

中性粒淋巴细胞比值与心血管疾病关系研究进展

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摘要

中性粒淋巴细胞比值(NLR)作为一种简便, 可靠, 容易获取的复合性指标逐渐在心血管, 肿瘤学科领域上被学者关注。越来越多的研究证实NLR与多种心血管疾病发病, 发展及其预后相关。本文主要综述NLR与冠状动脉粥样硬化性心脏病, 高血压, 心律失常, 心力衰竭, 心脏瓣膜病病因及预后的关系, 以便临床工作者对此类高危患者早识别早干预, 预防患者并发症, 改善患者预后。

关键词

中性粒与淋巴细胞比值, 心血管疾病, 预后, 综述

Advances in the Relationship between Neutrophil Lymphocyte Ratio and Cardiovascular Disease

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Abstract

Neutrophil lymphocyte ratio (NLR) is gaining attention as a simple, reliable, and easily accessible composite index in the field of cardiovascular and oncology. An increasing number of studies have

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confirmed the association of NLR with the pathogenesis, development and prognosis of various cardiovascular diseases. This article reviews the relationship between NLR and the etiology and prognosis of atherosclerotic heart disease, hypertension, arrhythmias, heart failure, and heart valve disease, in order to facilitate early identification and intervention of such high-risk patients, prevent complications, and improve their prognosis by clinical workers.

Keywords

Neutrophil-to-Lymphocyte Ratio, Cardiovascular Disease, Prognosis, Review

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1. 引言

随着社会发展, 老龄化加重, 心理压力过高, 生活及饮食习惯的改变等均促进心血管疾病发病率[1]。心血管疾病已成为中国人死亡和过早死亡的主要原因, 据统计中国人 40% 的死亡率与心血管疾病相关[2]。医疗技术的发展, 治疗方式的改善在降低急性心血管疾病患者死亡率同时, 也增加了现存心血管疾病患者数量, 严重挑战着我国医疗卫生事业。相关研究表明炎症反应在心血管疾病发病机制中起着重要作用[3] [4] [5]。中性粒细胞与淋巴细胞比值(neutrophil lymphocyte ratio, NLR)作为一种新型炎症指标, 既能反应中性粒细胞为代表的先天性免疫, 也能反映淋巴细胞为代表的适应性免疫, 且由于其简单, 便宜, 易获取的特点逐渐成为研究热点。近年来对于 NLR 与多种心血管疾病病因及不良预后的关系有诸多报道[6] [7] [8]。本文就 NLR 与冠状动脉粥样硬化性心脏病, 高血压, 心律失常, 心力衰竭及心脏瓣膜病的病因及预后的关系予以综述。

2. NLR 与冠状动脉粥样硬化性心脏病

冠心病是冠状动脉狭窄或闭塞所致的心脏病, 也是冠状动脉管壁的局部炎症性疾病。血管内皮损伤后, 局部发生的炎症反应可通过表达多种黏附因子引起大量中性粒细胞聚集并释放炎症因子引起单核细胞黏附于内皮下, 并逐渐分化成吞噬细胞, 吞噬细胞通过吞噬低密度脂蛋白进一步加速泡沫与粥样斑块的形成, 其后又进一步分泌致炎因子等趋化更多的炎性细胞, 增强局部炎症反应, 增加其粥样硬化斑块的不稳定性, 最终导致斑块破裂, 血栓形成甚至急性心肌梗死。而此时由于免疫系统受到抑制, 淋巴细胞数量降低[9] [10]。炎症反应参与冠状动脉粥样硬化发病, 发展全过程。NLR 作为一个复合炎症标志物, 已有研究证明可以作为冠心病严重程度和预后的预测指标[11] [12]。Verdoia 等人通过对 3738 名冠心病患者观察发现高 NLR 与冠状动脉病变数量, 阻塞程度, 冠状动脉内血栓形成相关[13]。Ramazan 等人发现 NLR 与急性梗死患者 GRACE 风险评分呈显著正相关($r = 0.803, P < 0.05$)。在多变量分析中, NLR 是独立于 GRACE 风险评分的住院期间预后不良的预测因子[14]。另一项研究中 Shah 等人通过对冠心病患者进行长达 14 年的随访发现, NLR > 4.5 组患者远期死亡率远高于 NLR < 1.5 组, 其 HR: 2.68 (95% CI 1.07~6.72, $P = 0.035$)。Wada 等人也发现 NLR 是急性冠状动脉综合征患者 PCI 术后长期预后的独立风险因素, 该研究通过对患者进行长达 7 年的随访发现高 NLR 是全因死亡和心源性死亡的独立风险因素, 其 HR 值分别为 1.73 和 1.87 [15]。同样 Edoardo 等人对 PCI 患者长达 5 年随访发现高 NLR 不仅仅是长期死亡的独立风险因素, 还是 MACCEs 发生的独立风险因素(HR 1.65, 95% CI 1.07~2.55, $P = 0.024$) [16]。

