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STEMI再灌注后微血管阻塞与心肌内出血：从CMR表型到预后与干预

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摘　要

急性ST段抬高型心肌梗死(STEMI)患者急诊经皮冠状动脉介入治疗后，心外膜血流虽可恢复至TIMI 3级，但组织水平仍常存在再灌注不足及无复流现象。微血管阻塞(MVO)与心肌内出血(IMH)是再灌注后微循环损伤的核心影像表型，与左心室不良重构、心功能恢复受限及主要不良心血管事件等风险增高密切相关。心脏磁共振(CMR)技术具有无创、高空间分辨率及多参数成像等优势，可精准识别和评估MVO及IMH，为缺血/再灌注损伤的关键病理过程提供一体化的表征，并有助于进行风险分层。本文围绕MVO与IMH，综述其发生机制、CMR判读要点、预后意义及干预策略，并展望表型驱动的精准治疗方向。

关键词

急性ST段抬高型心肌梗死，微血管阻塞，心肌内出血，心脏磁共振，预后，干预策略

Microvascular Obstruction and Intramyocardial Hemorrhage after Reperfusion in ST-Segment Elevation Myocardial Infarction: From CMR Phenotypes to Prognosis and Management Strategies

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Abstract

In patients with acute ST-segment elevation myocardial infarction (STEMI) undergoing emergent percutaneous coronary intervention (PCI), epicardial coronary flow may be restored to Thrombolysis in Myocardial Infarction (TIMI) grade 3; however, inadequate myocardial tissue reperfusion and the no-reflow phenomenon often persist at the microvascular level. Microvascular obstruction (MVO) and intramyocardial hemorrhage (IMH) are hallmark CMR phenotypes of post-reperfusion microvascular injury and are strongly associated with adverse left ventricular remodeling, limited recovery of ventricular function, and an increased risk of major adverse cardiovascular events. Cardiac magnetic resonance, a noninvasive high-spatial-resolution multiparametric imaging modality, enables robust detection and quantification of MVO and IMH, provides an integrated assessment of key pathological processes underlying ischemia-reperfusion injury, and supports risk stratification. Here, we review the mechanisms of MVO and IMH, highlight practical considerations for CMR acquisition and interpretation, summarize prognostic evidence, and discuss current and emerging therapeutic strategies, with an outlook toward phenotype-driven precision therapy.

Keywords

ST-Segment Elevation Myocardial Infarction, Microvascular Obstruction, Intramyocardial Hemorrhage, Cardiac Magnetic Resonance, Prognosis, Therapeutic Strategies

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1. 引言

急性 ST 段抬高型心肌梗死(ST-segment elevation myocardial infarction, STEMI)的救治核心在于尽早实现梗死相关动脉的再通[1] [2]。尽管急诊经皮冠状动脉介入治疗(primary percutaneous coronary intervention, PPCI)显著降低了 STEMI 急性期死亡率，但冠状动脉造影意义上的血管成功再通并不必然转化为心肌组织层面的有效再灌注[3] [4]。即便在获得 TIMI 3 级血流的患者中，仍有相当比例存在持续的微循环灌注障碍，即无复流(no-reflow)现象[5] [6]。

微血管阻塞(microvascular obstruction, MVO)和心肌内出血(intramyocardial hemorrhage, IMH)是无复流在组织层面的核心病理表现。大量研究表明，二者与不良左室重构、心功能恢复受限及主要不良心血管事件(major adverse cardiovascular events, MACE)显著相关[7]-[9]。深入理解 MVO 与 IMH 的病理生理机制、影像学特征及临床意义，对于优化 STEMI 患者的风险分层和个体化治疗具有重要意义。

2. 病理生理机制：从 MVO 到 IMH 的级联损伤

再灌注诱发的分子级联反应是微循环损伤的始动环节，通过触发内皮损伤、微血管通透性增高及毛细血管结构破坏，为 MVO 与 IMH 的发生奠定病理基础。该过程主要涉及三类核心介质：(1) 活性氧(reactive oxygen species, ROS)爆发：再灌注期线粒体电子传递链功能障碍，生成大量超氧阴离子、过氧化氢等 ROS，其与一氧化氮反应生成的过氧亚硝酸盐可诱发内皮细胞膜脂质过氧化、DNA 损伤及蛋白质失活，降低 NO 生物利用度并加重内皮功能障碍[10] [11]。(2) 细胞内钙超载：再灌注后缺血期累积的酸中毒迅速纠正，激活 Na^+-H^+及 Na^+-Ca^{2+}交换体，导致胞质及线粒体 Ca^{2+}超载；后者激活钙依赖性蛋白酶，

