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系统性炎症反应指数预测急性前循环大血管闭塞取栓预后的研究进展

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摘　要

急性前循环大血管闭塞(ACALVO)是神经血管外科的急重症，具有极高的致死致残率。尽管机械取栓(MT)已成为其标准治疗方案，但仍有约50%的患者面临“无效再通”的困境。因此急需一个简便、经济且易于获取的生物标志物来辅助临床进行早期风险分层和预后判断。系统性炎症反应指数(SIRI)作为一种基于外周血中性粒细胞、单核细胞和淋巴细胞计数所得的新型炎症标志物，对ACALVO患者MT后无效再通、功能预后具有独特的预测价值。本文系统地梳理了SIRI预测ACALVO患者MT预后的相关研究进展，旨在为临床医生提供有价值的参考，以促进其临床决策的科学化。未来还需多中心、大样本的前瞻性研究来验证其临床效用，以推动其在临床的广泛应用。

关键词

系统性炎症反应指数，急性前循环大血管闭塞，机械取栓，无效再通

Research Progress on the Systemic Inflammation Response Index in Predicting Prognosis after Thrombectomy for Acute Anterior Circulation Large Vessel Occlusion

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Abstract

Acute Anterior Circulation Large Vessel Occlusion (ACALVO) is a critical emergency in neurovascular surgery. It has extremely high rates of death and disability. Mechanical thrombectomy (MT) has become the standard treatment. Yet about 50% of patients still face the problem of "futile recanalization". Therefore, a simple, inexpensive, and easily accessible biomarker is urgently needed. It can assist in early risk stratification and prognosis assessment. The systemic inflammation response index (SIRI) is a novel inflammatory biomarker. It is calculated from peripheral blood neutrophil, monocyte, and lymphocyte counts. SIRI has unique predictive value for futile recanalization after MT in ACALVO patients. It also has predictive value for functional outcome. This article systematically reviews the relevant research progress. The aim is to provide a valuable reference for clinicians. This can help make clinical decision-making more scientific. Future multicenter, large-sample prospective studies are needed to validate its clinical utility. This will promote its widespread clinical application.

Keywords

Systemic Inflammation Response Index, Acute Anterior Circulation Large Vessel Occlusion, Mechanical Thrombectomy, Futile Recanalization

1. 引言

1.1. ACALVO 取栓治疗现状与“无效再通”的挑战

急性缺血性卒中(AIS)是全球第二大死亡原因，也是全球第三大致残原因[1]。在中国，每年新发 AIS 病例约 240 万例，死亡率为 159/10 万人，这使得其成为头号死因[2]。在 AIS 病例中，大血管闭塞的病例占 24%~46% [3]。由于大血管闭塞的严重性以及静脉溶栓治疗的疗效不佳，大血管闭塞性卒中患者死亡或功能障碍的风险约为非大血管闭塞性卒中患者的两倍[4]。近年来，以 MT 为核心的血管内治疗取得了突破性进展。多项随机对照试验和荟萃分析均表明，将 MT 与标准医学治疗相结合，能显著改善 ACALVO 患者的功能预后[4]。MT 已成为 ACALVO 所致缺血性卒中的标准治疗方法[5]。不过，尽管这些患者在规定的时间内实现了血管再通，但仍有约 50%的患者在 90 天后依然无法恢复自主生活能力。这类患者被称为“无效再通患者”[6]。因此，急需能早期、便捷反映这种全身炎症状态的标志物，来辅助早期风险分层和临床决策。

1.2. 卒中后免疫炎症的双重作用与 SIRI 的生物学基础

以往研究多通过临床评分和影像学检查来评估 AIS 患者的预后。但近年来，反映全身及神经炎症的生物标志物成为了临床研究的热点[7]。在 AIS 中免疫系统具有双重作用：一方面会增加血脑屏障(BBB)的通透性，促进神经元的损伤[8]-[10]。另一方面在其亚急性期和慢性期也会进行神经修复、血管生成和细胞碎片清除。此外，相关研究[11]-[13]发现 AIS 患者缺血的脑组织中有相关的炎症细胞(如中性粒细胞、淋巴细胞和单核细胞)浸润。这些炎症细胞在 AIS 中发挥着不同的作用。外周循环的中性粒细胞可在缺血后 6 小时内进入脑实质，通过释放氧自由基直接加重缺血区细胞坏死和凋亡[14]-[16]。此外，中性粒细胞

