doi: 10.13241/j.cnki.pmb.2017.02.019

超声造影技术评价颈动脉粥样硬化斑块稳定性的临床研究 *

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摘要 目的：探讨超声造影技术评价颈动脉粥样硬化斑块稳定性的临床价值，为动脉粥样硬化诊断准确性提供参考。**方法**：根据实时超声造影检查的回声图像特点将该院 53 例（59 个斑块）颈动脉粥样硬化斑块患者分为软斑组（24 个）、混合斑组（18 个）、硬斑组（17 个），比较 3 组的造影增强率、造影增强程度分级，并对各类型斑块的时间 - 强度进行定量分析。**结果**：59 个斑块中有 40 个呈现不同程度的增强，增强率为 67.80%，其中软斑组、混合斑组、硬斑组超声增强率分别为 87.50%、72.22%、35.29%，差异具有统计学意义（P<0.05）；造影增强程度Ⅰ级和Ⅲ级在三组间差异具有统计学意义（P<0.05），其中硬斑组造影增强程度Ⅰ级个数较软斑组和混合斑组多，软斑组造影增强程度Ⅲ级个数较混合斑组和硬斑组多，差异均有统计学意义（P<0.05）；软斑组达峰时间、平均渡越时间均低于混合斑组和硬斑组，斑块峰值强度高于混合斑组和硬斑组，混合斑组达峰时间、平均渡越时间均低于硬斑组，斑块峰值强度高于硬斑组，差异均具有统计学意义（P<0.05）。**结论**：超声造影技术可无创性地通过造影增强实时反映出颈动脉粥样硬化斑块内的新生血管情况，提供参数成像与定量分析，正确评价斑块的稳定性。

关键词：超声造影技术；颈动脉粥样硬化斑块；稳定性；临床研究

中图分类号：R543.5；R445 **文献标识码**：A **文章编号**：1673-6273（2017）02-280-03

Clinical Study on Evaluation of Carotid Atherosclerotic Plaque Stability by Contrast-enhanced Ultrasound*

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ABSTRACT Objective: To investigate the clinical value of evaluation of carotid atherosclerotic plaque stability by contrast-enhanced ultrasound, and to provide a reference for atherosclerosis diagnostic accuracy. **Methods:** 53 cases (59 patches)of patients with carotid artery atherosclerotic plaque were divided into soft plaque group (24 patches), mixed plaque group (18 patches)and hard plaque group(17 patches) according to the characteristics of real-time ultrasound echo image angiography, compared the the contrast enhancement rate and enhancement degree between the 3 groups,and quantitative analysis of time-intensity for each type of patch. **Results:** 40 of the 59 patches showed different degrees of enhancement and the enhancement rate was 67.80% . The ultrasound enhancement rates of soft plaque group, mixed plaque group and hard plaque group were 87.50%,72.22% and 35.29% respectively,and the difference was statistically significant (P<0.05); The I and III grade of contrast enhancement degree between the three groups was statistically significant (P<0.05), the number of I grade of contrast enhancement degree in hard plaque group was more than the soft and mixed plaque groups,the number of III grade of contrast enhancement degree in soft plaque group was more than the hard and mixed plaque groups, the difference was statistically significant (P<0.05); The peak time, average transit time of soft plaque group were lower than the mixed plaque group and hard plaque group, the plaque peak intensity is higher than the mixed plaque group and hard plaque group, the peak time and average transit time of the mixed plaque group was lower than the hard plaque group, the plaque peak intensity was higher than the hard plaque group, and the differences were statistically significant (P<0.05). **Conclusion:** The ultrasound contrast technique can be used to reflect the new blood vessel of carotid atherosclerotic plaque in real time, and provide the parameter imaging and quantitative analysis to evaluate the stability of plaque.

Key words: Contrast-enhanced ultrasound technique; Carotid atherosclerotic plaque; Stability; Clinical study

Chinese Library Classification(CLC): R543.5; R445 Document code: A

Article ID: 1673-6273(2017)02-280-03

前言

目前，心、脑血管意外的发病形势十分严峻，其发病率与病死率居全球疾病之最，动脉粥样硬化是其重要的一大危险因素。经研究证实，不稳定性的动脉粥样硬化斑块与易损斑块碎裂继发血栓是引发心、脑血管意外及缺血性脑卒中的主要原因[1]。有报道显示[2]，伴颈动脉粥样硬化斑块的缺血性脑卒中患者比例超过了 63%。外国学者 Sun X F 等[3]报道指出，新出现的同

* 基金项目：解放军总医院科技创新苗圃基金项目（14KMM26）

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（收稿日期：2016-04-29 接受日期：2016-05-25）

侧症状与斑块的出血呈正比，且不稳定斑块的缺血风险大于稳定斑块。因此，缺血性脑卒中的严重程度与颈动脉粥样硬化斑块的稳定性密切相关[4]，斑块稳定性主要在于斑块组分、斑块氧化应激及炎症反应有关。本研究对该院 53 例颈动脉粥样硬化斑块患者的 59 个斑块进行了定性分析与定量分析，具体报告如下。

