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颈动脉斑块易损性与血脂指标、炎症因子和冠心病的关系 *

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摘要 目的:探讨颈动脉斑块易损性与血脂指标、炎症因子和冠心病的关系。**方法:**选择 2016 年 1 月-2018 年 1 月在我院进行治疗的颈动脉斑块患者 95 例为研究对象,所有患者均进行颈动脉超声检查,根据超声检查结果的斑块性质将患者分为稳定组(n=43)和易损组(n=52)。检测两组患者的总胆固醇(TC)、甘油三酯(TG)、高密度脂蛋白胆固醇(HDL-C)、低密度脂蛋白胆固醇(LDL-C)等血脂指标,对比两组患者的血清白介素-8(IL-8)、超敏 C 反应蛋白(hs-CRP)、细胞黏附因子-1(ICAM-1)、趋化因子(RANTES)水平,统计两组患者的冠心病发生率。**结果:**易损组患者的 TC、TG、LDL-C 均高于稳定组,HDL-C 低于稳定组,组间比较差异有统计学意义(P<0.05)。易损组患者的 IL-8、hs-CRP、ICAM-1、RANTES 水平均高于稳定组,组间比较差异有统计学意义(P<0.05)。稳定组冠心病发生率为 53.49%(23/43),易损组冠心病发生率为 78.85%(41/52),两组冠心病发生率比较差异有统计学意义(P<0.05)。**结论:**颈动脉斑块易损性可导致患者的血脂指标、血清炎症因子指标进一步恶化,也会增加患者出现冠心病的发生机率。

关键词:颈动脉斑块;易损性;血脂指标;炎症因子;冠心病;关系

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Relationship between Carotid Plaque Vulnerability and Blood Lipids, Inflammatory Factors and Coronary Heart Disease*

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ABSTRACT Objective: To study the relationship between carotid plaque vulnerability and blood lipids, inflammatory factors and coronary heart disease. **Methods:** 95 patients with carotid artery plaque who were treated in our hospital from January 2018 to January 2016 were selected as the subjects. All the patients were examined by carotid ultrasound, and the patients were divided into stable group (n=43) and unstable group (n=52) according to the plaque character of ultrasonic examination results. Blood lipid indexes such as total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C) in two groups were detected. The serum levels of interleukin-8 (IL-8), hypersensitive C reactive protein (hs-CRP), cell adhesion factor-1 (ICAM-1) and chemokine (RANTES) were compared in the two groups, and the incidence of coronary heart disease in the two groups was statistically analyzed. **Results:** The TC, TG and LDL-C of the patients in the unstable group were higher than those in the stable group, while HDL-C was lower than that in the stable group, and the differences between the two groups were statistically significant (P<0.05). The levels of IL-8, hs-CRP, ICAM-1 and RANTES in the unstable group were all higher than those in the stable group, and the difference between the two groups was statistically significant (P<0.05). The incidence of coronary heart disease in the stable group was 53.49% (23/43), and the incidence of coronary heart disease in the vulnerable group was 78.85% (41/52), there was a significant difference in the incidence of coronary heart disease in the two groups (P<0.05). **Conclusion:** The vulnerability of carotid plaque can lead to further deterioration of blood lipid index and serum inflammatory factor index, and also increase the incidence of coronary heart disease.

Key words: Carotid plaques; Vulnerability; Blood lipid index; Inflammatory factor; Coronary heart disease; Relationship

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前言

颈动脉斑块是颈动脉粥样硬化的主要表现,主要是在患者颈动脉粥样硬化的基础上病变加剧而形成的,该病好发于颈总动脉分叉处。研究表明颈动脉粥样硬化斑块与老年缺血性脑卒

中、冠心病等发病有紧密关联^[1-3]。在患者的颈动脉斑块中,根据超声影像不同可分为稳定型斑块和易损型斑块,其中易损斑块因斑块在血液中的稳定性较差,容易出现斑块中栓子的脱落、破裂,导致患者出现急性脑梗死、脑栓塞、心肌梗死、冠心病等重型疾病,对患者的生命健康和生活质量造成严重威胁^[4-6]。因

