

冠心病相关危险因素研究进展

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摘要

冠心病(CHD)的发病率和死亡率逐年增加, 已经成为影响人类健康的一项公共卫生事件。对于导致冠心病的危险因素的研究仍在继续。随着研究的进展, 学者们发现同型半胱氨酸血症在内的诸多因素在CHD发生、发展过程中发挥关键作用。本文通过阐述近年来冠心病相关危险因素研究的进展, 为冠心病的预防和临床治疗提供参考。

关键词

冠心病, 冠状动脉粥样硬化, 危险因素

Advances in Research on Risk Factors Associated with Coronary Heart Disease

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Abstract

The incidence and mortality rate of coronary heart disease (CHD) have been increasing year by year, making it a public health event that significantly impacts human health. Research on the risk factors contributing to CHD is still ongoing. With the progress of research, scholars have discovered that various factors, including hyperhomocysteinemia, play a crucial role in the occurrence and development of CHD. This article aims to provide a reference for the prevention and clinical treatment of CHD by elucidating the recent advancements in the study of CHD-associated risk factors.

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Keywords

Coronary Heart Disease, Coronary Artery Atherosclerosis, Risk Factors

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1. 引言

冠心病(coronary heart disease, CHD)是一种常见疾病,对人类健康造成严重威胁。随着时间的推移,冠心病患病率和病死率逐年增加,其中急性心肌梗死是我国心血管疾病死亡的主要原因之一[1]。根据中国卫生健康统计年鉴 2021 年的数据,2020 年中国城市居民冠心病的死亡率为 126.91/10 万,而农村地区为 135.88/10 万[2]。值得注意的是,自 2012 年起,冠心病的死亡率呈现持续上升的趋势,尤其是在农村地区,上升幅度更为明显,至 2016 年已超过城市地区水平[2]。根据发达国家的经验,改善人群的危险因素对于减少冠心病致死率的效果最为明显[3]。冠心病的发病受多种因素影响,包括传统危险因素和新兴危险因素。以下对冠心病危险因素在近年来的研究进展进行综述,为冠心病的早期干预提供理论基础,也为制定个体化的防治策略和公共卫生政策提供指导意见。

2. 传统危险因素

冠心病的传统危险因素主要集中在个体的生活方式和遗传方面,包括年龄、性别、遗传因素、吸烟、高血压、血脂异常、糖尿病、超重、肥胖、缺乏运动、精神压力、不健康饮食以及过量饮酒等。最近的研究表明,初次心肌梗死患者在长时间从事工作时,面临着增加复发事件风险的可能性,这种风险可能是由于长期暴露于工作压力环境所引起[4]。Rong 等[5]的研究结果显示,不进行早餐摄入与心血管疾病发生率的增加存在关联。此外,长期饮用含糖或人工甜味剂的饮料还被发现与心血管疾病死亡率的增加存在关联[6]。除了年龄、性别和遗传等无法控制的因素外,其他因素均可通过调整生活方式或药物干预来进行控制。近年来,随着研究的深入,学者们发现了许多新的危险因素[7]。将这些新发现的危险因素与传统因素一起进行综合管理,可能会增加冠心病预防和治疗的疗效。

3. 新兴危险因素

3.1. 高同型半胱氨酸血症

同型半胱氨酸(homocysteine, HCY)是人体内的一种含硫氨基酸,在蛋氨酸和半胱氨酸代谢过程中充当重要的中间产物,对叶酸代谢起着关键作用。研究发现,高同型半胱氨酸(HCY)是冠心病的一种新型致病危险因素,它在动脉粥样硬化的形成和进展中扮演着重要的角色[8]。其可能的机制涉及凝血系统紊乱、血管内皮细胞受损以及促进血栓形成等因素[9]。Shenoy 等学者[10]使用 Gensini 评分系统来评估冠心病的严重程度,结果显示冠心病患者的同型半胱氨酸水平明显升高,并且同型半胱氨酸水平与疾病的严重程度呈正相关。此外,还有研究致力于探索同型半胱氨酸水平与心血管疾病预后之间的关系。Fu 等研究人员[11]发现,对于老年急性冠脉综合征(ACS)患者而言,高水平的同型半胱氨酸(HCY)血症是预测全因死亡率和心血管不良事件的重要指标。总的来说,同型半胱氨酸(HCY)的高水平与冠心病的发病和严重程度有较高的关联,且可能影响心血管疾病的预后,应给予重视。

3.2. 脂蛋白 a [Lp(a)]与脂蛋白磷脂酶 A2 (Lp-PLA2)

