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综 述

# 老年人肌少症发生机制

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**摘 要**：因年龄增长所致骨骼肌质量减少及功能衰退称为肌少症，其特点是随着年龄的增加，肌纤维的质量、力量、肌耐力、代谢能力下降，而脂肪、结缔组织增多。肌少症的本质是肌纤维数量与横截面积下降及蛋白质净降解，与炎症加剧、氧化应激损伤、线粒体功能障碍、细胞自噬异常和肌肉质量调控因子失调等因素密切相关。本文系统阐述了肌少症发生的分子机制，加深人们对肌少症的理解与认识，为肌少症的预防与治疗提供潜在靶点。

**关键词**：肌少症；机制；骨骼肌；衰老
**中图分类号**：R3

## Mechanism of the occurrence of sarcopenia in the elderly

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**Abstract:** The decline in skeletal muscle mass and function with age is referred as sarcopenia. It is characterized by the muscle fiber's quality, strength, muscle endurance and metabolic ability decreasing as well as the fat and connective tissue growing. Previous studies have shown that sarcopenia in itself features decreased number and cross-sectional area of muscle fibers and the net degradation of protein, which results from the joint effects of multiple factors such as the exacerbation of inflammation, oxidative stress injury, mitochondrial dysfunction, abnormal autophagy and dysregulation of muscle quality regulatory factors. In this review, we systematically displayed the molecular mechanism of sarcopenia, which will be helpful to deepen our understanding of sarcopenia and provide potential targets for the prevention and treatment of sarcopenia.

**Key words:** sarcopenia; mechanism; skeletal muscle; aging

因年龄增长所致骨骼肌质量减少及功能减退称为肌少症，其特点是随着年龄的增加，肌纤维的质量、力量、肌耐力、代谢能力下降，而脂肪、结缔组织增多[1]。肌少症和骨质疏松症相伴出现被统称为“活动障碍综合征”，该征可使老年人易于跌倒和骨折，因而成为了老年人群致残、致死的主要原因之一[2]。与骨质疏松症相比，肌少症近 10 年来才逐渐受到关注。肌少症与活动障碍、跌倒、低骨密度及代谢紊乱密切相关，是老年人生理功能逐渐减退的重要表现之一。肌少症的发生增加了老年人住院率及医疗花费，严重影响老年人的生活质量，甚至缩短老年人的寿命[3]。随着我国老龄化时代的提前到来，肌少症成为了老年医学领域亟待解决的重要问题。有很多研究关注肌少症，但肌少症发生的分子机制至今仍远未阐明。本研究对国内外最新文献进行了全面梳理，对肌少症发生的相关机制最新研究进展进行了系统总结，以期为肌少症的预防和治疗提供有价值的参考。

## 1 衰老对骨骼肌质量和功能的影响

### 1.1 衰老对骨骼肌质量的影响

年龄增长诱发的肌少症一般进展缓慢，首先是

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健康肌纤维出现纤维化、被脂肪填充，随后骨骼肌氧化受损加剧、还原能力减弱、神经肌肉接头功能障碍、肌肉类型发生转变、快 / 慢肌纤维比例降低，且二者绝对质量下降 [4]。有人对肌少症发病率进行了相关研究，如 Stephan 等研究显示，60~70 岁老年人肌少症发病率为 5%~13%，80 岁以上老年人为 11%~50% [5]；Cheng 等对上海 3 500 多名年龄 18~96 岁健康人群的研究显示，70 岁以上男性一级和二级肌少症患病率分别为 34.0% 和 13.2%，女性分别为 16.5% 和 4.8% [6]。也有人对肌肉流失量进行了研究，肌肉质量通常在年轻成年人中占总体重约 50%，但在 75~80 岁时减少至 25% [7]，尤其是下肢肌肉质量损失最为显著，与 20 岁时相比，80 岁时外侧肌横断面积减少了 40% [8]。

