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· 综述 ·

外周血单核细胞与高密度脂蛋白胆固醇比值与急性脑梗死关系的研究进展

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[摘要]　急性脑梗死是危害公民生命健康的最主要疾病之一。炎症反应与急性脑梗死的发生发展进程密切相关,炎性标志物水平的高低可反映炎症反应的严重程度。外周血单核细胞与高密度脂蛋白胆固醇比值(MHR)作为近年来新应用的代表炎症反应程度的指标,受到广泛关注。本文就外周血 MHR 与急性脑梗死的高危因素、风险预测、早期功能恶化、严重程度评估、出血转化及预后等方面的关系进行综述。

[关键词]　脑梗死;单核细胞;胆固醇,HDL;综述

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Research advances in the association between peripheral blood monocyte to high-density lipoprotein cholesterol ratio and acute cerebral infarction

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[**ABSTRACT**]　Acute cerebral infarction is one of the most important diseases that endanger the life and health of citizens. Inflammatory response is closely associated with the development and progression of acute cerebral infarction, and the levels of inflammatory markers can reflect the severity of inflammation. In recent years, monocyte to high-density lipoprotein cholesterol ratio (MHR) has attracted wide attention as a newly applied indicator for the degree of inflammatory response. This article reviews the association between peripheral blood MHR and acute cerebral infarction in terms of high-risk factors, risk prediction, early functional deterioration, severity assessment, hemorrhagic transformation, and prognosis.

[**KEY WORDS**]　Brain infarction; Monocytes; Chdesterol, HDL; Review

急性脑梗死是临床上一种常见的脑血管疾病,在我国具有高致残率、高复发率和高死亡率等特点[1]。在急性脑梗死的各个阶段,炎症和免疫反应发挥着重要作用,炎性反应也是急性脑梗死后继发性脑损伤的重要原因[2]。近年来,单核细胞与高密度脂蛋白胆固醇比值(MHR)作为一种新的炎性标志物受到广泛关注。在临床实验室检测指标中单核细胞、高密度脂蛋白胆固醇(HDLC)作为常规参数,容易获取并且经济快捷。其次,构成 MHR 的两个生化指标单核细胞和 HDLC 既参与了炎症发生过程,又参与了抗炎过程,相较于单一指标更能反应炎症程度。MHR 中的单核细胞是炎症反应的起始细胞,由单核细胞分化而成的巨噬细胞,是泡沫细胞的前体细胞,也是动脉粥样硬化起始阶段的重要炎性细胞[3-4]。单核细胞是在缺血后炎症反应中起重要作用的细胞,在脑梗死发生早期,单核细胞会快速聚集到缺血区域,通过释放炎性介质加速血脑屏障破坏[5-6];MHR 中 HDLC 与单核细胞在炎症反应中的作用相反,可诱导泡沫细胞中的胆固醇外排,启动胆固醇逆向转运途径,促进胆固醇向肝内转移[7-8],降低脑梗死发生风险。此外 HDLC 还具有抗炎和抗氧化作用[9],属于拮抗动脉硬化及防止斑块形成的保护性因子[10]。因此,MHR 作为单核细胞和 HDLC 的复合标志物,被发现是心血管疾病[11]、免疫系统疾病[12]和风湿性疾病[13]的新的预后标志物,越来越多的研究也表明 MHR 与急性脑梗死过程的关系密切。

1　MHR 与急性脑梗死高危因素的关系

1.1　MHR 与高血压

高血压是发生急性脑梗死的高危因素[14-15],炎症反应和氧化应激导致的血管内皮损伤对其发生发展起着重要作用,目前高血压与 MHR 的相关性研究多围绕高血压所致并发症与 MHR 的关系。KAPLAN 等[16]使用 MHR 预测高血压终末器官的损害状况,发现高血压相关性器官损害患者的 MHR 明显高于无高血压并发症患者。国外另一项临床研究探究了原发性高血压患者的 MHR 与无症状性亚临床靶器官损害间的关系,结果显示 MHR 与患者的颈动脉内膜、心脏、肾脏等靶器官损伤呈正相关,且 MHR 升高是患者发生无症状性器官损害的独立危险因素[17]。GEMBILO 等[18]通过对 214 例慢性肾脏病患者的回顾性分析结果显示,顽固性高血压患者的 MHR 明显高于非顽固性高血压,多元回归分析结果显示,MHR 升高是高血压发生的独立危险因素。在 YAYLA 等[19]的另一项关于高血压患者 MHR 与动脉弹性受损的研究中,高 MHR 患者的主动脉硬化程度明显高于低 MHR 患者,表明较高的 MHR 与动脉弹性受损存在明显相关性。