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此,采取积极有效的诊治手段对冠心病患者具有重要意义,使患者能够尽早确诊并展开相应的治疗,减少临床恶性心血管事件的发生。常规的冠心病诊断方法为冠状动脉造影或者CT血管造影,虽然准确度较高,但是存在一定的有创性,且操作复杂费时^[7,8]。为此,寻找一种新型的辅助诊疗方法对于冠心病患者的诊断、病情评估、预后效果判断均有着较好的疗效。本研究旨在探讨颈动脉斑块类型与患者血脂指标、炎症因子水平与冠心病的关系,现报道如下。

1 资料与方法

1.1 临床资料

选择2016年1月-2018年1月在我院进行治疗的颈动脉

斑块患者95例为研究对象,其中男性患者49例、女性患者46例,患者年龄46-78岁,平均(58.76±10.27)岁。纳入标准^[9]:①所有患者经彩色多普勒超声检查确诊为颈动脉斑块;②患者入院前2周内未服用降血脂、免疫抑制剂等相关治疗药物;③患者均进行冠状动脉血管造影以检查冠心病的发病情况;④患者签署知情同意书。排除标准:①并发其他心血管恶性疾病者;②全身恶性肿瘤疾病者;③原发性、继发性高脂血症者;④影像资料不全者。将上述患者按颈动脉斑块超声结果的斑块性质分为稳定组(n=43)和易损组(n=52)。两组患者的一般资料比较差异无统计学意义(P>0.05),见表1,提示组间具有可比性。本研究方案经我院伦理学委员会批准。

表1 两组患者一般资料比较

Table 1 Comparison of general data in two groups

Groups	n	Gender		Age (years)	Body mass index (kg/m ²)	Complication	
		Male	Female			Hypertension	Hyperglycemia
Stable group	43	20	23	59.13±11.45	22.09±1.98	12	11
Unstable group	52	29	23	57.56±11.47	23.68±2.02	15	17
t/x ²	-	0.808		0.665	0.872	0.150	
P	-	0.369		0.508	0.452	0.698	

1.2 超声检查

所有患者均采用ACUSON SC2000型彩色多普勒超声诊断仪(德国西门子公司)进行颈动脉超声检查,超声探头频率8-12 MHz,患者取仰卧位,颈部放松,从锁骨上端颈总动脉起始处开始进行横切面、纵切面两个方向的超声探查,对颈总动脉的近端、中端和分叉处以及双颈外动脉处进行检查,超声影像显示内中膜厚度≥1.5 mm并向管腔内突起即可判断为颈动脉斑块。易损性斑块的判断标准为^[10]:超声显示为不规则型低回声信号,斑块内有血流信号出现即为易损性斑块。

1.3 评价方法

所有患者在入院后次日清晨采集空腹静脉血5 mL,加入到抗凝管中,采用TGL-16型高速离心机(上海安亭科学仪器厂)以5000 rpm进行离心10 min后,分离得到血清。采用ES-200型全自动生化分析仪(南京颐兰贝生物科技有限责任公司)以过氧化酶法检测患者的血脂指标,包括:总胆固醇(Total cholesterol, TC)、甘油三酯(Triglyceride, TG)、高密度脂蛋白胆固醇(high density lipoprotein cholesterol, HDL-C)、低密度脂蛋白胆固醇(low density lipoprotein cholesterol, LDL-C),并进行

组间对比。采用酶联免疫吸附试验(Enzyme-linked immunosorbent assay, ELISA)检测血清中白介素-8(Interleukin-8, IL-8)、超敏C反应蛋白(Hypersensitive C reactive protein, hs-CRP)、细胞黏附因子-1(Cell adhesion factor-1, ICAM-1)、趋化因子(RANTES)的水平,SpectraMax i3x多功能酶标仪购自美国Molecular Devices公司,相关检测试剂盒购置于南京金斯瑞生物科技有限公司。对两组患者进行冠状动脉血管造影,统计两组患者冠心病的发病率,冠心病发病的判断标准为:冠状动脉造影狭窄≥50%。

1.4 统计学方法

采用专业统计学软件SPSS 20.0进行数据处理与分析,计量资料以($\bar{x} \pm s$)表示,组间比较实施t检验,计数资料以[n(%)]表示,组间比较实施 χ^2 检验,当P<0.05时表示差异有统计学意义。

2 结果

2.1 两组患者血脂指标比较

易损组患者的TC、TG、LDL-C均高于稳定组,HDL-C低于稳定组,组间比较差异有统计学意义(P<0.05),见表2。

表2 两组患者血脂指标比较($\bar{x} \pm s$)

Table 2 Comparison of blood lipid indexes in two groups($\bar{x} \pm s$)

