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· 专题报道 ·

# 不同机制大动脉粥样硬化型脑卒中基线特征和血管内治疗后结局比较：DIRECT-MT 研究亚组回顾性分析

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［摘要］ **目的**　比较颅内大血管伴 / 不伴同侧颈内动脉闭塞的前循环大动脉粥样硬化（LAA）型脑卒中患者行血管内治疗后的结局。**方法**　对多中心随机临床试验 DIRECT-MT 亚组进行回顾性分析，比较接受血管内治疗的孤立颅内动脉闭塞 LAA 型卒中患者（颅内闭塞组）和伴有同侧颈内动脉颅外段闭塞的串联闭塞 LAA 型卒中患者（串联闭塞组）的基线特征和预后，分析不同机制学特征（动脉粥样硬化或动脉－动脉栓塞）对临床结局的影响。**结果**　LAA 型卒中患者共 108 例，其中串联闭塞组 63 例，颅内闭塞组 45 例。颅内闭塞组有高血压史的患者比例高于串联闭塞组［77.8%（35/45）vs 52.4%（33/63），$P$=0.007］。颅内闭塞组闭塞部位最常见于大脑中动脉 M1 段（88.6%，39/44），而串联闭塞组颅内闭塞主要位于颈内动脉颅内段（49.2%，31/63）和大脑中动脉 M1 段（49.2%，31/63）（$P$<0.001）。两组患者在年龄、性别、术前抗栓和他汀类药物的使用、卒中史、心房颤动史、吸烟史、基线改良 Rankin 量表（mRS）评分、基线美国国立卫生研究院卒中量表（NIHSS）评分、是否行静脉溶栓、侧支循环以及救治流程时间等方面差异无统计学意义（$P$ 均>0.05）。两组 90 d mRS 评分为 0～2 分的患者比例差异无统计学意义［53.3%（24/45）vs 41.9%（26/62），$P$=0.243］。颅内闭塞组术后成功再灌注率高于串联闭塞组［93.3%（42/45）vs 77.4%（48/62），$P$=0.026］，但术后 24～72 h 血管再通率低于串联闭塞组［57.1%（24/42）vs 77.2%（44/57），$P$=0.034］，最终梗死体积小于串联闭塞组［20.1（0.3，65.3）mL vs 34.5（19.9，124.6）mL，$P$=0.025］。术后 NIHSS 评分、90 d 欧洲五维五水平量表评分和巴塞尔指数评分为 95 或 100 分的患者比例等其他次要结局在两组间差异无统计学意义（$P$ 均>0.05）。两组 90 d 内的死亡率、无症状性和症状性颅内出血的发生率、5～7 d 时其他血管区域脑梗死的发生率及新流域栓塞的发生率差异无统计学意义（$P$ 均>0.05）。**结论**　动脉粥样硬化导致的串联闭塞相较于孤立颅内闭塞，末次造影成功再灌注率较低，梗死体积更大，但术后 24～72 h 血管再通率较高，且神经功能良好预后率和不良事件发生率与颅内闭塞相仿。

［关键词］ 大动脉粥样硬化型脑卒中；串联闭塞；颅内闭塞；临床结局
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## Comparison of baseline characteristics and outcomes after endovascular treatment of large artery atherosclerosis stroke with different mechanisms: retrospective subgroup analysis of DIRECT-MT trial

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［**Abstract**］ **Objective**　To compare the outcomes of patients with anterior circulation large artery atherosclerosis (LAA) stroke with or without ipsilateral internal carotid artery occlusion after endovascular treatment. **Methods**　The subgroups of a multicenter randomized clinical trial DIRECT-MT were retrospectively analyzed. The baseline characteristics and prognoses of patients with LAA stroke with isolated intracranial artery occlusion (intracranial occlusion group) and LAA

