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冠状动脉疾病和C反应蛋白与白蛋白比值相关性的研究现状

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摘　要

冠状动脉疾病(Coronary artery disease, CAD)在全球范围内都是发病率和死亡率均较高的心血管疾病，鉴于此，寻找一条经济、可靠，方便的诊断和预测指标尤为必要，炎症反应是导致动脉粥样硬化的病理因素。近来，炎症生物标志物正在被深入研究，在最近的研究中，一种新的炎症反应指标，C反应蛋白/白蛋白(CAR)，被证明是一种中等价值的动脉粥样硬化标志物，因为它能够确定CAD患者的严重程度和预后价值。本文综述主要阐明CAR对冠状动脉疾病的相关研究现状。

关键词

C反应蛋白与白蛋白比值，冠状动脉疾病

Research Status of the Correlation between Coronary Artery Disease and C-Reactive Protein to Albumin Ratio

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Abstract

Coronary artery disease (CAD) is a cardiovascular disease with high incidence rate and mortality worldwide. In view of this, it is particularly necessary to find an economic, reliable and convenient diagnostic and predictive indicator. Inflammatory reaction is a pathological factor leading to atherosclerosis. Recently, inflammatory biomarkers are being further studied. In recent studies, a new inflammatory response indicator, C-reactive protein/albumin (CAR), has proved to be a moderately valuable atherosclerosis marker because it can determine the severity and prognostic value of CAD patients. This review focuses on clarifying the current research status of CAR related to coronary artery disease.

Keywords

C-Reactive Protein to Albumin Ratio (CAR), Coronary Artery Disease (CAD)

1. 引言

心血管疾病有很多种类，其中主要包括冠状动脉疾病(Coronary artery disease, CAD)、心力衰竭、颈动脉疾病、主动脉疾病和外周动脉疾病，是世界范围内最重要的死亡和发病原因[1]。冠状动脉粥样硬化性心脏病，也就是我们常说的冠心病(Coronary heart disease, CHD)，它常常影响到患者的心脏功能，在许多国家被认为是主要的公共卫生负担[2] [3]。CHD 是由冠状动脉血管进行性狭窄造成的，它是一种缓慢进行的慢性心血管疾病，冠状动脉主要作用是为心肌提供含氧血液，当运动量增大时，随着氧气需求量的增加，狭窄的冠脉会导致心肌的缺血。CHD 患者的预后与早期干预有关，其预后情况有很多种，临床终点包括心力衰竭、心律失常或急性冠状动脉综合征(ACS)，如心肌梗死和不稳定心绞痛，通常随后出现心脏性猝死[4]。

动脉粥样硬化是一种导致冠心病的炎症性疾病。冠状动脉内皮的炎症与急性期蛋白和细胞因子的增加有关。局灶性和全身性炎症在动脉粥样硬化斑块[5]的失稳和破裂中起关键作用。因此，炎症生物标志物正在被深入研究，因为它们能够确定 CAD 患者的严重程度和预后[6] [7]。其中一种生物标志物是 C 反应蛋白(CRP)，它是炎症过程的原型标志物，有助于 CAD，作为疾病的生物标志物备受关注[7] [8]。流行病学研究表明，低白蛋白血症与 CAD 的发展有关系[9] [10]。在最近的研究中，CRP/白蛋白比值(一种新的炎症反应指标)被证明是一种中等价值的动脉粥样硬化标志物，对预测经皮冠状动脉介入治疗(PCI)后支架再狭窄的发展和疾病预后有价值[11] [12] [13]，本文主要对 C 反应蛋白与白蛋白比值(CAR)对冠心病的影响作综述。

2. CAR 对心血管疾病应用价值

C 反应蛋白、白蛋白不仅是系统性炎症的标志，而且可能动脉粥样硬化形成和动脉粥样硬化斑块破坏的积极参与者[14] [15]。在文献报道中，已经证明 CRP 水平的升高，是稳定型心绞痛和 ACS 患者的冠状动脉狭窄程度和心血管事件复发独立相关因素[16] [17]。目前，虽然 CRP 导致冠脉病变狭窄的病理生

