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论著·临床

颈动脉狭窄及血清同型半胱氨酸、高敏 C 反应蛋白表达对中年脑梗死的评估价值

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【摘要】 目的 探讨颈动脉狭窄及血清同型半胱氨酸(Hcy)、高敏 C 反应蛋白(hs-CRP) 表达对中年脑梗死的评估价值。方法 选取 2019 年 5 月—2022 年 12 月四川大学华西广安医院/广安市人民医院神经内科收治中年脑梗死患者 98 例为脑梗死组, 依据美国国立卫生研究院卒中量表(NIHSS) 评分分为轻度亚组 30 例、中度亚组 40 例、重度亚组 28 例; 另选取同期非脑梗死患者 80 例为非脑梗死组。所有患者均行颈动脉数字减影血管造影(DSA) 检查, 并检测患者血清 Hcy、hs-CRP 水平, 比较所有受试者颈动脉血管狭窄情况及血清 Hcy、hs-CRP 水平, Pearson 法分析各项指标与脑梗死发生的相关性, 受试者工作特征曲线分析血清 Hcy、hs-CRP 对中年脑梗死的预测价值。结果 非脑梗死组颈动脉狭窄 12 例(15.00%), 低于脑梗死组 85 例(86.73%), 差异有统计学意义($\chi^2/P=91.398/<0.001$); 脑梗死组血清 Hcy、hs-CRP 水平高于非脑梗死组($t/P=44.901/<0.001, 44.365/<0.001$); 病情轻、中、重度患者的动脉狭窄程度比较差异均有统计学意义($\chi^2/P=77.729/<0.001$), 血清 Hcy、hs-CRP 水平重度亚组>中度亚组>轻度亚组($F/P=10.586/<0.001, 25.051/<0.001$); 动脉狭窄程度及血清 Hcy、hs-CRP 与脑梗死严重程度均呈正相关($r=0.421, 0.365, 0.452, P$ 均<0.001); 血清 Hcy、hs-CRP 及两者联合预测中年脑梗死的曲线下面积(AUC) 分别为 0.859、0.791、0.863, 两者联合检测 AUC 高于单一检测者($Z/P=2.251/0.005, 3.452/0.012$)。结论 DSA 检测颈动脉狭窄结合血清 Hcy、hs-CRP 检测有助于评估脑梗死发生风险, 为临床防治提供指导。

【关键词】 脑梗死; 数字减影血管造影; 同型半胱氨酸; 高敏 C 反应蛋白; 中年人**【中图分类号】** R743.33**【文献标识码】** A

The evaluation value of carotid artery stenosis and serum homocysteine and high sensitivity C-reactive protein expression in middle-aged patients with cerebral infarction Wang Mingyue, Wu Xiaoshan, Liu Maochun, Wang Yi. Department of Neurology, West China Guang'an Hospital of Sichuan University/Guang'an People's Hospital, Sichuan Province, Guang'an 638000, China

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【Abstract】 Objective To investigate the evaluation value of carotid artery stenosis and serum homocysteine (Hcy) and high sensitivity C-reactive protein (hs-CRP) expression in middle-aged cerebral infarction. **Methods** Ninety-eight middle-aged patients with cerebral infarction admitted to the Neurology Department of West China Guang'an Hospital/Guang'an People's Hospital of Sichuan University from May 2019 to December 2022 were selected as the cerebral infarction group. According to the National Institutes of Health Stroke Scale (NIHSS) score, they were divided into mild subgroup of 30 cases, moderate subgroup of 40 cases, and severe subgroup of 28 cases; Another 80 non cerebral infarction patients in the same period were selected as the non-cerebral infarction group. All patients underwent carotid artery digital subtraction angiography (DSA) examination, and serum Hcy and hs-CRP levels were measured. The carotid artery stenosis status and serum Hcy and hs-CRP levels were compared among all subjects. Pearson's method was used to analyze the correlation between various indicators and the occurrence of cerebral infarction. The predictive value of serum Hcy and hs-CRP for middle-aged cerebral infarction was analyzed using the subject's work characteristic curve. **Results** 12 cases (15.00%) of carotid artery stenosis in the non-cerebral infarction group were lower than 85 cases (86.73%) in the cerebral infarction group ($\chi^2/P=91.398/<0.001$).

