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急性脑梗死患者颈动脉斑块内新生血管超声造影评价及其与血脂指标和超敏 C 反应蛋白水平的关系研究 *

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摘要 目的:探讨急性脑梗死患者颈动脉斑块内新生血管超声造影评价及其与血脂指标和超敏 C 反应蛋白水平的关系。**方法:**选取 2018 年 6 月到 2019 年 6 月期间我院收治的 ACI 患者 186 例,根据患者的颈动脉内中膜厚度(IMT)数值以及颈动脉斑块内新生血管超声造影情况将其分为无斑块组、稳定斑块组和易损斑块组。对比各组患者的总胆固醇(TC)、低密度脂蛋白胆固醇(LDL-C)、三酰甘油(TG)、高密度脂蛋白胆固醇(HDL-C)、美国国立卫生研究院卒中量表(NIHSS)评分、改良的 Rankin 评分(mRS)、超敏 C 反应蛋白(hs-CRP)水平。**结果:**易损斑块组和稳定斑块组患者的 TC、LDL-C、TG、hs-CRP 水平均明显高于无斑块组($P<0.05$),易损斑块组患者的 LDL-C、hs-CRP 水平均明显高于稳定斑块组($P<0.05$),易损斑块组和稳定斑块组患者的 NIHSS 评分和 mRS 评分均明显高于无斑块组($P<0.05$),易损斑块组患者的 NIHSS 评分和 mRS 评分均明显高于稳定斑块组($P<0.05$),经 Pearson 分析显示,LDL-C、hs-CRP、NIHSS 评分和 mRS 评分与斑块分级均呈正相关($P<0.05$)。**结论:**颈动脉斑块内新生血管超声造影技术可有效评估 ACI 患者的斑块稳定性,ACI 患者的斑块分级与脂代谢紊乱、机体的炎症反应以及患者病情严重程度和预后均存在一定的相关性。

关键词:急性脑梗死;颈动脉斑块;超声造影;脂代谢;炎症反应;病情;预后

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Study on the Evaluation of Neovascularization in Carotid Plaque of Patients with Acute Cerebral Infarction by Contrast-enhanced Ultrasound and Its Relationship with Blood Lipid Index and High-sensitivity C-reactive Protein Levels*

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ABSTRACT Objective: To investigate the evaluation of neovascularization in carotid plaque of patients with acute cerebral infarction by contrast-enhanced ultrasound and its relationship with blood lipid index and high-sensitivity C-reactive protein levels. **Methods:** 186 patients with ACI who were admitted to our hospital from June 2018 to June 2019 were selected. According to the value of carotid intima-media thickness (IMT) and the condition of carotid plaque neovascularization, the patients were divided into plaque free group, stable plaque group and vulnerable plaque group. The total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), triacylglycerol (TG), high density lipoprotein cholesterol (HDL-C), national Institute of Health Stroke Scale (NIHSS) and modified Rankin scale (mRS), high sensitive C-reactive protein (hs-CRP) in each group were compared. **Results:** The TC, LDL-C, TG and hs-CRP levels in vulnerable plaque group and stable plaque group were significantly higher than those in non plaque group ($P<0.05$). The LDL-C and hs-CRP levels in vulnerable plaque group were significantly higher than those in stable plaque group ($P<0.05$). The NIHSS and Mrs scores in vulnerable plaque group and stable plaque group were significantly higher than those in stable plaque group, the differences were statistically significant ($P<0.05$). The NIHSS score and Mrs score in the vulnerable plaque group were significantly higher than those in the stable plaque group ($P<0.05$). Pearson analysis showed that LDL-C, hs-CRP, NIHSS score and Mrs score were positively correlated with the plaque grade ($P<0.05$). **Conclusion:** The plaque stability of patients with ACI can be evaluated by contrast-enhanced ultrasound. The plaque classification of patients with ACI are related to the disorder of lipid metabolism, the inflammatory response of the body, the severity of the disease and the prognosis.

