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硕士学位论文

（专业学位）

急性前循环大血管闭塞机械取栓复流程度与 NLR 值及血栓病理成分的关系

The relationship between the degree of reperfusion after mechanical thrombectomy and the NLR and the pathological components of thrombus in patients with acute anterior circulation large vessel occlusion

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急性前循环大血管闭塞机械取栓复流程度与 NLR 值及血栓病理成分的关系

中文摘要

第一部分 急性前循环大血管闭塞机械取栓术后复流程度与中性粒细胞和淋巴细胞比值的关系

目的：探索前循环大血管闭塞患者接受机械取栓（Mechanical Thrombectomy,MT）后闭塞血管复流程度与治疗前外周静脉血中性粒细胞和淋巴细胞比值（Neutrophil-to-Lymphocyte Ratio，NLR）的关系。

方法：回顾性分析2016年6月至2022年3月在本中心接受机械取栓治疗的前循环大血管闭塞性急性缺血性脑卒中（Acute Ischemic Stroke，AIS）患者的临床资料，根据改良脑梗死溶栓分级(Modified thrombolysis in cerebral infarction，mTICI）评估术后闭塞血管的复流程度，将所有成功复流患者分为部分复流组（mTICI=2b级）及完全复流组（mTICI=3级），比较两组患者的基本临床资料、疾病特征、介入治疗及预后的相关数据，行单因素分析及多因素Logistic分析，探索影响闭塞血管术后复流程度的相关因素。

结果：共纳入患者214例（部分复流组65例，完全复流组149例），单因素分析结果显示，两组患者的术前NLR值、闭塞血管位置、血栓负荷量、穿刺至再通时间、取栓次数、术后90d预后良好率存在统计学差异（$P<0.05$）。与部分复流患者相比，完全复流患者有更低的NLR值、闭塞血管更多位于大脑中动脉、更低的血栓负荷量、更短的手术时间、更少的取栓次数及更好的临床预后。多因素Logistic 回归分析显示，NLR值与低血栓负荷是前循环AIS患者术后完全复流的两个独立影响因素。

结论：机械取栓前有更低中性粒细胞和淋巴细胞比值及低血栓负荷量的前循环AIS 患者，接受机械取栓治疗后更容易达到完全复流。

【关键词】急性前循环大血管闭塞；缺血性脑卒中；机械取栓；复流程度；中性粒细胞和淋巴细胞比值

第二部分　急性前循环大血管闭塞机械取栓的血栓病理学与复流程度及中性粒细胞和淋巴细胞比值的关系

目的：研究前循环大血管闭塞性急性缺血性脑卒中（Acute Ischemic Stroke，AIS）行机械取栓治疗（Mechanical Thrombectomy,MT）取出血栓病理组织成分与术后闭塞血管复流程度及治疗前外周静脉血中性粒细胞和淋巴细胞比值（Neutrophil-to-Lymphocyte Ratio，NLR）的关系。

方法：收集2020年11月至2022年12月于本中心接受血管内机械取栓治疗的前循环急性缺血性脑卒中患者的血栓标本及相关临床资料。将取出血栓样本用苏木精和伊红(Hematoxylin-eosin Staining，HE)染色后观察，使用Image J软件对染色后血栓样本进一步分析并计算出各成分所占面积百分比。根据患者血栓中各成分占比，将所有患者分为富含红细胞型血栓组、混合型血栓组及少红细胞型血栓组。比较三组患者的基本临床资料、术后复流程度及术前NLR值等相关数据，采用单因素方差分析、非参数检验、卡方检验及Fisher’s精确概率法分析患者血栓病理组织成分与术后闭塞血管的复流程度及术前NLR的关系。

