

# D-二聚体与纤维蛋白原比值与青年急性脑梗死患者颈动脉粥样硬化斑块的相关性分析

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## 【摘要】

**目的** 探讨青年急性脑梗死 (young acute cerebral infarction, YACI) 患者D-二聚体与纤维蛋白原比值 (D-dimer to fibrinogen ratio, DFR) 与颈动脉粥样硬化斑块的关系。

**方法** 回顾性连续收集2014年2月—2020年9月进行了颈动脉斑块超声造影 (contrast-enhanced ultrasound, CEUS) 检查的首次发病的YACI患者为观察组, 根据CEUS检查结果将颈动脉斑块分为1~4级; 根据NIHSS评分将患者的神经功能缺损分为轻、中、重度。另外选取同期进行了颈动脉超声检查且结果正常的体检青年人作为对照组。收集两组的人口学信息、血管危险因素及实验室检查结果, 根据凝血功能结果中的D-二聚体及纤维蛋白原水平计算DFR。比较观察组和对照组上述指标的差异; 对观察组中DFR与颈动脉斑块分级和神经功能缺损的严重程度进行相关性分析。

**结果** 研究共纳入观察组96例, 对照组67例。观察组DFR数值高于对照组 [ $(102.06 \pm 13.05) \times 10^{-3}$  vs  $(71.35 \pm 18.13) \times 10^{-3}$ ], 差异有统计学意义 ( $P=0.019$ ); 观察组中DFR数值与神经功能缺损严重程度呈正相关 ( $r=0.716, P=0.038$ ), 与颈动脉斑块CEUS分级也呈正相关 ( $r=0.879, P=0.032$ )。

**结论** YACI患者的DFR数值与颈动脉斑块分级及神经功能缺损严重程度有关, 可能是判断YACI患者颈动脉斑块稳定性及病情严重程度的新的标志物。

**【关键词】** D-二聚体与纤维蛋白原比值; 急性脑梗死; 青年; 颈动脉斑块; 神经功能缺损; 危险因素

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## Correlation between D-dimer to Fibrinogen Ratio and Carotid Plaque in Young Patients with Acute Cerebral Infarction

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## 【Abstract】

**Objective** To explore the relationship between D-dimer to fibrinogen ratio (DFR) and carotid plaque in young acute cerebral infarction (YACI) patients.

**Methods** The first-onset YACI patients who underwent contrast enhanced ultrasound (CEUS) from February 2014 to September 2020 were retrospectively collected and taken as the observation group. The healthy young people with normal carotid ultrasound results in physical examination during the same period were selected as the control group. According to the results of CEUS, carotid plaque was divided into 1-4 grades. According to NIHSS score, the neurological deficits were divided into mild, moderate and severe grades. The demographic information, vascular risk factors and laboratory examination results of the two groups were collected, and DFR was calculated. The differences of the above indexes between the two groups were compared. The correlation of DFR with carotid plaque grade and the severity of neurological deficit in the observation group were analyzed.

**Results** 96 cases in the observation group and 67 cases in the control group were included in this study. The DFR value of the observation group was higher than that of the control group [ $(102.06 \pm 13.05) \times 10^{-3}$  vs  $(71.35 \pm 18.13) \times 10^{-3}$ ,  $P=0.019$ ]. In the observation group, DFR was positively correlated with NIHSS score ( $r=0.716, P=0.038$ ) and CEUS grade of carotid plaque ( $r=0.879, P=0.032$ ).

**Conclusions** The DFR value of YACI patients was positively correlated with CEUS carotid plaque



grade and NIHSS score. The DFR maybe a potential marker for evaluating carotid plaques stability and stroke severity in YACI patients.

**【Key Words】** D-dimer to fibrinogen ratio; Acute cerebral infarction; Youth; Carotid plaque; Neurological deficit; Risk factor

青年脑梗死一般指45周岁以下成年人发生的脑梗死,动脉粥样硬化是青年脑梗死的主要病因,也是青年脑梗死患者二级预防的重要靶点<sup>[1-4]</sup>。颈动脉斑块超声造影(contrast-enhanced ultrasound, CEUS)操作简单无创,可显示动脉粥样硬化斑块内的新生血管密度,从而较准确地评价斑块的稳定性<sup>[5-6]</sup>。血浆D-二聚体(D-dimer, DD)和纤维蛋白原(fibrinogen, FIB)是临床上常用的检测机体凝血和纤维溶解功能的指标,对血栓形成的诊断有重要价值<sup>[7]</sup>。D-二聚体与纤维蛋白原比值(D-dimer to fibrinogen ratio, DFR)的稳定性较好,已有报道DFR与冠心病患者的冠状动脉粥样硬化有关<sup>[8]</sup>。目前关于DFR与青年急性脑梗死(young acute cerebral infarction, YACI)患者颈动脉粥样硬化斑块关系的研究较少,本研究在伴有颈动脉粥样硬化斑块的YACI人群中,探讨DFR与此类患者颈动脉粥样硬化斑块之间的关系。

