·论著 临床诊治·

大血管闭塞性脑梗死患者桥接治疗转化性出血的危险因素

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【摘要】 **目的** 分析桥接治疗大血管闭塞性脑梗死出血性转化的危险因素。**方法** 回顾性分析2018-01—2020-12厦门大学附属中山医院收治的73例接受桥接治疗大血管闭塞性脑梗死患者的临床资料,根据治疗后患者是否出现转化性出血分为出血性组(21例)和非出血性组(52例)。比较2组患者性别、年龄、是否吸烟、是否合并高血压、是否合并糖尿病、是否合并房颤、是否合并高脂血症、血小板相关数值、肝肾功能、凝血功能、NIHSS评分等指标,采取多因素Logistic回归分析大血管闭塞性脑梗死出血性转化的危险因素。**结果** 出血组患者年龄>70岁(P=0.027)、血小板计数<185×10^9个/L(P=0.029)、APTT>30.3 s(P=0.014)、NIHSS评分>18分(P=0.015)是大血管闭塞性脑梗死转化性出血的危险因素。**结论** 年龄大、血小板计数低、APTT时间延长、NIHSS评分均可能会影响大血管闭塞性脑梗死的疗效,增加术后转化性出血的发生率,是大血管闭塞性脑梗死患者转化性出血的危险因素,应引起临床重视。

【关键词】 脑梗死;桥接治疗;大血管闭塞性;转化性出血;危险因素
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Risk factors of hemorrhagic transformation in bridging therapy for large vessel occlusive cerebral infarction

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【**Abstract**】 **Objective** To analyze the risk factors of hemorrhagic transformation in bridging therapy for large vessel occlusive cerebral infarction. **Methods** The clinical data of 73 patients with large vessel occlusive cerebral infarction who received bridging therapy from January 2018 to December 2020 in Zhongshan Hospital Affiliated to Xiamen University were retrospectively analyzed. According to the number of cases, they were divided into hemorrhagic group (21 cases) and non-hemorrhagic group (52 cases). Gender, age, smoking, hypertension, diabetes, atrial fibrillation, hyperlipidemia, platelet-related values, liver and kidney function, blood coagulation function, and baseline National Institutes of Health stroke scale (NIHSS) were compared between the two groups. Multivariate Logistic regression analysis was used to analyze the risk factors of hemorrhagic transformation of large vessel occlusive cerebral infarction. **Results** Age>70 years, blood platelet<185×10^9 L^{-1}, APTT>30.3 s, and NIHSS score>18 in the hemorrhagic group were risk factors for hemorrhagic transformation of large vessel occlusive cerebral infarction (P<0.05). **Conclusion** Older age, low blood platelet, prolonged APTT time, and NIHSS score may affect the curative effect of large vessel occlusive cerebral infarction, increase the incidence of postoperative hemorrhagic transformation, and are the risk of hemorrhagic transformation in patients with large vessel occlusive cerebral infarction. Factors risk factors for hemorrhagic transformation should be paid attention to by clinicians.

【**Key words**】 Cerebral infarction; Bridging therapy; Large vessel occlusion; Hemorrhagic transformation; Risk factors

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脑血管疾病是由于突然的动脉闭塞阻断大脑的血液供应而引起的[1]。在过去的几十年中，大量临床试验表明，与接受安慰剂的患者相比，接受静脉溶栓治疗的患者在3个月内的致残率和病死率显著降低[2-3]。目前，使用rt-PA静脉溶栓治疗急性脑梗死已成为国际临床标准[4-5]。然而一些研究表明，对于＞8 mm的栓子，静脉溶栓效果较差，血管开通的概率＜1%[6]。因此，桥接治疗被推荐用于治疗大血管闭塞性脑梗死[7-9]，旨在早期有效地再通，并获得更好的功能改善[10]。同静脉溶栓相同，桥接治疗最严重的并发症也是转化性出血，范围从轻微的颅内点状出血到脑实质血肿，这是不良预后的最重要因素之一[11]。本研究分析桥接治疗转化性出血的影响因素，预测术后出血的概率及患者预后，让更多大血管闭塞性脑梗死患者受益于桥接治疗。