The serum Hcy and hs-CRP levels in the cerebral infarction group were higher than those in the non-cerebral infarction group ($t/P = 44.901 / <0.001, 44.365 / <0.001$). There is a statistically significant difference in the degree of arterial stenosis among patients with mild, moderate, and severe conditions ($\chi^2/P = 77.729 / <0.001$), with serum Hcy and hs-CRP levels in the severe subgroup > moderate subgroup > mild subgroup ($F/P = 10.586 / <0.001, 25.051 / <0.001$). The degree of arterial stenosis, serum Hcy, and hs-CRP were positively correlated with the severity of cerebral infarction ($r = 0.421, 0.365, 0.452, P < 0.001$). The area under the curve (AUC) of serum Hcy, hs-CRP, and their combination in predicting middle-aged cerebral infarction were 0.859, 0.791, and 0.863, respectively. The combined detection of AUC was higher than that of single detection ($Z/P = 2.251 / 0.005, 3.452 / 0.012$). **Conclusion** DSA detection of carotid artery stenosis combined with serum Hcy and hs-CRP detection can help evaluate the risk of cerebral infarction and provide guidance for clinical prevention and treatment.

【Key words】 Cerebral infarction; Digital subtraction angiography; Homocysteine; Hypersensitive C-reactive protein; Middle-aged

脑梗死是指多种原因导致的脑部循环功能障碍,致使局部脑组织发生缺氧、缺血性坏死,是脑血管疾病中常见的一种^[1]。该病具有较高的发病率及致残率,已成为中年人群常发疾病。在预防脑梗死发生的过程中应明确脑供血动脉情况,到目前为止,颈部血管超声、数字减影血管造影(digital subtraction angiography, DSA)等血管检查方法可以有效评价脑梗死的供血动脉^[2-3]。研究指出,DSA能准确把握颈部及颅内动脉狭窄情况^[4]。动脉粥样硬化(AS)缺血性脑卒中的原因之一,文献资料显示,同型半胱氨酸(homocysteine, Hcy)与AS发生显著相关;当患者出现炎症反应时,高敏C反应蛋白(hypersensitive C-reactive protein, hs-CRP)水平明显升高,并且直接参与AS形成过程^[5-6]。关于DSA检查结合血清指标分析脑梗死的发生并不多见,现分析颈动脉DSA检测联合血清Hcy、hs-CRP与中年脑梗死发生的关系,报道如下。

1 资料与方法

1.1 临床资料 选取2019年5月—2022年12月四川大学华西广安医院/广安市人民医院神经内科收治中年脑梗死患者98例为脑梗死组;另选取同期非脑梗死患者80例为非脑梗死组。2组基线资料比较差异无统计学意义($P > 0.05$),具有可比性,见表1。本研究已经获得医院伦理委员会批准(2019年审014号),患者或家属知情同意并签署知情同意书。

1.2 病例选择标准 (1) 纳入标准: ①脑梗死患者均符合相关指南中的诊断标准^[7],且经MR或CT确定存在病灶; ②无脑卒中病史,且未接受过其他治疗; ③均为中年人,年龄45~59岁。(2) 排除标准: ①合并肝肾功能不全、恶性肿瘤、免疫系统疾病等; ②患有其他脑部病变,如颅内肿瘤等; ③精神异常者。

1.3 观测指标与方法

1.3.1 颈动脉狭窄程度检查: 患者取平卧位,完善术前准备后,借助Sledinger方法,对患者进行股动脉

表1 非脑梗死组与脑梗死组基线资料比较

Tab. 1 Comparison of baseline data between non cerebral infarction group and cerebral infarction group

项目	非脑梗死组 (n=80)	脑梗死组 (n=98)	χ^2/t 值	P值
性别(男/女)	48/32	56/42	0.148	0.700
年龄($\bar{x} \pm s$, 岁)	51.31 ± 5.18	51.26 ± 5.24	0.063	0.951
体质指数($\bar{x} \pm s$, kg/m ²)	22.47 ± 2.29	22.35 ± 2.36	0.342	0.733
高血压史[例(%)]	18(22.50)	23(23.47)	0.023	0.879
糖尿病史[例(%)]	22(27.50)	27(27.55)	0.195	0.658
吸烟史[例(%)]	20(25.00)	25(25.51)	0.006	0.938
饮酒史[例(%)]	36(45.00)	42(42.86)	0.082	0.774