已被证明是 AIS 后 24 小时内基质金属蛋白酶-9 (MMP-9)的重要来源，而 MMP-9 与 AIS 后血脑屏障破坏、脑组织水肿、出血性转化和神经功能障碍密切相关[17] [18]。单核细胞是 AIS 后另一个重要的炎症触发因子。AIS 发病后，外周单核细胞增加并向缺血脑组织迁移，扩大了损伤区域[19]。与中性粒细胞和单核细胞不同，一些特定的淋巴细胞，如 T-reg 细胞，是 AIS 后主要的脑保护性免疫调节细胞[20]。如前所述，实验研究表明中性粒细胞和单核细胞可加重 AIS 的损伤，而淋巴细胞却表现出一定的神经保护作用。SIRI 定义为中性粒细胞计数 × 单核细胞计数/淋巴细胞计数，因此，SIRI 的增加可能意味着更大的破坏作用和相对较弱的保护作用，其可以作为 AIS 炎症状态的重要指标[15] [19]-[21]。

2. SIRI 概述

2.1. SIRI 的定义、计算与免疫学内涵

2016 年在确定胰腺癌患者化疗的备选药物中，Qi 等人[22]首次提出了“SIRI = 中性粒细胞计数 × 单核细胞计数/淋巴细胞计数”的概念。大量研究[23]-[26]表明，SIRI 对癌症患者的预后具有独特的预测价值。随着研究的深入，其预测价值也被逐渐应用在以炎症为主的疾病(如 AIS)中[27]。

2.2. SIRI 在脑血管病领域的早期探索

尽管 SIRI 已被定义为可用于恶性肿瘤患者的预后标志物，但其诊断性能也在许多以炎症为主导的疾病中得到了研究。例如，一项 2021 年的研究[28]旨在评估 SIRI 在识别缺血性卒中患者中的诊断性能，结果发现 SIRI 是 90 天全因死亡率的独立预测因子，尽管其预测性能并不理想(AUC = 0.622；95%置信区间：0.598~0.645)。另一项 2022 年的研究[21]报道，SIRI 是缺血性脑卒中患者不良功能预后的独立预测因子，且具有中等的预测效能(AUC = 0.714；95%置信区间：0.658~0.765)。

3. SIRI 在 ACALVO 取栓中的核心研究进展

3.1. 预测功能预后

3.1.1. SIRI 对大动脉闭塞患者 MT 后临床预后的预测价值

2021 的一项研究[29]纳入了 440 名因大动脉闭塞接受 MT 治疗的患者，采集入院时的实验室指标用于计算 SIRI。3 个月时采用改良 Rankin 量表评估预后，将改良 Rankin 量表评分为 0~2 的定义为良好的临床结局。通过受试者工作特征(ROC)曲线分析，确定 SIRI 预测临床结局的最佳截断值。同时通过多因素分析评估 SIRI 与临床结局之间的关系。结果[29]：在 ROC 曲线分析中，SIRI 的最佳临界值分别为 2.9 (曲线下面积分别为 0.799，95%置信区间 0.756~0.843，$P < 0.001$)。多因素分析显示，SIRI < 2.9 (优势比为 2.27，95%置信区间 1.29~5.17，$P = 0.019$)是 MT 术后良好临床结局的独立预测因子。SIRI 的降低与 MT 术后的良好临床预后相关。因此，SIRI 是大动脉闭塞患者接受 MT 时的潜在预后因素[29]。