1 资料和方法

1.1 一般资料 纳入2018-01—2020-12大血管闭塞性脑梗死接受桥接治疗的患者73例，其中非出血性组52例，出血组21例。

1.2 纳入标准 (1)4.5 h内发生急性脑梗死的患者；(2)年龄18～85岁；(4)头颅CT扫描未见新发低密度缺血性病灶，排除脑出血；(4)未怀孕；(5)经rt-PA静脉溶栓后NIHSS评分未改善或改善不明显，急诊予以头颅CTA考虑前循环大血管闭塞性脑梗死患者[颈内动脉远端闭塞、颈内动脉、大脑中动脉串联闭塞、大脑中动脉M1段和M2段闭塞以及大脑前动脉(A1段)闭塞]；(6)患者或家属签署知情同意书。本研究经厦门大学附属中山医院伦理委员会批准。

1.3 排除标准 (1)短暂性脑缺血发作单次发作、脑梗死症状迅速好转；(2)既往蛛网膜下腔出血患者；(3)血压持续升高(收缩压≥185 mmHg或舒张压≥110 mmHg，1 mmHg=0.133 kPa)；(4)CT显示患者有出血、脑水肿、动静脉畸形和肿瘤；(5)感染性心内膜炎患者；(6)患者卒中前48 h内接受过抗凝剂或肝素治疗；(7)7 d内有动脉穿刺，14 d内有大手术或外伤，活动性持续出血；(8)血液系统疾病、凝血障碍患者，国际标准化比率(INR)>1.5；(9)血小板<100×10^{9}个/L；(10)有除高血压、心房颤动、糖尿病外的慢性疾病者；(11)后循环血管闭塞患者。

1.4 统计学方法 对所有收集到的数据采用SPSS 26.0统计软件包进行分析和处理。计量资料中的正态分布数据使用均数±标准差表示，组间比较采用独立样本t检验，非正态分布数据用中位数(四分位数间距)，组间比较采用非参数检验。计数资料以例数和百分率表示，组间比较采用卡方检验或Fisher确切概率法。采用Losgistic回归评估出血并发症的影响因素。以P<0.05为差异有统计学意义。

2 结果

单因素分析显示，2组在性别、吸烟史、高血压史、糖尿病史、高脂血症史等方面差异无统计学意义(P＞0.05)，心房颤动、年龄在出血组和非出血组间差异有统计学意义(P＜0.05)，见表1。

表1 2组患者临床基本信息比较

Table 1 Comparison of basic clinical information of two groups

资料	非出血组(n=52)	出血组(n=21)	P值
年龄/(岁，$\bar{x}\pm s$)	61.56±11.464	70.95±9.325	0.001
性别[n(%)]			0.295
男	33(67.3)	16(76.2)	
女	19(36.5)	5(23.8)	
吸烟[n(%)]	15(28.8)	6(28.6)	0.981
高血压[n(%)]	30(57.7)	14(66.7)	0.478
糖尿病[n(%)]	12(23.1)	9(42.9)	0.091
房颤[n(%)]	13(25.0)	12(57.1)	0.009
高脂血症[n(%)]	16(30.8)	8(38.1)	0.546

通过分析临床和生化数据，与非出血组相比，出血组NIHSS评分较高，APTT显著延长，而血小板计数显著降低(P<0.05)，见表2。

运用多元逻辑回归分析，选择年龄、房颤、NIHSS评分、血小板计数、肌酐数值作为分析因素，结果表明，年龄越大、NIHSS评分越高、APTT延长、血小板计数越少是大血管闭塞性脑梗死桥接治疗转化性出血的危险因素(表3)。

3 讨论

随着人类生活水平的不断提高，急性脑梗死目前是最常见的疾病之一[12]，其发病率和病死率居高不下，已成为危害人类健康的主要疾病之一[13-14]。如何选择最好的治疗方法是一个世界难题。目前，溶栓治疗已成为世界公认的最佳干预措施[15-17]，但对于大血管闭塞性脑梗死的患者，溶栓治疗不能起到很好的作用，与未接受桥接治疗的患者相比，大多数接受桥接治疗的患者预后良好。然而，出血性并发症是同样也是桥接治疗最严重的并发症之一。本研究表明，转化性出血的发生率为28.8%，与以往研究结果部分一致。