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1.2　MHR 与动脉粥样硬化

动脉粥样硬化是引起动脉狭窄或闭塞，造成急性脑梗死的关系也被广泛研究。OMAR 等[22]在对 MHR 与急性脑梗死患者颈动脉病变关系的研究中，首次发现颈动脉粥样硬化患者可能具有较高的 MHR，MHR 也被发现是急性脑梗死患者颈动脉粥样硬化发生的影响因素。MAYASARI 等[23]关于糖尿病患者 MHR 与动脉粥样硬化发生的相关性研究亦显示，MHR 与动脉粥样硬化的发生呈独立相关。另一项纳入了8 148 例患者的大规模人群横断面调查研究同样发现，MHR 是动脉粥样硬化的相关性指标，MHR 与急性脑梗死发生率呈显著正相关[24]。

1.3　MHR 与血栓形成

血栓的形成和栓塞是造成急性脑梗死的又一高危因素，急性脑梗死的主要病理生理机制是动脉粥样硬化导致的斑块破裂，从而导致脑动脉内血栓形成及血流中断，而炎症反应在血栓的形成、机化消退等方面发挥重要作用[25]。一项纳入 3 848 例体检人员的回顾性分析表明，MHR 或可作为判断颈动脉斑块形成及其严重程度的标志物[26]。ARISOY 等[27]关于 MHR 与心肌梗死(心梗)患者冠状动脉(冠脉)血栓负荷量的研究中，将 414 例接受经皮冠状动脉介入治疗的心梗患者分为了低血栓负荷组和高血栓负荷组，其中高血栓负荷组的 MHR 明显高于低血栓负荷组，且多因素 logistic 回归分析显示 MHR 升高是心梗患者冠脉高血栓负荷的独立危险因素。另一方面，心房颤动(房颤)引发的血栓形成与脱落，是造成心源性脑梗死的重要危险因素，而炎症反应参与了心房基质的改变，与房颤的发生与发展有关[28]。ULUS 等[29]的研究显示，MHR 升高是老年冠脉综合征患者行冠脉介入治疗术后新发房颤的独立危险因素。ADILI 等[30]通过回顾性分析 131 例瓣膜病房颤患者射频消融术后 3 个月复发概率与 MHR 的关系，发现 MHR 是房颤射频术后早期复发的独立危险因素。

2　MHR 与急性脑梗死发生的关系

国外的一项基于大样本普通人群的横断面研究证明，MHR 与急性脑梗死发生间存在线性关系，并且比传统危险因素具有更高预测价值，可能是预测急性脑梗死发生的更优生物标志物[24]。刘新萍等[31]通过比较 154 例急性脑梗死患者和 184 例正常健康查体者的 MHR，发现 MHR 升高可能是脑梗死发生的独立危险因素。LIU 等[32]的回顾性研究纳入 253 例确诊为急性脑梗死的患者和 211 例健康体检者，发现 MHR 及单核细胞/淋巴细胞比值(MLR)升高均是急性脑梗死发生的独立危险因素，且与单个指标相比，两者共同升高更具预测价值。

3　MHR 与急性脑梗死早期神经功能恶化的关系

较高的 MHR 可能预测急性脑梗死患者的早期神经功能恶化情况，并可能与病情严重程度呈正相关。动物实验和临床研究表明，脑梗死急性期局灶性脑损伤后，神经细胞死亡诱发了一系列炎症级联反应，这些反应以胶质细胞活化、外周免疫细胞募集和细胞因子释放为主要特点，引起外周血白细胞迁移至缺血性脑组织，炎症因子集中在病变部位和周围组织中并且持续数周，参与了急性脑梗死后的继发性脑损伤[33]。一项对 173 例接受静脉溶栓治疗的脑梗死患者的研究显示，入院时 MHR 高是接受静脉溶栓的急性脑梗死患者早期神经功能恶化的独立危险因素，入院 MHR 对溶栓后是否发生早期神经功能恶化具有一定预测价值[34]。BI 等[35]回顾性分析了 212 例急性孤立性脑桥梗死患者的临床资料，发现 MHR 升高可作为预测脑桥梗死早期神经功能恶化的生物标志物。一项纳入 154 例急性脑梗死患者的研究分别以 NHISS 评分和梗死灶体积作为评定脑梗死严重程度的指标，研究结果显示 NHISS 评分较高患者的 MHR 明显高于 NHISS 评分较低患者，梗死体积≥5 cm^3 患者的 MHR 明显高于梗死体积＜5 cm^3 患者，说明 MHR 与急性脑梗死的神经功能缺损程度及脑组织梗死体积均有关[31]。