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stroke with tandem occlusion (tandem occlusion group) with ipsilateral extracranial internal carotid artery occlusion were compared, and the effects of different mechanism characteristics (atherosclerosis or arterial embolism) on clinical outcomes were analyzed. **Results** There were 108 patients with LAA stroke, including 63 cases in the tandem occlusion group and 45 cases in the intracranial occlusion group. The proportion of patients with hypertension history in the intracranial occlusion group was higher than that in the tandem occlusion group (77.8% ［35/45］ vs 52.4% ［33/63］, $P$=0.007). The most common site of intracranial occlusion in the intracranial occlusion group was the middle cerebral artery M1 segment (88.6%, 39/44), while those in the tandem occlusion group were the internal carotid artery intracranial segment (49.2%, 31/63) and the middle cerebral artery M1 segment (49.2%, 31/63) ($P$<0.001). There were no significant differences in age, gender, preoperative use of antithrombotic drugs or statins, history of stroke, atrial fibrillation or smoking, baseline modified Rankin scale (mRS) or National Institutes of Health stroke scale (NIHSS) score, whether receiving intravenous thrombolysis or not, collateral circulation, or treatment process time between the 2 groups (all $P$>0.05). There was no significant difference in the proportions of patients with 90-d mRS score of 0-2 between the 2 groups (53.3% ［24/45］ vs 41.9% ［26/62］, $P$=0.243). The successful reperfusion rate in the intracranial occlusion group was higher than that in the tandem occlusion group (93.3% ［42/45］ vs 77.4% ［48/62］, $P$=0.026), but the proportion of vascular recanalization within 24-72 h after surgery was lower than that in the tandem occlusion group (57.1% ［24/42］ vs 77.2% ［44/57］, $P$=0.034), and the final infarct volume was smaller than that in the tandem occlusion group (20.1 ［0.3, 65.3］ mL vs 34.5 ［19.9, 124.6］ mL, $P$=0.025). There were no significant differences in other secondary outcomes such as postoperative NIHSS score, 90-d EuroQoL Group 5-dimension 5-level self-report questionnaire on health-related quality of life (EQ-5D-5L) score or Barthel index between the 2 groups (all $P$>0.05). The mortality within 90 d, the incidence of asymptomatic and symptomatic intracranial hemorrhage, the incidence of cerebral infarction in other vascular regions at 5-7 d, and the incidence of embolization in a new territory were similar between the 2 groups, with no significant differences (all $P$>0.05 ). **Conclusion** Compared with isolated intracranial occlusion, tandem occlusion caused by atherosclerosis has a lower successful reperfusion rate on the last angiography and a larger infarct volume, but the vascular recanalization rate is higher at 24-72 h after surgery, and the good prognosis rate of neurological function and the incidence of adverse events are similar to those of intracranial occlusion.

［**Key words**］ large artery atherosclerosis stroke; tandem occlusion; intracranial occlusion; clinical outcomes

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Org 10172急性脑卒中治疗试验（Trial of Org 10172 in Acute Stroke Treatment，TOAST）分型是国际上广泛采用的缺血性脑卒中分型方式[1]。而2011年提出的中国缺血性脑卒中亚型（Chinese ischemic stroke subclassification，CISS）一定程度上弥补了TOAST分型对发病机制探讨的欠缺，其中大动脉粥样硬化（large artery atherosclerosis，LAA）型在CISS分型体系中，进一步对颅内/外大动脉粥样硬化所导致急性缺血性卒中的潜在发病机制进行了分类，包括载体动脉斑块或血栓阻塞穿支动脉、动脉-动脉栓塞、低灌注/栓子清除下降和混合机制[2]。尽管同为LAA型卒中，伴或不伴同侧颈动脉闭塞的颅内动脉闭塞的患者其发病机制可能不同。