穿刺: 置入5F导管鞘,借助导丝引导送至5F猪尾巴管,选择飞利浦大型C臂数字减影机(DSA)检测颈动脉;以NASCET法^[8]对颈动脉狭窄率进行测算,狭窄率(%) = (1 - 狭窄处管径/狭窄远端管径) × 100%。狭窄率: 轻度 < 50%、中度 50% ~ 69%、重度 70% ~ 99%,血流信号消失,无血流通为血管闭塞。

1.3.2 血清Hcy、hs-CRP检测: 患者入院翌日晨采取空腹肘静脉血5ml,离心留取上清液于冰箱-70℃下保存待测。以酶联免疫法检测Hcy,胶乳法检测hs-CRP水平,日本Shimadzu公司提供对应试剂盒。

1.3.3 脑梗死病情严重程度判定^[9]: 应用美国国立卫生研究院卒中量表(NIHSS)评分对脑梗死患者病情严重程度进行评价,NIHSS评分 ≤ 6分为轻度亚组, >6 ~ 14分为中度亚组, >14分为重度亚组。

1.4 统计学方法 应用SPSS 20.0软件对数据进行统计学分析。正态分布的计量资料以 $\bar{x} \pm s$ 表示,多组间比较采用F检验,多组间两两比较采用q检验;计数资料以频数或率(%)表示,组间比较行 χ^2 检验;以Pearson分析血管狭窄程度、血清Hcy、hs-CRP与中年脑梗死发生之间的相关性;以受试者工作特征(ROC)曲线分析血清Hcy、hs-CRP对中年脑梗死的预测价值。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 2 组颈动脉狭窄程度比较 脑梗死组 98 例患者颈动脉狭窄或闭塞 85 例占 86.73% ,其中轻度 30 例、中度 42 例、重度 13 例;非脑梗死组 80 例患者颈动脉狭窄 12 例占 15.00% ,其中轻度 10 例、中度 2 例。脑梗死组动脉狭窄率显著高于非脑梗死组 ($\chi^2/P = 91.398/<0.001$) ,见图 1。

2.2 2 组血清 Hcy、hs-CRP 水平比较 脑梗死组血清 Hcy、hs-CRP 水平高于非脑梗死组 ($P<0.01$) ,见表 2。

表 2 非脑梗死组与脑梗死组患者血清 Hcy、hs-CRP 水平比较 ($\bar{x}\pm s$)

Tab.2 Comparison of serum Hcy and hs-CRP levels between non cerebral infarction group and cerebral infarction group patients

组别	例数	Hcy($\mu\text{mol/L}$)	hs-CRP(mg/L)
非脑梗死组	80	6.35 \pm 1.21	1.46 \pm 0.26
脑梗死组	98	17.14 \pm 1.85	5.36 \pm 0.75
<i>t</i> 值		44.901	44.365
<i>P</i> 值		<0.001	<0.001

2.3 脑梗死组轻、中、重度患者动脉狭窄程度及血清 Hcy、hs-CRP 比较 脑梗死组患者病情严重程度轻、

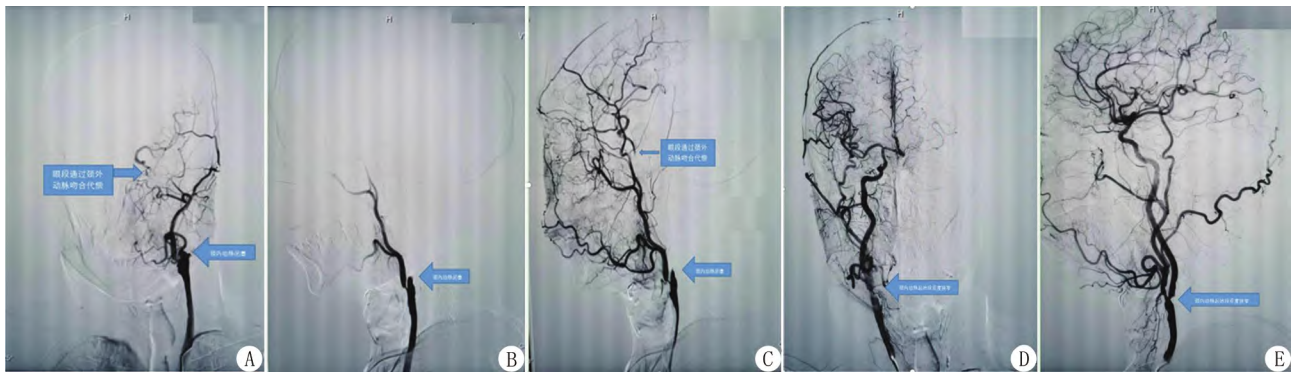
中、重度的动脉狭窄程度有差异 ($F = 77.729 P < 0.01$) ;血清 Hcy、hs-CRP 水平比较 ,重度亚组>中度亚组>轻度亚组 ($P < 0.01$) ,见表 3。

