

· 前沿进展 ·

冠心病患者贫血的发病原因、治疗及预后研究进展

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【摘要】 近年来我国冠心病发病率及病死率均呈持续上升趋势, 已成为威胁我国居民生命健康的主要疾病之一。研究表明, 冠心病患者常伴有贫血, 且贫血可导致患者病情加重, 病死率明显增加。因此, 临床应重视贫血与冠心病之间的关系, 积极给予基于循证医学的治疗, 以改善冠心病贫血患者预后。本文主要综述了冠心病患者贫血的发病原因、治疗及预后, 旨在为冠心病患者贫血的有效管理提供参考依据。

【关键词】 冠心病; 贫血; 发病原因; 治疗; 预后; 综述

【中图分类号】 R 541.4 R 556 **【文献标识码】** A DOI: 10.3969/j.issn.1008-5971.2018.10.001

郑思道, 杨翠. 冠心病患者贫血的发病原因、治疗及预后研究进展[J]. 实用心脑血管病杂志, 2018, 26(10): 1-5. [www.syxnf.net]

ZHENG S D, YANG C. Progress on etiology, treatment and prognosis of anemia in patients with coronary heart disease [J]. Practical Journal of Cardiac Cerebral Pneumal and Vascular Disease, 2018, 26(10): 1-5.

Progress on Etiology, Treatment and Prognosis of Anemia in Patients with Coronary Heart Disease ZHENG Si-dao¹, YANG Cui²

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【Abstract】 Coronary heart disease, as one of the major diseases threatening life and health in China, both the morbidity and mortality showed continuous upward trend in recent years. Previous studies showed that, anemia is relativity common in patients with coronary heart disease, moreover anemia may exacerbate the severity of illness and increase the risk of death, thus we should attach importance to relationship between anemia and coronary heart disease, actively adopt treatment based on evidence-based medicine to improve the prognosis in coronary heart disease patients accompanied with anemia. This paper reviewed the etiology, treatment and prognosis of anemia in patients with coronary heart disease, to provide a reference for effective management of anemia in patients with coronary heart disease.

【Key words】 Coronary disease; Anemia; Pathogenesis; Therapy; Prognosis; Review

冠心病是临床常见的心血管疾病, 包括稳定性冠心病和急性冠脉综合征 (acute coronary syndrome, ACS)。近年来我国冠心病发病率及病死率均呈持续上升趋势, 据统计目前冠心病患者人数约 1 100 万, 将给我国带来沉重的经济及社会负担^[1]。贫血和缺铁均与冠心病有关, 冠心病患者冠状动脉狭窄导致远端血供减少, 贫血导致血红蛋白携氧能力减弱, 而冠心病患者一旦合并贫血则会进一步导致心肌氧供减少, 当心肌无法代偿上述改变、不能满足心脏做功时症状加重、病情恶化^[2]。既往研究表明, 贫血及其合并症是行经皮冠状动脉介入治疗 (percutaneous coronary intervention, PCI) 及冠状

动脉旁路移植术 (coronary artery bypass grafting, CABG) 患者预后不良的独立预测因素之一^[3-4]。因此, 了解冠心病与贫血的关系及其相关机制对改善冠心病贫血患者预后具有重要意义。笔者通过检索国内外相关文献, 主要综述了冠心病患者贫血的发病原因、治疗及预后, 旨在为冠心病患者贫血的有效管理提供参考依据。

1 冠心病贫血的临床特征

一项有关英国 422 855 例 ACS 患者的调查结果显示, ACS 患者贫血 [血红蛋白 <120 g/L (女性) 或 130 g/L (男性)] 发生率为 27.7%^[5]; BRENER 等^[6]对多个国家共 16 318 例 ACS 患者调查发现, ACS 患者贫血发生率为 18.8%。上述研究表明, ACS 患者贫血发生率较高。WANHA 等^[7]通过分析 1 916 例 ACS 患者的临床资料发现, 老年、合并症较多、左心功能低下的 ACS 患者贫血发生率较高; ACS 贫血患者多表现为冠状动脉多支病变、复杂病变及陈旧性心肌梗死; 与无贫血患者相比, ACS 贫血患者急性心力衰竭住院风险、大出

