

# 支架术后即刻冠状动脉光学相干断层扫描结果的临床影响

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**【摘要】** 冠状动脉光学相干断层扫描的分辨率为 10  $\mu\text{m}$ , 它可为术者提供支架贴壁不良、组织脱垂、支架内血栓和支架边缘夹层等支架术后即刻结果, 但其对临床预后的影响一直存在争议。现总结既往研究, 并就支架术后即刻冠状动脉光学相干断层扫描结果的研究进展及临床影响进行综述。

**【关键词】** 支架术后; 血管内影像学; 冠状动脉光学相干断层扫描; 临床影响

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## The Clinical Influence of Poststent Optical Coherence Tomographic Findings of Coronary Artery

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**【Abstract】** Although the distinguishability of optical coherence tomography has been reach 10  $\mu\text{m}$  which can provides detailed information such as stent malapposition, tissue prolapse, stent thrombosis and stent edge dissection, the clinical influence of poststent optical coherence tomographic findings has been controversial. This article aims at summarize previous research findings and review the latest development and clinical influence of poststent optical coherence tomographic findings of coronary artery.

**【Keywords】** Poststent; Intravascular imaging; Coronary artery optical coherence tomography; Clinical influence

支架在经皮冠状动脉介入治疗 (percutaneous coronary intervention, PCI) 中已成为不可或缺的部分。光学相干断层扫描 (optical coherence tomography, OCT) 作为一种有效的腔内影像学技术, 其成像分辨率为 10  $\mu\text{m}$ , 对单个支架支柱具有良好的可视化, 相比其他影像学技术, 提供了更多研究支架部署细节的机会, 因此 OCT 在指导 PCI 方面的应用越来越广泛。临床实践表明, 支架植入术后即刻 OCT 结果的发生频率远高于早期设想, 且这些结果与不良心血管事件之间是否存在关系以及对临床预后的影响一直备受争议。考虑到支架在 PCI 中的广泛应用, 阐明支架术后即刻 OCT 结果的临床影响, 可避免不必要的操作, 从而优化支架治疗效果。

### 1 急性支架贴壁不良

支架贴壁不良为支架支柱的内表面与血管内腔的分离, 在没有侧支的部分, 其距离大于 OCT 的轴向分辨率 + 聚合物涂层厚度 + 支架小梁厚度, 按支架植入后观察到的时间分为急性贴壁不良 (即术后即刻)

和晚期贴壁不良 (即术后诊断和持续随访评估)。在临床工作中急性支架贴壁不良 (acute stent malapposition, ASM) 是一种常见现象, 常在支架近端边缘被发现<sup>[1]</sup>, 并且药物洗脱支架 (drug eluting stent, DES) 比裸金属支架 (bare metal stent, BMS) 更容易发生<sup>[2]</sup>。DES 植入后, 通过 OCT 观察到 50% 的支架可发生 ASM, 而血管内超声 (intravascular ultrasound, IVUS) 的检出率为 15%<sup>[3]</sup>。

目前认为 ASM 的发生是由于支架和血管管腔轮廓不匹配导致的, 一方面是支架部署不理想, 如支架尺寸过小或扩张不足, 另外一方面是继发于血管结构或病变本身特点, 如开口病变、分叉病变、长病变、成角病变和钙化病变等<sup>[1,4]</sup>。ASM 对支架失败率 (即支架内再狭窄和支架内血栓形成) 的潜在影响一直是一个有争议的问题<sup>[5]</sup>。体外实验<sup>[6]</sup>、小规模 IVUS 和 OCT 研究<sup>[7]</sup> 支持支架贴壁不良与支架内血栓形成有理论联系, 即可能通过引起局部血流干扰和延迟愈合引起支架植入失败。并且也有研究<sup>[8]</sup> 在支架内血栓

形成患者中发现了 ASM。几项使用 OCT 的大型研究<sup>[1,9-10]</sup>显示,ASM 与 DES 植入后的早期、晚期或极晚期支架内血栓形成无关。此外支架贴壁不良的严重程度与临床预后的相关性目前尚不明确。最近的荟萃分析<sup>[11]</sup>显示虽然急性和持续性支架贴壁不良与支架植入后的主要不良心血管事件(major adverse cardiovascular event, MACE) 无关,但严重贴壁不良(错位距离  $\geq 400 \mu\text{m}$  或贴壁不良总体积  $\geq 7.0 \text{ mm}^3$ ) 会增加 MACE 风险。Yonsei OCT 注册研究(以贴壁不良总体积评估贴壁不良严重程度)也指出:显著错位(错位距离  $\geq 400 \mu\text{m}$  且错位长度  $\geq 1 \text{ mm}$ ) 伴有贴壁不良总体积  $\geq 7.0 \text{ mm}^3$  与 MACE 具有显著相关性<sup>[12]</sup>。但此项研究只有 3 例经血管造影明确记录了支架内血栓形成,其余病例都是由研究者推测因支架内血栓形成导致的 MACE,所以未来还需更大规模、多中心的随机观察研究来核实这一结论。