### 1.2 衰老对骨骼肌功能的影响

老年人骨骼肌功能会因肌肉质量减少而下降，且肌力下降比肌肉体积减少更加明显 [9]。随着年龄的增加，骨骼肌强度降低 (40 岁左右表现明显 )，随后骨骼肌稳定性下降，自我修复能力减弱，致使跌倒风险增加，死亡率上升 [10–12]。骨骼肌质量下降，不仅改变肌肉蛋白的合成和降解，还影响功能性 α 运动神经元数量及对肌肉的支配作用 [13, 14]。70 岁以后，人体运动神经元数量显著减少，α 运动神经元丢失约 50%，肌肉强度和功能出现显著下降 [15]。此外，线粒体作为能量生成、活性氧 (reactive oxygen species, ROS) 产生、细胞信号传递过程中具有重要作用的细胞器，衰老可使其结构改变，功能下降 [16]。因此，衰老可使骨骼肌蛋白质代谢失衡、运动神经元减少、线粒体结构和功能出现异常，从而导致衰老骨骼肌再生能力、肌力及稳定性的下降。

## 2 肌少症的本质——肌纤维数量与横截面积下降及蛋白质净降解

肌少症表现为结构与功能的损害，但结构是决定功能的基础，骨骼肌功能下降的根本原因是肌肉结构上的异常。肌少症的本质可归结为肌纤维数量与横截面积下降及蛋白质净降解。

### 2.1 肌纤维数量与横截面积下降

肌纤维水平上，肌少症以 II 型肌纤维萎缩、纤维坏死增加以及纤维交联成分和线粒体减少为特征 [8]。研究显示，90 岁人体肌肉中 I 型和 II 型纤维含量仅为年轻人的一半 [17]。目前对于衰老诱发肌肉质量下降的直接原因仍有不同的观点。Nilwik 等研究表明，随着年龄的增长，肌纤维质量的损失具有纤维类型特异性，主要表现为 II 型肌纤维横截面积下降 [18]。且有实验结果显示，与年轻人相比，老年人 II 型肌肉纤维尺寸减少 10%~40%，而 I 型肌肉纤维尺寸基本不受影响 [19, 20]。也有研究显示，随着年龄的增长，肌肉质量的丢失不仅仅是由于肌纤维横截面积的下降，同时还伴有肌纤维数量的减少 [21, 22]。早期人体实验研究表明，与年轻人相比，老年男性外侧肌纤维的数量减少了 40%[23]。因为实验模型的差异，当前对于衰老是否伴有肌纤维数量的减少尚存争议。多数动物模型研究指出，肌纤维的数量随年龄增加有明显下降。而人体研究则认为，肌纤维横截面积降低是肌少症发生的主要原因。

### 2.2 骨骼肌蛋白质净降解

蛋白质约占肌肉质量的 20%，是维持人体肌肉质量的重要成分。蛋白质降解与合成之间的关系是决定人体肌肉质量的主要因素 [24]。肌少症发生时，蛋白质降解大于其合成，即出现蛋白质净降解。

#### 2.2.1 蛋白质降解增强

当老年人蛋白质摄入不足，肌肉蛋白分解超过合成时，会引起肌肉质量减少，增加肌少症发生的风险 [25]。泛素 - 蛋白酶体系统 (ubiquitin-proteasome system, UPS) 是调节蛋白质降解和维持蛋白质稳态的重要途径。肌萎缩素 1 (atrogin-1) 是泛素蛋白酶途径中泛素蛋白连接酶 E3s 的一种，atrogin-1 决定着 ATP- 泛素 - 蛋白酶体系统的特异性和速率。泛素蛋白连接酶 atrogin-1 和肌环指蛋白 1 (musclering-finger 1, MuRF-1) mRNA 表达的上调先于代谢的变化，可以作为肌少症等相关疾病的早期分子标志物 [26]。伴随机体衰老，UPS 发生改变，导致肌肉蛋白降解增加 [27]。肌肉萎缩盒 F 蛋白 (muscle atrophy F-box, MAFbx) 和 MuRF-1 是已知的与蛋白质分解代谢关系最为密切的两种泛素蛋白连接酶，也是 UPS 的重要组成部分 [28]。研究表明，随着年龄的增加，肌肉中 MAFbx 蛋白水平没有明显变化，但 Atrogin-1 和 MuRF-1 蛋白表达水平显著增加，进而促进肌蛋白降解 [29]。此外，衰老机体引起的蛋白激酶 B (protein kinase B, Akt) 和哺乳动物雷帕霉素靶蛋白 (mammalian target of rapamycin, mTOR) 活性降低及调亡信号增强也可激活 UPS，诱导蛋白质降解，使肌肉质量下降。这些都可能是诱发肌少症的重要原因 [30, 31]。