颅内动脉伴同侧颈动脉闭塞也称串联闭塞，在急性缺血性脑卒中患者中占比高达20%[3]。动脉粥样硬化和夹层是导致串联闭塞的主要机制，其中动脉粥样硬化占78%[4]。在急性动脉粥样硬化血栓形成中，斑块破裂是主要的诱发事件，其潜在的促血栓物质暴露会引发血栓形成[5]，而疏松的血栓脱落导致下游血管闭塞，闭塞可以发生在颈内动脉颅内段、大脑中动脉M1段或更远端，也称动脉-动脉栓塞，这是串联闭塞的重要机制之一。尽管静脉溶栓可以溶解或减少血栓，提高血管再通率，但由于串联闭塞的闭塞范围较长，其静脉溶栓的血管再通率仅为4%～32%[6]。因此，串联闭塞被认为是大血管闭塞性缺血性脑卒中单纯静脉溶栓治疗预后不良的独立预测因素[7]。尽管近年来血管内治疗被推荐为急性缺血性卒中大血管闭塞的首选方法，但在这些评估血管内治疗疗效的随机对照试验中，串联闭塞患者大多被排除在外[8-9]。血管内治疗的主要随机对照试验中包括的串联闭塞患者相对

较少，并且伴有同侧颈内动脉闭塞的患者通常没有设立单独研究方案或进行相关事后分析。有限的研究发现，前循环串联闭塞患者也可以受益于血管内治疗，并优于单纯静脉溶栓[10-11]。然而，与孤立的颅内闭塞相比，仍然缺乏关于串联闭塞患者血管内治疗策略的大型随机对照试验研究，相关指南无法给出关于其最佳管理的确切建议[9]。

本中心牵头的一项多中心随机临床试验DIRECT-MT结果显示，伴有大血管闭塞且症状出现时间不超过4.5 h的急性缺血性脑卒中患者，单纯血管内取栓的神经功能结局不劣于取栓术前给予阿替普酶静脉溶栓[12]。本研究对DIRECT-MT研究亚组进行了回顾性分析，比较接受血管内治疗的串联闭塞和颅内动脉闭塞前循环LAA型卒中患者的基线特征和预后，并探讨不同机制学特征（动脉粥样硬化或动脉-动脉栓塞）对临床结局的影响。

## 1　资料和方法

1.1　研究对象　DIRECT-MT是在中国开展的一项多中心随机临床试验（NCT03469206），旨在明确对于伴有大血管闭塞且症状出现时间不超过4.5 h的急性缺血性脑卒中患者，单纯血管内取栓的疗效是否不劣于取栓术前给予阿替普酶静脉溶栓。在41个中心筛选的1 586例患者中有656例被纳入DIRECT-MT试验，根据TOAST标准对卒中病因进行评估，包括心源性栓塞、LAA和不明原因。LAA卒中定义为血管内取栓后数字减影血管造影（digital subtraction angiography，DSA）显示在非分叉位置闭塞处局部残余狭窄超过50%，或由于同侧颈内动脉颅外段粥样硬化导致的串联闭塞。DIRECT-MT试验中LAA卒中患者全部纳入本研究，并根据是否伴有同侧颈内动脉颅外段闭塞分为颅内闭塞组（孤立颅内动脉闭塞患者）和串联闭塞组（伴有同侧颈内动脉颅外段闭塞的串联闭塞患者）。颅内闭塞的血管内治疗策略包括直接抽吸、支架取出器和2种血栓切除装置组合，串联闭塞患者颈内动脉颅外段的血管内治疗策略包括支架植入、球囊扩张、血管成形术和血栓抽吸。所有入选患者的颅内血管闭塞和串联闭塞患者的颈内动脉颅外段闭塞的血管内治疗策略由介入医师根据患者在手术中的血管状况选择。

1.2　观察指标与临床结局　提取入组患者的基线特征，包括但不限于年龄、性别、就诊时美国国立卫生研究院卒中量表（National Institutes of Health stroke scale，NIHSS）评分、既往病史（高血压、吸烟、糖尿病、心房颤动、卒中）、是否行静脉溶栓和颅内闭塞部位。

