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老龄化影响下寒冷对心血管疾病的影响研究

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摘　要

随着全球人口老龄化进程加速，心血管疾病已成为老年人群的主要健康威胁。寒冷环境作为重要的外部应激源，通过血管收缩、交感神经激活等机制加剧心血管负担。而老龄化伴随的血管弹性下降、体温调节能力衰退及慢性炎症状态，显著放大了寒冷对心血管系统的负面效应。本综述系统分析寒冷暴露与老龄化对心血管系统的交互作用机制，揭示低温环境下老年人群心血管疾病高发病率的病理生理机制；总结寒潮期间老年心血管事件的流行病学特征与高风险人群；并提出涵盖个体行为干预、医疗管理与社会支持的综合防控策略。通过整合最新研究成果，旨在为降低老年人群寒冷相关心血管风险提供理论依据和实践指导。

关键词

老龄化，寒冷暴露，心血管疾病，低温应激，炎症反应，预防策略

The Impact of Cold on Cardiovascular Diseases under the Influence of Aging

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Abstract

With the accelerating global aging population, cardiovascular diseases (CVD) have emerged as a primary health threat to older adults. Cold environments, as significant external stressors, exacerbate cardiovascular burden through mechanisms including vasoconstriction and sympathetic activation. Age-related declines in vascular elasticity, impaired thermoregulation, and chronic inflammation synergistically amplifies the adverse effects of cold exposure on the cardiovascular system. This review systematically analyzes the interaction mechanisms between cold exposure and aging in the

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cardiovascular system, elucidating the pathophysiological mechanisms underlying the high incidence of CVD among older adults in low-temperature environments. It summarizes epidemiological characteristics and high-risk populations during cold waves and proposes integrated prevention strategies encompassing individual behavioral interventions, medical management, and social support systems. By synthesizing the latest research, this review aims to provide theoretical foundations and practical guidance for reducing cold-related cardiovascular risks in the elderly.

Keywords

Aging Population, Cold Exposure, Cardiovascular Diseases, Low-Temperature Stress, Inflammatory Response, Prevention Strategies

1. 引言

随着人口结构转型加速，社会进入深度老龄化阶段，老年人比例显著提升[1]。这一趋势伴随心血管疾病负担的急剧加重，成为全球主要的死因之一，其中高龄群体尤其脆弱[2]-[4]。寒潮和长期低温事件作为独立风险因素，显著加剧了心血管事件的发生率[5] [6]。在老年人群中，冷暴露通过激活交感神经系统导致血压骤升和血管痉挛，进而诱发心肌梗死和脑卒中等急症[7]。同时，低温环境促进氧化应激和炎症反应，加速动脉粥样硬化进程，进一步提高了致命性心血管事件的风险[8] [9]。值得注意的是，老年群体由于生理储备下降和多种共病高发，对寒冷暴露的敏感性远高于其他年龄段[10]。寒潮发生时，65 岁以上老年人的心血管住院风险显著增加，死亡率增幅可达 32.4%，发病率上升 13.8%，这种敏感性在温带和热带气候区均有体现，低温每下降 1℃，心血管事件风险显著上升，老年亚群体尤甚[11]。此外，寒冷通过抑制自主神经调节和增加血栓形成倾向，放大衰老相关的血管功能障碍，形成恶性循环[12]。这一现象的复杂性表明，应对寒冷暴露的公共卫生干预应针对高危老年群体进行优化。