以往的研究已经观察到心血管疾病(CVD)患者普遍存在脂蛋白 a [Lp(a)]浓度的增加。然而, 由于对 Lp(a)在心血管疾病中的作用认识的不足, Lp(a)的重要性尚未得到充分的证实。最近的临床和遗传学研究均表明, Lp(a)在心血管疾病发病机制中扮演着关键的角色[12] [13]。根据 2022 年 JAMA 杂志的一篇研究论文, 研究人员验证了脂蛋白 a 水平升高与动脉粥样硬化性心血管疾病和主动脉瓣狭窄之间的关联, 并提出了潜在的因果关系[14]。此外, Tsimikas 等研究者[15]还对 191 例冠心病患者的冠脉斑块体积在 CT 血管成像下的动态变化进行了对比分析, 结果显示, LP(a)水平较高的 CHD 患者在 12 个月后冠状动脉斑块体积的增长也明显更高。同时, 一项对 LP(a)介导的血管钙化的研究也证实了 LP(a)与冠状动脉钙化的存在以及其严重程度之间的独立相关性[16]。

作为一种炎症标志物, 脂蛋白磷脂酶 A2 (Lp-PLA2)参与了动脉粥样硬化的发展过程, 并介导了相关的炎症反应。2000 年, 苏格兰西部冠状动脉预防研究首次报道了 Lp-PLA2 血浆水平升高与心血管事件之间的关联[17]。根据 2020 年的一项流行病学研究[18]结果显示, Lp-PLA2 水平与传统心血管风险因素之间存在相关性, 这些风险因素包括年龄, 低密度脂蛋白胆固醇, 高密度脂蛋白胆固醇, 总胆固醇以及甘油三酯等。然而, 研究者尽管对这些危险因素进行了调整, Lp-PLA2 水平的升高仍然与心血管事件的发生相关, 并支持将 Lp-PLA2 活性作为评估稳定型冠心病患者和一般人群不良结局风险的指标[18]。未来还需进一步研究, 以更好地了解 Lp-PLA2 如何调节血管炎症、促进动脉粥样硬化的进展, 这将有助于揭示 Lp-PLA2 在心血管疾病发展中的精细调控机制, 为相关疾病的预防和治疗提供新的治疗策略。

3.3. 血清可溶性尿激酶型纤溶酶原激活物受体(Soluble Urokinase Plasminogen Activator Receptor, suPAR)

作为细胞表面尿激酶原激活物受体的可溶性形式, suPAR 已被广泛运用于冠心病研究中, 成为一种新型的标志物[19]。George Hindy 等人[20]的一项荟萃分析研究表明, suPAR 在动脉粥样硬化的病理过程中起到致病因素的作用, 其中至少部分是通过调节单核细胞功能来实现的。还有研究人员还发现, 在无阻塞性冠状动脉疾病但有症状患者群体中, 较高水平的 suPAR 与不良事件风险的增加之间存在独立关联, 并且这种关联具有累加效应[21]。此外, Walter JE 等人[22]的研究还发现 suPAR 在已知冠心病患者中是全因死亡率的独立预测因子。综上所述, 虽然 suPAR 在冠心病中的预测价值已被确认, 但还需要进一步的研究来充分发挥其在临床上的价值。此外, 与其他生物标志物的联合应用以及不同治疗方法对 suPAR 水平的影响也值得进一步研究。

3.4. 炎症指标及相关疾病

C 反应蛋白(CRP)作为一种炎症标志物, 与冠心病的发生和发展密切相关[23]。白蛋白水平与冠状动脉病变的严重程度和发生急性心肌梗死的风险之间存在负相关关系[24] [25]。因此, C 反应蛋白和白蛋白的比值(CRP/ALB, CAR)能更准确地反映冠心病病程中炎症因素的作用[26]。2022 年的一项研究结果显示, CAR 与冠状动脉病变程度之间存在显著相关性, 可作为可靠的标志物, 用来预测心肌梗死的严重程度[27]。此外, Cinar 等人[28]提出, CAR 在预测急性 ST 段抬高型心肌梗死患者不良预后方面的能力优于中性粒细胞淋巴细胞比值(Neutrophil-to-Lymphocyte Ratio, NLR)。

痛风、炎症性肠病、自身免疫性疾病和牛皮癣等疾病与冠状动脉疾病的发生风险增加存在相关性, 可能源于它们对炎症活性的增加[29] [30] [31]。2022 年 JAMA 杂志发文, 发现近期痛风发作患者发生急性心血管事件的可能性呈现上升趋势[29]。Mahtta 等人[30]在研究中分析了大型退伍军人事务部数据库 VITAL (包括患有过早动脉粥样硬化的退伍军人), 发现被诊断为类风湿性关节炎、系统性红斑狼疮或两