主要结局指标是随机分组后90 d（评估时间窗为±14 d）的改良Rankin量表（modified Rankin scale，mRS）评分为0～2分[13]。由经过培训且不知晓分组结果的医师采用标准化表格对患者进行结构化访谈（面对面或电话访谈），并在这一过程中收集结局数据。每次访谈的标准化书面报告提交给结局委员会的2名成员，2人确认评分，达成一致意见。

次要结局指标如下：（1）90 d时的mRS评分；（2）术后成功再灌注，定义为在末次颅内血管造影时脑梗死溶栓扩展量表（extended thrombolysis in cerebral infarction，eTICI）分级为2b、2c或3级[14]；（3）术后24～72 h头颅计算机断层扫描血管成像（computed tomography angiography，CTA）显示血管再通；（4）术后24 h和5～7 d（或出院时）的NIHSS评分[15]；（5）最终梗死病灶体积（通过CT平扫计算）；（6）90 d时的欧洲五维五水平量表（EuroQoL Group 5-dimension 5-level self-report questionnaire on health-related quality of life，EQ-5D-5L）评分[范围为−0.39（最差）至1.00（最佳）]；（7）90 d时的巴塞尔指数（Barthel index，BI）评分[范围为0（重度残疾）至100（无残疾）]为95或100分[16-17]。

安全性结局指标包括：（1）90 d内的死亡率；（2）所有颅内出血和症状性颅内出血（根据Heidelberg出血分类标准判断）[18]；（3）5～7 d时在其他血管区域的新发脑梗死；（4）新流域栓塞。

1.3　统计学处理　采用SPSS 22.0软件分析数据。计数资料的描述使用例数和百分数，两组间比较采用$\chi^2$检验或校正$\chi^2$检验；计量资料的描述采用中位数（下四分位数，上四分位数），两组间比较采用秩和检验。检验水准（$\alpha$）为0.05。

## 2　结　果

2.1　患者基线资料　DIRECT-MT研究中108例LAA型卒中患者全部纳入本研究，其中颅内闭塞组45例，年龄为63（55，68）岁，男性占71.1%（32/45）；串联闭塞组63例，年龄为64（57，

73）岁，男性占84.1%（53/63）。颅内闭塞组患者有高血压史的比例高于串联闭塞组（$P$=0.007）。颅内闭塞组闭塞血管最常见于大脑中动脉M1段（88.6%，39/44），而串联闭塞组颅内闭塞主要位于颈内动脉颅内段（49.2%，31/63）和大脑中动脉M1段（49.2%，31/63）（$P$<0.001）。两组患者在术前抗栓和他汀类药物的使用、卒中史、心房颤动史、吸烟史、基线mRS评分、基线NIHSS评分、是否行静脉溶栓、侧支循环以及救治流程时间等方面差异均无统计学意义（$P$均>0.05）。见表1。

**表1　颅内闭塞组与串联闭塞组LAA型卒中患者基线资料比较**

**Tab 1　Comparison of baseline data of LAA stroke patients between intracranial occlusion group and tandem occlusion group**