2. 寒冷暴露对心血管系统的生理与病理影响

寒冷暴露被公认为是心血管系统的重要风险因素，可能加剧全球心血管疾病负担[5]。寒冷暴露通过激活皮肤瞬时受体电位 M8 (TRPM8)冷敏离子通道启动生理级联反应。TRPM8 受体感知低温刺激后，经 Aδ 神经纤维将信号传递至下丘脑体温调节中枢，触发蓝斑核－交感神经通路兴奋。脊髓侧角神经元随之释放去甲肾上腺素，同时肾上腺髓质儿茶酚胺分泌量显著增加，触发了肾交感神经活动(RSNA)和腰交感神经活动(LSNA)的增加，进而导致心率上升和动脉血压升高，这些效应具有可逆性，但长期寒冷暴露可引发时间依赖性的累积作用，从而启动冷诱导的高血压[13]。在此阶段(暴露时间 < 30 分钟)，β_1 肾上腺素受体介导的窦房结自律性升高导致心率加速(+12~18 bpm)，而 α_1 受体激活则促使外周小动脉持续性收缩，总外周阻力上升 20%~25%，协同血管紧张素II的缩血管效应，最终使平均动脉压(MAP)升高超过 15 mmHg。这种血流动力学变化伴随自主神经失衡、高频心功率(HF)增加、低频心功率(LF)和 LF/HF 比率降低，平均血压轻度升高，这些变化在暴露后 15 分钟内仍持续[14]。在真实世界极端寒冷条件下(如低温至−34℃)，上述矛盾进一步激化。初期儿茶酚胺的正性肌力作用可使左室射血分数(LVEF)短暂提升 8%~10% (代偿相)；但随着核心体温降至 35℃临界点，区域性心肌缺血引发室壁运动异常，导致 LVEF 下降超过 5% (失代偿相)。此时平均动脉压骤升 25%以上，反映了心功能代偿或失代偿的适应性过程[15]。此外，

寒冷暴露还影响体温调节和自主神经响应，例如躯体加热干预可减轻大气温度下降或连续寒冷对热知觉的不利影响(如手脚冰凉、鼻涕或寒颤)，但寒冷本身增加了整体生理压力[16] [17]。

在病理方面寒冷暴露通过激活 BAT 的产热功能，增加 T3 合成，促进有害的心脏重塑，包括结构破坏(如心肌肥大)和功能损伤(如心功能失代偿)，这些变化与心血管死亡率和发病率增加直接相关[18]。系统回顾和流行病学分析显示，寒冷暴露使心血管疾病死亡率风险增加 75%，寒潮更导致死亡率上升 32.4%和发病率增加 13.8%，累积风险显著高于对照组[5]。寒潮还影响血液指标如血细胞比容，进一步揭示其病理机制[19]。寒冷抑制脂肪酸合成，促进脂解，导致心肌能量代谢紊乱。脂滴蛋白 Plin5 通过调控脂质储存和氧化，影响心脏重塑的代谢适应。此外，mTOR 信号通路通过整合营养和能量信号，参与心肌肥厚和纤维化的调控[20] [21]。影响程度因个体差异而异，例如在 2 型糖尿病患者中，寒冷引发的收缩压增加和心率减少较弱，显示出代谢疾病状态下的不同响应[22]。年龄、气候带和国家收入水平也被确定为关键影响因素，加剧了寒冷对心血管系统的负担[5]。极端寒冷暴露还可能导致局部灌注不足，特别是存在动脉狭窄时，增加急症风险如紧急救护调度的发生[23] [24]。寒冷环境结合运动虽可能产生协同健康益处，但单靠寒冷暴露本身增加身体热损失和心血管风险，需要通过干预策略(如躯体加热)来缓解[25]。健康干预旨在减少发病率，但机制仍需深入探究。

3. 老龄化心血管系统的病理生理变化

在老龄化过程中，心血管系统经历了一系列显著的病理生理变化。这些变化主要涉及血管和心脏结构及功能的逐步衰退，导致心血管储备能力下降，并显著增加心血管疾病的风险。在血管层面，衰老通过降低 SIRT1 (NAD + 依赖性去乙酰化酶)活性，导致 eNOS (内皮型一氧化氮合酶)乙酰化水平升高，减少 NO 生物利用度。同时，NADPH 氧化酶(NOX2/4)表达上调促进超氧化物生成，进一步加剧氧化应激，引起弹性纤维断裂、胶原沉积及中层钙化，导致动脉僵硬度显著升高(脉搏波传导速度增快)，脉压差增大，舒张压降低而收缩压升高[13] [14]。这种结构重塑伴随内皮功能障碍，主要表现为一氧化氮生物利用度降低、内皮依赖性舒张能力下降，进而削弱血管调节能力[15] [17] [26]。内皮功能失调与炎症因子浸润及氧化应激共同加速动脉粥样硬化斑块形成和不稳定性[2] [20] [27]。