理机制尚未研究清楚，但 CRP 很可能通过直接损伤内皮、激活补体等过程，在动脉粥样硬化的所有阶段发挥凋亡作用，血管细胞活化，血栓形成。也有大量证据表明，血浆白蛋白浓度的降低可能与动脉粥样硬化的发展和进展有因果关系。冠心病低白蛋白血症的潜在病理生理机制可能主要与其抗氧化、抗炎、抗血小板聚集活性降低，导致内皮功能受损、血液黏度升高、氧化应激、血小板源性冠状动脉狭窄的重要介质增加[18]。此外，有研究表明，在 C 反应蛋白和白蛋白这两种生化指标在预非心脏疾病导致的全身炎症状态及预后方面，显然 CAR 作为一种新的炎症指标，具有更好地敏感性及特异性[19] [20] [21]。CAR 首先由 Fairclough 等[19]描述，并被提出作为预测急性疾病患者较单独血清 CRP 或白蛋白水平更好的预后参数。与我们的研究类似，Cagdas M 等[22]证实 CAR 可预测 CAD 严重程度。这些作者还报道，CAR 在预测 NSTEMI 患者中更有价值。此外，已有研究表明，CAR 在预测各种非心脏疾病的全身炎症反应综合征和预后方面更有优势[23] [24] [25] [26]。

3. CAR 与冠心病冠脉狭窄程度的关系

众所周知，在炎症反应过程中，血清 CRP 水平炎症的急性期反应物，可以反应一定时间体内的炎症反应严重程度。目前，CRP 水平是否与冠状动脉的狭窄程度有关，还存在一定的争议。在以往的研究中表明，CRP 的水平与冠状动脉的狭窄程度没有相关性[27]，但是，也有相关的研究表明，在冠状动脉疾病的患者中，其 CRP 水平的高低，与病变血管的狭窄严重程度存在相关性[23]。综上可以得知，文献中对 CRP 水平对冠脉的病变严重程度存在一些矛盾结论，暂且没有决断性的证据，但是，在大多数研究中一致发现，血清 CRP 水平的高低是 CHD 患者发病严重程度和预后的独立风险因素，血清 CRP 水平在 CHD 患者的冠状动脉狭窄程度方面，是存在显著差异性的。在最近的研究中文献中已经证明，CAR 在评估几种疾病的严重程度、预后效果及进展相关性等方面是明显优于血清 CRP 的[28]。在 Kalyoncuoglu 等[29]人的所研究的一项回顾性研究中同样发现，在冠状动脉病变严重程度方面，CAR 与其是显著相关的，作为一种容易测量且相对廉价的参数，可以用于预测冠状动脉粥样硬化严重程度的情况。相关的研究表明，通过计算所得的 CAR 在预测各种全身炎症疾病的反应程度和预后方面，是显著优越于 NLR 的。目前，Çinar 等人[30]也提出他们自己的结论，CAR 在预测 STEMI 患者预后不良方面，相对于 NLR 来说，显然具有更加说服力的价值。相关的研究在 CAR 与冠状动脉的狭窄程度方面也得出实验数据，就 Kalyoncuoglu 等人[29]的研究而言，就发现 CAR 在预测冠状动脉狭窄程度的能力方面比 NLR 更有价值。最终得出结论，计算所得的 CAR 数值升高，在预测冠状动脉狭窄程度方面，是一项独立得预测因子，具有临床参考价值。