#### 2.2.2 蛋白质合成代谢抵抗

衰老骨骼肌对蛋白合成刺激 ( 如补充蛋白质、

运动等 ) 的敏感性下降，即衰老引起蛋白质合成代谢抵抗作用 [32]。基础条件下老年人肌肉蛋白周转率出现异常，蛋白质合成代谢抵抗可能是老年人骨骼肌质量流失的重要原因 [33–35]。老年人骨骼肌出现合成代谢抵抗的发生机制还不太清楚，最近有研究指出，机体转运氨基酸至肌肉组织的速率可能是老年人肌肉蛋白合成的关键限制因素，老年人骨骼肌蛋白质合成代谢抵抗可能与外周组织氨基酸的转运速率及肌细胞对氨基酸摄取能力降低有关 [36]。机体向外周组织递送氨基酸的速率依赖于动脉氨基酸浓度和肌肉组织血流量，而机体血流量和毛细血管数量都随机体衰老而降低 [37]。即机体衰老引起血流量的降低及毛细血管数量减少，进而导致氨基酸递送至肌肉的速率下降，可能是肌蛋白合成代谢抵抗发生的根本原因 [36, 37]。

此外，老年人骨骼肌合成代谢抵抗也可能与 mTOR 通路中氨基酸刺激下的蛋白质磷酸化过程被钝化相关。必需氨基酸是刺激肌肉蛋白合成的主要因素，与 mTOR 通路相关的信号蛋白对氨基酸十分敏感，特别是亮氨酸 [38, 39]。研究表明，补充大剂量的必需氨基酸克服合成代谢抵抗能力主要取决于亮氨酸的含量，如果提高必需氨基酸中亮氨酸的含量，则可适当刺激老年人肌肉蛋白质合成 [40]。因此，有人提出了“亮氨酸阈”的概念，即骨骼肌要想达到蛋白质合成速率的最大化，氨基酸中的亮氨酸含量必须达到这个阈值 [16, 40]。对于年轻人，亮氨酸阈值约为 2 g，老年人约为 3g。由于老年人骨骼肌对氨基酸浓度敏感性下降，因此必须摄取足够的亮氨酸才能克服合成代谢抵抗，充分刺激肌肉蛋白质合成 [34, 41]。此外，年龄增加导致体内生长激素 (growth hormone, GH)、胰岛素样生长因子 -1 (insulin-like growth factor-1, IGF-1) 水平降低及胰岛素抵抗，也是诱发蛋白质合成抵抗的重要原因 [1]。

## 3 肌少症发生的分子机制

### 3.1 炎症加剧

越来越多的证据表明，较高的炎症水平与机体衰老有关 [42]。随着机体衰老，炎症和氧化应激水平显著升高，这被认为是诱发老年人肌少症的重要因素 [43]。老年人机体炎症标志物如白介素 -6 (interleukin-6, IL-6)、C- 反应蛋白 (C-reactive protein, CRP)、肿瘤坏死因子 -α (tumor necrosis factor α, TNF-α)、IL-1β 等循环水平显著升高，且与老年人肌肉质量和力量降低直接相关 [42, 44]。TNF-α 可通过抑制 Akt/mTOR 途径增强肌肉分解代谢，与其受体结合后，还可通过线粒体的电子传递产生 ROS，从而激活核因子 -κB (nuclear factor κB, NF-κB)，从而活化 UPS，显著增强 UPS 活性，加速骨骼肌蛋白质水解 [45, 46]。TNF-α 还可激活金属蛋白酶调控细胞凋亡，通过叉头蛋白转录因子 (forkhead box transcription factor O, FOXO) 激活溶酶体自噬途径。此外，血清中 CRP 水平升高也与蛋白质合成减少及蛋白质分解代谢增加有关 [47]。IL-6 参与肌蛋白更新调控，被认为是分解代谢细胞因子 [48]。炎症还可通过间接降低机体 GH 和 IGF-I 浓度，对骨骼肌产生负面影响，诱发肌少症的发生 [49]。