| Variable | Intracranial occlusion $N$=45 | Tandem occlusion $N$=63 | Statistic | $P$ value |
|---|---|---|---|---|
| Age/year, $M$ ($Q_L$, $Q_U$) | 63 (55, 68) | 64 (57, 73) | $Z$=1.03 | 0.301 |
| Male, $n$ (%) | 32 (71.1) | 53 (84.1) | $\chi^2$=2.65 | 0.103 |
| Medical history, $n$ (%) | | | | |
| Previous ischemic stroke | 3 (6.7) | 7 (11.1) | $\chi^2$=0.20 | 0.654 |
| Atrial fibrillation | 7 (15.6) | 5 (7.9) | $\chi^2$=1.54 | 0.214 |
| Hypertension | 35 (77.8) | 33 (52.4) | $\chi^2$=7.26 | 0.007 |
| Diabetes mellitus | 10 (22.2) | 15 (23.8) | $\chi^2$=0.04 | 0.847 |
| Smoking | 18 (40.0) | 24 (38.1) | $\chi^2$=0.04 | 0.841 |
| Statin use | 0 | 0 | $\chi^2$=0.00 | 1.000 |
| Antiplatelet agent use | 3 (6.7) | 5 (7.9) | $\chi^2$=0.00 | 1.000 |
| Oral anticoagulant use | 2 (4.4) | 1 (1.6) | $\chi^2$=0.09 | 0.767 |
| mRS score 1 or 2 before stroke onset, $n$ (%) | 2 (4.4) | 3 (4.8) | $\chi^2$=0.00 | 1.000 |
| Baseline NIHSS score, $M$ ($Q_L$, $Q_U$) | 17 (12, 20) | 16 (12, 19) | $Z$=0.45 | 0.653 |
| Baseline SBP/mmHg, $M$ ($Q_L$, $Q_U$) | 151 (132, 166) | 145 (128, 169) | $Z$=0.44 | 0.663 |
| Duration/min, $M$ ($Q_L$, $Q_U$) | | | | |
| From stroke onset to groin puncture | 215 (165, 240) | 200 (153, 248) | $Z$=0.57 | 0.569 |
| From start of alteplase to groin puncture | 37 (15, 45) | 22 (13, 25) | $Z$=1.75 | 0.080 |
| From start of alteplase to reperfusion | 92 (64, 182) | 119 (75, 168) | $Z$=0.56 | 0.576 |
| From groin puncture to reperfusion | 65 (37, 125) | 78 (52, 120) | $Z$=1.35 | 0.176 |
| From stroke onset to reperfusion | 291 (210, 359) | 281 (239, 347) | $Z$=0.04 | 0.970 |
| ASPECT score, $M$ ($Q_L$, $Q_U$) | 8.5 (7.0, 10.0) | 8.0 (7.0, 10.0) | $Z$=0.49 | 0.625 |
| Treatment with intravenous thrombolysis, $n$ (%) | 19 (42.2) | 29 (46.0) | $\chi^2$=0.15 | 0.695 |
| Collateral grade, $M$ ($Q_L$, $Q_U$) | 2 (1, 3) | 2 (1, 3) | $Z$=0.07 | 0.948 |
| Location of intracranial artery occlusion[a], $n$ (%) | | | $\chi^2$=18.79 | <0.001 |
| ICA | 4 (9.1) | 31 (49.2) | | |
| M1 | 39 (88.6) | 31 (49.2) | | |
| M2 | 1 (2.3) | 1 (1.6) | | |

[a]: The information was not available for 1 case in the intracranial occlusion group. 1 mmHg=0.133 kPa. LAA: Large artery atherosclerosis; mRS: Modified Rankin scale; NIHSS: National Institutes of Health stroke scale; SBP: Systolic blood pressure; ASPECTS: Alberta Stroke Program early computed tomography score; ICA: Intracranial artery; M1: M1 segment of middle cerebral artery; M2: M2 segment of middle cerebral artery; $M$ ($Q_L$, $Q_U$): Median (lower quartile, upper quartile).

2.2　*主要及次要结局比较*　串联闭塞组1例患者的主要和次要结局数据缺失，本研究未对缺失数据进行填补。主要结局90 d mRS评分为0～2分的患者比例在颅内闭塞组与串联闭塞组之间差异无统计学意义（$P$=0.243）。次要结局中，颅内闭塞组术后成功再灌注率高于串联闭塞组（$P$=0.026），但术后24～72 h血管再通率低于串联闭塞组（$P$=0.034）。颅内闭塞组最终梗死体积小于串联闭塞组（$P$=0.025）。术后NIHSS评分、90 d EQ-5D-5L评分和BI为95或100分的患者比例等其他次要结局在两组间差异无统计学意义（$P$均>0.05）。