4　MHR 与急性脑梗死后机械取栓治疗的关系

机械取栓术是急性大动脉闭塞所致脑梗死的重要治疗方法之一[36-37]，相关文献报道称急性脑梗死患者行机械性血栓切除术后再通率可达 90％以上[38-40]。然而，取栓后患者的预后受到许多因素影响，其中炎症反应对取栓后缺血再灌注过程有明显影响[41-43]。OH 等[44]对 411 例接受机械性血栓切除术治疗的急性脑梗死患者的预后影响因素进行研究，结果显示预后不良患者的 MHR 显著高于预后良好患者，说明高 MHR 可能是机械性血栓切除术后患者预后不良的独立危险因素。LI 等[45]收集了 286 例接受机械性血栓切除术治疗的急性缺血性脑梗死患者的临床资料，发现较高的 MHR 是机械性血栓切除术患者术后前 3 个月预后不良的独立危险因素。故而，MHR 对于机械性血栓切除术后患者预后评估具有一定价值。

5　MHR 与脑梗死出血转化的关系

脑梗死的出血转化是指急性脑梗死后缺血区域血管重新恢复血流，导致缺血区域产生再灌注损伤继发出血，是急性脑梗死常见并发症[46]。越来越多的证据表明，急性脑梗死后炎症反应参与了脑梗死的出血转化过程[47-48]。WANG 等[49]对 MHR 与脑梗死后出血转化的关系进行了相关性研究，将 974 例影像学诊断为脑梗死出血转化的患者根据是否存在脑梗死临床表现，分为无症状组和有症状组，该研究结果显示 MHR 的升高与脑梗死出血转化呈正相关，MHR 升高时症状性脑梗死出血转化的风险升高，高水平 MHR 可作为预测脑梗死后出血转化的独立危险因素。XIA 等[50]的另一项回顾性研究分析了 340 例急性脑梗死患者溶栓治疗前 MHR 与治疗后出血转化间关系，发现较高水平 MHR 是急性脑梗死溶栓后发生出血转化的独立危险因素。与此相同，ZHANG[51]等的一项研究也发现，MHR 是急性脑梗死后出血转化的独立危险因素。

6　MHR 与脑梗死预后的关系

越来越多研究表明，MHR 可能与脑梗死后的预后情况有显著相关性，较高水平的 MHR 可能是脑梗死患者预后不良的独立危险因素[52]。LIU 等[53]的研究纳入 1 090 例急性脑梗死患者，研究结果表明预后不良组的 MHR 显著高于预后良好组，且 MHR 升高与急性脑梗死发病 3 个月后的不良预后呈独立相关，MHR 是影响急性脑梗死患者预后的重要影响因素，且相比于其他炎性因子更具优势。苏玉蓉等[54]一项关于 MHR 与脑梗死预后的临床研究也有相似结论。LI 等[55]在 MHR 与大动脉粥样硬化型脑梗死的相关性研究中发现，功能预后不良患者的 MHR 明显高于功能预后良好患者。另一项研究对 985 例接受溶栓治疗的急性脑梗死患者进行早期（术后前 3 个月）预后分析，发现溶栓前 MHR 较低可能与早期良好预后相关[32]。另有国外研究发现，发病后 24 h 内死亡的急性脑梗死患者较存活患者 MHR 更高，且 MHR 是急性脑梗死发病 30 d 内病死率高的独立危险因素[56]。另外，在一项关于急性脑梗死后相关性肺炎的报道中同样显示，较高 MHR 可以预测急性脑梗死后相关性肺炎的发生情况[57-58]。因此，对 MHR 的检测有助于早期识别急性脑梗死预后不良患者，从而在临床上及早进行干预，以减少不良预后事件发生。

7　小结及展望

外周血 MHR 作为近年来新兴的炎症指标，能较好反应急性脑梗死后机体炎症反应程度，MHR 与急性脑梗死的发生风险、神经功能恶化、取栓疗效、并发症及预后等方面均有较强的相关性。但急性脑梗死发生后，一方面外周血 MHR 受脑动脉侧支循环、机体应激程度及炎症敏感性等诸多因素影响，另一方面 MHR 与不同类型急性脑梗死的发生、发展及预后的关系也有所不同[59]，这也是 MHR 预测急性脑梗死发病、治疗以及预后的局限性。另外，目前对于 MHR 与颈动脉斑块稳定性的关系，以及两者在预测急性脑梗死发生风险、脑梗死严重程度和预后方面的灵敏度及特异度的研究仍相对较少。因此外周血 MHR 是否可以作为指导急性脑梗死患者诊疗的生物标志物，仍需大量的实验室及临床研究提供理论依据。

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