破坏细胞骨架及内皮细胞间连接，进一步升高微血管通透性并加剧微循环堵塞[12] [13]。(3)线粒体通透性转换孔(mitochondrial permeability transition pore, mPTP)开放：ROS 与 Ca^{2+}超载协同促进 mPTP 开放，诱导线粒体膜电位崩溃及 ATP 耗竭，最终导致心肌细胞及微血管内皮细胞死亡，造成不可逆的微血管结构性损伤[14] [15]。

上述分子事件所导致的内皮损伤与功能障碍，是 MVO 形成的前提。在此基础上，MVO 的形成通常涉及多重因素的叠加：微血管痉挛、内皮细胞肿胀、炎症细胞浸润与血小板－白细胞聚集、微血栓形成以及心肌水肿所致的微血管外源性压迫等因素，共同导致毛细血管水平灌注缺失，促使 MVO 形成[16] [17] [18]。在微血管损伤程度更重的患者中，该病理过程可进一步发展为 IMH。在缺血再灌注持续损伤作用下，微血管发生一系列结构性改变：糖萼层迅速脱落，内皮细胞间紧密连接破坏，基底膜降解，使血管壁的机械支撑和屏障功能逐渐丧失。当结构性损伤累积至血管壁完整性彻底丧失时，红细胞外渗至心肌间质，最终形成 IMH [18] [19]。从 MVO 到 IMH 的演进，本质上是微血管从功能性阻塞向结构性破坏演变的连续病理生理过程。

3. 心脏磁共振成像评估：再灌注损伤的表型化工具

心脏磁共振成像(cardiac magnetic resonance, CMR)是评估 STEMI 再灌注后微循环损伤的无创“金标准”，其核心在于识别 MVO 与 IMH 两种关键表型[5] [18]。

3.1. MVO 的 CMR 识别

MVO 在延迟钆增强(late gadolinium enhancement, LGE)序列上典型表现为高信号梗死区内的低信号“无强化核心”，多位于梗死中心或跨壁较深的区域[5] [19]。其病理基础为微血管阻塞导致对比剂进入显著受限或延迟，导致在 LGE 时相仍呈低信号核心。判读时应注意：低信号需位于梗死高信号区内部、形态相对稳定，并结合多切面复核，以避免将边缘伪影或对比剂分布不均误判为 MVO [20] [21]。

3.2. IMH 的 CMR 识别

IMH 的识别依赖磁敏感成像技术。在 T2*加权成像或 T2* mapping 中，梗死或水肿相关区域内出现局灶低信号或 T2*明显缩短的低信号核心，提示心肌内出血[5] [22]。T2 或 T2 mapping 中亦可出现水肿高信号内的低信号核心，但特异性相对有限，应以 T2*作为确认依据，并与 LGE 上的 MVO 表现联合判读以完成微血管损伤表型分层[19] [23]。

IMH 多与 MVO 空间共定位，但并非所有 MVO 均伴发 IMH，其出现通常提示更为严重的微血管损伤表型[8] [19]。临床实践中，建议采用“LGE 定位梗死及 MVO＋T2*确认 IMH”的组合策略完成表型判读，并注意不同扫描时间窗及序列参数差异对检出率的潜在影响[24]。

4. 预后意义：从影像表型到临床结局

大量研究证实，通过 CMR 检出的 MVO 与不良左室重构、射血分数恢复受限及 MACE 风险升高显著相关。de Waha 等基于 7 项随机对照试验、纳入 1688 例患者的个体患者数据合并分析显示，MVO 与全因死亡及心力衰竭住院等不良事件显著相关，在校正梗死面积及基线临床特征后，MVO 仍保持独立预测价值[25]。后续的一系列研究进一步表明，MVO 并非单纯急性期现象，持续性 MVO 与更高的远期不良事件风险相关，并与更差的心功能恢复及不良左室重构密切相关[4] [26] [27]。

