本文引用：施 展，张步春. 光学相干断层成像对急性冠状动脉综合征患者易损斑块的新认识[J]. 中国动脉硬化杂志，2022，30(9)：817-820. DOI：10.20039/j.cnki.1007-3949.2022.09.012.

[文章编号] 1007-3949(2022)30-09-0817-04

·文献综述·

光学相干断层成像对急性冠状动脉综合征患者易损斑块的新认识

施 展[1]，张步春[2]

(1.安徽医科大学附属省立医院心血管内科,2.中国科学技术大学附属第一医院(安徽省立医院)心血管内科,安徽省合肥市 230001)

[关键词] 光学相干断层成像； 急性冠状动脉综合征； 易损斑块

[摘 要] 血管斑块的稳定性是影响急性冠状动脉综合征发生发展的主要因素,具有超高空间分辨率的光学相干断层成像(OCT)技术在易损斑块识别方面有着独特的优势。本文就近年来 OCT 在急性冠状动脉综合征患者易损斑块识别方面的临床新进展进行综述。

[中图分类号] R445；R5 [文献标识码] A

New recognition of vulnerable plaque in patients with acute coronary syndrome by optical coherence tomography

SHI Zhan[1], ZHANG Buchun[2]

(1. *Department of Cardiology, Anhui Provincial Hospital Affiliated of Anhui Medical University, Hefei, Anhui* 230001, *China*; 2. *Department of Cardiology, the First Affiliated Hospital of University of Science and Technology of China (Anhui Provincial Hospital), Hefei, Anhui* 230001, *China*)

[**KEY WORDS**] optical coherence tomography; acute coronary syndrome; vulnerable plaque

[**ABSTRACT**] Vascular plaque stability is a major factor contributing to the development of acute coronary syndrome, and optical coherence tomography (OCT) with ultra-high spatial resolution has a unique advantage in the identification of vulnerable plaques. This paper reviews the clinical progress of OCT in the identification of vulnerable plaques in patients with acute coronary syndrome in recent years.

急性冠状动脉综合征(acute coronary syndrome，ACS)是冠心病致死的主要原因,传统的冠状动脉造影不能真实反映病变血管情况。被誉为“活体组织显微镜”的光学相干断层成像(optical coherence tomography,OCT)由于其超高分辨率,可在体识别动脉粥样硬化易损斑块组织特征[1-2]。目前国内外指南一致推荐使用血管腔内影像工具 OCT 指导 ACS 患者的精准治疗[3-4]。本文就 OCT 在 ACS 患者易损斑块识别的临床新进展作一综述。

1 OCT 联合血清标志物检测在识别 ACS 患者易损斑块中的作用

血清炎症标志物与易损斑块发生密切相关,近年来国内外学者先后报道 ACS 患者血清标志物水平与血管内 OCT 测得的易损斑块特征影像之间有联系。Refaat 等[5]报道 ACS 患者血清低脂联素水平与 OCT 观察下的斑块破裂、微血栓和薄纤维帽动脉粥样硬化斑块(thin-cap fibroatheromas,TCFA)密切相关,且循环脂联素水平与斑块的富脂坏死核及最大脂质弧度负相关。国内有学者也报道平均血小板体积偏高是非 ST 段抬高型心肌梗死(non-ST-segment elevation myocardial infarction,NSTEMI))患者血管斑块破裂的独立危险因素[6]。既往研究报道,来自肝脏的 γ-谷酰基转移酶(gamma-glutamyl transferase,GGT)在冠状动脉粥样硬化斑块中表达;然而,近期的研究发现 GGT 血清浓度与 OCT 检测的冠状动脉斑块易损性无明显相关性[7]。蛋白质

[收稿日期] 2021-10-06 [修回日期] 2021-12-08

[基金项目] 国家自然科学基金面上项目(81670393)；安徽省卫生健康委科研资助项目(AHWJ2021b082)

[作者简介] 施展,硕士研究生,研究方向为冠心病临床研究,E-mail：shizhanah@163.com。通信作者张步春,医学博士后,副主任医师,副教授,硕士研究生导师,研究方向为冠心病基础及临床研究,E-mail：zhangbc68@ustc.edu.cn。

组学证实纤维蛋白原在男性冠状动脉硬化斑块中高表达,其机制与加速血液凝固、血小板聚集和内皮功能障碍而促进冠状动脉斑块的易损性相关[8],但血清纤维蛋白原浓度与 OCT 观察下的冠状动脉 TCFA 也无相关性[9]。此外,有研究认为外周血单核细胞与淋巴细胞比值(monocyte and lymphocyte ratio,MLR)可以用来判断 ACS 患者非罪犯血管斑块易损性[10-11]。对 ACS 患者精确的危险分层直接影响其治疗决策和预后判断。近期有学者报道,血液炎症标志物 C 反应蛋白(C-reactive protein,CRP)≥2 mg/L 联合 OCT 检测到的血管易损斑块特征可以用来作为 ACS 患者是否反复发生急性心血管事件的危险分层的新指标[12]。

