

# 冠心病多支病变患者PCI术后非罪犯血管病变进展的相关因素分析

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## 摘要

MVD患者在PCI术后发生不良心血管事件的发生率仍较高, 这与NCCL的进展密切相关。PCI后MVD患者炎症水平与冠心病危险因素与NCCL病变进展的相关性, 可作为PCI后MVD患者准确评估和早期干预的基础, 以期减少不良心血管事件的发生率, 从而降低患者死亡率, 改善患者预后。

## 关键词

冠心病, 经皮冠状动脉介入治疗, 非侵犯性血管疾病进展, 多血管疾病

## Analysis of Factors Related to the Progression of Non-Offender Vascular Disease in Patients with Coronary Heart Disease after PCI

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## Abstract

MVD patients still have a high incidence of adverse cardiovascular events after PCI, which is close-

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ly related to the progression of NCCLs. The correlation between the level of inflammation and risk factors of coronary heart disease in MVD patients after PCI and the progression of NCCLs lesions can be used as a basis for accurate assessment and early intervention of MVD patients after PCI, to reduce the incidence of adverse cardiovascular events, thereby reducing patient mortality and improving patient outcomes.

## Keywords

Coronary Heart Disease, Percutaneous Coronary Intervention, Progression of Non-Offender Vascular Disease, Multi-Vessel Disease

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## 1. 引言

冠状动脉粥样硬化性心脏病是指冠状动脉发生粥样硬化引起管腔狭窄或闭塞, 导致心肌缺血缺氧或坏死而引起的心脏病, 简称冠心病(coronary heart disease, CHD), 也称缺血性心脏病。以冠心病为代表的动脉粥样硬化性疾病是目前人类最主要的死因, 据世界卫生组织官网报道, 全球每年 1790 万人死于心血管疾病, 其中估计 740 万人死于冠心病[1]。目前我国冠心病患者达 1100 万, 死亡率达 113/10 万, 且自 2012 年以来继续呈增加态势[2] [3]。随着生活方式、环境条件、人口老龄化趋势的改变, 冠心病发作趋势正从单支病变向多支血管病变(multi vessel disease, MVD) [4]发展, MVD 是指至少两支主要冠状动脉或其主要分支直径狭窄超过 50%以上, 而近年来的研究发现, MVD 的发生率较前明显增加, 约 40%~60% 的患者在冠脉造影检查中发现有多支血管病变[5]。MVD 患者的冠状动脉情况更加复杂, 其血管病变多弥漫, 且常合并有慢性闭塞、钙化、分叉病变, 部分血管病变开通难度大, 常存在病情较重、治疗困难、预后较差、猝死风险高、并发症较多等特点, 与单支血管病变的患者相比预后更差, 1 年内死亡率增加 2 倍以上[6], 在临床工作中一直是冠心病综合治疗方案中的难题。

## 2. MVD 的病理基础

MVD 患者的病理基础同动脉粥样硬化, 是由于年龄、吸烟、肥胖、高血压病(essential hypertension, EH)、高脂血症(hyperlipidemia)、糖尿病(diabetes mellitus, DM)、高尿酸血症、高同型半胱氨酸血症、家族史等多种危险因素共同作用的结果。但随着对病理基础的深入研究发现, 人们逐渐发现动脉粥样硬化是一种综合性炎性疾病, 各种危险因素造成的动脉内膜损伤是冠状动脉粥样硬化发生的始动环节, 动脉内膜在各种因素的刺激下致内膜损伤, 并进一步发生纤维增生反应, 进而演变成动脉粥样硬化, 该过程有大量的生长因子、炎症因子、炎细胞和血管调节分子参与其中[7] [8]。在此过程中, 免疫机制与代谢性危险因素相互作用, 启动、传播和激活动脉粥样硬化病变[9]。

## 3. MVD 的治疗方案

MVD 患者的治疗方案中, 其无可置疑的核心地位是长期口服药物, 而除此之外, MVD 患者还需采用血运重建治疗, 重建策略包括不完全血运重建(incomplete revascularization, IR)和完全血运重建(complete revascularisation, CR) [10]。CR 相比 IR 的优势显而易见, 不仅可减少或消除局部心肌缺血风险, 也可以