与单纯 MVO 相比，IMH 在多项研究中携带更为不良的预后信息：基于 CMR 微血管损伤表型分层的临床研究显示，IMH 阳性患者的 MACE 风险通常高于仅有 MVO 者，且 IMH 对结局的预测力更强或可提供增量预后信息[8] [28]。系统评价与 Meta 分析亦提示，IMH 与不良临床结局风险显著相关，并支

持其作为更严重的微血管损伤表型用于风险分层[9]。影像学综述进一步强调，IMH 多与严重 MVO 共定位，代表更重的再灌注损伤表型并与更差的临床转归相关[22]。

5. 干预策略

目前，针对 PPCI 术后 MVO 及 IMH，尚未形成针对已确立 MVO/IMH 的特异性、统一 I 类推荐治疗方案[1] [2]。临床实践与研究层面，现阶段处理思路大致可归纳如下。

5.1. 标准化药物治疗

以尽早开通梗死相关动脉并实现有效再灌注为核心，STEMI 患者的指南推荐药物治疗主要包括：以阿司匹林联合口服 P2Y12 受体抑制剂为基础的双联抗血小板治疗，并在围术期及住院急性期根据再灌注策略及个体缺血–出血风险选择肠外抗凝方案；同时应尽早启动高强度他汀治疗，并在无禁忌证且符合适应证的人群中联合使用 β 受体阻滞剂及肾素–血管紧张素–醛固酮系统(RAAS)抑制剂等二级预防药物[1] [2]。这些药物治疗在减少再梗死、改善长期生存方面具有明确获益，但其主要作用靶点更偏向于降低血栓事件风险与促进整体心室重构；对于已形成的 MVO 或 IMH，目前缺乏一致的直接改善证据，相关获益更可能依赖总体风险下降而非表型逆转[17] [19] [29]。

5.2. 靶向微循环灌注不良的药物干预

针对微循环灌注不良的药物干预涵盖冠状动脉内给药与全身给药两种途径，根据作用靶点可分为以下两类：(1) 缓解微血管痉挛–主要针对再灌注后微血管的功能性收缩：血管扩张剂如腺苷、硝普钠、维拉帕米、尼可地尔等，通过扩张微循环、降低微循环阻力以改善即刻灌注[17] [30]。然而，随机对照研究结果显示，冠状动脉内应用腺苷或硝普钠对 CMR 测定的 MVO 范围及梗死面积的影响并不稳定，提示其疗效受给药时机、剂量及患者异质性的显著影响[31] [32]。(2) 调控上游损伤机制–主要针对再灌注引发的氧化应激与炎症级联反应：IL-6 信号通路抑制剂托珠单抗在 ASSAIL-MI 研究中显示出提高 CMR 心肌挽救指数、减轻 MVO 程度的趋势，提示其可能减轻再灌注相关组织损伤负荷[33]。N-乙酰半胱氨酸(N-acetylcysteine, NAC)通过清除活性氧并增强硝酸酯-NO 轴功能[34]，在 NACIAM 试验中，高剂量静脉 NAC 联合硝酸甘油可降低 CMR 测定的梗死面积、提高心肌挽救指数[35]。然而，上述策略多属于机制验证或小型随机试验探索性研究，针对 MVO/IMH 的特异性获益及其对硬终点的影响尚缺乏一致性证据。

上述药物干预策略尽管作用靶点各异，却共同面临一个核心困境：临床前研究中明确的心肌保护效应难以在 STEMI 患者临床试验中转化为稳定的临床获益，呈现出显著的“转化鸿沟”[17] [36]。这一困境的根源可概括为以下两方面：(1) 模型外推不足：现有缺血/再灌注动物实验多采用年轻、无合并症的健康个体，难以真实反映临床 STEMI 患者常见的高血压、糖尿病、动脉粥样硬化等共病状态。这些共病因素不仅影响微循环基线状态，还可能改变药物反应性，使得动物模型中观察到的疗效往往系统性高于真实临床场景[37] [38]。(2) 临床时机延迟与背景治疗的“稀释效应”：在临床实践中，STEMI 患者的有效缺血时间及再灌注起始时点常因院前就诊延迟、转运流程及院内操作等因素而难以精确界定。相当比例的患者在接受再灌注治疗时已存在显著的微循环损伤，导致其错失了多数药物所依赖的再灌注早期治疗时间窗[17]。同时，在 STEMI 规范化再灌注及多药联合治疗的背景下，单一试验药物的增量获益难以显现[39]。