Groups	n	TC (mmol/L)	TG (mmol/L)	LDL-C (mmol/L)	HDL-C (mmol/L)
Stable group	43	3.46±1.09	2.01±0.67	2.12±0.68	1.39±0.42
Unstable group	52	4.42±1.24	2.54±0.78	2.67±0.82	1.05±0.33
t	-	3.965	3.113	3.511	4.418
P	-	0.000	0.002	0.001	0.000

2.2 两组患者血清炎症因子指标比较

于稳定组,组间比较差异有统计学意义($P<0.05$),见表3。

易损组患者的 IL-8、hs-CRP、ICAM-1、RANTES 水平均高

表3 两组患者血清炎症因子指标比较($\bar{x} \pm s$)

Table 3 Comparison of serum inflammatory factors in two groups of patients($\bar{x} \pm s$)

Groups	n	IL-8(ng/L)	hs-CRP(mg/L)	ICAM-1(mg/L)	RANTES(ng/L)
Stable group	43	198.28± 21.12	4.14± 1.07	1.02± 0.42	2.97± 0.61
Unstable group	52	287.18± 31.56	7.51± 1.78	2.01± 0.67	5.61± 0.97
t	-	15.773	10.889	8.414	15.486
P	-	0.000	0.000	0.001	0.000

2.3 两组患者冠心病发生率比较

稳定组确诊为冠心病患者 23 例,冠心病发生率为 53.49%,易损组确诊为冠心病患者 41 例,冠心病发生率为 78.85%,两组冠心病发生率比较差异有统计学意义($\chi^2=6.885$, $P=0.000$)。

3 讨论

随着人们生活条件的改善以及各种不规律的饮食和生活方式的出现,颈动脉斑块在临床上的发生率逐渐增多,是临床引起各类不良事件的主要诱因。尤其随着颈动脉斑块病情的进展,冠心病、心肌梗塞等严重心血管事件的发生率逐渐增加^[11,12]。在数多的临床报道中显示^[13-15],患者颈动脉斑块症状越严重,其出现破裂斑块、易损斑块的概率就越大,导致形成血栓的机率也越大,从而造成患者的心血管的管腔出现狭窄或闭塞,上述结果均是诱发心脑血管疾病的主要原因。因此,对于颈动脉斑块患者的易损斑块的检测及严重程度判断将有助于预防患者的心血管不良事件的发生率。在实际临床中,颈动脉斑块多处于浅表,通过对颈动脉斑块易损性程度的检测判断,引入血脂指标、炎症因子指标作为颈动脉斑块与冠心病间的衔接指标,以期进一步探讨颈动脉斑块易损性与冠心病的预防及发生发展间的关联性^[16-18]。

本研究结果显示,易损组患者的 TC、TG、LDL-C 均高于稳定组,HDL-C 低于稳定组,这是因为易损型颈动脉斑块中脂质类物质及成分比例较高,易损斑块中见单核-巨噬细胞、T 淋巴细胞、肥大细胞浸润,这些细胞可直接或间接作用于斑块中的其他细胞间质成分,使斑块发生形态改变而易于破裂。hs-CRP 是目前发现的最重要的颈动脉斑块的炎性标记物,是由肝脏在白介素-1 (Interleukin-1, IL-1)、白介素-6 (Interleukin-6, IL-6) 的刺激下产生的^[19,20]。IL-8 系单核巨噬细胞合成产物,可以提高中性粒细胞的活动度,诱发其出现移位等情况,并可对其凋亡发挥抑制作用^[21]。ICAM-1 为黏附分子当中的免疫球蛋白之一,广泛分布于内皮细胞与白细胞中,在正常人群中低表达^[22]。趋化因子 RANTES 属于结构与功能类似的多肽类物质,主要由白细胞合成,平滑肌细胞与血管内组织细胞也可见其分泌与合成,可于白细胞朝向炎症病灶的活化趋化过程中发挥驱动作用,并且可促进内皮细胞与平滑肌细胞的异常增生及迁移^[23,24]。在本次研究中,易损组患者的 IL-8、hs-CRP、ICAM-1、RANTES 水平均高于稳定组,且易损组冠心病发生率

