

晚期慢性肾脏病患者冠状动脉粥样硬化性心脏病 治疗方案研究进展

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【摘要】 冠状动脉粥样硬化性心脏病(冠心病)是慢性肾脏病患者死亡的重要原因之一,尤其是晚期慢性肾脏病[估算的肾小球滤过率 $<30\text{ mL}/(\text{min}\cdot 1.73\text{ m}^2)$]。合并肾功能不全的冠心病患者心血管风险较高,预后较差。因警惕对比剂肾病风险,此类患者很少行冠状动脉造影检查来评估病变,且关于冠心病治疗的临床研究通常将晚期慢性肾脏病患者排除在外,导致此类患者最佳治疗方案尚无定论。现回顾冠心病合并晚期慢性肾脏病患者相关临床研究,总结目前对于该类患者最佳的治疗方法。在冠心病合并晚期慢性肾脏病患者中,对于 ST 段抬高型心肌梗死患者行血运重建治疗优于内科保守治疗。而非 ST 段抬高型心肌梗死及不稳定型心绞痛患者的最佳治疗方案尚无统一论,仍需更多的临床研究证实。对于稳定型冠心病患者首选内科保守治疗。临床中仍需权衡利弊,对不同患者的治疗方法进行个体化指导。

【关键词】 晚期慢性肾脏病;冠状动脉粥样硬化性心脏病;治疗

【DOI】10.16806/j.cnki.issn.1004-3934.2023.07.002

Treatment of Coronary Atherosclerotic Heart Disease in Patients with Advanced Chronic Kidney Disease

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【Abstract】 Coronary atherosclerotic heart disease (CHD) is one of the important causes of death in patients with chronic kidney disease, especially in patients with advanced chronic kidney disease [estimated glomerular filtration rate $<30\text{ mL}/(\text{min}\cdot 1.73\text{ m}^2)$]. CHD patients with renal insufficiency have high cardiovascular risk and poor prognosis. Due to the risk of contrast nephropathy, these patients seldom undergo coronary angiography to evaluate the pathological changes. Clinical studies on the treatment of CHD usually excluded patients with advanced chronic kidney disease, leading to the uncertainty of the best treatment scheme for these patients. This paper reviews the relevant clinical studies of patients with CHD complicated with advanced chronic kidney disease, and summarizes the best treatment methods for these patients at present. In the patients with CHD complicated with advanced chronic kidney disease, revascularization therapy is superior to medical conservative treatment for patients with ST segment elevation myocardial infarction. However, the best treatment for patients with non-ST segment elevation myocardial infarction and unstable angina pectoris has not been determined, and more clinical studies are needed to confirm it. Conservative medical treatment is the first choice for patients with stable coronary heart disease. In clinic, it is still necessary to weigh the pros and cons and give individualized guidance to the treatment methods of different patients.

【Key words】 Advanced chronic kidney disease; Coronary atherosclerotic heart disease; Treatment

冠状动脉粥样硬化性心脏病(冠心病)是目前世界范围内主要致死疾病之一,占全球死亡率的27%^[1]。随着社会城市化和老龄化进程的加快,冠心病发病率及死亡率逐年升高。慢性肾脏病(chronic kidney disease, CKD)也是全世界主要的公共卫生问题之一,相关数据表明,CKD 的全球患病率估计为14.9%^[1],并且有逐年增加趋势^[2]。

冠心病是 CKD 患者最常见的并发症之一,是 CKD

患者死亡的主要原因^[2-3]。合并 CKD 的冠心病患者除了暴露于糖尿病、高血压、肥胖、吸烟等传统心血管疾病危险因素外^[4],还暴露于其他非传统危险因素,包括炎症、氧化应激增加和钙磷代谢异常等^[5],可能会加速冠状动脉病变的进展^[6]。研究表明,心血管危害与 CKD 的严重程度呈正相关^[7],CKD 分期越严重,预后越差^[8]。

冠状动脉造影及介入诊疗技术是目前冠心病诊

断及治疗的主要方法,术中需使用到的对比剂经肾脏代谢,可能导致肾功能恶化^[9],因此在临床诊疗中,晚期 CKD 患者很少接受侵入性治疗,且大量临床研究几乎将重度肾功能不全患者排除在外^[10],导致此类患者的最佳治疗方案尚无定论。现对晚期 CKD 患者的冠心病治疗方案选择进行总结,为临床诊疗提供参考。