降低死亡率、心绞痛发作频率、再次心肌梗死和重复手术率[11],但在实际工作中由于患者意愿、血管钙化及血管迂曲、血管弥漫性病变等原因,IR 较 CR 更加常见[12]。血运重建的方式包括两种:经皮冠状动脉介入治疗(percutaneous coronary intervention, PCI)和冠状动脉搭桥手术(coronary artery bypass graft, CABG)。IR 又以经皮冠脉介入术(percutaneous coronary intervention, PCI)为主要治疗方式。PCI 技术发展至今,以其微创、快速开通血管等特点成为治疗 CHD 最有效、最直接的手段,在我国临床上普及飞快。随着 Mehta SR、Ibanez B, James S 等国外学者在近几年来研究中发现,血流动力学稳定的急性 ST 段抬高性心肌梗死合并多支血管病变的患者中,完全血运重建策略要明显优于仅开通罪犯血管策略[13],因此 ESC 的指南中,对非罪犯血管血运重建给出了 IIa 级的建议[14]。然而,在两项大型 Meta 分析中,STEMI 合并 MVD 的患者非罪犯血管 PCI 的最佳时机,尚未确定,完全血运重建的益处是否大于相关风险仍有待于进一步确定[15] [16] [17]。一方面,完全血运重建可以限制心肌梗死范围,并通过解除冠状动脉的严重狭窄防止再发心肌缺血。另一方面,非罪犯血管的完全血运重建通常需要更长的手术时间和更多的造影剂,因此可能会增加急性肾损伤和急性左心室容量超负荷的风险[18]。另有 Elgendy IY, Mahmoud AN 等学者在相关研究中发现,在早期干预非罪犯血管优于仅干预罪犯血管,这会使得患者获益变得更多。同时期的国内学者在研究中也同样证实早期行完全血运重建,可以显著减少患者全因死亡率、心力衰竭等不良结局的发生,让患者临床获益,改善预后。因为心肌损伤处于最危险的状态,非梗性狭窄也可能导致心肌损伤,所以在基于国内外的相关研究下,除非患者存在心源性休克,当前指南不鼓励在急性心肌梗死患者的急诊 PCI 治疗中同时预防性处理非罪犯血管。

#### 4. NCCLs 对 MVD 患者预后的影响

但随着 PCI 技术的发展,人们发现 PCI 术后不良心血管事件的相对发生率仍然较高,究其原因,这可能与 PCI 术后血管内膜局部炎症反应以及缺血再灌注损伤加重炎症反应密切相关[19],诸如 C 反应蛋白、白介素-6、白细胞、淋巴细胞、血小板等多种炎症因子、炎症细胞均参与此炎症反应过程,在实际的临床工作中,这些指标可以帮助对高危患者的未来风险的预测。2014 年, Hu B, Yang XR 等学者提出一个新的参数指标[20],并且命名为“系统免疫炎症指数”(SII: 血小板数  $\times$  中性粒细胞/淋巴细胞比值),SII 是一种综合了三种炎性外周细胞计数的新指标,最初是在肿瘤学领域进行风险预测的[21],高 SII 被报道与癌症患者的不良预后相关[22]。此后有学者研究发现 SII 也可能与慢性心力衰竭的不良预后相关[23]。基于以上研究成果的深入研究, SII 对评估 CHD 患者 PIC 术后的血管炎症反应水平有着一定的临床价值[24]。