高于稳定组,说明上述各炎症因子指标也可作用冠状动脉粥样硬化疾病的炎性标记物和疾病预测因子,并且炎症因子的共同作用加快了单核巨噬细胞、内皮细胞的异常增殖并向斑块病灶处汇集黏附,使斑块内部及机体处于炎性反应状态中,从而增加了斑块易损的风险性^[25,26]。再者,易损组患者血液中的纤维成分水平、平滑肌细胞比例均较低,相应的斑块质地较软使得斑块在动脉血流的作用下出现破裂糜烂的机率增加,继而引发血栓栓塞、心肌梗死等不良心血管疾病,使得患者的冠心病发生率增加^[27]。而稳定组患者由于颈动脉斑块处于相对稳定状态,其斑块中的纤维、胶质等成分的比例相对较高,并且在斑块形成的过程中还可出现纤维成分与胶质成分的比例升高,有些患者甚至出现钙化反应,造成斑块对于动脉血管壁的附着力进一步增强,斑块质地较硬且固定较为牢固,不易脱落或破损,因而稳定组患者引发的冠心病、脑梗死的发病率大为降低^[28-30]。

综上所述,颈动脉斑块易损性患者的血脂指标、血清炎症因子水平升高,且出现冠心病的机率也增加,这也为预测颈动脉斑块的发展及冠心病的发展提供新思路。

参考文献(References)

- [1] Thorsson B, Eiriksdottir G, Sigurdsson S, et al. Population distribution of traditional and the emerging cardiovascular risk factors carotid plaque and IMT: the REFIN-REYKJAVIK study with comparison with the Tromsø study[J]. BMJ Open, 2018, 8(5): e019385
- [2] de Haro J, Rodriguez-Padilla J, Bleda S, et al. Carotid stenting with proximal cerebral protection in symptomatic low-grade vulnerable recurrent carotid stenosis[J]. Ther Adv Chronic Dis, 2018, 9(6): 125-133
- [3] Hou Q, Li S, Gao Y, et al. Relations of lipid parameters, other variables with carotid intima-media thickness and plaque in the general Chinese adults: an observational study[J]. Lipids Health Dis, 2018, 17(1): 107
- [4] 孙翀, 顾敦星. CT 血管造影评价颈动脉易损性斑块与症状性缺血性卒中关系的价值 [J]. 现代中西医结合杂志, 2017, 26(3): 328-330, 342
- [5] Nakahara T, Narula J, Strauss HW. Molecular Imaging of Vulnerable Plaque[J]. Semin Nucl Med, 2018, 48(3): 291-298
- [6] Jin H, Li DY, Chernogubova E, et al. Local Delivery of miR-21 Stabilizes Fibrous Caps in Vulnerable Atherosclerotic Lesions [J]. Mol Ther, 2018, 26(4): 1040-1055
- [7] Liu W, Ming Q, Shen J, et al. Trimetazidine Prevention of Contrast-Induced Nephropathy in Coronary Angiography[J]. Am J Med Sci, 2015, 350(5): 398-402