结果：共纳入患者55例，其中富含红细胞型7例（12.7%）,混合型23例（41.8%），少红细胞型25例（45.5%）。三组患者的性别、年龄、合并基础疾病情况、术前NLR值、闭塞血管位置、血栓负荷量、穿刺至再通时间、取栓次数、术后90d预后良好率均无统计学差异（P＞0.05）。富含红细胞型血栓患者完全复流（mTICI=3）6例（6/7，85.7%），混合型血栓患者完全复流20例（20/23，87%），少红细胞型血栓患者完全复流13例（13/25，52%），三组间完全复流患者所占比例的差异具有统计学意义（P=0.015，＜0.05）。将55例患者按照术后靶血管复流程度分为完全复流组39例（39/55,70.9%）和部分复流组16例（16/55,29.1%），两组间取出血栓内红细胞所占百分比的差异具有统计学意义（P=0.016，＜0.05）。

结论：血栓中红细胞含量较高的前循环大血管闭塞急性缺血性脑卒中患者，行机械取栓后闭塞血管更容易达到完全复流，血栓病理组织构成与患者的术前 NLR 值无关。

【关键词】急性前循环大血管闭塞；机械取栓；血栓病理；复流程度；中性粒细胞与淋巴细胞比值

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The relationship between the degree of reperfusion after mechanical thrombectomy and the NLR and the pathological components of thrombus in patients with acute anterior circulation large vessel occlusion

Abstract

Part One: The relationship between the degree of reperfusion after mechanical thrombectomy and the ratio of neutrophil to lymphocyte in patients with acute anterior circulation large vessel occlusion

Objective: To investigate the relationship between the degree of reperfusion of the occlusive vessel in the patients with acute anterior circulation large vessel occlusion after mechanical thrombectomy (MT) and the pretherapeutic neutrophil-to-lymphocyte ratio (NLR) in peripheral venous blood of the patients.

Methods: The clinical data of patients with anterior circulation acute ischemic stroke (AIS）who received mechanical thrombectomy in our center from June 2016 to March 2022 were analyzed retrospectively. The degree of reperfusion after MT was evaluated according to the modified thrombolysis in cerebral infarction (mTICI). All patients with successful reperfusion after MT were divided into partial reperfusion group (mTICI=2b) and complete reperfusion group (mTICI=3). The basic clinical data, disease characteristics, interventional therapy and prognosis of the two groups were compared. Univariate analysis and multivariate logistic analysis were used to analyze the factors affecting the degree of reperfusion after MT.

Results: A total of 214 patients were included (65 cases in partial reperfusion group and 149 cases in complete reperfusion group). There were statistical differences between the two groups in preoperative NLR value, location of occluded vessels, clot burden, time from puncture to recanalization, times of thrombus removal, and the rate of 90-day good prognosis(P<0.05). Compared with partial reperfusion patients, complete reperfusion patients had lower NLR value, more occluded vessels which locate in the middle cerebral

artery, lower clot burden, shorter operation time, fewer thrombus removal times and better clinical prognosis. Multivariate logistic regression analysis showed that NLR value and low clot burden were influencing factors for the occlusive vessels' complete reperfusion in the patients with anterior circulation AIS after MT.

Conclusions: Patients with anterior circulation AIS who had lower pretherapeutic neutrophil to lymphocyte ratio and lower clot burden were more likely to achieve complete reperfusion after mechanical thrombectomy.

【Keywords】: acute anterior circulation large vessel occlusion; ischemic stroke; mechanical thrombectomy; degree of reperfusion; neutrophil to lymphocyte ratio

Part Two: The relationship between the thrombus histology and the degree of reperfusion and the ratio of neutrophil to lymphocyte in patients with acute anterior circulation large vessel occlusion

Objective: To explore the relationship between the thrombus histology of the patients with acute ischemic stroke (AIS) caused by anterior circulation large vessel occlusion and the degree of the occlusive vessel's reperfusion and the pretherapeutic neutrophil to lymphocyte ratio (NLR) in peripheral venous blood of the patients.

Methods: The thrombus samples and relevant clinical data of patients with acute ischemic stroke of anterior circulation who received mechanical thrombectomy (MT) in our center from November 2020 to December 2022 were collected continuously. The thrombus samples were observed after stained with hematoxylin and eosin Staining (HE). Image J software was utilized to analyze and calculate the percentage of different component in the thrombus sample. According to the proportion of different component in the thrombus, the patients were divided into rich erythrocyte group, mixed group and low erythrocyte group. The basic clinical data, the degree of reperfusion and the NLR of patients were compared between the three groups. The relationship between thrombus histology and degree of reperfusion and the preoperative NLR were analyzed by one-way ANOVA test, non-parametric test, chi-square test and Fisher's precision probability test.