2 OCT 辅助判断 ACS 患者血管斑块形态特征的作用

近年来系列 OCT 研究对 ACS 患者病变血管的斑块特征进行了描述,并探讨了影响易损斑块形成的新因素。来自国内的研究认为,吸烟是引起年轻 ACS 患者发生急性心血管事件的主要危险因素,其原因在于吸烟患者冠状动脉血管纤维斑块增生较少,斑块更易发生破裂[13]。另一项通过 OCT 技术探究具有残余胆固醇风险[关键生物学指标—低密度脂蛋白胆固醇(low density lipoprotein cholesterol,LDLC)≥1.8 mmol/L]的 ACS 患者斑块特征,结果发现在 ACS 患者高敏 C 反应蛋白(high sensitivity C-reactive protein,hs-CRP)水平正常的前提下,具有残余胆固醇风险的患者更有可能表现出动脉粥样硬化性斑块及破裂,但在 TCFA 方面并无显著差异[14],提示这类患者仍具有高度易损性。ST 段抬高型心肌梗死(ST-segment elevation myocardial infarction,STEMI)患者的非罪犯病变血管斑块形态的 OCT 特点如何? COMPLETE 试验的亚组研究结果显示,近 50% 的 STEMI 患者阻塞性非靶病变血管斑块含有更多的脂质含量和易损斑块形态[15],该结论为 STEMI 患者合并多支血管病变进行完全血运重建术提供了新的循证医学证据。在对 245 名 ACS 患者的 OCT 检测分析显示,含有裂隙的不稳定斑块同破裂斑块相比,其坏死脂质核心和血管正性重构减少,裂隙斑块位于冠状动脉近端部位,主要包括斑块破裂和侵蚀[16]。此外,OCT 检测 32 名初次发作的 NSTEMI 患者的原位冠状动脉血管发现,罪犯病变血管巨噬细胞含量和巨噬细胞周向伸展明显增多[17]。研究还发现 ACS 合并胰岛素抵抗患者的病变血管富有较多的巨噬细胞和微血管通道,最小纤维帽厚度与稳态模型胰岛素抵抗指数(homeostasis model of assessment insulin resistance,HOMA-IR)呈负相关,且 HOMA-IR 是不稳定斑块-点状钙化斑块的独立危险因素[18]。

3 OCT 检测的愈合斑块在 ACS 发病机制中的作用

在猝死患者的尸检标本中,愈合斑块(healed plaque)形态上呈现为分层表型,故又被称为分层斑块(layered plaque),愈合斑块之前被认为是斑块破裂后的一种血管自我修复过程。近年来,随着 OCT 在 ACS 患者中的临床广泛应用,发现大于 1/4 的 ACS 患者靶病变血管存在愈合斑块。愈合斑块通常表现出 OCT 的易损性特征,并伴有局部和全身炎症的迹象。斑块易损性、局部炎症和斑块负荷增大以及全身炎症的结合可能会超过斑块愈合的保护机制,并使这些斑块容易形成闭塞性血栓[19]。OCT 检测发现 ACS 患者的非靶病变血管也存在愈合斑块,同时合并斑块易损性特征[20]。在一项前瞻性纳入 325 名急性心肌梗死患者行 3 支冠状动脉原位血管 OCT 检测中,3/4 的急性心肌梗死患者有冠状动脉愈合斑块,其中 STEMI 患者的罪犯血管中愈合斑块更常见,此类患者愈合斑块局限性分布于左前降支和回旋支中,而右冠状动脉愈合斑块分布比较均匀。无论在罪犯病变还是非罪犯病变血管,与非愈合斑块相比,愈合斑块导致管腔狭窄更明显[21]。影响愈合斑块的临床危险因素有哪些? 来自国外研究的多因素回归模型证实,稳定型心绞痛和多支血管病变患者 B2/C 型血管病变和血管狭窄直径大于 70% 都是罪犯血管愈合斑块存在的独立危险因素。该研究认为愈合斑块可能是泛血管易损性和内源性抗血栓保护机制之间的一种平衡[22]。国内陈韵岱教授团队通过回顾性分析来自 85 名 ACS 患者的 113 处非罪犯血管的 OCT 影像学检查图片,结果发现,愈合斑块是血管斑块进展的独立危险因素,ACS 患者愈合斑块的形成原因与合并较高的低密度脂蛋白水平、接受过抗血小板治疗以及血管分叉病变有关[23]。一项针对 265 名冠心病患者 OCT 检测的 2 年随访结果显示,罪犯血管存在愈合斑块,有较高的血运重建发生率[24]。ACS 患者与稳定型心绞痛患者相比较,罪犯病变血管愈合斑块是否存在差异? 一项研究显示,同长期的稳定型心绞痛患者相比,反复发

作的 ACS 患者有着独特的动脉粥样硬化表型,即 TCFA 发生率高,而愈合斑块发生率低,提示斑块愈合可能在冠心病的发病自然史中也发挥作用[25]。另一项来自国内的研究也表明,同近期发作的 ACS 患者相比,愈合斑块更多见于稳定型心绞痛或陈旧性心肌梗死患者,通常合并更多的血管腔狭窄[26]。

根据上述 OCT 观察试验结果,近年来认为动脉粥样硬化斑块的愈合被认为是 ACS 另一潜在致病机制。ACS 的发生很可能是因为动脉粥样硬化斑块不稳定("活化")和愈合("钝化")之间的平衡被打破。改善斑块愈合将成为治疗 ACS 的新靶点。

4 小 结

OCT 在识别 ACS 患者血管易损斑块和揭示其病理机制方面有着独特的优势,且不同类型的 ACS 患者 OCT 影像学冠状动脉斑块特征存在差异,这些信息将为指导疾病的临床干预和术后随访用药等提供重要参考。

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(此文编辑 文玉珊)