2.4 脑梗死严重程度与动脉狭窄程度、血清 Hcy、hs-CRP 之间相关性 经 Pearson 分析结果显示 ,血清 Hcy、hs-CRP 水平与脑梗死严重程度呈正相关 ($r = 0.365、0.452$, P 均 < 0.001) ,动脉狭窄程度与中年脑梗死严重程度呈正相关 ($r/P = 0.421/<0.001$) 。

2.5 血清 Hcy、hs-CRP 对中年脑梗死的预测价值分析 绘制血清 Hcy、hs-CRP 对中年脑梗死的预测价值 ROC 曲线 ,并计算曲线下面积 (AUC) 结果显示 :血清 Hcy、hs-CRP 及两者联合预测中年脑梗死的 AUC 分别为 0.859、0.791、0.863 ,两者联合检测的曲线下面积高于单一检测者 ($Z/P = 2.251/0.005、3.452/0.012$) ,见表 4、图 2。

3 讨论

脑梗死是 AS 导致的脑动脉闭塞性病变 ,对患者生活质量造成严重威胁 ,其中高血压、卒中家族史、高血脂、吸烟等均为发病的危险因素^[10]。在控制危险因素的同时 ,为预防及控制病情 ,明确脑血管情况也对患者意义重大。DSA 对于供血动脉有无病变、病变程度、病变部位均能准确判断 ,在脑血管疾病中应用价值



注: A~C 均提示左侧颈内动脉慢性闭塞 左侧颈内动脉眼段通过颈外动脉吻合代偿; D~E.DSA 均显示右侧颈内动脉起始段出现重度狭窄。

图 1 脑梗死患者脑动脉血管造影情况

Fig.1 Cerebral artery angiography in patients with cerebral infarction

表 3 脑梗死组轻、中、重度患者动脉狭窄程度及血清 Hcy、hs-CRP 比较 ($\bar{x}\pm s$)

Tab.3 Comparison of arterial stenosis degree and serum Hcy , hs-CRP in mild , moderate , and severe patients with cerebral infarction

组别	例数	动脉狭窄程度[例(%)]			Hcy($\mu\text{mol/L}$)	hs-CRP(mg/L)
		轻度狭窄($n = 30$)	中度狭窄($n = 42$)	重度狭窄($n = 13$)		
轻度亚组	30	25(83.33)	5(16.77)	0	16.02 \pm 1.78	4.01 \pm 0.58
中度亚组	40	5(12.50)	32(80.00)	3(7.50)	17.25 \pm 1.89	5.23 \pm 1.12
重度亚组	28	0	5(17.86)	10(35.71)	18.21 \pm 1.76	5.98 \pm 1.35
χ^2/F 值			77.729		10.586	25.051
<i>P</i> 值			<0.001		<0.001	<0.001

表 4 血清 Hcy、hs-CRP 对中年脑梗死的预测价值分析

Tab.4 Analysis of the predictive value of serum Hcy and hs-CRP for middle-aged cerebral infarction

指标	临界值	AUC	95%CI	敏感度	特异度	约登指数
Hcy	12.85 μmol/L	0.859	0.803~0.916	0.837	0.812	0.775
hs-CRP	2.86 mg/L	0.791	0.720~0.862	0.837	0.800	0.752
两者联合		0.863	0.803~0.923	0.937	0.787	0.901

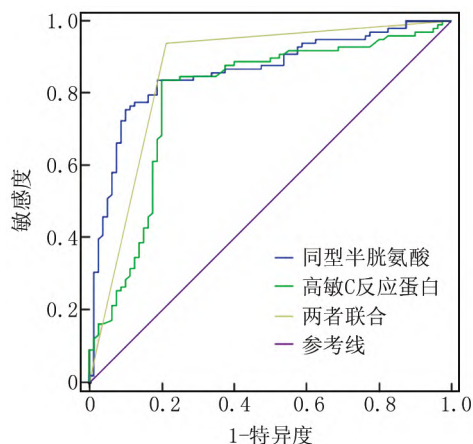


图 2 血清 Hcy、hs-CRP 预测中年脑梗死的 ROC 曲线分析

Fig.2 ROC curve analysis of serum Hcy and hs-CRP predicting middle-aged cerebral infarction