在心肌层面，年龄相关性心肌肥厚和间质纤维化导致左心室僵硬度增加，引发舒张功能障碍(早期充盈受限)，成为老年射血分数保留性心力衰竭(HFpEF)高发的主要病理基础[15] [28]。值得注意的是，心肌纤维化在衰老过程中持续进展且难以逆转[29]。神经内分泌系统也发生显著失调：自主神经系统压力反射敏感性下降(降幅 40%~60%)，显著损害血压稳态调节能力[30]，而肾素－血管紧张素－醛固酮系统(RAAS)过度激活[31]-[33]，通过促进氧化应激、炎症反应及钠潴留，进一步加剧血管重塑、心肌肥厚和胰岛素抵抗[34] [35]。

体温调节功能障碍是老龄化另一关键特征。皮肤温度感受器敏感性降低延迟寒冷感知[36]，棕色脂肪组织(BAT)活性衰退(下降 30%以上)，严重削弱非寒战产热能力[15]，加之行为调节能力受限，共同导致核心体温维持能力下降。尤其重要的是“炎性衰老”现象：慢性低度炎症状态表现为循环促炎因子持续升高，炎症细胞向血管壁浸润增加，抗炎机制减弱。这种炎症环境与 RAAS 激活、内皮功能障碍及胰岛素抵抗相互交织[37]，形成恶性循环，放大动脉粥样硬化风险和斑块易损性。

上述病理改变的综合效应表现为：寒冷暴露时血管收缩反应亢进加剧血压波动(因压力反射障碍)，同时心肌耗氧量增加诱发缺血风险。RAAS 激活及炎症反应增强更直接促进血管痉挛、血小板活化和斑块破裂，最终解释观察到的老年人心血管系统对寒冷暴露的敏感性增加及心血管死亡率升高现象。

4. 老龄化与寒冷的交互作用机制

老龄化与寒冷暴露之间的交互作用机制涉及多个生理层面，表现出高度复杂性。在衰老过程中，寒

冷暴露通过激活交感神经系统(SNS)触发儿茶酚胺释放，进而过度激活肾素–血管紧张素–醛固酮系统(RAAS)，导致血管紧张素 II (Ang II)生成增加[38]。Ang II 作为 RAAS 的主要效应分子，通过激活 NF-κB 信号通路促进炎症反应，同时诱导活性氧(ROS)大量产生，加剧氧化应激[39]。在衰老背景下，慢性低度炎症(inflammaging)和抗氧化防御系统功能衰退形成恶性循环：Ang II 诱导的 NF-κB 活化进一步促进促炎因子释放，而氧化应激又通过激活 TLR4/NF-κB 等通路放大炎症反应[40]。这种持续放大的炎症–氧化应激轴直接损害血管内皮功能，导致一氧化氮生物利用度下降、血管收缩增强及血栓形成倾向[41]。衰老个体因交感张力基线升高(SNS 过度活跃)、RAAS 调控失衡、内皮修复能力下降以及线粒体功能障碍等因素，使得该恶性循环的破坏阈值显著降低[42]。研究表明，老年人群对寒冷诱发的心血管死亡率敏感性增加，这与衰老相关的 β-肾上腺素能受体信号衰减、UCP1 介导的产热能力下降以及 NF-κB/NLRP3 等炎症通路持续激活密切相关，最终导致心血管事件风险显著升高[3]。