表2 2组患者临床指标对比 ［中位数(四分位数间距)］

Table 2 Comparison of clinical indicators between the two groups ［*M*(IQR)］

指标	非出血组($n=52$)	出血组($n=21$)	*P*值
NIHSS评分	15.94(13.00,19.00)	21.05(18.50,23.50)	0.001
PT	11.70(11.00,13.40)	11.6(11.10,12.25)	0.933
APTT	26.41(24.52,29.00)	28.80(26.25,32.10)	0.006
FIB	3.12(2.60,3.700)	3.15(2.56,4.03)	0.730
TT	17.70(17.10,18.47)	17.90(17.00,18.10)	0.391
血小板计数	235.06(187.75,278.75)	184.52(159.00,210.50)	<0.001
血小板压积	2.15(1.80,2.60)	2.10(1.70,2.40)	0.380
平均血小板体积	9.75(9.32,10.90)	9.90(9.45,11.00)	0.263
血小板体积分布宽度	10.75(9.90,12.57)	10.80(10.20,12.15)	0.730
大血小板比例	22.90(19.27,31.60)	22.5(20.50,27.70)	0.855
丙氨酸氨基转移酶	17.35(12.00,23.62)	15.9(10.95,23.00)	0.633
天门冬氨酸氨基转移酶	20.90(19.125,26.15)	20.2(16.25,28.15)	0.804
γ-谷氨酰基转移酶	32.35(16.82,50.00)	30.2(19.75,68.2)	0.865
碱性磷酸酶	82.950(61.45,93.05)	85.00(73.50,105.85)	0.506
糖	7.29(6.34,8.78)	8.27(6.58,12.74)	0.261
肌酐	65.85(57.52,78.42)	74.00(70.5,83.35)	0.015

表3 多元回归分析相关危险因素

Table 3 Analysis of related risk factors by multiple regression analysis

变量	*OR*值	95%置信区间		*P*值
		下限	上限	
血小板计数 < 185×10^9个/L	6.242	1.212	32.150	0.029
NIHSS评分 > 18分	10.187	1.583	65.535	0.015
APTT > 30.3 s	17.390	1.785	169.438	0.014
年龄 > 70岁	6.697	1.243	36.079	0.027
房颤	1.969	0.385	10.063	0.416
肌酐	1.026	0.986	1.068	0.205

年龄是缺血性脑卒中的主要不可改变的危险因素之一[18-19]。与年轻患者相比,大血管闭塞性脑梗死患者转化性出血的风险更高,神经功能恢复更差[20-21],与本研究结果一致,>75岁的老年人经桥接治疗更加容易转化性出血,可能与老年人大脑发生明显退行性改变,且常伴随动脉粥样硬化等有明显关系。

通常来说,NIHSS评分越高的患者侧支循环越差,梗死的面积越大[22-24]。相关研究表明,NIHSS评分能反映颅内病灶体积和病灶影响功能的大小,且随着NIHSS评分的增加,功能缺损越厉害[25-26],入院时患者的NIHSS评分也是预测转化性出血的独立风险因素,并具有良好的预测能力[27]。本研究也表明,NIHSS评分>18分是大血管闭塞性脑梗死患者桥接治疗后转化性出血的危险因素之一,较高的NIHSS评分会影响桥接治疗大血管闭塞性脑梗死患者的预后,增加了转化性出血的概率,提示桥接治疗在取栓前需要严格评分,NIHSS评分较高的患者选择桥接治疗时仍需谨慎。NIHSS评分>18分的脑梗死患者梗死面积更大,取栓后血管再通的过程中会使大血管的内皮受损严重而造成转化性出血的形成。

本研究发现,APTT>30 s、血小板计数<185×10^9个/L是转化性出血的危险因素。众所周知,APTT是临床常用的反映凝血因子活性的指标,数值越高,凝血因子活性越低,越容易出血,而血小板除在聚集后能产生止血功能外,还参与内皮的修复[28-32],虽在桥接治疗适应证内的患者,APTT>30 s以及血小板计数<185×10^9个/L的患者仍需要注意出血风险[33-36]。

本研究也有一些局限性:这是一项单中心回顾性研究,样本量相对较小,可能会导致一些偏差,因此,应设计大样本量的前瞻性多中心临床试验证实本研究结果,并需要进一步的实验探索这些预测因子导致出血并发症的机制。

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