4. CAR 与 STEMI 发生 MACE 事件的关系

大家都知道，STEMI 是动脉粥样硬化病变中冠状动脉的急性阻塞。CRP 作为炎症介质，直接影响动脉粥样硬化的进展。有研究表明，CRP 升高可增加活性氧水平，通过对氧化低密度脂蛋白的摄取量的增加，诱导内皮细胞的功能障碍及凋亡，最终使血管平滑肌细胞不断增殖，这样就大大增加了动脉斑块破裂的风险性[31] [32] [33]。据报道，CRP 水平升高与不同 CAD 表型患者心血管不良结局风险增加相关[34] [35]。炎症可诱发营养不良，营养不良可能对炎症的管理产生负面影响[36]。前白蛋白作为评价营养状态的一个参数在炎症环境中被抑制[37]。在营养不良的患者中，低水平的前白蛋白可能与维生素 C 缺乏类似[38]，这可能与不良的心脏事件有关，因为维生素 C 在抗氧化和抗炎过程中起着关键作用[39]。前白蛋白水平的降低可以增加游离甲状腺素，这与急性心肌梗死患者的不良结局相关[40]。越来越多的证据表明，低白蛋白血症与动脉粥样硬化风险增加和不良结局相关[41]。相关研究表明，系统性炎症反应和营养不良是 CAD 患者预后不良的原因[42]。心肺复苏术可以揭示体内 CRP 和前白蛋白之间的平衡，评估患者的炎

症和营养状况，这与动脉粥样硬化密切相关。心肺复苏术已被证明在预测急性疾病和癌症患者的预后方面优于 CRP 或单独的前白蛋白[19] [43]。目前的研究证明 CPR 是 STEMI 患者 MACE 和全因死亡率的独立预测因子[44]。

5. CAR 与 CAD 预后之间的关系

Söğüt Ö 等[45]对 2243 名接受 pPCI 的 STEMI 患者研究人群的血管造影特征的评估表明，高 CAR 患者左前降支频率明显升高，为梗死相关动脉，近端/口病变为梗死相关动脉，基线 TIMI 流量 < 3，血栓级别高，血管造影无再流，左主干冠状动脉疾病，与低三次组 CAR 组相比，非梗死相关血管的慢性完全闭塞。与使用中三次组、低三次组 CAR 的患者相比，使用高三次组 CAR 的患者有更高的 TIMI 风险评分。共有 86 例(3.8%)患者在住院期间死亡。高三次组 CAR 患者的全因死亡率显著高于中、低三次组 CAR 患者(分别为 1.3%:1.3%:8.8%；$p < 0.001$)。我们注意到，在住院期间，不良的次要结果在高三次组中比在中三次组和低三次组中更常见。该研究的平均长期随访时间为 34 ± 15 个月。长期随访中，共有 145 例(6.5%)患者死亡。全因死亡率、心肌再梗死和晚期心力衰竭发生率在高 CAR 组比中、低三次组更常见。通过 Kaplan-Meier 生存分析得知，高三次组 CAR 患者的住院存活率(log rank = 45.7, $p < 0.001$)和长期生存率(log rank = 95.1, $p < 0.001$)显著降低。值得注意的是，我们的结果表明，CAR 可能在个体风险方法的发展和 pPCI 的 STEMI 患者的监测中具有附加的预后价值。特别是，CAR 水平升高的患者可能需要更频繁的随访和强化治疗。

6. 结语

综上所述，CAR 值水平升高在 CAD 的发生、发展以及预后中有重要的预测和预后价值，可以评估 CAD 患者冠脉狭窄程度、疾病预后和并发症等相关风险性，它是一种实用、廉价、准确且高效的新型心血管疾病的生化标志物。CAR 在临床实践中具有其潜在的优点，比如，计算简单就是其优点之一，可以在临床中推广使用。然而，CAR 在早期临床干预的具体节点仍未清楚，我们期待今后有多中心、更大规模的关于 CAR 与 CAD 的临床研究结果和实验数据，用以支撑 CAR 在评估 CAD 的预后价值，并为早期干预可能发生的不良心血管事件提供有力依据。此外，CAR 作为一个易于获取的参数，计算简单，可标准化，无需额外费用，这些为患者的预后提供了更多的便利。

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