**表 2　颅内闭塞组与串联闭塞组 LAA 型卒中患者主要结局及次要结局比较**

**Tab 2　Comparison of primary and secondary outcomes of LAA stroke patients between intracranial occlusion group and tandem occlusion group**

| Outcome | Intracranial occlusion $N$=45 | Tandem occlusion $N$=62 | Statistic | $P$ value |
|---|---|---|---|---|
| Good function at 90 d, $n$ (%) | | | | |
| mRS score 0-2 | 24 (53.3) | 26 (41.9) | $\chi^2$=1.36 | 0.243 |
| mRS score 0-1 | 15 (33.3) | 19 (30.6) | $\chi^2$=0.09 | 0.768 |
| mRS score at 90 d, $M$ ($Q_L$, $Q_U$) | 2 (0, 5) | 3 (1, 4) | $Z$=0.20 | 0.843 |
| NIHSS score, $M$ ($Q_L$, $Q_U$) | | | | |
| After 24 h | 9 (3, 17) | 10 (4, 18) | $Z$=0.71 | 0.475 |
| At 5-7 d or discharge | 4 (1, 13) | 6 (1, 13) | $Z$=0.38 | 0.704 |
| Barthel index of 95 or 100 at 90 d, $n$ (%) | 26 (57.8) | 36 (58.1) | $\chi^2$=0.00 | 0.976 |
| EQ-5D-5L score at 90 d, $M$ ($Q_L$, $Q_U$) | 0.98 (0.78, 1.00) | 0.89 (0.60, 1.00) | $Z$=1.87 | 0.061 |
| Successful reperfusion (eTICI 2b-3), $n$ (%) | 42 (93.3) | 48 (77.4) | $\chi^2$=4.94 | 0.026 |
| Recanalization rate at 24-72 h[a], $n$ (%) | 24 (57.1) | 44 (77.2) | $\chi^2$=4.52 | 0.034 |
| Median lesion volume on CT/mL, $M$ ($Q_L$, $Q_U$) | 20.1 (0.3, 65.3) | 34.5 (19.9, 124.6) | $Z$=2.24 | 0.025 |

[a]: The information was not available for 3 cases in the intracranial occlusion group and 5 cases in the tandem occlusion group. LAA: Large artery atherosclerosis; mRS: Modified Rankin scale; NIHSS: National Institutes of Health stroke scale; EQ-5D-5L: EuroQoL Group 5-dimension 5-level self-report questionnaire on health-related quality of life; eTICI: Extended thrombolysis in cerebral infarction; CT: Computed tomography; $M$ ($Q_L$, $Q_U$): Median (lower quartile, upper quartile).

见表 2。

2.3　*安全性结局比较*　两组在 90 d 内的死亡率、无症状性颅内出血和症状性颅内出血的发生率、5～7 d 时其他血管区域脑梗死的发生率及新流域栓塞的发生率均相似，差异无统计学意义（$P$ 均＞0.05，表 3）。

**表 3　颅内闭塞组与串联闭塞组 LAA 型卒中患者 90 d 内安全性结局比较**

**Tab 3　Comparison of safety outcomes of LAA stroke patients within 90 d between intracranial occlusion group and tandem occlusion group**

$n$ (%)

| Variable | Intracranial occlusion $N$=45 | Tandem occlusion $N$=63 | $\chi^2$ value | $P$ value |
|---|---|---|---|---|
| Death | 11 (24.4) | 8 (12.7) | 2.50 | 0.114 |
| Asymptomatic intracranial hemorrhage | 11 (24.4) | 23 (36.5) | 1.77 | 0.183 |
| Symptomatic intracerebral hemorrhage | 2 (4.4) | 4 (6.3) | 0.00 | 1.000 |
| Infarction in new territory at 5-7 d | 4 (8.9) | 1 (1.6) | 1.73 | 0.188 |
| Embolization in a new territory | 0 | 6 (9.5) | 2.90 | 0.088 |

LAA: Large artery atherosclerosis.