Key words: Acute cerebral infarction; Carotid plaque; Neovascular ultrasound; Lipid metabolism; Inflammatory response; Condition; Prognosis

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前言

据统计卒中是我国第一位死亡原因,是全球第二大死亡原因^[1],急性脑梗死(Acute cerebral infarct, ACI)又被称为急性缺血性脑卒中,是卒中最常见的类型^[2]。颈动脉斑块破裂或糜烂导致的急性血栓形成会堵塞供应脑部血流的血管,使得脑组织出现血供障碍,进而发生缺血缺氧现象,造成脑部损伤,由此可见易损斑块是引发 ACI 的重要原因^[3,4]。随着超声影像学技术的飞速发展,其在临床得到了广泛的应用,颈动脉斑块内新生血管超声造影技术可无创检测斑块内新生血管的情况,进而对斑块的稳定性进行有效评估^[5-7]。目前的研究已经证实^[8-10],大部分 ACI 患者均存在明显的脂代谢紊乱,且体内存在炎症反应,其在 ACI 患者的病情进展中均起到了重要作用。本研究采用颈动脉斑块内新生血管超声造影技术对 ACI 患者的斑块稳定性进行了评估,并进一步分析了其与患者病情严重程度、预后情况、血脂指标和超敏 C 反应蛋白(High sensitive C-reactive protein, hs-CRP)的关系,现将研究结果整理报道如下,以期为临床无创评估 ACI 患者的病情及预后提供新的切入点。

1 资料与方法

1.1 病例选取

纳入标准:(1)诊断标准参考《中国急性缺血性脑卒中诊治指南 2018》^[11];(2)年龄 30~80 岁;(3)经治疗后生存时间超过 90d;(4)患者家属知情并签署同意书。排除标准:(1)脑出血、心源性脑梗死或低灌注性脑梗死;(2)合并恶性肿瘤、严重心肺肝肾功能障碍者;(3)存在声诺维(SonoVue)使用禁忌者;(4)随访失联者;(5)合并有严重感染性疾病,可能明显影响 hs-CRP 水平;(6)正在参与其他研究者。依据上述标准选取 2018 年 6 月到 2019 年 6 月期间我院收治的 186 例 ACI 患者,此研究已获取我院伦理学委员会批准进行。

1.2 方法

1.2.1 颈动脉内中膜厚度(intima-media thickness, IMT)检测 所有患者均采用东芝 Aplio 500 超声诊断仪检查双侧颈总动脉和颈内动脉,测量患者的 IMT 数值,根据 IMT 数值判断是否存在颈动脉斑块,IMT<1.5 mm 被认为无斑块,纳入到无斑块组,IMT $\geq$ 1.5 mm 则认为有斑块,纳入到斑块组。

1.2.2 颈动脉超声造影 所有斑块组的患者均进行颈动脉超声造影检查,采用东芝 Aplio 500 超声诊断仪,9L 线阵探头,频率为 6-8MHz,低机械指数 0.13,造影剂为 SonoVue,将其与 5 mL 的生理盐水混合,轻轻震荡溶解,制成微气泡混悬液备用。快速推注造影剂后用 5 mL 的生理盐水冲洗,在检查过程中需将探头保持稳定,观察 2 min 并存储动态图像,记录斑块的位置、大小、形态及回声特征。检查结果由高年资的医师进行解读,根据文献中的方法对斑块进行分级^[12],若斑块内无增强则为 0 级,若斑块内存在稀疏点状增强则为 I 级,若斑块内存在多个点状增强或线状增强则为 II 级,若斑块内存在密集的点线状增强或片状增强则为 III 级。其中 0-I 级的患者纳入到稳定斑块组,

II-III 级的患者纳入到易损斑块组。

1.2.3 血脂指标检测 抽取所有患者入院时的静脉血 3 mL,采用全自动生化分析仪(日立,7600)检测总胆固醇(total cholesterol, TC)、低密度脂蛋白胆固醇(Low density lipoprotein cholesterol, LDL-C)、三酰甘油(triacylglycerol, TG)、高密度脂蛋白胆固醇(High density lipoprotein cholesterol, HDL-C)的水平。

1.2.4 血清 hs-CRP 检测 抽取所有患者入院时的静脉血 3 mL,以 3000 r/min 的转速离心 15 min,半径 10 cm,提取血清,采用酶联免疫吸附试验检测血清中的 hs-CRP 水平,相关检测均严格遵循对应试剂盒(南京建成生物工程研究所)的操作指南进行。

1.2.5 神经功能检测 所有患者在入院时进行神经功能检测,采用美国国立卫生研究院卒中量表(National Institute of Health stroke scale, NIHSS)评分评定神经功能,该量表总分为 45 分,得分越高代表神经功能越差,患者病情越严重^[13];在治疗 90d 后采用改良的 Rankin 评分(Modified Rankin Scale, mRS)评估患者的远期神经功能恢复情况,mRS 总分为 6 分,得分降低代表患者的远期神经功能逐渐改善^[14]。

