=52) with the histogram of the frequency distribution of the grey tones of the pixels included in the outlined area of interest (plaque).

were determined to measure echodensity. Multiple regression analysis revealed that the GSM and the PEP were the variables related most significant to the presence or absence of ispilateral hemispheric symptoms.[29] Furthermore, computer-assisted plaque characterisation with B-mode image normalisation has led to identification and quantification of differences in echostructure between carotid plaques associated with retinal and hemispheric symptoms. The study[30] has shown that plaques associated with amaurosis fugax (AF) were hypoechoic (mean GSM=7.4) and severely stenotic (mean degree of stenosis=85.6%). Plaques associated with hemispheric TIAS and stroke had the same echodensity and the same degree of stenosis (mean GSM=14.9 vs 15.8 and mean degree of stenosis=79.3% vs 78.1%). These findings support the hypothesis that AF has a pathophysiological mechanism different from that of TIA and stroke.

In conclusion, there is strong evidence to suggest that the surface characteristics and ultrasonic internal structure of carotid plaque are factors which contribute to the development of hemispheric cerebrovascular end-points. Ultrasonic carotid plaque characterisation may have the potential to improve the selection of patients for carotid endarterectomy and/or carotid angioplasty and stenting. Prospective studies are needed to test this hypothesis.

ΠΕΡΙΛΗΨΗ

Υπερηχογραφικά χαρακτηριστικά καρωτιδικής πλάκας

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Το κύριο κριτήριο που χρησιμοποιείται σήμερα για την εκτίμηση του κινδύνου αγγειακού εγκεφαλικού επεισοδίου (ΑΕΕ) από αθηρωματικές βλάβες του καρωτιδικού διχασμού είναι ο βαθμός της στένωσης του αυλού της έσω καρωτίδας. Παρόλο που προοπτικές τυχαιοποιημένες κλινικές μελέτες έχουν αποδείξει τα οφέλη της καρωτιδικής ενδαρτηρεκτομής στην προφύλαξη από ΑΕΕ, τα οφέλη αυτά παραμένουν περιορισμένα, ιδιαίτερα σε ασυμπτωματικούς ασθενείς. Άλλοι παράγοντες κινδύνου έχουν επίσης προταθεί, όπως ο υπερηχογραφικός χαρακτηρισμός της καρωτιδικής πλάκας, που ίσως βοηθήσουν στον εντοπισμό υποομάδων υψηλού κινδύνου που θα ωφεληθούν τα μέγιστα από τυχόν καρωτιδική ενδαρτηρεκτομή. Σκοπός του παρόντος άρθρου είναι η

ανασκόπηση της βιβλιογραφίας όσον αφορά την κλινική σημασία του χαρακτηρισμού της καρωτιδικής πλάκας –τόσο ιστολογικά όσο και υπερηχογραφικά– με έμφαση στη συμβολή της ποσοτικής μέτρησης της ηχογένειάς της στον εντοπισμό μιας ομάδας ασθενών υψηλού κινδύνου για ΑΕΕ.

