

裴泽华, 蔡轶男, 王乐兵, 等. 肌少症现状及蛋白质对其预防作用的研究进展 [J]. 食品工业科技, 2022, 43(24): 469–477. doi: 10.13386/j.issn1002-0306.2022010094

PEI Zehua, CAI Yinan, WANG Lebing, et al. Research Progress of Current Situation of Sarcopenia and the Preventive Effect of Protein on It [J]. Science and Technology of Food Industry, 2022, 43(24): 469–477. (in Chinese with English abstract). doi: 10.13386/j.issn1002-0306.2022010094

· 专题综述 ·

肌少症现状及蛋白质对其预防作用的研究进展

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摘要: 随着老龄化社会的到来, 老年人的骨骼肌体积减少, 肌力下降, 易患肌肉减少症 (Sarcopenia)。肌少症对于老年人的生活造成了许多不便, 目前对于肌少症的对症医学治疗办法并不完善, 了解其发病机制和治疗措施很有必要, 其中补充蛋白质作为最健康、有效、便捷的方法受到人们的关注。本文总结了肌少症的发病机理和目前的预防治疗办法, 阐明了蛋白质作用与肌少症的重要意义和蛋白质对于肌少症的预防治疗作用, 为蛋白质在不同途径下应用与治疗肌少症奠定了理论基础。

关键词: 蛋白质, 肌少症, 骨骼肌, 预防治疗

中图分类号: TS550.50

文献标识码: A

文章编号: 1002-0306(2022)24-0469-09

DOI: 10.13386/j.issn1002-0306.2022010094

本文网刊:



Research Progress of Current Situation of Sarcopenia and the Preventive Effect of Protein on It

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Abstract: With the advent of aging society, the skeletal muscle volume and muscle strength of the elderly are reduced, and they are prone to sarcopenia. Sarcopenia has caused a lot of inconvenience to the life of the elderly. At present, the symptomatic medical treatment for sarcopenia is not perfect. It is necessary to understand its pathogenesis and treatment measures. Protein supplementation, as the most healthy, effective and convenient method, has attracted people's attention. This paper summarizes the pathogenesis and current prevention and treatment methods of sarcopenia, the significance of protein action and sarcopenia and the role of protein in the prevention and treatment of sarcopenia are clarified. It lays a theoretical foundation for the application of protein in different ways and the treatment of sarcopenia.

Key words: protein; sarcopenia; skeletal muscle; preventive treatment

自从 20 世纪九十年代以来, 我国老龄化进程加快, 根据最新人口普查数据显示 2021 年的老年人数相对于 2020 年上升了 5.44%。随着年龄的增长, 老年人的骨骼肌质量和力量水平呈下降趋势^[1], 会导致

肌肉纤维萎缩、运动能力减弱, 以及生活自理能力下降, 这种疾病被称为肌肉减少症 (Sarcopenia)^[2]。从 30 岁开始, 人体骨骼肌肌量达到峰值, 此后骨骼肌肌量每年减少 1%~2%, 骨骼肌力量每年减少 1.5%~

收稿日期: 2022-01-14

基金项目: 黑龙江省“百千万”工程科技重大专项 (2020ZX07B01-3); 中央高校基本科研业务费专项资金资助 (2572019BA04); 哈尔滨市科技局创新研究基金项目 (2017RAQXJ091)。

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3%^[3]。由此可见肌肉减少症在老年人中患病风险极高。

