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通过血管内超声评估冠脉支架贴壁不良的研究进展

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摘　要

支架贴壁不良(stent malapposition, SM)现象普遍存在于经皮冠脉介入治疗后，根据发生的时间将支架贴壁不良分为急性支架贴壁不良(acute stent malapposition, ASM)和晚期支架贴壁不良(late stent malapposition, LSM)。LSM可能对术后患者的心肌梗死和晚期支架内血肿的发生有影响，但ASM与预后结局的关系仍有争议。通过血管内超声(intravascular ultrasound, IVUS)评估SM及其对预后的影响时，支架种类可能影响SM的发生率，弥漫性的钙化病变、支架对称性、炎症反应和支架长度等可能是SM的相关危险因素，SM的严重程度和支架内最小面积可能是预测临床结局的有效指标。IVUS在防治支架贴壁不良中具有不可忽视的作用，尤其对于左主干这类疾病的患者行介入干预时。在晚期支架内血栓病变的患者中，SM的发生率更高，此类患者建议长期口服双重抗血小板药物治疗。

关键词

经皮冠状动脉介入治疗，血管内超声，支架贴壁不良，预后

Research Advances in the Assessment of Stent Malapposition in Coronary Artery by Intravascular Ultrasound

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Abstract

Stent malapposition (SM) is a common phenomenon after percutaneous coronary intervention (PCI), and it is categorized into acute stent malapposition (ASM) and late stent malapposition (LSM) according to the time of occurrence. LSM may have an impact on the development of myocardial infarction and late in-stent thrombus in postprocedural patients, but the relationship between ASM and prognostic outcomes remains controversial. When assessing SM and its prognosis by intravascular ultrasound (IVUS), stent type may influence the incidence of SM. Diffuse calcified lesions, stent symmetry, inflammatory response and stent length may be relevant risk factors for SM. The severity of SM and the minimal stent area may serve as effective indicators for predicting clinical outcomes. IVUS plays a crucial role in preventing SM, particularly when treating patients with left main coronary artery disease. The incidence of SM is higher in patients with late stent thrombotic lesions, and long-term dual antiplatelet therapy is recommended for such patients.

Keywords

Percutaneous Coronary Intervention, Intravascular Ultrasound, Stent Malapposition, Prognosis

1. 引言

经皮冠状动脉介入术(percutaneous coronary intervention, PCI)是目前治疗冠心病的有效方法[1]。近年的研究表明，与传统冠脉造影相比，血管内超声(intravascular ultrasound, IVUS)指导下的 PCI 具有更好的临床结局，因此也彰显了 IVUS 在指导冠心病介入治疗中的应用价值与地位，其中对于支架贴壁不良的评估及处理具有不可忽视的作用[2] [3] [4]。本文将从支架贴壁不良的定义与发生率、发生原因与影响因素、临床影响及其防治等方面作一综述。

2. 支架贴壁不良的定义与发生率

支架贴壁不良(stent malapposition, SM)是指支架小梁与冠脉内膜之间未能完全贴合并遗留腔隙，其间可见血流影像[5]。严重的 SM 被定义为支架小梁到血管壁的距离(轴向距离) ≥ 0.4 mm 或支架未贴壁的长度(纵向长度) ≥ 1 mm [6]。根据 SM 发生的时间,可以分为急性支架贴壁不良(acute stent malapposition, ASM)和晚期支架贴壁不良(late stent malapposition, LSM)。ASM 是指在支架植入后即刻出现的 SM，LSM 是指在 PCI 术后即刻支架完全贴壁，而在随访检查中发现存在 SM [7] [8]。

SM 的发生率与支架种类有关。文献报道，植入药物洗脱支架(drug-eluting stent, DES)的患者合并 LSM 的发生率高于植入裸金属支架(bare metal stent, BMS)的患者[9] [10]。Guo 等人[11]研究发现在 ST 段抬高型心肌梗死的患者中，ASM 的发生率在 BMS 为 40.3%，高于 DES 的 34.3%，而 LSM 的发生率在 DES 为 46.8%，显著高于 BMS 的 29.0%，但是该研究排除了左主干病变患者。RAVEL 研究[12]表明，植入 BMS 的患者合并 LSM 的发生率为 4%，而植入 DES 的患者 LSM 发生率为 21%。Hur 等人[13]通过荟萃