基金项目: 北京市优秀人才培养资助青年骨干个人项目 (2014000057592G296)

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血发生风险及1年全因死亡率明显升高,但心肌梗死、脑卒中、靶血管再血管化发生率间无差异;此外,ACS贫血患者应用一代和二代药物涂层支架后主要不良心血管事件和靶血管再血管化发生率相似,提示应用二代药物涂层支架无明显优势。SHACHAM等^[8]研究结果显示,男性ST段抬高型心肌梗死(ST-elevation myocardial infarction, STEMI)患者中发病3h内就诊者血红蛋白水平高于发病3h后就诊者,提示随着病情发展STEMI患者贫血发生风险升高。

目前,有关稳定性冠心病患者贫血发生情况的研究报道较少。JANKOWSKA等^[9]研究结果显示,约50%的稳定性冠心病患者存在骨髓铁缺乏,提示稳定性冠心病患者贫血发生风险较高。

2 冠心病贫血的发病原因

生理学研究表明,人体内环境可通过感知组织氧及调节红细胞生成而维持血红蛋白水平稳定,当红细胞生成减少、破坏增加(溶血)、血液丢失(出血)时会导致上述调节机制障碍,进而引发贫血^[10]。目前,冠心病贫血的主要发病原因包括高龄、骨髓造血功能下降、血红蛋白异常及药物。

2.1 高龄 MORICI等^[11]研究结果显示,非ST段抬高型心肌梗死(non ST-elevation myocardial infarction, NSTEMI)贫血患者多为高龄,主要原因可能与老年人肌肉萎缩导致外周组织氧摄取能力下降、肾功能不全导致促红细胞生成素(erythropoietin, EPO)减少、干细胞功能衰退、EPO对红系祖细胞缺氧耐受及炎症反应紊乱等有关。

2.2 骨髓造血功能下降 既往研究表明,STEMI贫血患者白细胞计数、血小板计数及网织红细胞计数明显降低,提示骨髓造血功能下降可能是导致STEMI患者发生贫血的主要原因之一^[12]。

2.3 血红蛋白异常 OGUNBAYO等^[13]研究表明,镰刀形红细胞贫血患者ACS发生风险较高,该疾病发病年龄偏小,但病死率较高。CHEN等^[14]研究表明,珠蛋白生成障碍性贫血患者冠心病发生风险明显升高,约为健康对照者的1.5倍。表明血红蛋白异常贫血患者冠心病发生风险较高。

2.4 药物 铁是重要的造血原料,缺铁是发生贫血的常见原因,而ACS患者缺铁发生率较高可能与长期应用抗血小板药物治疗等有关^[15]。另有研究表明,应用质子泵抑制剂治疗的缺血性心脏病患者贫血发生率较高^[16]。表明抗血小板治疗和质子泵抑制剂等药物可增加冠心病患者贫血发生风险。

3 冠心病贫血的治疗

3.1 抗栓/抗血小板治疗 目前ACS贫血患者抗栓治疗策略缺少足够证据。MORICI等^[11]研究显示,与未贫血患者比较,NSTEMI贫血患者阿司匹林使用者所占比例明显降低。WANG等^[17]通过对我国4109例冠心病患者进行分析发现,贫血可增加药物涂层支架术后1年死亡风险,而采用双联抗血小板治疗可降低术后1年死亡风险,故对ACS贫血患者还是应该考虑使用双联抗血小板治疗。FREEMAN等^[18]研究表明,对合并慢性、亚急性贫血及非慢性肾病、心力衰竭、炎症相关贫血的NSTEMI患者和不稳定型心绞痛患者可参考RICHARD ANDERSON等提出的治疗流程,该流程是综合考虑出血/凝