## 1 对象与方法

**1.1 研究对象** 回顾性收集宝鸡市中心医院神经内科2014年2月–2020年9月住院的YACI患者的病历资料。入选标准:①年龄18~45岁;②脑梗死符合《中国急性缺血性脑卒中诊治指南2018》诊断标准<sup>[9]</sup>,经头颅MRI明确诊断;③首次脑梗死,发病时间在48 h内;④入院24 h内完成NIHSS评分,入院次日进行了血液DD和FIB水平检测;⑤颈部血管超声检查发现有颈动脉粥样硬化斑块,并进一步进行了针对斑块的CEUS检查。排除标准:①出血性卒中或其他病因(心源性及其他少见病因)所致脑梗死;②临床资料不完善;③伴有严重的心脏、肝脏或肾脏疾病;④发病前使用抗炎或免疫抑制剂

等药物;⑤血液检查前使用过抗凝或纤溶药物。选取同期体检的无脑梗死病史且颈部血管超声检查结果正常的青年人(18~45岁)作为对照组。

颈部血管超声检查中颈动脉粥样硬化斑块的判断标准为血管内-中膜厚度 $\geq 1.3$  mm<sup>[10]</sup>。根据CEUS结果对颈动脉粥样硬化斑块进行分级:1级,斑块无增强;2级,斑块基底部或肩部增强;3级,斑块基底部和肩部均增强;4级,斑块基底部、肩部和内部均增强<sup>[11]</sup>。

**1.2 资料收集和比较** 收集观察组和对照组的人口学特征(性别、年龄),血管危险因素(高血压病<sup>[12]</sup>、吸烟<sup>[13]</sup>、饮酒<sup>[14]</sup>)等资料。收集观察组入院24 h内的NIHSS评分,入院次日血常规、血脂、糖化血红蛋白、Hcy等实验室检查结果,记录凝血功能检查中的DD和FIB水平,并计算DFR(计算公式为DD/FIB)。根据NIHSS评分对患者神经功能缺损程度进行分级:<5分为轻度缺损,5~15分为中度缺损, $\geq 16$ 分为重度缺损<sup>[15]</sup>。收集对照组就诊当日的血常规、血脂、糖化血红蛋白、Hcy及凝血功能检查结果并计算DFR。

比较观察组和对照组的一般资料、血管危险因素、实验室检查结果及DFR;进一步在观察组中对DFR与颈动脉斑块分级,DFR与神经功能缺损的严重程度进行相关性分析。

**1.3 统计学处理** 采用SPSS 20.0软件进行统计学分析。先对计量资料进行正态检验,符合正态分布的计量资料以 $\bar{x} \pm s$ 表示,两组间比较采用独立样本 $t$ 检验,不符合正态分布的计量资料用 $M(P_{25} \sim P_{75})$ 表示,组间比较采用非参数检验;计数资料用率表述,组间比较采用卡方检验。DFR与神经功能缺损程度及斑块等级的相关性分析采用Spearman相关分析,计算相

关系数 ( $r$ )。以 $P<0.05$ 为差异有统计学意义。

## 2 结果

**2.1 观察组与对照组基线资料比较** 本研究共入组163例受试者,其中观察组96例,男性71例,女性25例,年龄29~44岁,平均 $36.2\pm 7.8$ 岁;对照组67例,男性51例,女性16例,年龄27~43岁,平均 $34.9\pm 8.6$ 岁。观察组吸烟、高血压比例高于对照组,糖化血红蛋白和LDL-C水平及DFR高于对照组,差异均有统计学意义(表1)。

**2.2 相关性分析** 在观察组中,DFR与神经损伤程度呈正相关( $r=0.716$ ,  $P=0.038$ ),与斑块等级也呈正相关( $r=0.879$ ,  $P=0.032$ )。

## 3 讨论

YACI发病率近年有逐渐上升趋势,有研究报道YACI占全部脑梗死的9.78%<sup>[1, 16-17]</sup>。YACI最主要的病因仍为动脉粥样硬化,预防青年颈动脉粥样硬化是YACI一级预防和二级预防的重要目标<sup>[2]</sup>。本研究结果显示,YACI患者中吸烟、高血压比例高于对照组,糖化血红蛋白和LDL-C水平高于对照组,提示上述传统血管危险因素与YACI的发病可能相关。