1 治疗方案选择

目前冠心病主要有 3 种治疗方法:药物治疗、经皮冠状动脉介入治疗(percutaneous coronary intervention, PCI)和冠状动脉旁路移植术(coronary artery bypass grafting, CABG)。但对于冠心病合并晚期 CKD 患者仍无统一的治疗标准^[5],且临床更倾向于内科保守治疗^[11],其原因有:(1)大多数心血管疾病临床试验排除了晚期肾脏病患者^[5],此类患者治疗方案的选择依据不足;(2)CKD 患者的冠状动脉病变复杂且严重,多支血管病变比例较高,血运重建术难度增大^[12];(3)此类患者行血运重建术后并发症较多^[5],尤其是对比剂急性肾损伤(contrast-induced acute kidney injury, CI-AKI)发生率为 30.6%^[13];(4)侵入性治疗后长期抗血小板或抗凝治疗会增加出血风险^[7]。此外,冠心病类型、临床状态和危险层次不同,治疗方案的选择策略也不同,对于各类冠状动脉疾病患者的治疗方案需进一步讨论。

1.1 急性冠脉综合征

急性冠脉综合征(acute coronary syndrome, ACS)包括 ST 段抬高型心肌梗死(ST segment elevation myocardial infarction, STEMI)和非 ST 段抬高型急性冠脉综合征(non-ST segment elevation acute coronary syndrome, NSTEMI/ACS),其特征是心脏血液供应突然减少,常合并不良事件,具有较高的死亡率^[14]。在 ACS 患者中,晚期 CKD 的患病率为 30%~40%^[15]。近年来,针对此类患者的侵入性治疗证据逐渐积累,血运重建的益处逐渐被熟知。

1.1.1 STEMI

对于肾功能正常的 STEMI 患者,PCI 是最有效的治疗方法^[14],而在合并晚期 CKD 的 STEMI 患者中,循证再灌注治疗的使用频率较低^[16]。Panchal 等^[17]的一项纳入 534 845 例 STEMI 合并 CKD 患者的回顾性研究显示,接受血运重建的晚期 CKD 患者与较低的死亡率相关。Schmucker 等^[18]还观察到此类患者接受血运重建治疗后的缺血事件减少了一半以上。在肾功能方面,有研究^[19]表明接受内科保守治疗与血运重建治疗后患者的肾功能不全的进展无显著差别;Panchal 等^[17]还发现,对于接受 PCI 的患者,需透析的急性肾衰竭的远期发生率相比内科保守治疗有所降低。2017 年

欧洲心脏病学会(European Society of Cardiology, ESC) STEMI 指南^[15]指出,STEMI 患者的再灌注决定必须独立于任何肾功能评估,缺血症状持续时间 < 12 h 且 ST 段持续抬高的所有患者都应接受血运重建治疗。

关于血运重建治疗的方法选择,合并晚期 CKD 的 STEMI 患者更有可能接受使用药物洗脱支架的紧急 PCI^[18],但 CABG 可能优于 PCI^[20-22],尤其是对于多支病变患者^[23]。一项荟萃分析^[22]表明与 PCI 相比,CABG 改善了主要不良心脑血管事件、全因死亡、重复血运重建和急性心肌梗死等结局,优势比分别为 1.75 (95% CI 1.26 ~ 2.42)、1.13 (95% CI 1.00 ~ 1.28)、4.24 (95% CI 3.29 ~ 5.47) 和 2.16 (95% CI 1.59 ~ 2.91)。也有研究^[21,24]指出与 PCI 相比,CABG 远期获益较为突出。

越来越多的证据表明无论 STEMI 患者肾功能状况如何,血运重建都是治疗的基石^[25-26]。然而,尽管侵入性治疗可能不会加速肾衰竭的进展,但由于 CKD 患者冠状动脉病变较为复杂,完全血运重建率较低^[22],且在 PCI 期间往往需要更高的对比剂负荷,术后 CI-AKI、出血、支架内血栓形成等并发症发生率较高,故应结合患者实际情况,注重术后并发症的预防与治疗^[27]。

1.1.2 NSTEMI/ACS

NSTEMI/ACS 包括不稳定型心绞痛和非 ST 段抬高型心肌梗死。2021 年的 ACC/AHA/SCAI 冠状动脉血运重建指南^[28]强调应对 NSTEMI/ACS 进行危险分层,包括 GRACE 评分及 TIMI 评分,高危 NSTEMI/ACS 患者应早期行血运重建治疗,对于中低危患者出院前行血运重建即可。部分研究^[29-30]认为与仅接受药物治疗相比,NSTEMI/ACS 患者受益于血运重建治疗。然而 Sharon 等^[31]对 2008—2021 年的 7 107 例非 ST 段抬高型心肌梗死患者进行回顾性研究后发现,早期侵入性策略可显著降低死亡率($HR = 0.70$, 95% CI 0.56 ~ 0.85),但这种益处随着肾功能下降而下降,对于估算的肾小球滤过率 < 45 mL/(min · 1.73 m²) 的中重度 CKD 患者($n = 483$)无显著的生存优势($HR = 0.89$, 95% CI 0.64 ~ 1.24)。2020 年 ESC 关于 NSTEMI/ACS 患者管理指南^[32]也指出了类似的情况,但并未进一步就治疗方案选择作出推荐。