## 3　讨　论

本研究共纳入 TOAST 分型为 LAA 的颅内大血管闭塞导致的急性缺血性脑卒中患者 108 例，其中孤立颅内动脉闭塞患者（颅内闭塞组）45 例，伴有同侧颈内动脉颅外段闭塞的串联闭塞患者（串联闭塞组）63 例。颅内闭塞组有高血压史的患者比例高于串联闭塞组，且两组颅内闭塞部位的分布不尽相同；术后 90 d 良好预后率（mRS 评分为 0～2 分的患者比例）两组差异无统计学意义，术后成功再灌注率颅内闭塞组高于串联闭塞组，早期再通率则相反；最终梗死体积颅内闭塞组小于串联闭塞组；90 d 生活质量评估（EQ-5D-5L 评分和 BI 为 95 或 100 分的患者比例）两组间差异无统计学意义。

本研究中两组患者的高血压、吸烟、糖尿病史比例高，这些均为动脉粥样硬化的危险因素。ESCAPE 研究的事后分析数据发现，与颅内闭塞患者相比，串联闭塞患者更年轻、以男性为主、糖尿病患病率和吸烟者比例更高[19]。此外，在 WAKE-UP 研究中，吸烟在大动脉疾病中更常见[20]。吸烟主要对颅外血管有影响，这一观点已在中国人和白种人人群中被确认，男性和高血压被确定为独立的额外危险因素[21-22]。而串联闭塞患者中有高血压史的比例相较于颅内闭塞患者更高[23]。但本研究中串联闭塞组有高血压史的患者比例低于颅内闭塞组，可能与研究对象均为 LAA 型卒中造成的选择

偏倚有关。

尽管本研究两组患者合并动脉粥样硬化相关危险因素比例高，但卒中前抗血小板及他汀类药物使用率低，提示动脉粥样硬化的早期筛查和一级预防应予以重视。此外，颅内闭塞组闭塞血管最常见于大脑中动脉M1段，而串联闭塞组颅内闭塞主要位于颈内动脉颅内段和大脑中动脉M1段。在颅内动脉粥样硬化狭窄导致的大血管闭塞性急性缺血性脑卒中患者中，闭塞多位于大脑中动脉M1段的平直段和基底动脉中段，而栓塞导致的大血管闭塞性急性缺血性脑卒中闭塞多位于血管分叉段[24]，提示串联闭塞可能为动脉－动脉栓塞机制有一定的合理性。

本研究结果显示，颅内闭塞组术后最终成功再灌注率高于串联闭塞组。串联闭塞即为再灌注失败的因素之一，此外血栓特性、其负荷或不同的闭塞病理机制（动脉粥样硬化闭塞）及闭塞血管的解剖学特征也影响再灌注结果[25]。一项大型国际多中心队列研究比较了大血管串联闭塞的急性缺血性脑卒中患者，在颅内动脉取栓前先行颈动脉成形和/或支架成形术与先治疗颅内动脉闭塞的成功再灌注率，结果显示2种处理方式的成功再灌注率相似，但前者达到成功再灌注的速度更快[26]。也有研究报道，颅内动脉粥样硬化性狭窄（intracranial atherosclerotic stenosis，ICAS）导致的大血管闭塞同样也会出现再通失败，作为ICAS典型特征的主干型闭塞与取栓支架回收失败相关[27]。

尽管本研究中颅内闭塞组最后成功再灌注比例高于串联闭塞组，但24～72 h经CTA证实的血管再通率前者却低于后者，提示颅内闭塞患者术后恢复灌注后发生再闭塞的比例高于串联病变组。与栓塞引起的大血管闭塞相比，支架回收和抽吸血栓切除技术在ICAS所致的大血管闭塞中效果较差，血管内手术期间再通率明显较低，再闭塞率较高，穿刺至再灌注时间较长[28]。而串联闭塞的颅内病变类似于栓塞事件，因此血管再通治疗后再闭塞的风险较低。此外，颅内闭塞血管经机械取栓或吸栓后，对存在残余狭窄的血管较少行支架植入术，而串联闭塞的颅内血管再通后残余狭窄发生率低，颅外闭塞段行球囊扩张、支架植入等血管成形术的比例高，相应地降低了颅内血管再闭塞的风险[29-30]。