支架贴壁良好为支架优化标准之一,但既往 OCT 研究未显示 ASM 与 MACE 的相关性,且大多数研究<sup>[1,13-14]</sup>认为 ASM 可通过血管重建得到纠正,从而在随访期间实现新生内膜完全整合。然而,ASM 可能持续存在,并最终演变成晚期贴壁不良,引起支架内血栓的形成。此外,支架近端贴壁不良还可能干扰导丝进入,导致器械进出困难或支架变形。为此欧洲经皮心血管介入协会建议,在血管解剖结构可行的情况下,应纠正最大错位距离  $\geq 400 \mu\text{m}$  且最大错位长度  $\geq 1 \text{ mm}$  的急性贴壁不良<sup>[15]</sup>。然而不同类型的支架因其支架小梁和聚合物涂层厚度不同,其贴壁不良的标准也不同<sup>[16]</sup>。对于 DES 支架, OCT 显示错位距离  $\leq 260 \mu\text{m}$  为可修复的支架贴壁不良的临界点,其敏感性为 89.3%,特异性为 83.7%。对亲水聚合物涂层的佐他莫司药物洗脱支架(Resolute, 美敦力, 美国)、含氟聚合物的依维莫司药物洗脱支架(XienceV, 雅培, 美国)以及 BMS 术后 OCT 发现,术后即刻错位距离  $< 270 \mu\text{m}$  的贴壁不良到随访时均可完全修复,只有少数支架小梁一直未被覆盖。对于生物可吸收支架,因其主体材料半晶态左旋聚乳酸较金属柔软,在后扩张不充分的情况下更易出现 ASM,建议其错位距离  $\leq 300 \mu\text{m}$ <sup>[17]</sup>。Foin 等<sup>[18]</sup>对不同等级的支架贴壁不良进行了流体动力学及愈合效果的随访分析,发现  $300 \mu\text{m}$  的错位距离是贴壁不良产生影响变化最为显著的界值,提示术者错位距离  $\geq 300 \mu\text{m}$  时可进行必要的后扩张处理。因后扩张支架所需压力与处理膨胀不良支架所需压力不同,所以无需使用非顺应性球囊进行高压扩张,而使用半顺应性球囊进行低压扩张即可。

## 2 支架组织脱垂和血栓

支架组织脱垂(instent tissue prolapse, ITP)即相邻

支架支板之间血管组织物向管腔突出,组织物脱垂位于支架小梁上方,有或没有破坏管腔血管表面的连续性。根据形态特征, OCT 可将 ITP 分为三类:平滑组织脱垂、非连续性纤维组织脱垂和不规则脱垂(irregular prolapse, IP)<sup>[19]</sup>。由于支板有时埋在内膜内,大多数研究只能通过 OCT 识别最大高度  $\geq 100 \mu\text{m}$  的支架内脱垂。冠状动脉内血栓为直径  $\geq 25 \mu\text{m}$  的肿块附着于腔体表面、支架支撑或漂浮在体腔内。OCT 可区分红色血栓和白色血栓,当血栓与 IP 不能完全区分时,大多数研究将其归类为 IP<sup>[19-21]</sup>。研究<sup>[22]</sup>汇总发现, OCT 能够检测出 58.1%~98.0% 的 ITP, 相比于 IVUS, 具有更高的敏感性。