者兼具的患者发生冠状动脉疾病的风险较高。Lee 等人[31]的研究结果显示,患有炎症性肠病(如克罗恩病和溃疡性结肠炎)的患者存在发生冠状动脉疾病的增加趋势。研究表明[32],银屑病会增加炎症环境中多种因子(如肿瘤坏死因子 α 、干扰素和细胞因子)的激活,而牛皮癣患者相较于非患者,其患心血管疾病的风险增加 50%。总的来说,这些疾病可能可以通过改变血液中的凝血系统和纤溶系统,导致血栓形成和血管功能异常,加剧动脉硬化的进展。因此,控制炎症对于预防和治疗冠心病具有重要意义。

3.5. 环境因素

冠状动脉疾病发病率的增加与两个环境因素相关,而这两个因素本身可能存在相关性:社会经济地位较低和空气污染[33][34][35]。Hamad 等人[33]指出,多个因素可能导致社会经济地位较低的个体冠状动脉疾病增加,包括心理社会压力的增加、有限的教育和经济机会,以及同龄人缺乏对更健康生活方式选择的支持。据估计,2019 年全球约有 900 万人死于空气污染,其中 62% 的死亡与心血管疾病有关,其中冠状动脉疾病占 31.7%,中风占 27.7% [34]。与空气污染相关的病因包括高血压和糖尿病的发病率增加,这可能是由于空气污染中的细颗粒物和有害气体对心血管系统的直接损害效应[34]。空气污染会对血管的张力产生影响,导致动脉内膜的增厚和钙化,从而助长动脉粥样硬化的进展。此外,空气污染中的有毒物质还可能包括铅、汞、砷和镉等有毒金属,这些有毒金属通过吸入进入人体,与血管内皮细胞发生作用,导致炎症反应和血管功能异常,进而增加心血管疾病的风险[34]。根据 Chen 等人[35]的研究报告,短暂接触各种空气污染物即有可能会急性冠脉综合征的发生。总的来说,对于不同环境因素的改善可以有效降低对心血管系统的损害。

4. 女性特有危险因素

女性进入绝经期后,由于缺乏雌激素的保护作用,常常出现冠心病的发病率显著增加。研究表明,女性相较于男性更易患上冠状动脉疾病(Coronary Artery Disease, CAD),且其死亡率也高于男性[36]。同时,吸烟和糖尿病在女性中会显著增加 CAD 发生的风险,因此对女性 CAD 进行早期识别显得尤为重要[36]。

Yoon 等[37]的研究结果表明,乳腺动脉钙化(Breast Arterial Calcification, BAC)与心血管事件风险增加之间存在关联,该现象被认为是女性冠状动脉疾病(CAD)潜在风险的标志物,并与冠状动脉粥样硬化的进展密切相关。Kadioglu 等学者[38]认为,乳腺动脉钙化(BAC)可作为预测冠状动脉疾病(CAD)的一个额外危险因素,尤其在冠状动脉钙化评分较高的患者中。总的来说,BAC 可能作为冠状动脉钙化进程的一个准确指标,从而有可能降低与冠状动脉粥样硬化相关的发病率和死亡率。

患有妊娠期糖尿病、先兆子痫和早产史的女性与冠状动脉疾病风险增加相关。然而,具体导致这一关联的机制和因素尚不完全清楚,可能涉及细胞因子和氧化应激等生物学过程的增加[39][40][41]。近期的研究发现在女性中存在带有先兆的偏头痛与心血管疾病之间的关联,目前尚未完全理解这种联系的机制[42]。一种可能的解释是先兆偏头痛与心血管疾病共享一些共同的病理生理机制,例如血管内皮功能紊乱、炎症反应或血小板聚集异常[42]。

冠心病的发生和发展除了研究危险因素,还需要考虑与动脉粥样硬化无关的其他因素。在一项研究中,研究者以社会心理和生物行为因素为切入点,发现社会心理因素在男性和女性冠心病中扮演着重要的角色[43]。然而,对于女性而言,社会心理因素的影响可能更为显著,这或许是因为女性更容易体验焦虑情绪,并且在应对社会压力的负面影响时可能表现出较低的应对能力[43]。

5. 小结

冠心病作为一种常见且严重的心血管疾病,其危险因素的研究仍然存在许多尚待探索的领域。我们有理由相信,随着科学技术的不断进步,将会有更多新兴危险因素的出现,这些新发现将为我们提供更

全面的认识和理解, 从而为冠心病的预防和治疗提供新的突破口。

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