分析也显示，DES 组患者 LSM 发生率显著高于 BMS 组(11.8 vs 4.2%)。据报道，西罗莫司药物洗脱支架(sirolimus-eluting stents, SES)植入后 SM 发生率为 25% [14]；而在 TAXUS-II 和-IV 试验中，紫杉醇药物洗脱支架(paclitaxel-eluting stents, PES)植入后 6~9 个月 SM 发生率在 4.4%~8.0%之间[15] [16] [17]。Cook 等人[5]研究也得出了同样的结论，即 SES 组的 SM 比 PES 组发生更常见(27% vs 9%, p = 0.001)。作者认为产生这种现象的原因可能是 SES 组比 PES 组的晚期血管内丢失报告率低，其次也可能与支架植入时不均匀的扩张或慢性回缩有关。

3. 支架贴壁不良的发生原因与影响因素

SM 的原因在 ASM 与 LSM 中有所不同。ASM 发生的原因[18]有：① 支架尺寸和管腔直径不匹配；② 支架植入时的膨胀压力不够，或者病变相关因素如巨大斑块、严重钙化或血管扩张导致的支架扩张不足[19]；③ 急性血栓阻挡了支架金属梁与血管内膜的紧密接触，但在随后几周内血栓消退，导致了 SM [20]。LSM 产生的机制主要有：① 血管壁正性重塑。对植入 DES 患者的 IVUS 随访研究显示，LSM 患者支架段存在血管壁正性重塑，并可能与过敏反应(嗜酸性粒细胞的浸润)和炎症过程有关[21]。Cook 等人在 28 例非常晚期的支架内血栓患者中对 10 例患者进行血栓抽吸后 IVUS 影像分析，LSM 发生率为 73%，这些患者的支架段血管横截面积显著高于参考段血管横截面积，且嗜酸性粒细胞的数量与支架贴壁不良的横截面的面积存在相关性，表现为明显的血管壁正性重塑。② 支架部位的急性血栓在后续随访中溶解，因此 IVUS 检查可表现为 LSM [11] [22] [23]。

SM 的影响因素有：① 钙化：严重的钙化程度可能会影响支架植入后的效果。Kyodo 等人认为[24]，即使在旋磨术后再进行高压球囊后扩张，靶病变处钙化的存在也可能增加 SM 的风险，并且 SM 的严重程度(支架小梁到血管壁的最大距离)与靶病变处的最大钙化角度有显著相关性，但是与钙化的厚度无关。② 支架偏心率：通过 IVUS 测得理想的支架植入标准是支架完全贴壁以及支架偏心率 ≥ 0.7 [25]，后者是指在每一帧图像测得最小支架直径/最大支架直径后计算的平均值，并与 SM 可能存在相关性。Hoffmann 等人认为[26]，在弥漫性钙化病变的患者中，钙化程度越高，支架偏心率越小。③ 支架对称性：是指(最大支架直径 − 最小支架直径)/最大支架直径，以上的最小支架直径和最大支架直径可能来自于不同的横断面[27]。支架对称性的阈值定义为 0.3 [28]。研究表明[29]，支架对称性比偏心率更有意义。值得注意的是，支架对称性 < 0.3 和支架偏心率 ≥ 0.7 是否有关联需要进一步证实。④ 炎症介质：炎症与冠状动脉疾病的发生、进展及预后密切相关。Peng 等人[30]研究表明，血清 hs-CRP、miRNA-21 和 MMP-2 是 LSM 发生的危险因素，MMP-2 升高和 MMP-2/TIMP-2 失衡可能是导致 PCI 术后 LSM 的潜在机制。⑤ 其它：Hong 等人[31]研究表明，支架长度、急性心肌梗死患者直接支架植入术和 CTO 病变是发生 LSM 的独立的相关因素。Enrico 等人[32]探讨了 864 例患者 1020 个病灶，其中左主干病变部位有 55 个(5.4%)，研究发现左主干疾病、稳定性心绞痛、支架预扩张或后扩张、残余性狭窄、支架内斑块脱垂与 SM 具有相关性。

4. 支架贴壁不良的临床影响

目前普遍认为 ASM 与患者 PCI 术后长期的临床影响无关。Enrico 等人[32]纳入了 864 例患者，在中位随访 302 天(IQ 127-567)时，ASM 并不影响主要心脏不良事件发生的风险。前瞻性研究显示，IVUS 检查中的 SM 与随访后的心血管事件无明显相关。在支架植入后即刻影像的相关研究中，ASM 并不是支架内血栓形成的独立预测因子[2] [11]。尽管如此，保证最佳的支架贴壁在冠脉病变患者人群中依然是必要的。