患肌少症会令老年人骨骼肌强度降低,与非肌少症患者相比肌少症患者的跌倒风险更高^[4],肌肉质量下降可能导致一系列负面后果,如致使老年人的身体虚弱、残疾甚至死亡^[5],最新研究表明肌肉质量低会延长 COVID-19 患者的住院时间^[6],所以预防和治疗肌少症对于老年人的身体健康十分有必要。除大众目前所公认的运动量减少会导致肌肉质量下降之外,研究发现营养不良也会导致肌少症的发生^[7],而单独的蛋白质补充或与抵抗训练相结合被认为是抵消与年龄有关的肌肉质量和力量损失的有效方法^[8]。蛋白质是生命的物质基础,身体中每一个重要细胞和各种形式的生命活动都与蛋白质紧密相关。在生活中摄入足够多的膳食蛋白质有助于维持骨骼肌质量^[9],所以补充蛋白质是预防老年人肌肉损失的一种理想的补充方式^[10]。建议健康老年人平均每天可摄入 1.0~1.2 g/kg 的高质量蛋白质^[11]。蛋白质获取途径多且方便,肉、蛋、奶等都是丰富的蛋白质来源。对于老年肌少症患者进行有效的营养干预是不可避免的,而对于肌少症有益的营养元素大多与蛋白质相关^[12]。

社会对于肌少症认识还不够全面,关于利用摄入蛋白质来预防肌少症发生的意识不够成熟。本文通过介绍肌少症的发病机理进而对不同种类蛋白质作用于肌少症的效果及应用情况进行综述。对于将蛋白质应用于预防肌少症提供理论基础,为治疗肌少症提供一种新思路。

1 肌少症的发病机理

骨骼肌是人体运动系统的发动机,肌肉除作为身体连接、活动的基本功能器官之外,还有助于加快新陈代谢和保护骨骼等功能^[13]。当肌肉发生衰老和萎缩时标志着人体开始衰老,当肌力减退即会容易引起骨折以及关节损伤等问题。患有肌肉减少症的老年人站立困难、行走缓慢、容易跌倒受伤。即使是健康的老年人随着年龄的增长也会不可避免的出现肌少症^[14]。了解肌少症发病机理才可以更好地对不同情况引起的肌少症进行针对性治疗。

1.1 营养缺乏

老年人由于生活习惯、饮食习惯的改变可能会导致蛋白质摄入不足,再加上肌肉纤维逐渐纤维化被脂肪组织代替,导致肌少症的发病率大大增加。随着年龄的增长老年人体内的泛素-蛋白酶体系统(UPS)平衡会被打破,UPS 是调节蛋白质分解和维持蛋白质稳态的重要途径,当年龄逐渐增加,UPS 中的肌萎缩素 1(Atrogin-1)和肌环指蛋白 1(MuRF-1)表达水平显著增加,进而促进肌蛋白降解^[15]。全身骨骼肌质量取决于肌肉蛋白质合成(MPS)和肌肉蛋白质分解(MPB)的速率,统称为肌肉蛋白质周转。在健康状态下,MPS 和 MPB 与食物摄入量的关系不断变化,以维持肌肉质量。为了实现肌肉合成代谢生长,MPS

平均必需长期超过 MPB,以获得正向蛋白质平衡^[16]。当老年人摄入营养不足时会导致肌肉蛋白质分解速率超过肌肉中蛋白质合成速率^[17],从而使得肌肉质量下降。此外老年人机体易患各种炎症同时伴随食欲不振情况,因此致使其他营养物质摄入不足^[18],这种情况同样会增大肌少症的患病风险。例如维生素 D 的缺乏会引起肌少症的发生。老年人普遍存在维生素 D 缺乏现象。缺乏维生素 D 被证实与骨骼肌下降及肌肉衰减等密切相关^[19],缺乏维生素 D 更容易发生肌少症。研究发现,为期 13 周的维生素 D 和含丰富亮氨酸的乳清蛋白口服营养补充剂的补充能改善老年人肌肉质量和下肢功能^[20]。随着年龄的增长,肌肉质量的下降会增加跌倒的风险^[21],而补充维生素 D 可改善人群的肌力下降,预防跌倒,25 羟基维生素 D 血清水平缺乏和不足的老年人都应补充维生素 D,使其达到适宜的水平^[22]。