通过对 MVD 患者 PCI 术后随访结果的分析发现,在对罪犯血管成功实 PCI 后,并规律冠心病二级预防药物治疗的情况下,出现严重不良心血管事件(major adverse cardiac events, MACE)的几率却居高不下,需要住院或再次血运重建。而继续研究发现非罪犯血管(non-culprit coronary lesions, NCCLs)病变进展与 MACE 关系密切[25] [26]。NCCLs 病变进展是指:(1) 间隔 6 个月或以上重复行冠脉造影的患者中,发现有至少 1 处冠脉病变直径狭窄增加  $\geq 20\%$ 和(或)任何病变发展为完全闭塞;(2) 原来造影正常的血管出现新发的  $\geq 20\%$ 的狭窄[27]。而在多数情况下, MVD 患者初次行 PCI 治疗时,因 NCCLs 病变较轻,不是支架植入的适应症,未做相应干预,但是在临床工作中发现,有相当一部份 MVD 患者在 PCI 术后,  $\geq 6$  月后复查冠状动脉造影结果中显示, NCCLs 有不同程度的进展[28],这将会极大提高 MVD 患者的不良心血管事件发生率。

#### 5. NCCLs 进展的相关因素

随着今年来的研究发现,在 PCI 的治疗过程中,球囊扩张时和支架植入后,人为的原因导致了斑块

的破裂,破坏了原有的炎症因子之间的相互平衡状态,有研究证实 PCI 术后的炎症程度和临床预后相关[22]。也有研究表明,PCI 术后患者会出现心肌损伤的情况,其直接原因是球囊预扩张时间的长短、预扩张的次数、扩张压力之大小,导致肌钙蛋白 1 (CTNI)的升高,其压力和扩张时间过长导致病人不稳定斑块破裂,斑块内所含脂质成分渗透到病人的管腔,其具有促进炎症因子的作用,会使炎症因子升高,具有很强的促凝作用,能激活病人血小板,促进血栓形成[29] [30]。而对 MVD 患者 PCI 术后间隔 3~6 月后再次行冠状动脉造影(coronary angiography, CAG)后发现,此类患者 NCCLs 病变由临界病变逐渐发展成严重病变,NCCLs 病变逐渐加重,并由稳定性斑块变成不稳定性斑块,导致心血管不良事件发生率增加,已成为 MVD 患者 PCI 术发生不良预后的一个重要原因[31] [32]。NCCLs 病变进展显著的影响了 MVD 患者 PCI 术的预后,其快速进展是 PCI 术后面临的一个重要问题[33] [34]。当前,在国内外众多学者针对 NCCLs 病变进展的研究下发现,其机制可能与脂质代谢紊乱、炎症反应学说、氧化应激学说、肾功能不全、血小板功能亢进学说、血栓形成学说、免疫功能异常、服药依从性及行 PCI 术时导管等相关器械对 NCCLs 内皮细胞的损伤有关。异物置入引起机体的炎症反应,可使 C 反应蛋白水平升高,有学者认为其可促进 AS 的进展;各脂质代谢因子水平的紊乱与心血管疾病密切相关;Reddan 等学者发现,肾功异常也会在不同程度上影响 MVD 患者预后;血小板激活后可参与 AS 的发生发展等,这些危险因素均得到大家的关注[35] [36]。而以上这些结果会不同程度的导致管腔阻塞(主要是斑块和血栓碎片的微栓塞)、炎症以及心肌水肿和坏死可出现短暂的微血管功能障碍[37],这种微血管损伤并不局限于罪犯血管,还可能延伸到非罪犯血管[38]。而非罪犯血管的斑块位置、斑块特征和斑块类型等也与上树因素共同影响非罪犯血管的病变进展[39]。

## 6. 小结

综上所述,冠心病多支血管病变的综合性治疗在临床工作中一直都是较为复杂和棘手的问题,在规律的冠心病二级药物预防的基础之上,冠心病多支病变患者在 PCI 术后仍有很高的不良心血管事件发生率,远期预后非常差,这与非罪犯血管的进展密切相关,在此后的研究方向中,我们应该多加探索多支血管病变患者在 PCI 术后相关炎症水平、冠心病危险因素的变化水平,同非罪犯血管病变进展程度之间的关联性,以此为依据对多支血管病变患者 PCI 术后进行精准评估和及早干预,这符合心血管治疗中的精准原则,从而降低不良心血管事件发生率,从而降低患者死亡率,乃至改善患者预后。

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