### 3.2 氧化应激损伤

随着年龄增加，细胞内氧化应激增强，引起骨骼肌 ROS 产生增加。ROS 不仅可以抑制肌卫星细胞功能，还可促进 atrogin-1 和 MuRF-1 基因表达，增强 UPS 活性，加速蛋白质水解。此外，骨骼肌内 ROS 水平升高还可降低细胞膜内 $Ca^{2+}$-ATP 酶活性，引起细胞质 $Ca^{2+}$ 浓度及钙蛋白酶活性升高，促进细胞内蛋白质水解。另有研究显示，ROS 增加还可激活天冬氨酸特异性半胱氨酸蛋白酶 (caspase-3)，引起细胞凋亡 [50]。因此，氧化应激损伤可能参与了肌少症的发生和发展。

### 3.3 线粒体功能障碍

线粒体是肌肉收缩所需 ATP 的主要生成场所，伴随着机体的衰老，多种细胞器出现缺陷，线粒体结构和功能也发生了一系列的变化，如线粒体出现体积增大和嵴的损失 [51]。目前，线粒体自由基衰老理论 (mitochondrial free radical theory of aging, MFRTA) 认为 ROS 产生增多导致线粒体 DNA (mitochondrial DNA, mtDNA) 氧化损伤，进而引起线粒体功能障碍，这被认为是驱动机体衰老的中心机制 [52]。由于 mtDNA 表面没有组蛋白的保护，使其不断受到自由基的攻击，导致线粒体功能紊乱。线粒体功能障碍引起能量缺乏、ROS 和脂类上升，继而引发肌肉发育不良和损伤，这是诱发老年人肌少症的重要因素之一 [53]。此外，骨骼肌线粒体严重的氧化损伤，影响 $Ca^{2+}$ 转运，导致骨骼肌收缩功能下降。线粒体功能紊乱还可加速衰老动物去神经改变，最终致使老年人肌肉功能紊乱，衰老肌细胞死亡，诱发肌少症 [54, 55]。

### 3.4 细胞自噬异常

自噬是一种基本的细胞清洁过程，可以清除活

细胞中功能失调的细胞器和变性蛋白[56]。骨骼肌占据人体体重的40%~55%，是人体质量最大的组织，也是人体主要的代谢器官[57]。然而骨骼肌细胞的自噬功能状态却一直被人们所忽视。过度和有缺陷的自噬都与骨骼肌质量丢失高度相关[58]。肌细胞自噬缺陷可导致错误折叠蛋白的异常聚集，而过度自噬则会引起细胞应激，导致蛋白质降解增加，骨骼肌质量损失。研究表明，衰老大鼠骨骼肌中调控自噬发生的标志性相关蛋白自噬相关蛋白13 (autophagy-related protein 13, Atg13)、Unc样激酶1 (Unc 1ike kinase 1, ULKl)、自噬效应蛋白Beclin1、自噬相关蛋白LC3和溶酶体膜蛋白-2 (lysosomal membrane protein 2, LAMP-2)等表达均出现显著上调[31]。而自噬水平升高与衰老小鼠骨骼肌质量、力量降低密切相关[59]。此外，最近研究表明，磷脂酰肌醇3-激酶 (phosphatidylinositol 3-kinase, PI3K)/Akt/mTOR信号通路与自噬的激活密切相关，机体衰老导致TORC1活性降低，可使Atg13部分去磷酸化，进而导致与Atg1和Atg7的结合能力增强，从而提高Atg1的激酶活性，使细胞自噬活性增强[60, 61]。

### 3.5 骨骼肌质量调控因子失调

骨骼肌质量既受外周血多种激素 ( 如GH、睾酮、甲状腺激素 ) 的调控，也受到骨骼肌局部产生的多种活性因子 ( 如PGC-1α、IGF-1、Myostatin) 的影响。随着年龄增长，体内GH、睾酮、甲状腺激素和IGF-1等含量下降，可导致肌肉质量及功能的降低[62]。