医学建议老年人在正常进食的情况下一定要注意营养管理^[23],科学的摄入营养成分预防肌少症的发生。

1.2 炎症反应与细胞自噬

炎症反应是临床常见的一个病理过程,可以生于机体各部位的组织和各器官。目前已经证实炎症因子能引起老年肌少症的发生^[24]。各种炎症标识物如白介素-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)等标识物在老年人体内显著增加,机体炎症加剧反应^[25]。炎症因子 TNF- α 和 IL-6 水平的升高会引起肌肉减少症的发生^[26]。炎症因子可加速老年人肌肉组织分解,导致肌纤维纤维化,减少肌肉量,研究发现^[27]因炎症引发疾病后患者在 50 岁后肌肉力量逐年下降、肌肉逐年减少。因此炎症因子被认为是患肌少症的一种象征^[28]。

细胞自噬是细胞自我将细胞内物质进行周转的过程,细胞内成分的合成和降解之间的平衡决定了整个肌肉纤维的质量^[29],由于神经、免疫和激素因素导致的卫星细胞活化和增殖受损,当出现细胞过度自噬或细胞自噬不足的现象会导致肌肉再生能力降低^[30]增加患肌少症风险。细胞自噬不足会诱导骨骼肌萎缩^[31],细胞过度自噬会抑制骨骼肌生长^[32]。研究发现由于细胞自噬的情况出现会导致小鼠出现明显的骨骼肌疲劳和肌无力等功能障碍^[33]。而年龄衰老会引起细胞自噬能力不足或者功能异常,使蛋白质合成出现不平衡导致骨骼肌蛋白质合成能力下降进而出现肌少症的情况。

1.3 激素变化

此外随着年龄的增长,身体内分泌激素失调,例如性激素、胰岛素和一些生长激素的分泌减少,导致肌肉质量下降。研究发现性激素分泌水平会随着年龄的增长而降低,进而影响肌肉质量。自 30 岁起,男性睾酮水平每年下降 1%,睾酮水平降低与下肢肌

肉功能有关^[34]。雌激素可能导致更年期女性的骨骼肌密度变低并逐年衰减,研究显示绝经后女性体内雌激素水平减少与肌肉减少症有相关性^[35]。糖尿病会使得胰岛素出现分泌缺陷,而同时出现的胰岛素抵抗现象会引起肌少症的发生。肌肉中储备有大量的糖原,而肌肉组织减少会减少糖原储备,导致体内过多的血糖,高于正常胰岛素水平维持血糖稳态,形成胰岛素抵抗^[36]。同时骨骼肌是胰岛素的主要靶器官之一,胰岛素抵抗会引起骨骼肌摄取以及葡萄糖利用量减少,研究发现患者肌肉减少与 2 型糖尿病有关^[37]。肌生长抑制素会在人体的骨骼肌中表达并抑制肌肉生长进而致使肌少症的出现。研究发现抑制肌肉生长抑制素可用于治疗肌肉减少症^[38]。在关于肌少症患者的临床试验的第二阶段中,抑制肌肉生长抑制素抗体在增加肌肉质量、力量和步行速度等方面显现出阳性结果^[39]。研制出抑制肌生长抑制素可成为治疗肌少症的关键因素。

2 肌少症预防及治疗方法的研究进展

肌少症全称肌肉衰减综合症早在 1991 年就被国外学者提出,但文献资料显示,目前对于肌少症的对症医学治疗办法并不完善^[40]。并且对于肌少症的预防也仍处于摸索阶段^[41]。