5.3. 新兴器械辅助治疗

新兴器械辅助治疗旨在改善微循环回流、减轻再灌注损伤，目前多处于探索阶段，代表性技术包括：(1) 压力控制间歇性冠状静脉窦阻塞(Pressure-controlled Intermittent Coronary Sinus Occlusion, PiCSO)：通

过间歇性阻塞冠状静脉窦、改变静脉回流压力梯度，以促进微循环灌注。然而，PiCSO-AMI-I 试验未显示其对短期 CMR 测定的梗死面积、MVO 或 IMH 具有明确改善，提示需进一步优化适用人群与干预时机[40]。(2) 选择性冠状动脉内低温(selective intracoronary hypothermia, SIH)通过在再灌注期对梗死相关动脉行局部降温，试图抑制损伤级联反应。EURO-ICE 随机试验未能证实选择性冠脉内低温的临床获益：尽管该策略在前壁 STEMI 急诊 PCI 中安全可行且可实现快速局部降温，但并未降低患者 3 个月时的 CMR 梗死面积，也未改善 MVO 或 IMH 等微循环损伤表型[41]。(3) 再灌注前左心室卸载(Left Ventricular Unloading Before Reperfusion)：旨在通过机械辅助降低左室壁张力与心肌代谢需求，从而减轻再灌注损伤。STEMI-DTU 试验提示其可能缩小梗死负荷，但对 MVO 的稳定获益仍需更大样本研究确认[42]。上述器械策略尽管机制各异，但均面临与药物干预相似的困境：人群异质性与干预时机可能是影响疗效的关键变量。这提示，未来的器械研究有必要引入影像表型进行人群富集，以精准筛选可能获益的患者。

5.4. 表型导向的精准治疗

急性期 CMR 可精准评估 STEMI 再灌注后微血管损伤(microvascular injury, MVI)表型，将风险分层从心外膜血管开通深化至组织灌注层面。基于 MVO 与 IMH 的检出，可将再灌注损伤表型分为三类：低危型(MVO^-/IMH^-)、中危型(MVO^+/IMH^-)及高危型(IMH^+，常伴 MVO) [19] [28] [43]。多项研究证实，MVI 与远期不良预后的关联主要由出血性表型(IMH^+)所驱动，而单纯 MVO 未合并 IMH 者的风险梯度相对较低[9] [28]。基于上述证据及病理生理学机制，我们提出以下基于 CMR 表型的分层管理思路(其临床获益仍待前瞻性研究验证)：低危组(MVO^-/IMH^-)：遵循现行指南推荐的二级预防及抗心室重构治疗路径进行常规随访。中危组(MVO^+/IMH^-)：在基础治疗之上，建议适当加强随访及心功能监测频率，重点确保 β 受体阻滞剂与 RAAS 抑制剂达到目标剂量，并于出院后 8~12 周复查心功能以动态评估心室重构进展。高危组(IMH^+)：应在指南推荐的基础治疗框架内，更积极地推进抗心室重构及心力衰竭预防治疗的规范化与达标管理，考虑提高随访密度、强化心功能监测[1] [2] [19] [27] [28]。

在靶向干预层面，目前尚无表型特异性的常规治疗。然而，CMR 表型(尤其 IMH^+)可用于富集临床试验人群，优先筛选患者纳入以改善微循环灌注为目标的干预研究(如 PiCSO、SIH 等)，以探索逆转微血管损伤表型演变的潜在治疗路径[19] [40] [44]。这一“表型导向的精准治疗”模式，有望破解当前药物与器械干预面临的转化困境。

6. 结论与展望

MVO 与 IMH 是 STEMI 再灌注后微循环损伤的关键影像学表型，二者构成从功能性灌注障碍到结构性微血管破坏的连续性病理谱系。大量研究表明，其存在与左室不良重构、心功能恢复受限及不良临床结局密切相关，其中 IMH 携带尤为不良的预后信息。然而，正如前文所述，针对 MVO/IMH 的干预研究长期受困于“转化鸿沟”——临床前模型中明确的心肌保护效应难以在真实世界患者中复现。破解这一困境的关键，在于从“一刀切”的治疗模式转向基于影像表型的精准干预。表型驱动的个体化治疗策略，有望将 CMR 从“预后判断的工具”转化为“指导干预的罗盘”，最终实现 STEMI 患者长期预后的实质性改善。

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