- [8] Roifman I, Rezai MR, Wijesundera HC, et al. Utilization of cardiac computed tomography angiography and outpatient invasive coronary angiography in Ontario, Canada [J]. *J Cardiovasc Comput Tomogr*, 2015, 9(6): 567-571
- [9] 宋爱霞,纪蓉,刘俊峰,等.脑梗死患者血清生物标志物水平与颈动脉斑块的相关性研究[J].*中国临床药理学杂志*, 2016, 32(3): 195-197, 201
- [10] 栗静,石正洪.颈动脉易损性斑块的研究进展[J].*中风与神经疾病杂志*, 2017, 34(1): 88-91
- [11] Badacz R, Przewłocki T, Gacoń J, et al. Circulating miRNA levels differ with respect to carotid plaque characteristics and symptom occurrence in patients with carotid artery stenosis and provide information on future cardiovascular events [J]. *Postępy Kardiologii Interwencyjnej*, 2018, 14(1): 75-84
- [12] Yi X, Lin J, Luo H, et al. Interactions among variants in TXA2R, P2Y12 and GPIIa are associated with carotid plaque vulnerability in Chinese population[J]. *Oncotarget*, 2018, 9(25): 17597-17607
- [13] 茆丽娜,门琛,贾坚,等.脂蛋白相关磷脂酶 A2 对急性前循环脑梗死患者颈动脉斑块易损性的预测价值[J].*现代生物医学进展*, 2017, 17(36): 7132-7136
- [14] Petroglou D, Didagelos M, Chalikias G, et al. Manual Versus Mechanical Compression of the Radial Artery After Transradial Coronary Angiography: The MEMORY Multicenter Randomized Trial[J]. *JACC Cardiovasc Interv*, 2018, 11(11): 1050-1058
- [15] Glisic M, Franco OH, Muka T. Response by Glisic et al to Letter Regarding Article, "Associations of Endogenous Estradiol and Testosterone Levels With Plaque Composition and Risk of Stroke in Subjects With Carotid Atherosclerosis"[J]. *Circ Res*, 2018, 122(8): e69-e70
- [16] Scarabin-Carré V, Scarabin PY. Letter by Scarabin-Carré and Scarabin Regarding Article, "Associations of Endogenous Estradiol and Testosterone Levels With Plaque Composition and Risk of Stroke in Subjects With Carotid Atherosclerosis" [J]. *Circ Res*, 2018, 122(8): e67-e68
- [17] Chen J, Zhang YM, Song ZZ, et al. The inter-observer agreement in the assessment of carotid plaque neovascularization by contrast-enhanced ultrasonography: The impact of plaque thickness [J]. *J Clin Ultrasound*, 2018, 46(6): 403-407
- [18] Alonso N, Traveset A, Rubinat E, et al. Correction to: Type 2 diabetes-associated carotid plaque burden is increased in patients with retinopathy compared to those without retinopathy[J]. *Cardiovasc Diabetol*, 2018, 17(1): 49
- [19] 薛国华,马惠芳,张守彦,等.非 ST 段抬高型急性冠脉综合征患者血清 Hcy,hs-CRP 与冠状动脉斑块易损性的关系[J].*实用医学杂志*, 2016, 32(19): 3241-3244
- [20] Machino-Ohtsuka T, Seo Y, Ishizu T, et al. Combined assessment of carotid vulnerable plaque, renal insufficiency, eosinophilia, and hs-CRP for predicting risky aortic plaque of cholesterol crystal embolism[J]. *Circ J*, 2010, 74(1): 51-58
- [21] Marino F, Tozzi M, Schembri L, et al. Production of IL-8, VEGF and Elastase by Circulating and Intraplaque Neutrophils in Patients with Carotid Atherosclerosis[J]. *PLoS One*, 2015, 10(4): e0124565
- [22] Palenkić H, Bačun T, Čosić A, et al. Serum levels of ICAM-1, VCAM-1 and E-selectin in early postoperative period and three months after eversion carotid endarterectomy [J]. *Med Glas (Zenica)*, 2014, 11(2): 313-319
- [23] 刘延东.急性冠脉综合征患者血清趋化因子 RANTES 含量检测及其与炎症反应、心肌损伤程度的关系[J].*海南医学院学报*, 2015, 21(11): 1477-1479, 1482
- [24] Gross MD, Bielinski SJ, Suarez-Lopez JR, et al. Circulating soluble intercellular adhesion molecule 1 and subclinical atherosclerosis: the Coronary Artery Risk Development in Young Adults Study [J]. *Clin Chem*, 2012, 58(2): 411-420
- [25] Im CH, Kim NR, Kang JW, et al. Inflammatory burden interacts with conventional cardiovascular risk factors for carotid plaque formation in rheumatoid arthritis [J]. *Rheumatology (Oxford)*, 2015, 54(5): 808-815
- [26] 周亮亮,宫剑滨,李德润,等.心外膜脂肪定量及其炎症状态与冠状动脉粥样硬化斑块易损性的关系[J].*中华心血管病杂志*, 2015, 43(2): 134-140
- [27] Akkuş O, Topuz M, Koca H, et al. The relationship between low thiol levels and major adverse cardiovascular events after primary percutaneous coronary intervention in patients with STEMI[J]. *Türk Kardiyol Dern Ars*, 2018, 46(4): 248-259
- [28] Goldstein JA. Coronary CT Angiography: Identification of Patients and Plaques "At Risk"[J]. *J Am Coll Cardiol*, 2018, 71(22): 2523-2526
- [29] Chang HJ, Lin FY, Lee SE, et al. Coronary Atherosclerotic Precursors of Acute Coronary Syndromes [J]. *J Am Coll Cardiol*, 2018, 71(22): 2511-2522
- [30] 曹衡玉.超声探讨颈动脉斑块易损性与脑血管意外的关系[J].*中南医学科学杂志*, 2016, 44(1): 64-66, 70