2.1 营养补充

有效正确的营养补充对肌肉质量有着积极的影响,是预防肌少症最有效的方法,其中补充蛋白质和多种维生素等营养素有益于肌肉组织合成^[42],对抗肌少症效果显著^[43]。国外学者强调了营养补充在增强肌肉质量和力量方面的关键作用,营养补充不仅显示出增强物理干预的积极效果,而且对作为肌肉质量和功能关键调节器的肠道微生物群产生积极影响^[44]。补充必需氨基酸对于抵抗肌肉衰减有良好效果^[45],研究发现补充亮氨酸可以对肌减少症产生一些有益影响,比如增强肌肉减少症患者的肌肉质量、力量和身体功能^[46]。例如让老年人定期摄入亮氨酸,结果显示亮氨酸的服用具有良好的耐受性,并显著改善了老年人的肌肉质量、肌力和功能,降低了肌少症的发生概率^[47]。补充亮氨酸可对肌减少症产生一些有益影响。当前中国老龄化进程加快,在更易受影响的群体中(如农村老年人和老年居民),他们对于蛋白质丰富的食物(如乳制品、大豆、坚果、鸡蛋、鱼和海鲜)摄入量较低,而对高脂肪和高钠食物(如泡菜、榨菜、香肠、罐头)摄入量较高^[48]导致蛋白质摄入不足,易患肌少症。因此正确的卫生营养宣传和有针对性的进行营养补充对预防老年人患肌少症至关重要。

2.2 运动预防

进行抗阻运动是大众所熟悉的保持肌肉弹性,防止肌肉衰退的有效途径。运动对于肌肉减少症有着积极影响^[49],可以有效增加老年人肌肉力量^[50]。运动抵抗力训练提供了有效、相对较低成本的预防肌肉减少症的方法,有益于人体整体健康^[51]。国外通

过弹力带抗阻运动对于老年肌肉减少症的对照实验显示,运动对肌肉减少性肥胖的老年妇女的肌肉质量、肌肉力量和身体功能产生了显著的有益影响^[52]。肌肉质量差与衰老性肌肉减少症的发病进展相关,运动是改善线粒体健康和减缓肌肉萎缩的理想方法^[53]。但考虑到大部分老年人行动不便,肌肉力量不足,难以完成标准有效的抗阻训练,所以强度较高的抗阻训练并不是老年人预防及治疗肌少症的最佳办法。

2.3 其他方面

胰岛素生长因子是一组重要的促生长因子。但胰岛素生长因子会随着年龄的增加而呈现负增长,研究表明胰岛素生长因子与骨骼肌质量呈正相关^[54],说明其减少可能会引起老年人患肌肉减少症。一项对比研究^[55]中通过对于两组不同受试者的数据研究得出,胰岛素治疗可以减轻 2 型糖尿病患者产生肌肉减少症风险的结论。其他激素例如睾酮也对肌肉细胞凋亡具有保护作用^[56]。睾酮不仅仅可以诱导男性肌纤维肥大和肌核增加,而且对女性肌肉纤维也有性能增强作用^[57],可以改变女性的肌肉形态,使得 II 型纤维肥大。一项综述显示联合雌激素-孕酮、脱氢表雄酮、生长激素、生长激素释放激素、联合睾酮-生长激素、胰岛素样生长因子-1、吡格列酮、睾酮和血管紧张素转换酶抑制剂等激素对于老年人肌肉质量都有一定程度的良性影响^[58]。血管紧张素转换酶与血管紧张素的信号通路可以增加肌肉摄取葡萄糖功能从而改善肌肉功能^[59]。

多不饱和脂肪酸在延缓肌肉衰减方面也有一定的作用, ω -3 多不饱和脂肪酸通过降低促炎细胞因子缓解肌肉减少症^[60]。但是对于其具体合适剂量和一些不利影响研究很少^[61],其在临床上的安全性依旧不能确定,所以并不能作为有效预防肌少症的具体措施进行实施。

综上所述,虽然肌少症的针对预防治疗方法种类繁多,但最安全有效、实用性强的办法依然是通过正确补充蛋白质及必需氨基酸的途径预防疾病发生。在自身条件允许的情况下,可以辅以抗阻运动以达到最佳效果,预防肌少症发生。