3.1.2. SIRI 对预测“无效再通”的特殊价值

尽管血管内治疗(EVT)技术和设备的不断更新，导致再通率高达 94% [30] [31]，但其临床疗效尚未完全实现。近一半成功再通的患者(mTICI 2b-3 级)在 90 天后没有实现功能独立(mRS 0~2 分) [32]。这种血管造影再灌注成功与临床结果不佳之间的差异被称为“无效再通”，发生在 30%~50%的病例中[33]。2026 年的一项研究[34]结果表明，较高的基线 SIRI 水平是大血管闭塞性卒中患者在接受血管内治疗并实现成功再通后 90 天功能预后不良风险增加的独立相关因素。SIRI 可以作为一种与早期预后相关的现成生物标志物，并可能在预后评估中具有潜在价值，因为它的预测价值可能对功能恢复更有意义，而非出血性并发症，因此在临床预后评估中有其独特的潜在价值[34]。

3.2. 预测出血转化

3.2.1. SIRI 与中性粒细胞源性基质金属蛋白酶-9、血脑屏障损伤的理论联系

中性粒细胞是 AIS 后的第一反应者。研究表明[35]，术前中性粒细胞已被确定为 ACALVO 患者 EVT 后不良预后的独立预测因子。淋巴细胞对炎症消退和修复至关重要[36]。AIS 发生后由于生理应激，淋巴细胞发生反应性减少，而淋巴细胞的减少与更大的梗死面积和早期神经功能恶化相关[37]。单核细胞通过释放蛋白酶如基质金属蛋白酶-9 导致组织损伤[38]。在炎症反应的初始阶段，外周血单核细胞和内皮细胞释放组织因子[39] [40]，并上调内皮细胞中纤溶酶原激活物抑制剂-1 (PAI-1)的表达[41]。这一系列反应可能最终导致缺血脑组织的进一步损伤[42]。

3.2.2. SIRI 对出血性转化的预测

已有充分证据表明，出血性转化(HT/sICH)是 AIS 患者接受再灌注治疗后出现神经功能恶化及长期预后不良的独立危险因素[43]-[45]。2024 的一项研究[46]结果表明，第 1 天的 SIRI 可作为 ACALVO 取栓后 sICH 发生的独立预测因子。但 2026 的一项研究[34]结果却显示，SIRI 与 HT/sICH 之间未见关联。尽管已有研究[47] [48]表明炎症可破坏血脑屏障并促进 HT 的发生，但其阴性结果提示，以入院时采集的单次 SIRI 所反映的全身炎症状态，可能并非 EVT 术后 HT 并发症的主要驱动因素。这可能是因为 HT 受到其他因素(例如缺血性损伤的范围、再灌注的强度以及操作技术)的影响。此外，再灌注后炎症的动态变化并未被基线值所捕捉，而这些变化或许与 HT 的发病机制更为相关。有必要开展后续研究，通过连续的 SIRI 来验证这一假设[34]。

3.3. SIRI 在 AIS 中预后评估与临床管理中的应用价值

研究表明[49] [50]，AIS 患者 SIRI 水平升高与早期神经功能恶化、卒中相关性肺炎及认知障碍风险增加有关[51]-[53]。另有研究表明[54]，较高的 SIRI 水平可能会对颅内斑块易损性产生不利影响，从而导致脑缺血患者更严重的缺血和复发。还有研究[55]的荟萃分析显示了 SIRI 作为指导治疗决策和优化卒中护理资源分配的预后生物标志物的潜在优势。将 SIRI 纳入预后模型可以加强风险分层，使临床医生能够尽早地识别高风险个体，从而在卒中的急性期获得更积极的治疗干预(例如靶向抗炎治疗或强化康复计划)和更密切的监测，以便改善功能恢复和减轻残疾负担[55]。

4. SIRI 与 AIS 不良预后的关联：混杂因素分析及独立预测价值

4.1. 影响 SIRI 的各类混杂因素

研究结果[21]显示，与 AIS 预后良好组相比，预后不良组的年龄更高、NIHSS 评分更高，且心血管疾病和房颤的患病率也更高(所有 P 值均<0.05)。在实验室指标方面，预后不良的患者其中性粒细胞计数、淋巴细胞计数、空腹血糖水平及血清同型半胱氨酸浓度均高于预后良好组(所有 P 值均 $P < 0.05$)。