#### 3.5.1 GH与IGF-1

GH与IGF-1在维持骨骼肌质量和功能方面发挥重要作用。IGF-1是GH的下游因子。IGF-1可能是Akt-mTOR-p70S6K信号转导、促进肌肉生长和修复的重要介质，其过度表达可诱发骨骼肌肥大，并增强正常和肌营养不良小鼠的肌肉再生[63–65]。由垂体分泌的GH与受体结合，可促进局部组织产生IGF，IGF-1与其受体结合后可激活mTOR，磷酸化胰岛素受体底物-1 (insulin receptor substrate 1, IRS-1)和PI3K，诱导质膜中磷脂生成，募集和激活Akt激酶共同促进蛋白合成[66]。此外，IGF-1分泌下降同时伴随有GH脉冲释放显著降低，IGF-1还可通过增加肌卫星细胞数量和刺激蛋白质合成提高肌肉功能[67, 68]。随着机体的衰老，GH和IGF-1分泌减少，其量与肌力下降成正相关，同时伴有肌肉质量的丢失[69]。即GH与IGF-1可能在肌少症的发生中发挥了重要作用。

#### 3.5.2 睾酮

大量研究已表明，睾酮在调节机体代谢、维持骨骼肌质量和骨密度、抑制脂肪生成中发挥重要作用。临床研究也证实，睾酮缺乏是诱发老年人肌少症和肥胖症的重要因素[70]。在骨骼肌中，睾酮可通过雄激素受体 (androgen receptor, AR) 的介导作用影响蛋白质合成与分解代谢，使蛋白质合成增加并促进肌肉生长[71]。老年男性睾酮水平与肌肉量、强度和功能的下降均相关。研究显示，给予老年人适量的睾酮补充剂干预，可促进I型和II型肌纤维的横截面积和肌核数量增加，但I型和II型肌纤维的绝对数量没有变化[70]。体外实验也证实睾酮可促进星状细胞数量增加，且是其功能的主要调控因子[72]。有证据表明，肌少症的男性患者体内睾酮水平与正常男性相比显著降低[73]。纵向来看，随着年龄增长，男性体内睾酮水平约以每年1%的速度下降。此外，女性循环血液中睾酮水平也随年龄的增加而下降，特别是处在更年期和绝经后的女性循环血液中睾酮水平下降速度更快[74]。因此，机体衰老伴随的睾酮水平的下降可能是诱导肌少症发生的重要因素之一。

#### 3.5.3 甲状腺激素

甲状腺激素对生长、分化、发育和保持代谢平衡具有极其重要的作用。甲状腺激素有T3和T4两种主要形式，其中T3的生物活性最强。研究表明，T3对骨骼肌功能、代谢及损伤修复至关重要[75]。在胚胎发育期间，T3可通过激活肌源性调节因子 (myogenic regulatory factors, MRF) 诱导肌祖细胞分化；T3可调控骨骼肌转录因子MyoD和肌细胞生成素的表达；T3还可通过增加肌纤维的数量和直径来刺激骨骼肌生长[76, 77]。甲状腺激素发挥生理作用需由甲状腺激素受体 (thyroid receptor, TR) 介导，其中TRα在骨骼肌中呈高表达。最近研究表明，TRα基因敲除小鼠成肌细胞增殖和和肌原细胞的分化水平都显著降低，表明TRα在成肌细胞动态平衡中有重要作用[78]。

当甲状腺激素分泌异常时，骨骼肌可出现功能障碍，如甲状腺功能亢进症患者骨骼肌中II型肌纤维的比率增加，而甲状腺功能减退则会引起骨骼肌中II型肌纤维的比率下降，ATP酶活性降低，骨骼肌肌浆网摄取$Ca^{2+}$能力下降，肌球蛋白轻链比例下降[79]。多数甲状腺功能减退症患者都伴随有骨骼肌形态和功能的病变，导致肌肉力量下降及质量丢失[80]。与甲状腺功能减退症患者相似，老年人血清

中甲状腺激素浓度与年轻人相比显著降低[81]，这可能是引起骨骼肌质量和功能下降、诱发肌少症的重要因素。

### 3.5.4 过氧化物酶体增殖活化受体γ辅助活化因子1α (α subunit of peroxisome proliferators-activated receptor-γ coactivator-1, PGC-1α)

PGC-1α 是过氧化物酶体增殖活化受体 γ 辅助活化因子 1 (peroxisome proliferators-activated receptor-γ coactivator-1, PGC-1) 的成员之一。PGC-1α 是线粒体生物合成的主要调节因子，也是机体内氧化应激反应的标志分子[82]。研究表明，衰老状态下 PGC-1α 参与骨骼肌质量的调节[83]。PGC-1α 表达升高可抑制蛋白质降解，预防各种刺激诱导的骨骼肌萎缩。PGC-1α 过表达可预防衰老骨骼肌质量丢失，降低凋亡标志物的产生，抑制自噬及 UPS 相关基因的表达，预防肌少症的发生和发展[84]。此外，PGC-1α 过表达还可抑制 FOXO3 与基因 ( 如 atrogin-1) 的结合和激活，抑制转录因子 NF-κB 的表达，进而预防肌少症发生[85–87]。研究表明，与年轻人相比，老年人肌肉中 PGC-1α 基因表达量呈降低趋势，这