Λέξεις ευρετηρίου: Ηχογένεια, Καρωτιδική πλάκα, Καρωτιδική στένωση, Υπέρηχοι

References

1. EXECUTIVE COMMITTEE FOR THE ASYMPTOMATIC CAROTID ATHEROSCLEROSIS STUDY. Endarterectomy for asymptomatic carotid artery stenosis. *JAMA* 1995, 273:1421–1428
2. POLAK JI, SHEMANSKI L, O'LEARY D, LEFKOWITZ D, PRICE TR, SAVAGE P ET AL. Hypoechoic plaque at US of the carotid artery: An independent risk factor for individual stroke in adults aged 65 years or older. *Radiology* 1998, 208:649–654
3. ELIASZIW M, STREIFLER JY, FOX AJ, HACHINSKI VC, FERGUSON GG, BARNETT H ET AL. Significance of plaque ulceration in symptomatic patients with high grade carotid stenosis. *Stroke* 1994, 25:304–308
4. FITZGERALD DE, O'FARRELL CM. Prognostic value of ultrasound morphology in carotid atherosclerosis. *Int Angiol* 1993, 12:337–341
5. SITZER M, MULLER W, RADEMACHER J, SIEBLER M, HORT W, KNIEMEYER HW ET AL. Colour-flow Doppler-assisted duplex imaging fails to detect ulceration in high grade internal carotid artery stenosis. *J Vasc Surg* 1996, 23:461–465
6. O'DONNELL TF, ERDOES L, MACKEY WC, McCULLOUGH J, SHEPARD A, HEGGERICK P ET AL. Correlation of B-mode ultrasound imaging and arteriography with pathologic findings at carotid endarterectomy. *Arch Surg* 1985, 120:443–449
7. COMEROTA AJ, KATZ ML, WHITE JV, GROSH JD. The preoperative diagnosis of the ulcerated carotid atheroma. *J Vasc Surg* 1990, 11: 505–510
8. JOHNSON JM, KENNELLY MM, DECESARE D. Natural history of asymptomatic carotid plaque. *Arch Surg* 1985, 120:1010–1012
9. REILLY LM, LUSBY RJ, HUGHES L, FERRELL LD, STONEY RJ, EHRENFELD WK. Carotid plaque histology using real-time ultrasonography. *Am J Surg* 1983, 146:188–193
10. BLUTH EI, KAY D, MERRITT CR, SULLIVAN M, FARR G, MILLS NL ET AL. Sonographic characterisation of carotid plaque: Detection of hemorrhage. *Am J Roentgenol* 1986, 146:188–193
11. GRAY-WEALE AC, GRAHAM JC, BURNETT JR, BYRNE K, LUSBY RJ. Carotid artery atheroma: Comparison of preoperative B-mode ultrasound appearence with carotid endarterectomy specimen pathology. *J Cardiovasc Surg* 1988, 29:676–681
12. GEROULAKOS G, RAMASWAMI G, NICOLAIDES A, JAMES K, LABROPOULOS N, BELCARO G ET AL. Characterisation of symptomatic and asymptomatic carotid plaques using high resolution real time ultrasound. *Br J Surg* 1993, 80:1274–1277
13. GEROULAKOS G. Ultrasound imaging of the arterial wall and of atherosclerotic plaque. Ph.D. Thesis, University of London, 1994: 173–177
14. WOLVERSON MK, BASHITI HM, PETERSON GJ. Ultrasonic tissue characterisation of atheromatous plaques using a high resolusion real time scanner. *Ultrasound Med Biol* 1983, 9:599–609
15. GOES E, JANSSENS W, MAILLET B, FRESON M, STEYAERT L, OSTEAUX M. Tissue characterization of atheromatous plaques. Correlation between ultrasound image and histological findings. *J Clin Ultrasound* 1990, 18:611–617
16. SEEGER J, KLIGMAN N. The relationship between carotid plaque composition and neurological symptoms. *J Surg Res* 1987, 43: 78–85
17. FEELY TM, LEEN EJ, COLGAN MP, MOORE DJ, HOURIHANE DO, SHARIK GD. Histologic characteristics of carotid artery plaque. *J Vasc Surg* 1991, 13:719–724
18. FRYER JA, MYERS PC, APPLEBERG M. Carotid intraplaque hemorrhage: the significance of neovascularity. *J Vasc Surg* 1987, 6:341–349
19. IMPARATO AM, RILES TS, MINTZER R, BAUMANN G. The importance of hemorrhage in the relationship between gross morphologic characteristics and cerebral symptoms in 376 carotid artery plaques. *Ann Surg* 1983, 197:195–203
20. LUSBY RJ, FERRELL LD, EHRENFELD WK, STONEY RJ, WYLIE EJ. Carotid plaque haemorrhage: its role in the production of cerebral ischaemia. *Arch Surg* 1982, 117:1479–1488
21. LUSBY RJ. Plaque characterisation: Does it identify high risk groups? In: Bernstein EF, Callow AD, Nicolaides AN, Shifrin EG (eds) *Cerebral Revascularisation*. Med-Orion, 1993:93–107
22. STEFFEN CM, GRAY-WEALE AC, BYME KE, LUSBY RJ. Carotid artery atheroma: ultrasound appearance in symptomatic and asymptomatic vessels. *Aust N J Surg* 1989, 59:529–534
23. GEROULAKOS G, DOMJAN J, NICOLAIDES A, STEVENS J, LABROPOULOS N, RAMASWAMI G ET AL. Ultrasonic carotid plaque characterisation and the risk of cerebral infarction on computed tomography. *J Vasc Surg* 1994, 20:263–266
24. EUROPEAN CAROTID PLAQUE STUDY GROUP. Carotid artery plaque composition. Relationship to clinical presentation and ultrasound B-mode imaging. *Eur J Vasc Endovasc Surg* 1995, 10:23–30
25. BOCK RW, GRAY-WEAL AC, MOCK PA, ROBINSON DA, IRWING L, LUSBY RJ. The natural history of asymptomatic ulcerative lesions of the carotid artery. *J Vasc Surg* 1993, 17:160–171
26. SRODON PD, GEROULAKOS G, LUMLEY JSP. Asymptomatic intracranial embolic events are related to carotid plaque structure. *Br J Surg* 1997, 84(Suppl):166
27. DEBRAY JM, BAUD JM, DAUZAT M FOR THE CONSENSUS CONFERENCE. Consensus concerning the morphology and the risk of carotid plaques. *Cerebrovasc Dis* 1997, 7:289–296
28. EL-ATROZY T, NICOLAIDES A, TEGOS T, ZARKA AZ, GRIFFIN M, SABETAI M. The effect of B-mode image standardisation on the echodensity of symptomatic and asymptomatic carotid bifurcation plaques. *Int Angiol* 1998, 17:179–186
29. ELATROZY T, NICOLAIDES A, TEGOS T, GRIFFIN M. The objective characterisation of ultrasonic carotid plaque features. *Eur J Vasc Endovasc Surg* 1998, 16:223–230
30. SABETAI MM, TEGOS TJ, NICOLAIDES AN, EL-ATROZY TS, DHANJIL S, GRIFFIN M ET AL. Hemispheric symptoms and carotid plaque echomorphology. *J Vasc Surg* 2000, 31:39–49

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