在 PCI 过程中,血管壁损伤是由于球囊或支架对血管壁的挤压引起的。病理研究<sup>[19]</sup>发现,平滑组织脱垂表现为轻微的血管损伤,非连续性纤维组织脱垂表现为轻中度的血管损伤,IP 表现为重度血管损伤。既往研究<sup>[23]</sup>显示脂质斑块负荷对病变处发生 IP 有着重大影响,可能是薄纤维帽覆盖的富脂斑块相比其他斑块,其最大可承受应力较低,因此在术中易受破坏,易发生组织脱垂。而急性冠脉综合征患者病变多为易损斑块,如脂质弓较大、纤维帽较薄、薄纤维帽粥样斑块,这也与多项研究观察到 ACS 患者 ITP 发生率高有关<sup>[23-24]</sup>。而且 CLI-OPCI II 研究<sup>[3]</sup>和 HORIZONS-AMI 研究<sup>[25]</sup>发现,与临床表现较稳定的患者相比,ACS 患者的 ITP 多为 IP,且更易导致不良临床事件。目前大多数研究认为 IP 是早期支架内血栓形成的 OCT 预测因子,并且与 PCI 后不良临床事件相关,因为 IP 的发生与支架植入过程中脂质核心的渗透和血管深部损伤有关,它可能引起动脉炎症和血栓形成,引起新生内膜的增生,从而增加早期支架内血栓的形成和支架内再狭窄的风险。一项结合 OCT 和血管镜对组织突出的研究<sup>[26]</sup>发现,IP 与血管镜观察到的高级别黄色斑块相关,黄色斑块作为富含脂质的一种特征表现,其亮度越高提示斑块存在较大的脂核和较薄的纤维帽,预示着斑块破裂的危险性高,血栓形成风险增加。并且该研究发现 IP 组的血栓发生率明显高于其他脱垂组。为进一步研究不同形态的 ITP 所导致的临床结局, Soeda 等<sup>[19]</sup>将 ITP 细分为三类,发现 OCT 检测到的 IP 是 1 年器械导向临床终点和目标病变血运重建术的有力预测因子。Bryniarski 等<sup>[21]</sup>也发现合并 IP 的患者的 MACE 发生率增加 150%。为进一步量化 IP 情况,一项评估 ST 段抬高型心肌梗死患者 IP 体积与临床事件之间关系的研究<sup>[27]</sup>发现,最大 IP 角  $\geq 180^\circ$  是 ST 段抬高型心肌梗死合并 IP 患者临床事件的独立预测因子,但 IP 角测量受测量者主观影响较大,可能

影响数据的真实性,并且减少 IP 体积是否可预防未来的心血管事件还需进一步研究。此外支架类型对于 IP 的临床预后影响也不同。最新研究<sup>[28]</sup>表明,虽然第二代 DES 与第三代 DES 在支架植入后的 IP 发生率相似,但使用第三代 DES 后观察到新生内膜多为均质型,这可能对血管愈合有积极的影响。

临床中对于支架内 ITP 的处理策略,首先应考虑降低 ITP 的发生率,尤其是 IP 的发生率。目前认为高水平的血清低密度脂蛋白与薄纤维帽粥样斑块和富含脂质斑块的发生之间存在明显的关联。高水平的低密度脂蛋白会促进斑块内脂质聚集,加速斑块形成,并且影响纤维帽的稳定性<sup>[29]</sup>,而血清低密度脂蛋白水平的降低显示脂质核心纤维帽的厚度增加并稳定内膜斑块<sup>[30]</sup>,因此在支架植入前更积极地降低低密度脂蛋白水平,可能会降低 IP 的发生率。此外在斑块负荷和脂质含量大的病变中使用长支架也可降低 IP 的发生率<sup>[21]</sup>。选择合适的支架尺寸和成像方式对于避免 IP 的发生也至关重要。OPINION 研究<sup>[31-32]</sup>比较了 IVUS 和 OCT 引导的 PCI,结果显示 OCT 引导的 PCI 支架面积更小以及 IP 发生率更低。其次,若出现了 ITP,首先评估 ITP 的严重程度,对于重度组织脱垂(即支架内组织脱垂最大厚度  $>200\ \mu\text{m}$ ,组织脱垂面积与支架面积比  $\geq 10\%$  且最小支架内血流面积  $<$  近端或远端参考面积的  $90\%$ )或影响血流的组织脱垂,《光学相干断层成像技术在冠心病介入诊疗中应用的中国专家共识》<sup>[33]</sup>建议进一步使用 1:1 球囊低压力、长时间扩张,必要时可考虑再次植入 BMS 或 DES。