衰老过程中，棕色脂肪组织(BAT)功能衰退表现为 β3 肾上腺素受体信号减弱、UCP1 表达下降及线粒体呼吸受损，导致其产热能力显著降低[43]。长期寒冷暴露时，衰老个体的 BAT 无法通过非战栗产热(NST)有效维持核心体温，引发代偿性交感神经过度激活[44]。这种持续的交感兴奋通过去甲肾上腺素释放诱发全身血管收缩，尤其在已有内皮功能障碍和血管硬化的老年人群中，会进一步加剧外周血管阻力[45]。研究表明，衰老个体的血管周围脂肪组织(PVAT)功能异常，丧失对血管张力的正常调节能力，使得寒冷诱导的血管收缩反应更强烈且持久。这种病理循环导致心肌氧供需失衡，在冠状动脉粥样硬化基础上显著增加心肌缺血风险。动物实验证实，BAT 功能缺陷模型会出现心脏收缩功能受损，且寒冷暴露时低体温与心力衰竭不良预后直接相关[46]。临床观察显示，老年人在寒冷环境中血浆 T3 水平波动更剧烈，提示其体温调节系统处于失代偿状态[47]，这种“代偿过度”机制可能是老年心血管事件季节性高发的重要诱因。

内皮功能障碍作为寒冷暴露与衰老进程的共同病理交汇点，其机制表现为多因素协同攻击内皮稳态。寒冷通过儿茶酚胺和血管紧张素 II (Ang II)的急性刺激诱发血管收缩反应，而衰老则通过慢性低度炎症和线粒体氧化应激导致内皮细胞持续损伤[48]。这两种病理过程均靶向破坏一氧化氮(NO)合成通路：寒冷通过 α1-肾上腺素受体激活减少内皮型一氧化氮合酶(eNOS)活性，衰老则因活性氧(ROS)积累直接降解 NO 并引发 eNOS 解偶联，共同导致 NO 生物利用度显著降低[49]。这种双重打击进一步损害内皮依赖性血管舒张功能，表现为 TRPV4 钙信号异常和血管平滑肌反应性下降，同时促进组织因子释放和纤溶抑制，形成促凝状态[50]。值得注意的是，衰老内皮细胞的线粒体功能障碍和 GPR35-TRPV4 相互作用缺失使其对寒冷诱导的血管痉挛更为敏感，而慢性炎症背景下的细胞衰老标志物(如 SA-β-gal)进一步削弱内皮修复能力。这种协同作用最终导致老年个体在寒冷应激下更易出现微循环障碍和血栓事件，证实内皮细胞是环境–衰老交互作用的关键枢纽。

5. 流行病学证据与高风险人群

寒冷暴露与心血管疾病的流行病学关联已在多项研究中得到证实，其中对老年人群的影响尤为显著。全球疾病负担研究显示，寒冷暴露可使心血管疾病死亡率增加 32.4%，发病率增加 13.8%，且这种效应在不同气候带和收入水平国家中存在显著差异[5]。在中国非季风区，极端寒冷天气对冠心病死亡率的负面影响尤为突出，女性及儿童亚组表现出更高的易感性[13]。年龄是寒冷致心血管风险的关键调节因素，研究证实寒冷效应随年龄增长呈现梯度增强，75 岁以上老年人在寒潮期间的全因死亡率较年平均水平显著升高，其中 52%可归因于心血管疾病[14] [15]。

在急性冠脉综合征(ACS)方面，寒冷暴露与 ST 段抬高型心肌梗死(STEMI)和非 ST 段抬高型心肌梗死(NSTEMI)的关联具有人群异质性。老年心肌梗死患者往往缺乏典型心血管危险因素，但其寒冷相关死

亡率可达 14%，显著高于年轻群体[17]。值得注意的是，伴有外周动脉疾病的老年急性冠脉综合征患者心血管死亡率更高，且寒冷诱发的心肌损伤机制与冠状动脉狭窄、血栓形成等病理改变密切相关[51] [52]。热带地区研究揭示，气温每降低 1℃会导致急性心梗风险整体增加 12%，而老年人群的风险增幅可达年轻群体的 1.5 倍[20]。