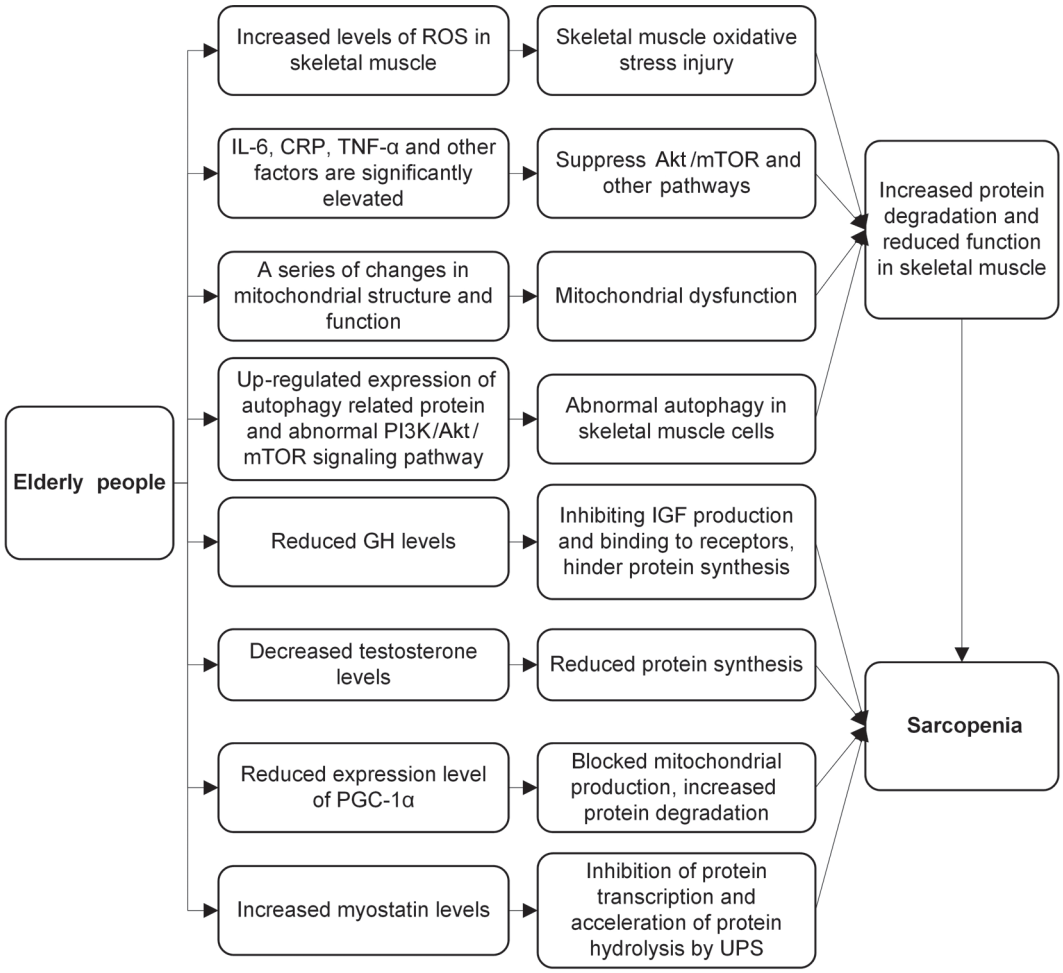


图 1. 老年人肌少症发生机制示意图

Fig. 1. A schematic of mechanism of the occurrence of sarcopenia in the elderly. With increased age, inflammatory factors such as IL-6 and TNF-α and ROS levels in the skeletal muscle tissue of body increase significantly, and the autophagy level and mitochondrial structure and function become abnormal, thus causing abnormal mitochondrial dysfunction of skeletal muscle, oxidative stress injury, and inhibition of Akt/mTOR pathway so as to strengthen muscle catabolism, which results in sarcopenia. In addition, excessive autophagy can cause cell stress, leading to increased protein degradation, and loss of skeletal muscle-induced sarcopenia. With the increase of age, skeletal muscle mass is regulated and controlled by multiple hormones (such as GH, testosterone, and thyroid hormones) in peripheral blood, and is also influenced by multiple active factors (such as PGC-1α, IGF-1, and myostatin) that are locally produced in skeletal muscle. As age increases, the levels of GH, testosterone, thyroid hormone, and IGF-1 in body decrease, and the level of myostatin in serum increases, resulting in decreased muscle mass and function, so that sarcopenia is induced.

可能是衰老诱导肌少症发生的重要因素之一 [83]。