1.3 统计学方法

采用 SPSS22.0 进行统计分析。计数资料以例数及率的形式表示,采用卡方检验,符合正态分布的计量资料以均值 $\pm$ 标准差($\bar{x} \pm s$)的形式表示,多组间比较采用单因素方差分析,两组间的比较采用 LSD-t 检验。采用 Pearson 法进行相关性分析。以 $\alpha=0.05$ 为检验标准。

2 结果

2.1 各组患者的一般资料比较

各组患者的年龄、性别比例、体质量指数、吸烟史、高血压、糖尿病、颅内动脉狭窄比例等比较差异无统计学意义($P>0.05$),数据见表 1。

2.2 各组患者的血脂指标及血清 hs-CRP 比较

各组的 HDL-C 水平整体比较差异无统计学意义($P>0.05$),各组患者的 TC、LDL-C、TG、hs-CRP 水平整体比较差异均有统计学意义($P<0.05$),易损斑块组和稳定斑块组患者的 TC、LDL-C、TG、hs-CRP 水平均明显高于无斑块组,差异均有统计学意义($P<0.05$),易损斑块组患者的 LDL-C、hs-CRP 水平均明显高于稳定斑块组($P<0.05$),数据见表 2。

2.3 各组患者的 NIHSS 评分和 mRS 评分比较

各组患者的 NIHSS 评分和 mRS 评分整体比较差异均有统计学意义($P<0.05$),易损斑块组和稳定斑块组患者的 NIHSS 评分和 mRS 评分均明显高于无斑块组($P<0.05$),易损斑块组患者的 NIHSS 评分和 mRS 评分均明显高于稳定斑块组($P<0.05$),数据见表 3。

2.4 血脂指标、血清 hs-CRP、NIHSS 评分以及 mRS 评分与斑块分级的相关性

经 Pearson 相关分析显示,LDL-C、hs-CRP、NIHSS 评分和 mRS 评分与斑块分级均呈正相关($P<0.05$),而 TC、HDL-C、TG

则与斑块分级无明显的相关性($P>0.05$),数据见表4。

表1 各组患者的一般资料比较

Table 1 Comparison of general data of patients in each group

Groups	n	Age(year)	Male/female	Body mass index(kg/m ²)	Smoking history [n(%)]	Hypertension [n(%)]	Diabetes [n(%)]	Intracranial artery stenosis [n(%)]
Plaque free group	33	58.36±8.92	18/15	22.15±1.59	15(45.45)	24(72.73)	11(33.33)	5(15.15)
Stable plaque group	54	59.63±10.26	34/20	22.58±2.46	27(50.00)	38(70.37)	22(40.74)	12(22.22)
Vulnerable plaque group	99	60.15±11.38	56/43	22.24±2.18	52(52.53)	71(71.72)	45(45.45)	30(30.30)
F/ χ^2		0.349	0.791	0.552	0.504	0.061	1.538	3.383
P		0.706	0.673	0.577	0.777	0.970	0.463	0.184

表2 各组患者的血脂指标及血清 hs-CRP 比较($\bar{x}\pm s$)Table 2 Comparison of blood lipid index and serum hs CRP in each group($\bar{x}\pm s$)

Groups	n	TC(mmol/L)	LDL-C(mmol/L)	TG(mmol/L)	hs-CRP(mg/L)	HDL-C(mmol/L)
Plaque free group	33	4.72±0.92	3.89±0.58	1.45±0.49	7.18±2.46	1.25±0.35
Stable plaque group	54	5.49±1.06 ^a	4.45±0.61 ^a	2.08±0.54 ^a	8.94±3.14 ^a	1.21±0.42
Vulnerable plaque group	99	5.68±1.13 ^a	4.87±0.52 ^{ab}	2.14±0.67 ^a	10.26±2.87 ^{ab}	1.18±0.53
F		9.897	40.051	16.722	14.798	0.568
P		0.000	0.000	0.00	0.000	0.842

Note: compared with non plaque group, ^a $P<0.05$; compared with stable plaque group, ^b $P<0.05$.

表3 各组患者的 NIHSS 评分和 mRS 评分比较($\bar{x}\pm s$)Table 3 Comparison of NIHSS score and Mrs score in each group($\bar{x}\pm s$)

Groups	n	NIHSS(score)	mRS(score)
Plaque free group	33	5.62±1.48	0.68±0.42
Stable plaque group	54	7.34±2.13 ^a	1.03±0.51 ^a
Vulnerable plaque group	99	9.56±3.65 ^{ab}	1.35±0.57 ^{ab}
F		25.062	21.419
P		0.000	0.000

Note: compared with non plaque group, ^a $P<0.05$; compared with stable plaque group, ^b $P<0.05$.