3. NLR 与高血压

高血压病是心脑血管风险的第一危险因素,其发病原因复杂多种,其中炎症反应起到至关重要作用。一方面人体内炎症可能通过氧化应激反应引发内皮功能障碍,导致动脉硬化和动脉粥样硬化,增加全身血管阻力引起高血压,另一方面促炎因子通过激活 RASS 系统促进高血压发生[17] [18]。在一项研究中,研究人员通过 NLR 五分位数来评估高血压发病率的风险比,与 NLR 最低值组相比,其余组高血压发生率的风险比分别为 1.0 (0.92, 1.26), 0.97 (0.83, 1.14), 1.10 (0.94, 1.28)和 1.23 (1.06, 1.43) [19]。此研究肯定了炎症在高血压发病率背后的潜在意义。高 NLR 是高血压病发病的独立风险因素这一结论在另一项研究中同样的得到支持[20]。除此之外 Cimen 等人通过对 NLR 和 24 h 平均动态血压和血压负荷进行评估发现 NLR 高值组与 NLR 低值组在临床和超声心动图特征方面无差异,但在日间收缩压、日间舒张压、24 小时舒张压,日间收缩压负荷、24 小时舒张压负荷和日间舒张压负荷方面前者显著高于后者[21],证明 NLR 与高血压严重程度有关。Sun 等人对年龄大于 80 岁高血压患者入院 90 天死亡率进行研究发现 NLR 与全因死亡率正相关,其临界值为 2.97 时,roc 曲线下面积(AUC) = 0.74, 敏感性为 92.6%, 特异性为 52.5%。NLR 第三四分位数患者和第四四分位数患者入院 90 天后死亡率为第一四分位数患者的 9.64 和 16.45 倍 [22]。

4. NLR 与心率失常

心律失常是由于窦房结激动异常或激动产生于窦房结以外,激动的传导缓慢、阻滞或经异常通道传导,即心脏活动的起源和(或)传导障碍导致心脏搏动的频率和(或)节律异常。心房颤动为最常见的持续性心律失常,严重时可导致血流动力障碍,可突然发作而致猝死,亦可持续累及心脏而致其衰竭。目前有多项研究支持高 NLR 是房颤发作的独立风险因素。Karatas 等人发现 NLR 是 PCI 术后患者在住院期间发生房颤的独立预测因子[23]。在另一项研究中 Canpolat 等发现射频消融前高 NLR 水平是房颤复发的危险因素[8]。Akdag 等人发现在非瓣膜性房颤患者中, NLR 与 CHA2DS2-VASc 评分所显示的血栓栓塞风险有关[24]。Alexander 等人通过对 22 项研究 6098 患者进行 meta 分析发现,在接受冠状动脉搭桥术,瓣膜手术或联合手术中患者中,术前 NLR 水平与新发房颤显著相关[25]。

5. NLR 与心力衰竭

心力衰竭简称心衰,是指各种原因导致心脏泵血功能受损,心排量不能满足全身组织基本代谢需要的综合征。目前有较多研究证明 NLR 与心力衰竭发生及预后相关[26] [27] [28]。Karagoz 等人通过对比发现在舒张功能障碍患者平均 NLR 水平显著大于对照组($P < 0.05$),舒张功能不全与较高的 NLR 水平正相关[29]。Erdal 等人的研究显示 NLR 与左室射血分数呈负相关($r = -0.409, P < 0.01$), NLR 预测 HF 的最佳临界值为 3.0, 敏感度为 86.3%, 特异性为 77.5%, 同时 NLR 也是心衰死亡的预测指标[30]。Anil 等人发现 NLR 与 NYHA 功能分级相关性有统计学意义($r = 0.68, P < 0.001$),是独立于 BNP 的心力衰竭的阳性预测因子[31]。Khalil 等人通过研究发现 NLR 对经导管主动脉瓣置换术后患者术后 1 年内发生心力衰竭也有较好的预测能力,其曲线下面积(AUC)为 0.61, 当患者 NLR 处于 cut-off 值 4.0 时, 敏感度为 60%, 特异度为 57% [32]。以上大部分研究证明,高 NLR 水平与心力衰竭发生及不良预后相关,但其预测心力衰竭及不良预后的最佳临界值尚未明确,仍需进一步研究探讨。

6. NLR 与心脏瓣膜病

心脏瓣膜病是先天性发育异常或风湿等各种疾病引起心脏瓣膜狭窄或关闭不全导致的心脏疾病。多项研究表明 NLR 与风湿性瓣膜病严重程度有关。Polat 等人发现风湿性二尖瓣狭窄患者 NLR 水平较非二

尖瓣狭窄患者显著升高($P < 0.05$), NLR 可用于预测 RMVD 患者的 MS 的存在和严重程度[33]。Serkan 等人也发现在风湿性心脏病患者 NLR 与瓣膜返流严重程度呈正相关($r = 0.34, P < 0.001$) [34]。而 Sinan 等人发现 NLR 是瓣膜置换术后院内死亡的预测指标, 其中第二个三分位数的危险比(HR)为 1.8 ($P = 0.11, 95\% \text{ CI } 0.88\sim 3.79$), 第三个三分位数的危险比为 2.8 ($P = 0.003, 95\% \text{ CI } 1.40\sim 5.59$) [35]。Separham 等人发现 NLR 是预测经皮球囊二尖瓣分离术后二尖瓣再次狭窄的独立于测指标[36]。

7. 小结及展望

近年来, 我国心血管疾病发病率、病死率及复发率逐年升高, 严重危害人们生命健康。早发现, 早期对可能出现不良预后的患者进行干预具有重要意义。相比白细胞, 中性粒, 淋巴细胞等指标, NLR 对局部炎症的反映更加全面。在预测心血管疾病的发生及预后评估中有非常重要的作用, 为临床工作者诊治心血管疾病提供新的方向。相信随着 NLR 与心血管之间研究进一步深入, 它在心血管领域中的作用进一步被挖掘, 将发挥出更多的作用。

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