1 资料与方法

1.1 一般资料

回顾分析 2014 年 1 月～2015 年 12 月期间我院收治的颈动脉粥样硬化斑块患者 53 例，患者均经多普勒超声检查确诊为颈动脉粥样硬化斑块形成，且所有患者斑块厚度≥ 1.8 mm；排除心源性心肌梗死、恶性肿瘤者。其中男 29 例，女 24 例，年龄 44～76 岁，平均年龄（55.93± 4.76）岁；短暂性脑缺血发作病史患者 21 例，脑梗死病史患者 13 例；按 Salcuni 标准[4]（颈动脉内 - 中膜厚度局部增厚程度在 1.2 mm 以上）经超声造影分析发现 59 个斑块，根据斑块的回声图像特点分为软斑组（24 个，斑块回声小于管壁回声）：男 11 例，女 13 例，年龄 40～75 岁，平均年龄（54.89± 3.65）岁、混合斑组（18 个，斑块回声表现为强、底或者无回声，钙化影较少）：男 10 例，女 8 例，年龄 41～73 岁，平均年龄（53.26± 3.82）岁、硬斑组（17 个，斑块回声强于管壁，后方伴有阴影）：男 8 例，女 9 例，年龄 40～80 岁，平均年龄（58.76± 3.58）岁，各组患者基线资料间差异无统计学意义（P>0.05），具有可比性。患者及家属签署知情同意书且经医学伦理委员会批准。

1.2 方法

常规超声检查：患者取仰卧位、颈后垫枕后仰、头偏向对侧，探头按照前位、侧位、侧后位和超后侧位探查，探头按照颈部颈总动脉近心端、中部、远端、颈动脉分叉处及颈内、外动脉检查，显示观察有无颈动脉粥样硬化斑块，如果发现斑块，测量斑块厚度；纵向探查测量内膜 - 中膜厚度，部位在颈总动脉远端近分叉处 1 cm，分叉部及颈内动脉起始部 1 cm 处后壁进行测量，并且对测量结果进行详细记录。

超声造影检查：超声造影检查采用仪器为 GE LogiqE9 超声诊断仪，配备 contrast 超声造影成像技术，选择 9L 线阵探头，频率 2.4～10MHz。指导患者取平卧位，保持呼吸平静，充分暴露出需检查的颈部位置，顺颈动脉从下开始纵向于横向的扫查，观察并记录斑块的大小、部位、颈动脉内 - 中膜厚度 。造影前将 Sono Vue 超声造影剂（意大利 Braacco 公司）与 5mL 的生理盐水进行混合，获得白色乳状的微泡悬液，后取 2mL 微泡悬液经患者的上臂肘静脉弹丸式注射，并继续快速推注 5 mL 的生理盐水。与此同时，同时计时进行实时观察 90 s，注意斑块内造影剂显影变化情况，待至造影微泡消失。使用自带 Sonoliver CAP 软件系统对图像进行定量分析，选择感新区（斑块）和参考区（管腔内），观察颈动脉粥样硬化斑块和颈动脉管腔内参与随时间变化的趋势（DVP 曲线），Sonoliver CAP 软件系统可以对斑块、边界、参考、分析四种感兴趣区进行分析，主要分析的指标有斑块峰值强度、达峰时间、平均渡越时间等，在造影剂注射后的 100s 内完成对每个颈动脉粥样硬化斑块的分析，当斑块参考拟合质量及斑块拟合质量都达到 75%以上，方可判定为良好水平。

1.3 观察指标

观察 3 组增强斑块，计算造影增强率、造影增强程度分级以及对各类型斑块的时间 - 强度进行定量分析。超声造影增强分级标准[4]：斑块内未出现增强回声为Ⅰ级；斑块内出现小范围的增强回声或出现星点状回声为Ⅱ级；斑块内出现短条状及斑点状的增强回声为Ⅲ级；斑块内出现网状或条索状的增强回声为Ⅳ级。

1.4 统计学处理

应用 SPSS13.0 统计软件进行，计量资料以均值± 标准差（$\bar{x}$± s）表示，检验符合正态分布方差齐性行多个均值之间的比较应用方差分析；计数资料用百分比表示，采用卡方检验（x^2）；等级资料利用秩和检验。P 小于 0.05，统计学具有意义。

2 结果

2.1 三组超声造影增强率及造影增强程度分级比较

59 个斑块中有 40 个呈现不同程度的增强，增强率为 67.80%，软斑组、混合斑组、硬斑组超声增强率分别为 87.50%、72.22%、35.29%，差异具有统计学意义（P<0.05），其中软班组超声增强率明显高于混合斑组和硬斑组超声增强率，混合斑组超声增强率高于硬斑组超声增强率，差异均具有统计学意义（P<0.05）；造影增强程度分级Ⅰ级和Ⅲ级在三组间差异具有统计学意义（P<0.05），其中硬斑组造影增强程度Ⅰ级个数较软斑组和混合斑组多，软斑组造影增强程度Ⅲ级个数较混合斑组和硬斑组多，差异均有统计学意义（P<0.05），见表 1。