3 不同蛋白质对肌少症预防作用的研究进展

3.1 乳源蛋白

乳清蛋白含有多种活性成分,具有营养价值高、易消化吸收等特点,是公认的人体优质蛋白质补充剂之一。乳清蛋白中所含的 β -乳球蛋白有助于增强机体中枢抗疲劳能力^[62]。因此乳清蛋白对于肌肉的蛋白质补充效果远远高于其他蛋白质,效果最佳。刁福寿^[63]研究表明,乳清蛋白对于老年肥胖小鼠的各项肌肉指标均有增强效果。在补充乳清蛋白方面,每天两次食用乳清蛋白为主的营养补充剂可以增加老年男性的肌力和瘦体重^[64]。可以说乳清蛋白对于修复肌肉以及治疗肌少症的能力也是所有蛋白质中最强的。因为乳清蛋白富含亮氨酸,而亮氨酸有助于促进

肌肉恢复,是最有效的一种支链氨基酸。研究表明亮氨酸及其代谢产物 β -羟基- β -甲基丁酸盐(HMB)直接激活 mTOR 信号通路而促进蛋白质的翻译和合成,进而改善肌肉功能^[65]。一项研究通过双盲对照实验发现长期补充 HMB 可能会对老年男性产生长期益处^[66]。可以认为乳清蛋白是一种针对肌少症的理想补剂。

酪蛋白是哺乳动物包括牛、羊和人奶中的主要蛋白质。其氨基酸含量丰富,是十分优质的氨基酸供给源,但其吸收效率远低于乳清蛋白^[67],所以作为抗肌肉衰减补充剂效果并不理想。但补充消化率低的酪蛋白,虽然不能促进蛋白质的氧化和合成,但却可以抑制蛋白质的分解^[68]。通过抑制蛋白质的分解即可起到保护肌肉流失的作用。

乳源蛋白作为一类公认的高营养价值蛋白质,在抗肌肉衰减方面展现出了巨大的应用价值。

3.2 植物源蛋白

大豆蛋白是植物蛋白中营养价值最高的蛋白质,大豆蛋白中含有一般植物蛋白缺乏的两种人体必需氨基酸(Essential Amino Acids, EAA)色氨酸与赖氨酸,它们是刺激肌肉蛋白质合成的主要因素^[69]。研究证明大豆蛋白可有效增强动物的肌肉质量,提高大鼠的抗疲劳能力、抗氧化能力^[70],并且也有大量实验证明,大豆蛋白具有降低血脂、胆固醇,提高胰岛素敏感性和减肥的功效^[71]。这些功效可以从侧面表明,大豆蛋白对于肌少症的治疗起到了不同方面的积极影响。尤莉蓉^[72]通过人群试验确定大豆蛋白肽可以有效提高肌肉含量。花生蛋白是从花生中制取,具有高营养价值的一种植物蛋白,国外研究^[73]通过使用花生蛋白粉与抗阻训练联合进行人群试验,结果表明,高蛋白脱脂花生粉与抗阻训练联合使用对未经训练的老年人肌肉衰退有积极影响。核桃蛋白水解肽同样具有一定的抗氧化和免疫调节等预防肌肉衰减的功能^[74]。一些常见的植物食物如紫苏叶、豌豆等均可以在一定程度预防肌肉衰减症状的发生^[75]。植物蛋白种类繁多、容易获取,在抗肌肉衰减方面具有一定的潜在应用价值。

3.3 肉源蛋白

肉源蛋白主要来源于鱼虾、禽畜肉等。一般说来肉源蛋白质大多属于优质蛋白质,因为肉源蛋白质其中所含的必需氨基酸种类齐全,相对于植物蛋白来说在人体内吸收率更高,营养价值也相对较高^[76]。肉源蛋白与乳清蛋白相似,都含有丰富的亮氨酸,可促进蛋白合成抑制蛋白质分解^[77]。鱼类是十分优质的肉蛋白来源,研究发现食用鱼类对骨骼肌具有保护和抗炎作用,其生物活性化合物有助于保持良好的肌肉性能^[78]。在对罗非鱼鳞胶原蛋白的研究中发现其可以有效延长小鼠负重游泳时间,并影响其体内疲劳性指标提升其肌肉耐力^[79],具有一定的预防肌少症功效。蚕蛹蛋白作为一种天然全价动物蛋白具有抗氧