Results: A total of 55 patients were included, including 7 (12.7%) cases of rich erythrocyte group, 23 (41.8%) cases of mixed group, and 25 (45.5%) cases of low erythrocyte group. There were no statistical differences in the gender, age, basic disease,

NLR value, location of occluded vessels, clot burden, time from puncture to recanalization, times of thrombus removal, and the rate of 90-day good prognosis among the three groups (P>0.05). There were 6 cases (6/7, 85.7%) in rich erythrocyte group, 20 cases (20/23, 87%) in mixed group and 13 cases (13/25, 52%) in low erythrocyte group respectively, the occlusive vessels of which got the complete reperfusion (mTICI=3). The difference of complete reperfusion rate among the three groups was statistically significant (P=0.015, P <0.05). According to the degree of the occlusive vessel's reperfusion after MT, 55 patients were divided into a complete reperfusion group of 39 cases (39/55, 70.9%) and a partial reflow group of 16 cases (16/55, 29.1%). There was a statistically significant difference in the percentage of red blood cells from the thrombus between the two groups (P=0.016, P <0.05)

Conclusions: In acute ischemic stroke patients with anterior circulation large vessel occlusion with high red blood cell content in thrombus, complete reperfusion of the occluded vessels was more likely to be achieved after mechanical thrombectomy, and the pathological structure of thrombus was independent of preoperative NLR value.

【 Keywords 】: acute anterior circulation large vessel occlusion; mechanical thrombectomy; thrombus histology; degree of reperfusion; neutrophil to lymphocyte ratio

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目　录

引 言

脑卒中是全世界范围内导致人类死亡和残疾的重要疾病之一，其中 70%为急性缺血性脑卒中[1]（Acute Ischemic Stroke,AIS）。约有近一半的 AIS 患者是大血管急性闭塞所致[2]，被称之为大血管闭塞性急性缺血性脑卒中（Acute Ischemic Stroke With Large Vessel Occlusion,AIS-LVO）。AIS-LVO 具有高致残率及高死亡率的特点[3]，其治疗方式主要有以下两种，以静脉溶栓（intravenous thrombolysis，IVT）为代表的药物治疗和以机械取栓（mechanical thrombectomy,MT）为代表的血管内介入治疗。静脉溶栓是 AIS 的一线治疗方法，但其应用受患者发病至入院的“时间窗”限制，且对于 AIS-LVO 患者，静脉溶栓后的闭塞血管再通率低[4]。2015 年在新英格兰杂志发表的 MR CLEAN[5]、SWIFT PRIME[6]、EXTEND-IA[7]、ESCAPE[8]、REVASCAT[9]共五项临床随机对照研究结果显示，对于筛选后的 AIS-LVO 患者，以使用支架取栓装置为代表的动脉内机械取栓治疗可为其带来显著临床疗效。机械取栓治疗目的是尽快使闭塞血管恢复血流，进而恢复缺血脑组织的灌注，挽救处于缺血半暗带的脑组织。闭塞血管复流程度是影响 AIS-LVO 患者 MT 术后临床结局的重要和潜在的可被改变的因素之一。目前最常采用改良脑梗死溶栓血流分级（modified Thrombolysis in Cerebral Infarction,mTICI）评分评估闭塞血管的复流程度。闭塞血管成功复流被定义为前向血流恢复至 mTICI≥2b 级，即 mTICI2b 级或 3 级，其中 3 级被定义为完全复流[10]。随着 MT 技术的发展，支架取栓联合颅内支撑导管抽吸取栓技术 （Solitaire FR with intracranial support catheter for mechanical thrombectomy，SWIM）开始得到广泛地应用，其使得闭塞血管的成功复流率明显提升[11]。使用 SWIM 技术行机械取栓后，绝大多数患者的闭塞血管都能达到成功复流（mTICI≥2b），但在成功复流的基础上，只有部分患者能达到完全复流（mTICI 3 级）。近年来，多项研究显示行 MT 治疗的患者，其闭塞血管术后复流达 mTICI3 级，比 2b 级有更好的临床预后，临床上应将复流至 mTICI3 级作为取栓手术技术成功的理想目标[12, 13]。