研究显示，LSM 可影响 PCI 患者术后长期的临床结局，尤其在晚期支架内血栓的发生方面。Cook 等人[5]共对 194 例病变患者进行了 5 年的前瞻性随访，在 8 个月时对患者进行 IVUS 评估，显示有 37 例(19.1%)患者存在 LSM，结论提示 LSM 与患者发生主要不良心脏事件有关。虽然在死亡方面没有差异，

但心肌梗死和晚期支架内血肿的发生率均高于支架贴壁良好的患者。在分析支架内血栓的患者中发现支架贴壁不良并不少见[33]，其中 PRESTIGE 研究和 PESTO 研究表明[34] [35]，在急性支架内血栓形成的患者中，SM 的发生率分别为 27%和 60%，在晚期支架内血栓形成的患者中，SM 的发生率分别为 10%和 44%。

SM 的严重程度也作为 PCI 术后是否进行后扩张的一个参考因素，当 SM 的严重程度超过一定的水平是否是安全的值得进一步探讨。一系列研究发现,支架贴壁不良轴向距离 < 0.35 mm 的支架小梁在随访过程中会完全与血管内皮细胞融合[36] [37] [38]。有研究发现在晚期支架内血栓形成的患者中，SM 的轴向距离普遍在 0.3~0.6 mm 之间，纵向长度在 1.0~2.1 mm 之间[39]。Kim 等人[40]研究了 SM 的轴向距离、纵向长度以及周长等指标，进行了三维测量支架贴壁不良的标准，将 SM 的严重程度用总贴壁不良体积(total malapposition volume, TMV)来表示，通过前瞻性随访表明，TMV ≥ 7 mm^2 与心脏不良事件的发生具有显著相关性。

此外，最小支架内面积(minimum stent area, MSA)亦可影响患者的临床结局。有研究通过 IVUS 将左主干支架内 MSA < 8 mm^2、分叉部 MSA < 7 mm^2、左前降支开口 MSA < 6 mm^2、左回旋支开口 MSA < 5 mm^2 定义为支架扩张不良，存在支架扩张不良的患者其再狭窄率较高[41]。研究显示,支架内 MSA ≤ 5 mm^2、支架边缘斑块负荷 $\geq 50\%$、支架边缘夹层、弥漫的支架贴壁不良是远期不良事件的独立预测因素[28] [42] [43] [44]。Lee 等人[45]研究了由 IVUS 引导的支架植入后对 1254 例患者 3 年临床结局的影响，文章指出，若达到 MSA > 5.5 mm^2 或 MSA/远端参考官腔面积 $> 90\%$的标准，将与长期的临床终点改善相关，因此为了实现远期效果的改善，应尽量使支架膨胀。EXCEL 的研究[46]结论也表明 MSA 对患者的全因死亡、心肌梗死、支架内血栓形成具有不良影响。

5. IVUS 在支架贴壁不良防治中的作用

IVUS 在防治 SM 中具有如下作用：① IVUS 可以提供更多的病变细节，如管腔直径、斑块特点、斑块在病变管腔中的分布等，从而可以指导支架直径和长度的选择及定位；② IVUS 有助于优化支架策略(即单支架还是双支架)；③ PCI 术后行 IVUS 可以发现支架贴壁不良和支架膨胀不全，可通过后扩张进一步优化，从而获得更大的支架尺寸；④ 能及时发现急性并发症如支架边缘夹层/血肿或支架变形[47] [48] [49] [50]。更重要的是，对于左主干病变的诸多特征如左主干分叉前后的直径差异、不规则管腔结构、偏心斑块、严重钙化等，这些很难仅通过血管造影进行正确判别[51] [52] [53]，因此 IVUS 在冠脉病变患者的介入干预中具有独特的应用价值作用。

由于 SM 的发生机制尚不完全清楚，目前仍无法完全避免其发生。在 PCI 术中及随访过程中运用 IVUS 等先进的影像学技术，既可以提供更多的病变细节，也能够帮助优化支架策略，可以早期发现支架贴壁不良，通过后扩张去进行优化，从而可以获得更大的支架尺寸，对降低 SM 的发生率有一定的作用。针对 LSM 患者，应该加强临床监测，并且延长双联抗血小板药物治疗的时间，有望降低晚期支架内血栓形成的风险。目前关于 LSM 患者介入干预策略尚无一致的结论。此外，未来随着新型支架的不断研发和应用于临床实践，可能为解决 SM 提供更优的选择。

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