DD是反映凝血酶生成和继发纤溶亢进的指标,有研究报道DD水平与脑梗死的发病风险及严重程度相关<sup>[18-19]</sup>。研究表明,急性脑梗死发病24 h内血浆DD水平即开始升高,高峰期在发病5 d时,之后逐步降低<sup>[20]</sup>。FIB是凝血反应的关键因子之一,参与动脉粥样硬化斑块的形成过程<sup>[21]</sup>,Swarowska等<sup>[22]</sup>报道血浆FIB水平与脑梗死患者的长期死亡风险正相关。DFR是DD与FIB的比值,可反映纤溶/凝血过程的平衡,DFR增高,该平衡向纤溶偏移,患者血栓形成的风险升高<sup>[23]</sup>。本研究结果表明,观察组DFR显著高于对照组,提示DFR可能与YACI的发生有关。

本研究相关性分析结果表明,YACI患者中DFR与NIHSS评分呈正相关,DFR数值随着神

表1 观察组与对照组患者基线资料比较

|                     | 观察组 (96例)                   | 对照组 (67例)                  | P值    |
|---------------------|-----------------------------|----------------------------|-------|
| 男性/例 (%)            | 71 (74.0)                   | 51 (76.1)                  | 0.112 |
| 年龄/岁                | $36.2\pm 7.8$               | $34.9\pm 8.6$              | 0.088 |
| 吸烟/例 (%)            | 32 (33.3)                   | 14 (20.9)                  | 0.042 |
| 饮酒/例 (%)            | 28 (29.2)                   | 16 (23.9)                  | 0.059 |
| 高血压/例 (%)           | 34 (35.4)                   | 11 (16.4)                  | 0.031 |
| 血小板/ ( $10^9/L$ )   | $269.21\pm 45.08$           | $229.11\pm 36.94$          | 0.063 |
| 白细胞/ ( $10^9/L$ )   | $6.23\pm 1.38$              | $5.91\pm 1.29$             | 0.581 |
| 中性粒细胞/ ( $10^9/L$ ) | $5.20\pm 1.11$              | $4.26\pm 1.23$             | 0.055 |
| 淋巴细胞/ ( $10^9/L$ )  | $1.19\pm 0.33$              | $1.49\pm 0.44$             | 0.062 |
| 胆固醇/ (mmol/L)       | $4.32\pm 1.13$              | $4.06\pm 1.20$             | 0.079 |
| TG/ (mmol/L)        | $1.71\pm 0.69$              | $1.49\pm 0.67$             | 0.550 |
| LDL-C/ (mmol/L)     | $3.36\pm 0.61$              | $2.11\pm 0.46$             | 0.040 |
| Hcy/ (mmol/L)       | $20.09\pm 2.84$             | $11.16\pm 3.26$            | 0.055 |
| 糖化血红蛋白/%            | $6.20\pm 1.29$              | $3.87\pm 0.71$             | 0.021 |
| D-二聚体/ (mg/L)       | $0.47\pm 0.12$              | $0.23\pm 0.13$             | 0.053 |
| 纤维蛋白原/ (g/L)        | $4.52\pm 0.08$              | $2.89\pm 0.07$             | 0.050 |
| D-二聚体与纤维蛋白原比值       | $(102.06\pm 13.05) 10^{-3}$ | $(71.35\pm 18.13) 10^{-3}$ | 0.019 |

经损害加重而增高,提示DFR可作为YACI患者早期病情监测的指标。研究表明,动脉粥样硬化斑块的易损性是脑梗死发生的主要原因,斑块易损性主要取决于斑块内血管新生的程度<sup>[11]</sup>,而评估斑块内血管新生的情况能够为斑块性质的判断提供依据<sup>[24-25]</sup>。超声造影可以无创性评估动脉粥样硬化斑块内新生毛细血管增生的情况,并对斑块进行危险分层<sup>[26]</sup>。本研究结果表明,DFR数值与YACI患者颈动脉粥样硬化斑块等级呈正相关,提示DFR越高,YACI患者的颈动脉粥样硬化斑块越不稳定。这也为临床提供了一个简单、易获取的预测患者动脉粥样硬化程度的可能的标志物。

本研究的不足:①本研究的样本来自单中心,样本量较小,代表性不足,结果可能存在一定的偏倚;②超声造影检查对斑块进行半定量视觉分级,有一定主观性,可能造成结果的偏差;③本研究为回顾性研究,结果可能受到其他混杂因素的影响,需要后续的前瞻性研究来进一步证实本研究的结论。



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【点睛】本研究对伴有颈动脉粥样硬化斑块的YACI患者资料进行了回顾性分析,发现DFR可能反映患者颈动脉粥样硬化斑块的病变程度及神经功能缺损的严重程度。

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《中国卒中杂志》经过16年的积淀与发展,为推进我国脑血管病临床和科研发展起到了应有的作用,同时得到了业界的普遍认可。于2021年入选《我国高质量科技期刊分级目录》(T3级,业界认可的国内外优质期刊)。内容注重临床实践、前沿信息、行业规范推广等。

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