表 1 三组超声造影增强率及造影增强程度分级比较

Table 1 Comparison of the contrast enhancement rate and enhancement degree of contrast-enhanced ultrasound in three groups

Groups	Number of plaques	Number of contrast-enhanced ultrasound	Contrast enhancement rate(%)	Contrast enhancement degree			
				Grade Ⅰ (number)	Grade Ⅱ (number)	Grade Ⅲ (number)	Grade Ⅳ (number)
Soft plaque group	24	21	87.50	3	7	11	3
Mixed plaque group	18	13	72.22*	5	5	6	2
Hard plaque group	17	6	35.29*#	10	5	1	1
x^2	-	-	12.655	10.163	0.014	7.589	0.502
P	-	-	0.002	0.006	0.993	0.022	0.778

Note:Compared with the soft plaque group,*P <0.05;Compared with mixed plaque group, # P <0.05

2.2 三组时间 - 强度定量分析比较

斑块峰值强度、达峰时间、平均渡越时间在三组间差异具有统计学意义(P<0.05),其中,软斑组达峰时间、平均渡越时间均低于混合斑组和硬斑组,斑块峰值强度高于混合斑组和硬斑组,混合斑组达峰时间、平均渡越时间均低于硬斑组,斑块峰值强度高于硬斑组,差异均具有统计学意义(P<0.05),见表 2。

表 2 三组时间 - 强度定量分析比较($\bar{x}\pm s$)

Table 2 Comparison of times-quantitative intensity analysis in three groups($\bar{x}\pm s$)

Groups	Number of plaques	Plaque peak intensity(%)	Peak time(s)	Average transit time(s)
Soft plaque group	24	-88.73± 9.05	8.33± 2.57	20.34± 2.36
Mixed plaque group	18	-103.16± 8.57*	9.83± 3.75*	24.68± 3.28*
Hard plaque group	17	-117.52± 9.66*#	10.37± 4.81*#	29.67± 2.34*#
F	-	4.856	3.451	3.986
P	-	0.006	0.026	0.018

Note:Compared with the soft plaque group,*P <0.05;Compared with mixed plaque group, # P <0.05

3 讨论

颈动脉粥样硬化与冠心病的关系十分紧密,是导致缺血性脑卒中的重要诱因[5]。动脉粥样硬化斑块内往往会出现病理性的新生血管,而这些新生血管会影响到病变的发展。稳定的动脉粥样硬化斑块会因易一些并发症的产生而发展为不稳定斑块,这些并发症包括斑块破损、斑块内出血等[6,7]。颈动脉粥样硬化斑块中一旦出现血管新生,不仅会影响到斑块的稳定性,而且还会引起斑块破裂与斑块局部出血[8]。超声造影技术是在造影剂作用使回声增强,通过回声增强提高诊断分辨力和敏感性,可精确识别到 32～99 nm 直径的微血管[9,10],超声造影可以有效增强心、肝、肾等器官二维超声影像和血流多普勒信号[11-13],反映和观察正常组织和病变组织的血流灌注情况等[14],明显的提高了临床上对疾病诊断的灵敏度和准确度等,超声造影增强所表示的则是新生血管的出现[15,16]。国外学者研究指出,动脉粥样硬化斑块内新生血管的组织学密度与超声造影增强程度之间存在一定的关联性[17,18],Sun J 等[19]研究已经发现超声造影强度增强程度可能与斑块内新生血管程度具有一定相关性。

本研究结果显示:59 个斑块中观测到 40 个有回声增强现象,其中造影增强率以软斑组最高,混合斑组其次,硬斑组最小,软斑组造影增强率与其它两组形成明显差异,这种情况与软斑的性质有关,此外斑块内出血也会一定程度地刺激、滋养血管更为丰富地生成,从而促使病理性的新生血管进一步延伸扩大,因此临床上软班组更加容易生成新生血管,患者更加容易恢复。除此,本研究还对 3 种类型的斑块进行了斑块峰值强度与达峰时间等定量分析,结果显示:与硬斑组与混合斑组比较,软斑组斑块峰值强度明显增强,达峰时间明显缩短,差异有统计学意义,而这反映出软斑内的血流信号更强,说明其内的新生血管的丰富程度要明显多于硬斑与混合斑。研究已证实,颈动脉粥样硬化斑块病情的严重程度与斑块内新生血管的密度与数目有关系,随着新生血管密度的变大,患者病变的风险性也随之增大,这与 Lin L 等研究相同[20]。促使颈动脉粥样硬化斑块快速发展的两个主因包括:其一为斑块表面破裂但又愈合的血管;其二为斑块内血管新生。

综上所述:在三种类型的斑块中,软斑的新生血管最为丰富,稳定性最差,最易发生破裂,最易引起重大心、脑血管意外。评价斑块的稳定性主要可通过斑块内新生血管来反映,而超声造影技术可无创性地通过造影增强实时反映出颈动脉粥样硬化斑块内的新生血管情况,提供参数成像与定量分析,正确评价斑块的稳定性,可在临床推广应用。

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