高^[11]。另外血清指标对疾病的诊断可促进患者预后的改善,如血清 Hcy、hs-CRP 对冠状动脉病变具有加重作用,但临床对两者相关性研究较少,本研究主要通过 DSA 在颈动脉斑块内新生血管中的检测,评估颈动脉狭窄程度,并结合血清 Hcy、hs-CRP 在脑梗死患者中的研究,以阐述临床应用价值。

脑梗死患者主要风险取决于患者症状和颈动脉狭窄程度,因此及时对上述指标进行准确评估,并制定相关治疗措施,对于预防脑梗死的发生与复发具有显著的临床价值^[12]。DSA 检测颈内动脉血管,能将图像清晰、明确显示出来;同时 DSA 还能测量动脉血流量^[13];对 AS 引起的缺血性脑血管疾病也有较高的应用价值,不仅清晰显示斑块具体情况(如大小、形态、数量等),还能识别斑块引起的动脉血管管腔狭窄、闭塞,以及侧支循环建立等情况^[14-15]。在本次研究中,98 例脑梗死患者颈动脉血管狭窄率为 86.73% (85/98),而非脑梗死患者血管狭窄率为 15.00%。脑梗死组血管狭窄率高于非脑梗死组,说明颈动脉血管狭窄是脑梗死发生的危险因素。其原因在于脑梗死与 AS 紧密相关,而大脑供血主要是通过颈动脉血流维持,为大脑大部分区域提供血液及营养,因此脑梗死的发生与

颈动脉病变有关,颈动脉狭窄或闭塞导致血液动力学发生变化,继而诱发脑部缺血情况发生^[16-17]。进一步比较不同病情严重程度患者的血管狭窄程度,发现重度神经缺损脑梗死患者的血管狭窄程度较高,提示可以通过 DSA 检测颈动脉血管狭窄程度反映脑梗死患者病情严重程度。血清 Hcy 是一种人体内反应性血管损伤氨基酸,其水平显著升高,可加重对血管内皮细胞的损伤,并使血管平滑肌得到增殖,临床该指标多用于预测心血管疾病^[18]。据相关文献报道,当患者发生心血管系统疾病时,其水平会显著升高,同时也可作为 AS 性疾病发生的独立危险因素^[19]。另外,当脑部发生缺氧或者缺血时,会引发一系列炎症反应的发生,从而导致脑组织损伤;在炎症反应发生时,血清 hs-CRP 水平急性升高,在预测炎症反应发生方面敏感度较好^[20]。本研究发现,脑梗死组血清 Hcy、hs-CRP 水平较非脑梗死组显著升高,说明上述血清指标与脑梗死的发生紧密相关。另一方面,贯穿整个 AS 发生及发展过程的是炎症反应,Hcy 可介导机体氧自由基以及炎症因子生成,继而对血管内皮产生损伤,使机体发生炎症浸润,增加脑梗死发生概率^[21]。而脑梗死患者所出现的功能障碍主要与局部炎症反应有关,作为一种炎症因子,hs-CRP 可直接参与炎症反应中,提示该指标可能是脑梗死发生的重要预测因子^[22]。另外,比较病情程度轻度、中度、重度患者血清 Hcy、hs-CRP 发现,重度亚组>中度亚组>轻度亚组($P<0.05$),提示上述血清指标还能体现出脑梗死患者病情严重程度。Pearson 分析血清 Hcy、hs-CRP 水平与血管狭窄程度及脑梗死严重程度均呈现正相关($P<0.01$),表明 DSA 检测联合上述指标对脑梗死严重程度具有评估价值。此外,ROC 曲线分析结果显示,血清 Hcy 联合 hs-CRP 预测中年脑梗死的曲线下面积较大,价值亦较高($P<0.05$)。

综上所述,联合颈动脉斑块内新生血管 DSA 与血清 Hcy、hs-CRP 检测有助于评估脑梗死发生风险,为临床防治提供指导。

利益冲突:所有作者声明无利益冲突

作者贡献声明

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