高风险人群的特征分析表明，长期职业性寒冷暴露(≥4 小时/日)使老年劳动者卒中风险增加 2.3 倍，这种效应在男性及 65 岁以上人群中更为显著[53]。代谢综合征患者合并急性心梗时，寒冷诱发的炎症反应和氧化应激加剧可导致血运重建术后死亡率升高 37% [54]。特别值得关注的是，患有风湿性免疫介导炎症疾病的老年患者，其寒冷相关 ACS 发生率是普通人群的 2.1 倍，且长期预后更差[55]。气候适应能力下降、合并多系统慢性病以及社会防护不足共同构成了老年群体对寒冷心血管效应的三重脆弱性。

6. 预防与管理策略

为有效降低老年人群寒冷相关心血管风险，需构建涵盖个体行为、医疗优化及社会支持的综合防护体系。在个体行为层面，倡导实践适应性防护措施，研究表明寒冷暴露会显著增加心血管疾病死亡率 32.4%和发病率 13.8% [5]，因此需特别注意保暖和活动调节。采用分层穿衣法保护核心体温，避免极端寒冷天气长时间户外活动，同时通过规律运动增强寒冷适应能力，证据显示运动虽增加心血管系统压力，但能提高机体对不良刺激的耐受性[13]。医疗管理层面强调循证干预策略，针对老年人群实施强化血压控制可显著降低心脑血管事件风险，同时需注意调整用药方案，避免使用加重低温反应的药物如血管扩张剂。疫苗接种是重要预防手段，特别是流感疫苗可显著降低老年心血管死亡率[15]。对于高风险人群，应考虑采用分子氢等新型干预手段，研究显示其具有预防和治疗年龄相关疾病的潜力。社会支持层面需建立多维度保障网络，确保室内适宜温度(≥18℃)对预防心血管事件至关重要，同时推广可穿戴设备进行实时健康监测[56]。社区应组织定向干预项目，针对寒冷天气实施特殊防护措施，如对高风险老人进行定期巡访。在机制研究基础上，针对 NLRP3 炎症小体等关键靶点开发干预策略可能为寒冷相关心血管疾病提供新的防治途径。值得注意的是，不同气候区域和年龄群体对寒冷的敏感性存在差异[6]，需制定区域化、年龄特异性的防护方案。通过整合生理监测、环境调控和靶向治疗等综合措施，可有效缓解寒冷暴露对老年心血管系统的不良影响，同时需进一步研究阐明寒冷适应与衰老的复杂关系，以优化防护策略。

7. 结论与展望

本研究综合分析表明，老龄化显著加剧了寒冷暴露对心血管疾病的不良影响，通过加速心血管系统的功能衰退、增加内皮损伤及血栓形成倾向，与寒冷诱导的交感神经激活、血压上升和心脏重塑相结合，协同提升老年人群的心血管事件风险。具体而言，寒冷暴露被确认为心血管疾病的重要危险因素，尤其在极端冷浪事件中，老年个体的心血管死亡率和发病率显著上升，且这种效应在特定气候区和低收入国家人群中更突出，反映了年龄与气候环境相互作用的复杂性。尽管寒冷暴露在理论上可能通过激活棕色脂肪组织、改善代谢调控和减轻慢性炎症提供潜在抗衰老益处，但长期冷暴露的实际风险在老年人中仍占主导，导致心血管功能恶化。应对这一挑战需多维干预，包括个体行为调整(如避免极端寒冷)、医疗管理优化(如针对血压控制)及社会支持(如供暖保障)。

研究应优先聚焦于深入探索寒冷与衰老协同作用的分子机制，特别是在线粒体功能障碍、氧化应激调控及免疫衰老－感染－心血管事件链接等路径。开发针对性干预策略至关重要，包括推进基于传统中医的延缓衰老制剂(如茶多酚)的临床应用，并研制新型药物如非寒战产热激活剂(如线粒体解偶联剂)以增强老年体温适应力。同时，结合人工智能技术构建寒潮健康风险预测模型，整合公共卫生监测体系(如实时气候风险评估)，推动制定老龄友好型城市供暖标准，从社区层面降低暴露风险。随着基因编辑、细胞

疗法及远程医疗的整合发展，未来有望实现从分子靶向治疗到社会支持的多层级防护网络，最终提升老年群体在寒冷环境中的心血管适应力，达成健康老龄化目标。

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