4.2. 多变量分析：SIRI 独立预测 AIS 不良预后，且呈剂量–反应趋势

多变量逻辑回归分析揭示了 SIRI 与 AIS 不良预后之间的关联。在未调整模型中，SIRI 每增加 1 个标准差，AIS 的不良预后风险升高 2.077 倍($P < 0.01$) [21]。在调整了年龄、性别、种族、BMI、吸烟、饮酒、高血压、糖尿病、心血管疾病史、房颤史、脑卒中后遗症史、低密度脂蛋白、高密度脂蛋白、空腹血糖、同型半胱氨酸、入院时的 NIHSS 评分以及卒中亚型等因素后，SIRI 每增加一个标准差会使不良预后风险额外增加 58.9% ($P = 0.37$)。将 SIRI 划分为四分位时，在全模型中观察到最高四分位的风险是最低四分位的 6.152 倍，且各四分位之间存在显著的趋势(P 趋势检验 P 值为 0.006) [21]。

5. SIRI 与其他炎症指标的横向比较

5.1. SII 与 SIRI 在 AIS 预后预测中的价值比较与研究现状

事实上，提出 SII 和 SIRI 的概念初衷就是通过结合不同的外周血细胞标志物来提升它们的预测能力。SII 是通过血小板计数 × 中性粒细胞计数/淋巴细胞计数计算的，而 SIRI 则是通过差异性白细胞计数来衡量，即中性粒细胞计数 × 单核细胞计数/淋巴细胞计数[56]。研究发现[57]，SII 和 SIRI 均为 AIS 后功能性结局不良的独立预测因子。高 SII 和 SIRI 分别与功能不良风险增加 2.35 倍和 1.69 倍相关。比较两者时，SII 样本量更大，结果更稳健，因为敏感性分析中未丢失统计显著性。目前相关研究不仅样本量较小，而且 SIRI 的相关研究也非常少[57]。未来随着样本量的增加以及研究的深入，SIRI 在预测 AIS 后功能性结局不良的简化与稳健性优势可能会进一步凸显。

5.2. 炎症与免疫生物标志物在 AIS 预后评估中的价值比较

尽管现有研究显示，免疫生物标志物(如 CRP、IL-6 和 TNF-α)浓度升高与 AIS 复发风险增加及不良预后相关[58]。此外，Tu 等人[59]的一项研究结果也显示，鸦铵素浓度降低(其水平与 hs-CRP 和 IL-6 呈负相关)与 AIS 的不良预后有关。然而 CRP、IL-6、TNF-α 和鸦铵素浓度的测定需要在特定的实验室检测，未纳入常规生化检测，因此在入院时不能及时获取其结果。但 SIRI 是通过外周血中性粒细胞计数 × 单核细胞计数/淋巴细胞计数计算所得，其通过外周血常规检查即可获得。因此，SIRI 在临床上更易推广和应用[21]。

6. 现有研究的不足与未来的临床展望

6.1. 从宏观指数到细胞亚群精细化评估

尽管 SIRI 对 ACALVO 患者 MT 后的预后具有其特殊的预测价值，但其作为免疫状态的宏观指标有一定的自身局限性。未来研究有望结合细胞亚群功能(如流式细胞术、单细胞测序等)更精细的炎症指数，以便进行更密切的监测和早期干预，进一步降低 ACALVO 患者的致死致残率，改善患者的预后。

6.2. 从单次基线评估走向标准化动态监测

现有研究多为入院时的 SIRI 与 ACALVO 取栓预后之间的关系，但 SIRI 在住院期间的动态变化尚无明确结论。未来研究应在特定的时间点(如 MT48 小时后、7 天后)进行外周血常规检验并计算出相应的 SIRI，以便进一步探索其与 ACALVO 取栓预后之间的关系。

6.3. 从单中心回顾性研究走向多中心前瞻性验证

目前研究多为样本量较小的单中心回顾性研究。回顾性研究大多未获得有关潜在混杂因素的数据(如饮食摄入和户外体育活动等)，未收集的潜在混杂因素是造成偏倚的主要来源，其研究结果是否适用于所有首次发生 ACALVO 的患者仍有待进一步探讨。未来应开展大规模多中心的前瞻性研究、充分考虑潜在的混杂因素并进行长期随访，以进一步验证其临床疗效，促进其在临床的推广和应用。

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