血风险、血红蛋白动态变化等因素后根据不同风险分级推荐相应治疗策略。

3.2 血运重建

3.2.1 PCI 贫血与造影剂肾病密切相关,是造影剂肾病的独立预测因素^[19]。但早期行PCI能提高患者30d及1年生存率,且不增加大出血发生风险,故对合并贫血的ACS患者建议应早期行PCI^[20]。需要注意的是,ACS贫血患者行PCI时选择经桡动脉路径较股动脉路径具有明显优势,可降低严重出血发生率和院内病死率^[21]。

3.2.2 CABG SPIEGELSTEIN等^[22]研究表明,CABG围术期伴有贫血的冠心病患者预后较差,且升高血红蛋白水平能降低患者输血需求并改善患者预后。PAPARELLA等^[23]研究表明,行非体外循环CABG患者的重症监护室(ICU)停留时间较短、输血治疗需求较低、术后肌酐清除率恢复较快;但对围术期伴有贫血患者而言,行非体外循环CABG者早期并发症发生率及病死率低于行体外循环CABG者,但6个月后并发症发生率及病死率却高于行体外循环CABG者。

3.3 改善贫血

3.3.1 促红细胞生成 红细胞生成主要分为EPO依赖期和铁依赖期,部分改善贫血的药物是通过抑制铁调素生成、中和铁调素或阻断铁调素与膜铁转运蛋白结合等机制调节铁调素表达,抑制分化生长因子11阳性细胞表达,进而不同程度地刺激红细胞生成,达到改善贫血的目的^[24]。但采用促红细胞生成刺激药物治疗合并轻中度贫血的冠心病患者常无获益,甚至还会增加静脉血栓栓塞、高血压发生风险^[25-26]。美国医师协会(American College of Physicians, ACP)提出对合并轻中度贫血的冠心病或充血性心力衰竭患者不建议使用红细胞生成刺激药物^[27]。

3.3.2 输血 输血是快速增加血红蛋白水平、提高氧输送的有效措施之一,但输注红细胞后血小板活性增加,主要表现为二磷酸腺苷-P2Y₁₂受体信号通路活化,而炎症因子、血栓标志物未发生明显改善,这可能是ACS输血患者PCI后虽给予P2Y₁₂受体拮抗剂治疗但缺血事件仍高发的原因之一^[28]。KARROWNI等^[29]研究表明,输血与行介入治疗的ACS患者发生急性肾损伤有关,分析原因可能与氧输送受损、炎症、氧化应激等有关,故对行介入治疗的ACS患者有必要实施限制性输血策略。且既往研究证实,与自由输血策略相比,选择限制性输血策略对ACS患者有利^[30-31]。GARFINKLE等^[32]研究结果显示,ACS患者血红蛋白<80g/L时输注浓缩红细胞可以获益,血红蛋白>110g/L时输血则对患者不利或呈中性影响。近期有研究结果显示,ACS患者血红蛋白<80g/L时不予输血治疗会增加患者全因死亡率,而血红蛋白为80~100g/L时是否给予输血治疗不影响患者全因死亡率^[33]。此外,也有学者建议根据贫血症状或体征而不仅是血红蛋白水平来指导ACS患者进行输血治疗^[34]。

HOLLIS等^[35]研究结果显示,对行非心脏手术治疗的稳定性冠心病患者采用限制性输血策略能够获益。CAMASCHELLA^[36]认为,缺铁性贫血引发的心绞痛应输注红细胞,以快速改善低氧和缺铁状态。既往也有研究建议,对