#### 3.5.5 肌肉生长抑制素(myostatin)

肌肉生长抑制素主要在骨骼肌中表达，其功能缺失可引起肌肉肥厚、功能增强，是肌肉生长的重要负调节因子。对年轻、中年和老年人群进行横断面研究结果显示，随着年龄增长，血清中肌肉生长抑制素水平增加，其中身体虚弱的老年妇女水平最高，且与骨骼肌质量呈负相关 [88]。衰老机体中肌肉生长抑制素水平升高，可与活化素受体蛋白 2B (activin receptor 2B, ActR2B) 结合，激活 Smad (drosophila mothers against decapentaplegic protein) 蛋白家族，后者可以抑制蛋白质转录并通过 UPS 加速蛋白质水解 [89, 90]。此外，衰老机体肌肉干细胞功能降低，其可能与肌肉生长抑制素表达增强有关 [91]。相反地，抑制肌肉生长抑制素的生成则可以改善骨骼肌的质量和功能 [92]。因此，肌肉生长抑制素水平升高可能是老年人肌肉流失的一种重要机制。

## 4 肌少症的防治——运动疗法

基础及临床研究均显示运动训练对预防和治疗肌少症有较好的疗效，如有氧运动对提高老年人机能状态和健康水平、预防心血管疾病和肌少症有积极意义，而抗阻训练对神经肌肉系统有积极影响，并增加激素水平及蛋白质合成，进而提高骨骼肌质量 [93]。抗阻训练不仅可提高骨骼肌质量，还可改善骨骼肌功能。如老年人以 60%~80% 一次重复最大负荷 (1 repetition maximum, 1RM) 的负荷，每天练习 1~3 组 (8~12 次 / 组 )，组间歇 1~3 min，频率为每周 2~3 d，对预防老年人肌少症有显著效果 [94]。Fiatarone 等对均龄为 87 岁的老年人进行 10 周抗阻运动和营养补充干预，结果显示骨骼肌肌力提高 125%，而对照组却降低 3% [95]。周期更短一些的抗阻训练，也能使骨骼肌获益，如 61~85 岁的老年人进行为期 6 周的抗阻训练，也可使其肌肉相对力量提高 28% [96]。此外，最新研究显示，全身震动训练和肌肉电刺激也能显著改善老年人肌少症 [97]。这些研究表明运动疗法在防治肌少症中具有积极意义，特别是抗阻训练，应成为治疗肌少症的基本方法。

## 5 总结

肌少症是老年人群常见疾病，肌少症的本质是肌纤维数量与横截面积下降及蛋白质净降解，其发生是多因素共同作用的结果 ( 图 1)。随年龄增加，机体炎症加剧，引起 UPS 活化，UPS 活性增强，加速骨骼肌蛋白的水解。氧化应激损伤增强，抑制肌卫星细胞活性，加速细胞凋亡。此外，衰老导致机体结构异常与功能障碍，特别是线粒体功能障碍在肌少症的发生中扮演了重要角色，这也被视为推动机体衰老的中心机制。最新研究显示，PI3K/Akt/mTOR 等信号通路异常所致肌细胞自噬增强也被视为诱发肌少症的重要因素 [61]。此外，肌少症的发生还与 PGC-1α、GH、AR 等多种肌再生调控因子失调密切相关。针对肌少症发生的分子机制，采取相应措施 ( 如运动、营养补充、抗氧化剂等 ) 对相关靶点进行干预，是未来防治肌少症相关研究的重点方向。

* * *

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