有研究报道，炎症反应也是AIS的重要病理生理学基础之一。AIS发生时，体内炎症反应被激活，进而在后续的继发性神经损伤中发挥重要作用[14]。近年来，炎症反应不仅是AIS治疗的新靶点，同时也被部分研究者用于预测AIS患者的预后[15]。研究显

示，中性粒细胞与淋巴细胞在AIS发展过程中的作用不尽相同，中性粒细胞会在AIS早期浸润缺血部位并释放导致脑组织损伤的相关化学物质[16]，而淋巴细胞则被认为是神经细胞的重要保护性调节剂之一，其数量的减少可能导致神经功能恶化[17]。已有研究表明中性粒细胞与淋巴细胞比值（Neutrophil-to-Lymphocyte Ratio，NLR）可以反映全身炎症水平，与心脑血管疾病的发生和预后关系密切[18-20]。并且最近已有研究结果显示患者血小板和淋巴细胞比值（Platelet-to-Lymphocyte Ratio,PLR）与接受机械取栓治疗的AIS患者的闭塞血管复流程度之间存在关系[21]，这可能是因为炎症反应与血小板活化及血栓形成之间也存在一定关系。

机械取栓术的中心环节是将闭塞段血管内的血栓从体内取出到体外，这使得对血栓的病理组织成分进行研究成为可能。研究血栓的病理组织成分，可能有利于术前筛选更适合行MT治疗的AIS-LVO患者，或对术中手术器材选择提供依据。研究者通常对血栓行病理学染色后将其分为红细胞、纤维蛋白/血小板、白细胞成分[22, 23]。Shin [24]及Hashimoto等[25]的研究均发现，MT术后成功复流（mTICI≥2b）患者取出血栓中的红细胞百分比，显著高于未成功复流（mTICI＜2b）患者的血栓红细胞百分比。这可能是因为高红细胞含量的血栓，在其红细胞聚集区域更柔软，且具有较低摩擦系数，所以更易于血栓的清除[26]。但也有研究显示，富含红细胞的血栓在取栓的过程中更容易“碎片化”[27, 28]，这可能在术中更容易出现“血栓逃逸”，导致远端小血管栓塞进而影响闭塞血管是否能成功复流。但目前在MT术后已成功复流（mTICI≥2b）的患者中，闭塞血管是否能够完全复流与血栓病理组织成分之间的关系尚缺乏有效研究。

NLR值可以一定程度上反映炎症反应水平。而炎症反应一方面在血栓形成过程中可以促进相关化学物质分泌，以促进血小板聚集及血栓形成。另一方面，炎症细胞，尤其是中性粒细胞又可以削弱血栓的稳定性进而改变血栓结构和物理特性[29]。目前，NLR是否与AIS-LVO患者血栓的病理组织成分之间存在一定的关系，尚缺乏相关研究。如果NLR也能一定程度上反映患者血栓病理组织成分组成，则可在患者在接受MT治疗之前通过简单的外周血检查初步判定患者的血栓病理组织组成。

基于上述研究背景，本研究第一部分探索接受机械取栓治疗后，成功复流的前循环大血管闭塞性急性缺血脑卒中患者，其术前中性粒细胞和淋巴细胞比值（NLR），是否为影响闭塞血管达到完全复流的相关影响因素。第二部分探索机械取栓术取出血栓的病理组织学成分与闭塞血管是否完全复流之间的关系，以及血栓病理组织成分与

NLR值之间是否同样存在一定关系。进而为接受机械取栓治疗的，前循环大血管闭塞性急性缺血脑卒中患者的筛选、取栓技术的应用、以及预后的判定提供更多参考依据。

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