表4 血脂指标、血清 hs-CRP、NIHSS 评分和 mRS 评分与斑块分级的相关性

Table 4 Correlation of blood lipid index, serum hs CRP, NIHSS score and Mrs score with plaque grade

Index	Plaque grading	
	r	P
TC	0.268	0.064
LDL-C	0.423	0.000
TG	0.215	0.076
hs-CRP	0.517	0.000
NIHSS	0.398	0.000
mRS	0.327	0.005
HDL-C	0.126	0.125

3 讨论

ACI 起病急、病情进展快,患者主要表现为口角歪斜、言语

障碍,严重时可导致神经功能明显受损,具有极高的致死率和致残率^[15,16]。据统计^[17],我国近年来 ACI 的患病率一直居高不下,且该病多发于中老年人群,随着近年来我国老龄化社会的

到来,其患病率将进一步上升,因此合理地防治 ACI 已成为医务工作者的重点工作内容。急性血栓形成是引起 ACI 的重要原因,而颈动脉粥样硬化和斑块的形成是血栓形成的病理基础,易损斑块的破裂或糜烂是引发急性血栓的重要因素^[18,19]。在斑块的形成及破裂的过程中,多种因素均起到了重要作用,如脂代谢紊乱、炎症反应、斑块内新生血管形成等,在这些因素的共同作用下促进了斑块的形成,并使其从稳定斑块发展为易损斑块,促使斑块破裂形成血栓^[20-22]。

TC、LDL-C、TG、HDL-C 均是临床常用的脂代谢指标,其中 TC 是指血液中所有脂蛋白所含胆固醇之总和^[23];TG 是长链脂肪酸和甘油形成的脂肪分子,是人体内含量最多的脂类^[24];LDL-C 是一种脂蛋白胆固醇,其极易被氧化,在被氧化后可形成氧化型低密度脂蛋白 (oxidized low density lipoprotein, ox-LDL),HDL-C 主要在肝脏合成,是一种抗动脉粥样硬化的脂蛋白^[25]。hs-CRP 在机体发生炎症反应时其水平可迅速升高,是敏感的炎症反应标志物^[26]。本研究结果显示,易损斑块组和稳定斑块组患者的 TC、LDL-C、TG、hs-CRP 水平均明显高于无斑块组,提示存在斑块的 ACI 存在明显的脂代谢紊乱和炎症反应,二者可能在斑块的形成与发展中起到了重要的作用。而进一步的比较发现,易损斑块组患者的 LDL-C、hs-CRP 水平均明显高于稳定斑块组,提示 LDL-C、hs-CRP 的表达水平可能与斑块的易损性有关,这主要是因为 LDL-C 被氧化后可形成 ox-LDL,而 ox-LDL 可诱导巨噬细胞凋亡形成泡沫细胞,并可促进斑块表面组织溶解,且还可有效促进机体的炎症反应^[27];而 hs-CRP 水平越高则代表机体的炎症反应程度越高,大量炎症因子可促进基质金属蛋白生成,促进斑块的纤维帽降解,进而增加斑块的易损性^[28]。NIHSS 评分和 mRS 评分均是临床评估 ACI 神经功能的常用量表,其中 NIHSS 评分多用于近期疗效和病情严重程度的评估,而 mRS 评分多用于远期疗效的评估^[29]。本研究结果显示,易损斑块组和稳定斑块组患者的 NIHSS 评分和 mRS 评分均明显高于无斑块组,且易损斑块组患者的 NIHSS 评分和 mRS 评分均明显高于稳定斑块组,提示斑块的存在可加重患者的病情,并影响患者的预后。进一步的研究发现,LDL-C、hs-CRP、NIHSS 评分和 mRS 评分与斑块分级均呈正相关,这说明斑块分级与患者的脂代谢紊乱、机体的炎症反应存在一定的相关性,采用颈动脉斑块内新生血管超声造影技术可有效对 ACI 患者的斑块稳定性进行评估,进而有效预测患者的病情和预后,具有一定的临床应用价值^[30]。

综上所述,采用颈动脉斑块内新生血管超声造影技术能有效评估 ACI 患者的斑块稳定性,并可对其进行有效分级,患者的斑块分级与患者的脂代谢紊乱、机体的炎症反应以及患者的病情严重程度和预后均存在一定的相关性。因此在临床诊治 ACI 患者时,可通过颈动脉斑块内新生血管超声造影技术有效筛查易损斑块,对预后不良的高危人群进行重点及针对性的监测,以更好地改善患者的预后。

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