颅内大血管闭塞的可能原因包括颅内动脉粥样硬化、来自近端血管的动脉－动脉栓塞、心源性栓塞或隐源性原因[31]。LAA型卒中的颅内闭塞通常是由于动脉粥样硬化原位血栓形成，而串联病变引起的颅内闭塞更常见的原因是颈内动脉颅外段的动脉粥样硬化病变导致的颅内动脉栓塞（动脉－动脉栓塞）[32]。本研究中颅内闭塞组平均梗死体积小于串联闭塞组，可能的原因是颅内动脉粥样硬化原位血栓形成引起的急性闭塞侧支循环代偿良好，核心梗死体积较小。而串联闭塞组颅外段颈内动脉闭塞导致的缺血脑组织体积更大，且发生动脉－动脉栓塞后闭塞血管供血区侧支代偿不能及时建立，加上闭塞血管早期成功再灌注率低于颅内闭塞组，从而梗死体积亦较颅内闭塞组增大。

多项回顾性研究发现串联闭塞和颅内闭塞之间的临床结局相当[33-35]，本研究结果与之一致，串联闭塞和颅内闭塞组获得良好临床结局的患者比例分别为41.9%（26/62）和53.3%（24/45），死亡率分别为12.7%（8/63）和24.4%（11/45）。ESCAPE研究和MR CLEAN研究在比较串联病变患者和非串联病变患者的结局和死亡率时亦发现两者差异没有统计学意义[19,36]。

本研究两组患者无症状性及症状性颅内出血、90 d内死亡及其他临床不良事件之间比较，差异均无统计学意义。关于机械取栓单独、联合血管成形术或联合使用颈动脉支架植入术治疗串联闭塞的效果哪个更好，目前还缺乏相关数据。有研究比较了急性前循环串联闭塞患者颈动脉支架植入术联合机械取栓术和颈动脉血管成形术联合机械取栓术的疗效，发现在紧急情况下，接受2种不同方式治疗的患者在功能结局、死亡率和围手术期卒中率方面没有显著差异。然而，支架植入术联合机械取栓治疗的患者出现症状性颅内出血的风险增加，这可能是因为支架植入后使用了额外的抗血小板药物[37]。

串联病变常指颅内大血管闭塞合并同侧颈内动脉颅外段闭塞或重度狭窄[38]。HERMES分析确认了血管内治疗在串联病变中的有效性[5]。据报道，大血管闭塞约占急性缺血性脑卒中的30%[39]，其中串联闭塞约占大血管闭塞的10.7%[40]。串联闭塞的病理变化比单一大血管闭塞更复杂，由于其在大型队列研究中往往被排除在外，对其临床特征及预后等因素知之甚少。

本研究存在以下局限性。（1）这是一项亚组数据的回顾性研究，存在一定的偏倚。（2）研究对象为LAA型卒中患者，排除了来源不明的栓塞

性卒中患者中一部分因动脉粥样硬化导致颅内闭塞的患者，存在一定的选择偏倚。后期还需要开展更全面、随访时间更长的多中心临床研究，以进一步验证本研究结果。

综上所述，TOAST 分型同为 LAA 型卒中的患者发病机制不尽相同，动脉粥样硬化导致的串联闭塞相较于孤立颅内动脉闭塞，虽然总体成功再灌注率较低、梗死体积更大，但术后 24～72 h 血管再通率却更高，且神经功能良好预后率和不良事件发生率均与颅内闭塞相仿。尽管在串联闭塞患者中存在病理生理学机制的不同和对颅外病变最佳治疗方法的不确定性，但经血管内治疗后串联闭塞和孤立颅内动脉闭塞患者取得了近似同等的效果，因此对串联闭塞病例应积极进行治疗。

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