心血管衰老机制研究进展（一）专题

·综 述·

心血管衰老概述

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摘要：目前血压升高、血脂异常等心血管疾病高危因素已获得有效管理，但心血管疾病仍是全球致残、致死的主要原因。衰老是人类不可避免的生命进程，心血管系统亦是如此。心血管衰老与心血管疾病发生风险升高密切相关。探究心血管衰老机制对心血管疾病的治疗、药物研发及改善患者预后均有重要意义。现就心血管衰老机制作简要综述，以期为后续研究提供参考。

关键词：心血管系统；衰老；机制
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Overview of cardiovascular aging

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Abstract: At present, high-risk factors for cardiovascular disease such as hypertension and dyslipidemia have been effectively managed, but cardiovascular diseases remain the main cause of disability and mortality worldwide. Aging is an inevitable process in human life, and the cardiovascular system is no exception. Cardiovascular aging is closely related to an increased risk of cardiovascular diseases. Exploring the mechanisms of cardiovascular aging is of great significance for the treatment of cardiovascular diseases, drug development, and improvement of patient prognosis. This article reviewed the mechanism of cardiovascular aging, in order to provide reference for future research.

Key words: cardiovascular system; aging; mechanism

人类心血管系统由多种不同类型的细胞组成，包括内皮细胞、平滑肌细胞、心肌细胞、成纤维细胞及免疫细胞等，上述细胞协同作用，以维持体内血液供应及代谢产物的排泄。值得注意的是，大多数心血管系统细胞均具有高度特异性，需在特定条件下方可发挥作用。然而，各类心血管系统细胞的独特功能（如心肌细胞的收缩功能）是以细胞周期衰退为代价的，且相关细胞修复缓慢、增殖能力有限，心血管衰老不可避免[1—3]。研究证实，年龄是心血管疾病危险因素之一[4]。随着年龄增长，细胞衰老加重，心脏、血管及微循环均会发生结构及功能改变[4—8]，心血管疾病发生风险随之增加[9]。尽管目前血压升高、血脂异常等心血管疾病危险因素已获得有效管理[10—11]，但心血管疾病仍是全球致残、致死的主要原因[12]。探究心血管衰老机制或对心血管疾病的治疗、相关药物的研发以及患者预后的改善具有重要意义。

1 衰老与心血管疾病

有证据表明，即使心血管事件主要危险因素获得有效控制，但仍有部分心血管事件无法避免，这

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被称为心血管事件残余风险[13—15]，且其机制与衰老密切相关[16]。心血管疾病发生风险与衰老存在相似的性别差异[5,17—18]，提示二者可能存在共同机制。动物试验显示，通过干预胰岛素样生长因子1、血管内皮生长因子不仅能改善衰老状况、提升健康水平，还可改善心功能，延长模型动物寿命[19—20]。提示抗衰老或是心血管疾病防治的可行切入点。

2 心血管系统衰老机制

抗衰老的前提是了解衰老相关分子机制。但目前相关研究多在动物模型中开展，且心血管细胞功能障碍的具体机制尚待评估[21—22]。Abdellatif等[23]提出，基于严格标准的8个分子特征作为心血管系统衰老标志。这8项标志涵盖主要衰老机制，包括巨自噬功能丧失、蛋白稳态丧失、基因组不稳定、表观遗传学改变、线粒体功能障碍、细胞衰老、神经激素信号失调及炎症。同时，其还指出针对上述机制进行干预可能降低心血管事件残余风险，延长机体寿命；此外，相关机制亦有潜力成为心血管疾病治疗新药研发靶点。

心血管衰老机制相互交织、相互影响。例如，巨自噬功能丧失会导致蛋白稳态崩溃、线粒体功能障碍、神经激素信号失调和炎症增加[24—25]。反之，诱导巨自噬能改善线粒体功能，防止蛋白稳态丧失，减少细胞衰老，减轻炎症[26—28]。同样，基因组不稳定是衰老的主要驱动因素，随后通过衰老相关分泌表型因子促进炎症；表观遗传不稳定可通过染色质免疫沉淀物410直接促进炎症。此外，非编码RNA及组蛋白的表观遗传学改变会使巨自噬失效，诱导细胞衰老，并破坏心血管系统中各种神经激素信号通路。

心血管衰老机制中巨自噬功能丧失、蛋白稳态丧失、基因组不稳定及表观遗传学改变为主要特征，会随年龄增长而逐渐发展，并成为基因组、表观遗传组、蛋白组及细胞器退化的基础，应被视为在上游水平启动心血管老化的主要标志。而线粒体功能障碍、神经激素信号失调和细胞衰老在心血管衰老中起到更微妙的作用，是拮抗性特征。当主要特征及拮抗性特征损伤累及达到阈值水平时，炎症这一机制随之发挥作用。

3 结语与展望

现有证据表明，持续暴露于外部因素，如营养不良、不良生活方式、心理和社会压力、吸烟及污染等，可能通过前文所述机制加速心血管疾病进展[29]。肥胖作为心血管疾病高危因素，其所涉及的机制亦涉及蛋白稳态丧失、表观遗传不稳定、线粒体功能障碍、细胞衰老、神经激素信号转导失调及慢性炎症[30—37]，并与加速心血管衰老相关[38—39]。多项研究表明，适当限制饮食、控制体质量对改善心血管衰老具有积极作用[40—43]。

心血管事件残余风险的存在意味着对心血管疾病传统危险因素进行有效管理并不能完全消除心血管事件的发生风险[44]，而针对心血管衰老机制研发新药，有望为全面开展心血管风险管理提供新思路、新方向。此外，对心血管衰老机制进行深入研究，还有助于探究针对不同心血管衰老机制的药物间协同作用，以进一步提高疗效。衰老相关疾病的发生不可避免，但目前相关研究仍以动物模型为主，无法完全涵盖人体内相关机制的复杂性，故仍需不断完善相关动物模型，以使其进一步贴近人体内环境。

除药物治疗之外，还需深入了解生活方式干预（如饮食和锻炼）的优化程度，以使心血管系统适应各种环境压力，减缓衰老过程。在未来的研究中，应致力于建立客观、以生物标志物为指导的干预建议，结合特定的药物预防策略，以进一步改善心血管疾病患者预后。

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