慢性心脏病患者血红蛋白 <80 g/L 或出现贫血症状时应进行输血治疗^[34]。

2013年, ACP发布的《心脏病患者贫血治疗管理》推荐对院内冠心病患者应实施限制性输血策略(即血红蛋白为70~80 g/L时考虑输血治疗)^[27]。2016年, 美国血库协会更新了红细胞输血指南, 建议对行心脏手术和已有心血管疾病的成年患者采取限制性输血策略时血红蛋白的阈值定为80 g/L, 但因证据不足未对ACS患者输血治疗做出推荐^[37]。英国《成人重症患者贫血与红细胞输血管理指南》建议, ACS患者应维持血红蛋白>80 g/L, 而稳定型心绞痛并重度贫血患者应维持血红蛋白>70 g/L^[38]。我国相关指南则建议对NSTEMI和 unstable型心绞痛贫血患者应在血流动力学不稳定或红细胞比容<25%或血红蛋白<70 g/L时进行输血治疗^[39]。

4 冠心病贫血的预后

既往研究表明, 贫血与心肌梗死患者主要不良心血管事件密切相关^[40], 合并贫血的初发心肌梗死患者预后不良、全因死亡风险及再发心血管事件发生风险升高^[41], 贫血可增加行PCI的急性心肌梗死患者院内死亡风险^[42], 上述研究均提示贫血与心肌梗死患者预后相关。既往多个研究显示, 贫血是ACS患者30 d、1年病死率的独立预测指标^[5, 43-44]。近期有研究表明, 合并贫血的ACS患者大出血发生率、输血需求及1年全因死亡率均高于未合并贫血的ACS患者; 此外, 贫血严重程度还与ACS患者预后呈负相关, 即贫血越严重则患者预后越差, 提示贫血是ACS患者预后的独立预测因子^[6]。另有研究表明, 贫血还是STEMI患者1年心血管死亡率的危险因素^[45-46], 可增加行介入治疗的STEMI患者微循环障碍发生风险及长期全因死亡率^[47-48]。

KALRA等^[49]研究结果显示, 血红蛋白是预测稳定性冠心病患者4年病死率、心血管事件、大出血风险的独立危险因素, 持续存在或新发贫血可预测冠心病患者心血管及非心血管死亡风险, 提示贫血与稳定性冠心病患者预后相关。

5 小结

冠心病患者贫血的发生率较高, 可能与高龄、骨髓造血功能下降、血红蛋白异常、药物等有关; 目前其治疗主要为药物及输血, 但不建议使用促红细胞生成素治疗轻中度贫血患者, 而新型抗贫血药物的使用还需更多研究支持。心肌供主要发生在心脏舒张期, 静息状态下心肌能摄取冠状动脉血供中约75%的氧气, 故心肌血供-氧输送-氧利用思维方法对冠心病贫血患者的诊疗可能更具有指导价值, 尤其对冠状动脉病变广泛、狭窄严重、保守治疗的患者^[50]。既往研究表明, 冠心病贫血患者心功能及最大氧输送代偿能力下降, 机体通过提高心率、每搏输出量等增加心输出量, 而重症冠心病患者全身氧需求增加, 心脏负荷加重, 冠状动脉血供减少并激活儿茶酚胺, 进一步加重心脏缺血和心功能不全^[50]。冠心病与贫血相互影响, 然而贫血导致冠心病患者不良结局还是冠心病导致贫血发生和发展目前尚未明确, 仍需大样本量、前瞻性研究及相关分子生物机制研究进一步证实。

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(收稿日期: 2018-08-20; 修回日期: 2018-10-15)

(本文编辑: 谢武英)

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《实用心脑血管病杂志》“医学循证”栏目征稿启事

循证医学的核心思想是“任何医疗卫生方案、决策的确定都应遵循客观的临床科学研究产生的最佳证据”,从而制订出科学的预防对策和措施,达到预防疾病、促进健康和提高生命质量的目的,实用性、针对性、可行性强,是临床医务工作者青睐的一个诊断和治疗疾病的有效方法。“医学循证”是本刊的特色栏目,栏目主要刊登心、脑、肺血管疾病领域的系统评价/Meta分析类型文章及心、脑、肺血管病领域的循证诊疗经验、思路、方法等,为您提供交流与分享的平台,欢迎您踊跃投稿!

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