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饮食与血管钙化的相关研究

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摘　要

血管钙化(Vascular calcification, VC)作为多种心血管疾病(Cardiovascular disease, CVD)的共同病理表现过程，与心血管疾病高发病率和死亡率密切相关。而慢性炎症已被证明在VC的进展中起重要作用。饮食模式主要是促炎性饮食，可影响全身炎症的强度，进而参与VC的发生和进展。本文就促炎性饮食成分与VC的关系及由饮食诱导的慢性全身性炎症及氧化应激从而诱导VC的过程做一综述，以期通过考虑饮食对VC的影响在改善心血管健康和延缓血管钙化方面取得进展。

关键词

饮食成分，炎症，血管钙化

Research on the Relationship between Diet and Vascular Calcification

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Abstract

Vascular calcification (VC), as the common pathological course of cardiovascular disease (CVD), has been proved to be closely related to the high incidence of a disease and mortality. Chronic inflammation has been shown to play an important role in the progression of VC. Dietary patterns, primarily pro-inflammatory diets, can influence the intensity of systemic inflammation and, in turn, participate in the occurrence and progression of VC. This article reviews the relationship between pro-

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inflammatory dietary components and VC and the process of oxidative stress and VC induction by diet-induced chronic systemic inflammation.

Keywords

Dietary Component, Inflammation, Vascular Calcification

1. 引言

目前，心血管疾病(Cardiovascular disease, CVD)仍是导致人类死亡的最常见原因，《2022 年中国心血管健康与疾病报告》显示，中国城市和农村居民的疾病死亡比例最高的是心血管疾病，分别占农村和城市地区死亡人数的 48%和 46%左右[1]。现有研究认为血管钙化(Vascular calcification, VC)是 CVD 的一个重要病理过程，极大地增加了不良心血管事件发生的风险。最近的证据表明，炎症是促进钙化的关键因素[2]，慢性炎症在心血管疾病的发病机制中起着重要作用。因此，解决炎症问题可能是有效预防 CVD 的一个重要方面。近年来的研究发现，食物代谢与炎症过程密切相关，促炎性饮食在慢性炎症性疾病的发生中发挥着重要作用[3]。一项包括 14 项研究的荟萃分析显示，具有高促炎潜力的饮食模式与 CVD 和相关死亡率风险增加呈正相关[4]。因此，重视膳食炎症对 VC 的影响具有重要意义。

膳食成分是指我们每天摄入的食物中存在的不同营养素和物质，包括常量营养素(碳水化合物、蛋白质和脂肪)和微量营养素(维生素和矿物质) [5]。研究结果表明，坚持健康的饮食模式，如地中海式饮食、高纤维饮食和富含水果、蔬菜及其他植物性食物的饮食，与较低的炎症水平独立相关[6]。而一些促炎饮食成分，如高糖负荷的碳水化合物、饱和脂肪酸、反式脂肪酸、胆固醇等则促进 VC 的发生发展。

2. 碳水化合物

血糖指数(Glycemic index, GI)反映了食物中碳水化合物血糖上升的速度，血糖负荷(Glycemic load, GL)则综合考虑了 GI 值及碳水化合物含量，更准确地反映食物对血糖的实际影响。不同的 GI 食品与动脉粥样硬化风险之间的不同相关性主要归因于其对餐后血糖水平的不同影响[7]。研究表明，高血糖水平通过诱导氧化应激、增加炎症反应和产生晚期糖基化终末产物对血管内皮细胞造成损伤，从而促进动脉粥样硬化的发生[8]。因此，高 GI/GL 的碳水化合物消耗与 CVD 风险增加之间的关联可能部分由低度慢性炎症介导。一项纳入 135 名乳腺癌遗传高风险的绝经前妇女的研究证实了高 GI 水平饮食与 IL-10 和瘦素升高的相关性[9]。一项横断面研究表明，久坐不动的生活方式和高碳水化合物摄入与绝经后低级别慢性炎症有关[10]。此外，在血管平滑肌细胞(Vascular smooth muscle cell, VSMC)中进行的体外研究发现，葡萄糖水平升高(浓度为 50 mM)可促进 VSMC 分化为成骨细胞进而促进中膜的血管钙化[11]。

3. 饱和脂肪酸(Saturated Fatty Acids, SFAS)和胆固醇(Cholesterol)

饱和脂肪酸凭借其对脂蛋白胆固醇水平的影响来参与血管钙化及心血管疾病的发生发展。与碳水化合物或不饱和脂肪酸相比，较高的 SFA 摄入量会增加低密度脂蛋白胆固醇(Low density lipoprotein, LDL)的循环浓度。减少饱和脂肪酸和反式脂肪酸的摄入，代之以不饱和脂肪酸，可能有助于改善脂质状况[12]。来自观察性研究和随机对照心血管结局试验的大量证据表明，LDL 循环浓度较低与重大血管事件风险降

低相关[13]。血液中 LDL 水平升高可导致 LDL 渗透血管壁并氧化为氧化 LDL (Oxidized low density lipoprotein, oxLDL)，引发炎症反应并诱导单核细胞浸润血管壁[14]。单核细胞在血管壁内分化为巨噬细胞，吞噬 oxLDL 并形成泡沫细胞，其逐渐扩大并发展成斑块，同时刺激平滑肌细胞向血管内层迁移和增殖。该过程触发骨形成，最终导致血管钙化[15]。在一项单独的随机对照试验中，一组 8 名轻度高脂血症患者和 5 名血脂水平正常的健康人随机接受了三种不同的标准化脂肪餐，其中包括 SFA、单不饱和脂肪酸或中链脂肪酸。研究结果显示，在 10 小时内，与其他组相比，食用 SFA 饮食的参与者的血浆甘油三酯水平显著升高，动脉粥样硬化发生率增加[16]。显然，大量摄入 SFA 和胆固醇会增加 VC 及 CVD 的风险。