### 3 支架边缘夹层

支架边缘夹层(stent edge dissection, SED)是指在支架近端和远端 5 mm 内,血管腔表面连续性中断,可观察到内膜撕裂片或内膜下血肿。OCT 将 SED 分为内膜撕裂与血管被拉伸、内膜分离两种类型<sup>[34]</sup>。夹层的严重程度按夹层的长度和角度来划分,分为重度(夹层角度  $\geq 60^\circ$  且长度  $\geq 3\ \text{mm}$ )和轻度(夹层角度  $< 60^\circ$  或长度  $< 3\ \text{mm}$ ),同时也可通过衡量血管损伤的深度进一步评估,分为以下三种类型:(1)内膜型,撕裂局限在斑块或内膜层;(2)中膜型,撕裂延伸到中膜层;(3)外膜型,撕裂延伸通过外弹力膜<sup>[35]</sup>。OCT 检测到的 SED 的比例为  $19.0\% \sim 39.1\%$ <sup>[35-37]</sup>。其中远端边缘的发生率几乎是近端边缘的 2 倍<sup>[35,38-39]</sup>。

有研究<sup>[35,40]</sup>表明发生 SED 的决定因素是支架植入到纤维钙化或脂质斑块等明显处。此外,管腔偏心是 SED 的另一个危险因素,对于有较大管腔偏心率的病变,在支架扩张时,血管壁受力不均易损伤内膜形成夹层<sup>[38]</sup>。既往只有少数研究<sup>[3,35,41-42]</sup>报道了支架植

入后 OCT 检测到的 SED 与不良临床预后相关,但可能因为患者数量较少,未能显示这种显著的相关性。目前已有相关研究表明 SED 与支架内血栓形成的高发生率和 MACE 有关,其中 CLI-OPCI 注册研究<sup>[43]</sup>表明远端厚度  $>200\ \mu\text{m}$  的夹层片被认为是主要夹层,在长期随访中与较差的临床预后相关,并且使 MACE 发生率升高 2.5 倍。最新公布的 ILUMIEN IV 研究<sup>[44]</sup>表明 OCT 指导 PCI 虽然实现了更好的支架植入即刻效果,降低了严重 SED 的发生率,但可能因为新冠疫情的原因,该研究并未发现 OCT 指导组与血管造影组 2 年内靶血管重建失败率的差异。

对 SED 的评估主要关注夹层深度、位置、长度、角度、对血流的影响、剩余有效管腔面积等几个指标<sup>[45]</sup>,一般来说,局限于内膜、角度  $< 45^\circ$  且长度  $< 2\ \text{mm}$  的夹层可不作处理<sup>[42]</sup>。而夹层累及中膜/外膜、残余斑块负荷明显、位于支架远端、角度  $> 60^\circ$  或长度  $> 2\ \text{mm}$  的夹层需要进一步处理<sup>[15,40,42]</sup>,包括植入新的支架以覆盖夹层全长,或行冠状动脉旁路移植术。此外正确的支架着陆位置、支架尺寸及扩张压力可减少 SED 的发生。在选择支架着陆位置时,应避免进行性动脉粥样硬化斑块和管腔偏心率较大的病变。在确定支架长度时,应考虑到支架可能在非计划区域着陆的情况而选择稍长支架。对于最小支架面积较小的血管,建议行支架扩张,以降低靶血管重建和 MACE 的发生率,但积极的支架扩张会增加发生 SED 的风险,所以应谨慎选择扩张位置及压力。

### 4 总结与展望

支架术后即刻 OCT 结果是常见且具有重要意义的。通过使用 OCT 技术进行支架术后即刻检查,可提供关键信息,评估支架植入后的效果,能及时发现支架贴壁不良、ITP 及 SED 等问题,为术后优化提供清晰的影像学支持,同时帮助术者预测 PCI 后临床不良事件风险。

ILUMIEN 系列研究肯定了 OCT 在评估冠状动脉病变、指导介入治疗、评价治疗效果等方面具有重要的应用价值,目前中国对于 OCT 指导的支架置入优化标准为:(1)支架膨胀率  $> 80\%$ ,在非左主干病变中,最小支架内面积  $> 4.5\ \text{mm}^2$ ;(2)无重度边缘夹层,夹层局限于内膜且无明显血肿发生风险;(3)无严重贴壁不良(轴向距离  $< 400\ \mu\text{m}$ ,长度  $< 1\ \text{mm}$ );(4)无重度组织脱垂,且组织脱垂不影响血流;(5)支架边缘不存在富含脂质区域。相信随着支架的迭代发展,相应的 OCT 指导的支架置入优化标准也会与时俱进。未来研究支架术后即刻 OCT 结果与支架失败的直接关系,需要考虑支架类型、纳入更多的人群、更规范的操作

作和评估方法。相信将来随着 OCT 技术的不断进步及临床数据的积累, OCT 在冠状动脉介入治疗的应用会越来越广泛。

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