因此,目前国内外对于 NSTEMI/ACS 合并晚期 CKD 患者治疗方案尚无定论^[5,33],仍需前瞻性研究进一步提供证据。但由于 NSTEMI/ACS 进展为心肌梗死或再次发生心肌梗死的危险性高,目前临床医生对符合适应证的患者多倾向于血运重建治疗。

1.2 稳定型冠心病

药物治疗是无肾脏疾病的稳定型冠心病患者的

首要治疗策略^[34-35],仅对于左室射血分数 <35%、左主干狭窄 ≥50%、药物难以控制的心绞痛、近期曾患 ACS 及纽约心功能分级Ⅲ级和Ⅳ级的心力衰竭患者应考虑 PCI 联合药物治疗。对于合并 CKD 的患者,CKD 与稳定型心绞痛患者的院内、短期和长期预后不良相关,且患者更有可能死于心血管病因,而不是发展为需透析或移植的终末期肾病^[36],其治疗方案的选择一直是研究的热点之一。

部分研究^[22,37]表明进行血运重建的稳定型冠心病合并晚期 CKD 患者心血管死亡或心肌梗死的风险较低。但由于上述研究多是观察性、无对照的单中心试验,循证等级相对不足。近期,ISCHEMIA-CKD 试验^[38]公布了 5 年随访结果,该试验纳入 777 例患有晚期 CKD 和中重度心肌缺血的稳定型冠心病患者,是目前规模最大的、对比此类人群有创治疗策略(最佳血运重建+最佳药物治疗)和保守治疗策略(单纯最佳药物治疗)的多中心、随机对照试验,结果表明侵入治疗组和保守治疗组全因死亡($HR = 1.12, 95\% CI 0.89 \sim 1.41, P = 0.322$)与心血管死亡($HR = 1.04, 95\% CI 0.80 \sim 1.37, P = 0.753$)均无显著差异。

因此,对于稳定型冠心病患者,虽然预先血运重建策略可改善生活质量,减少症状发作,但可能不会提供显著的生存益处,甚至会将患者暴露于术后并发症的风险中,故临床应首选最佳药物治疗。而侵入性治疗策略的制定,需依据患者对改善生活质量的要求以及患者自身的意愿等进行全面考量。

2 对比剂肾病风险应对

考虑到对比剂肾病相关风险,《2019 ESC 慢性冠脉综合征诊断和管理指南》^[39]支持患有严重 CKD 的患者应尽量减少碘对比剂的使用,以防止肾功能进一步恶化。近期有研究^[40]通过低剖面导管和双翼系统,成功实现以极微量对比剂对晚期 CKD 患者高度复杂的冠状动脉病变进行检查和血运重建。同时,基于血管内超声成像的零对比剂 PCI 也是保护 CKD 患者肾功能的一种安全且有前景的方法,且该方法在复杂冠状动脉病变中也是可行的^[41]。此外,应采取积极措施预防 CI-AKI 的发生,比如术前用等渗盐水水化^[42]。其他几种特定的药物虽不能显著降低 CI-AKI 的发生率,但也可用于保护肾功能,包括他汀类药物、碳酸氢盐、N-乙酰半胱氨酸、抗坏血酸、腺苷拮抗剂和血管扩张剂等^[42]。

3 总结与展望

冠心病合并晚期 CKD 患者逐年增多,其预后差,心血管死亡率较高,带来的经济负担巨大,故应更加重视这一亚群患者的最佳治疗策略。对于 STEMI 合

并晚期 CKD 患者,早期行血运重建治疗与降低死亡率相关,且肾损害不应成为侵入性治疗的阻碍,其中,CABG 可能优于 PCI,但需前瞻性研究进一步证实。对于非 ST 段抬高型心肌梗死患者的最佳治疗方案仍缺乏充足证据,但临床对于符合适应证的患者更倾向于选择血运重建治疗。对于稳定型冠心病,优先推荐最佳药物治疗。

因 CKD 患者存在尿毒症相关机制可能加速冠状动脉病变的发展,未来应继续探究其病理生理机制。同时,晚期 CKD 合并冠心病患者冠状动脉病变严重且复杂,且相关危险因素仍无定论,未来应建立相关风险模型以便识别出高风险人群,并对高风险人群进行个体化诊疗。冠心病合并晚期 CKD 患者行冠状动脉血运重建术是具有挑战性的,存在相关的高死亡率,但对于此类患者行血运重建治疗后并发症的预防尚未明确,未来仍需大量临床研究明确对此类高风险人群术后并发症的预防方案。临床对于治疗方案的选择,应积极评估患者心血管疾病风险,权衡利弊,实行个体化的治疗方案。

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收稿日期: 2023-03-31