4. 反式脂肪酸(Trans-Fatty Acids, TFAs)

反式脂肪酸包括天然存在和人工制造两种情况，人体研究已经确定了工业反式脂肪酸的摄入量和心血管疾病发展之间的正相关。一些研究检查了反式脂肪酸对血浆胆固醇浓度和脂蛋白动力学的影响。1990 年在瓦赫宁根大学进行的一项随机交叉试验将 59 名受试者随机分配到 3 种等热量饮食中的一种，持续 3 周，其中每日能量的 10%由油酸、十八碳烯酸的反式异构体或棕榈酸和月桂酸提供。与油酸饮食相比，反式脂肪酸饮食显著降低血清高密度脂蛋白胆固醇浓度(12%)，并增加总胆固醇和 LDL 胆固醇浓度分别为 5.8%和 13.9% [17]。大量摄入 TFA (>每日能量的 1%)可导致脂质变化：甘油三酯和 LDL-C 水平升高、高密度脂蛋白水平降低，轻度炎症和内皮功能障碍[18]。此外，反式脂肪酸也可能通过激活炎症促进血管钙化。在一项随机对照试验中，观察到当 TFA 平均摄入量达到总膳食脂肪的 4.7% (范围为 1.5%~9.2%)时，TFA 摄入量与 IL-6 和 C 反应蛋白浓度呈正相关[19]。在一项健康男性的随机对照试验中，与不含反式脂肪酸的对照饮食相比，每日能量含有 8%来自工业反式脂肪酸的饮食在摄入 5 周后导致 C 反应蛋白血浆浓度增加 3.4 倍[20]。另一项研究 TFAs 是否与心衰患者的全身炎症相关[21]的试验结果表明，在调整各种因素后，富含工业反式脂肪酸的食物摄入量与炎症标志物如 C 反应蛋白、TNFα、趋化因子配体 2 和 IL-6 的血浆浓度呈正相关。

5. 矿物质

一般来说，金属对巯基有很高的亲和力，使许多酶反应、氨基酸和含硫抗氧化剂失活，从而增加了氧化应激，导致炎症、血管平滑肌及内皮功能障碍。多种矿物质如钙、磷等已被发现与炎症反应过程相关。在正常生理条件下，身体采用由钙化抑制剂组成的矿物质缓冲系统严格控制血清磷水平。该系统有效地防止了磷–钙矿物质在细胞外的沉淀。然而，血液中磷水平升高会破坏这种平衡，导致钙在血管壁中沉积。该过程与诱导 VSMC 成骨/软骨转分化的激活炎症信号(Wnt/β-连环蛋白和 NF-κB)有关[22] [23]。有研究表明，在含有正常生理水平磷的培养基中培养的 VSMC 不会钙化，而在含有高水平(3.5 mM P)磷的培养基中培养的 VSMC 确实会诱导钙化[24]。此外，一些报告还描述了钙和磷在体外加速和增加矿化方面的协同作用归因于炎症因子(即 IL-1、IL-6 和 TNF-α)的表达[25]。

6. 饮食诱导慢性炎症的机制

饮食可能通过影响炎症因子的释放、炎性信号通路的激活及氧化应激等方面参与炎症反应过程。已有研究证明高浓度的 SFA 可激活炎症细胞，如巨噬细胞[26]-[28]。活化的巨噬细胞释放各种炎症介质，如细胞因子(TNF-α、IL-1β 等)和趋化因子[29]。炎症反应还可诱导内皮细胞分泌细胞因子和趋化因子，进一步引发炎症反应[30]。释放的炎症细胞因子可触发 VSMCs 的成骨分化，这是 VC 发展的关键过程。一项研究表明，高葡萄糖浓度(24 mM)增加了骨唾液蛋白、骨钙素以及 IL-1β、IL-6、IL-8、单核细胞趋化蛋白-1 (MCP-1)和 IL-10 mRNA 表达增加进而增加成骨细胞的矿化[31]。此外，炎性细胞因子和血管壁内的

其他信号分子之间的相互作用产生了维持成骨分化过程的正反馈回路。例如，炎性细胞因子上调 Runx 2 表达进一步增强了促炎性细胞因子的产生，形成了一个自我延续的循环[32]。氧化应激作为 VC 产生的关键介质，使细胞膜和脂蛋白内的磷脂、胆固醇酯等容易受到自由基诱导的脂质过氧化反应的影响，从而形成复杂的氧化产物组合。大量证据表明，这些氧化脂质通过与免疫细胞相互作用，在动脉粥样硬化相关的炎症反应中发挥积极作用[33]。高葡萄糖水平也显示通过激活 AGE/GSMA 信号通路增加氧化应激，导致 VSMC 在 AGE 诱导的钙化中表型转化为成骨细胞样细胞，促进 VC [34]。

7. 小结

综上，饮食因素在炎症诱导的 VC 中发挥着重要作用。高 GI/GL 的碳水化合物、高饱和脂肪饮食及微量元素不足的碳水化合物可能导致慢性炎症从而诱导 VC。而目前饮食诱导慢性炎症的机制尚需进一步研究，未来的研究应进一步阐明膳食成分与 VC 之间的关系以及与其他危险因素(如高血压和高脂血症)之间的相互作用，以期更好地预防和治疗血管钙化，进而降低心血管疾病的发生率及死亡率。

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