化和抗肌肉疲劳等保健功效^[80]。研究发现保持体育锻炼的生活方式并摄入肉蛋白食品,可以保持肌肉质量并提高运动能力,摄入这类食物较多的男性和女性的体力活动能力更强^[81]。在防止肌肉减少方面,肉源蛋白优势在于功能全面易被成人消化吸收与利用,但因其一部分高热量、高脂肪、高胆固醇的缺点^[82],如果摄入不当会使老年人产生肥胖而导致肌肉衰减症的风险^[83]。因此并不建议动物源蛋白作为预防及治疗肌少症的最佳蛋白质来源。

4 蛋白质与其他因素协同作用预防肌少症的研究

4.1 蛋白质与必需氨基酸(EAA)的联合作用

氨基酸是蛋白质营养与代谢的基本单位。支链氨基酸(BCAA)包括亮氨酸、异亮氨酸和缬氨酸,它们都是人体所需的必需氨基酸(EAA)^[84]。研究发现补充必需氨基酸可以促进蛋白质合成^[85]。亮氨酸与其他必需氨基酸相比,能更有效地防止各种肌肉消耗状况,补充服用富含亮氨酸的蛋白质可以显著改善老年人的肌肉减少症,改善肌肉质量^[86],经过亮氨酸干预后的肌肉蛋白质部分合成率显著增加,说明补充亮氨酸有助于解决与年龄相关的肌肉萎缩问题^[87]。研究发现^[88]摄取富含亮氨酸的营养来源,在一些情况下结合抗阻运动,可能是促进蛋白质合成的有效干预措施,在常规膳食中加入亮氨酸可提高老年肌肉中蛋白质合成的能力。HMB(β -羟基- β -甲基丁酸盐)是亮氨酸的下游代谢产物,饮食中摄取的亮氨酸约有 5%~10% 被转化为 HMB^[89]。研究表明 HMB 对于肌肉质量的促进有积极作用^[90]。Ryota 等^[91]的综合分析显示补充氨基酸/蛋白质对骨骼肌质量有着积极影响。一项对照实验^[92]对 120 名社区健康成人进行为期 12 周的干预,每天补充两次亮氨酸强化蛋白质补充剂,补充强化蛋白组的体重标准化 LBM(LBM/Wt)显著增加,证明补充富含亮氨酸的蛋白质可以通过预防肌肉损失而产生有益的效果。

4.2 蛋白质与运动的联合作用

运动是最有效的非药物干预措施之一,可以提高老年人的行动能力和活动独立性^[93]。mTOR(雷帕霉素靶蛋白)含量的减少减慢人体新陈代谢速率可能是造成肌肉衰退的原因之一^[94],有效的抗阻运动可以有效地增加新陈代谢速率。在非药物干预下,运动同时补充蛋白质已被证明能有效改善肌肉质量和功能^[95]。蛋白质补充结合抗阻运动比单纯进行抗阻运动在增加老年人群的骨骼肌量及肌力方面更加有效^[96]。李玲等^[97]的人群试验表明蛋白质联合抗阻运动对于患者乏力情况改善效果最佳。抵抗运动和蛋白质结合的方法可以增加小鼠血清中亮氨酸、胰岛素和葡萄糖水平^[98],从而提高肌肉质量。在对荷兰老年人群中进行为期四周的联合运动和蛋白质的补充方案对骨骼肌增长相关结果有效性的测试中显示,通过每周两次有监督的阻力和 75% 的高强度有氧运动

训练然后结合每日补充蛋白质,持续测量两周和四周后,证明运动和蛋白质协同干预可以改善老年人的肌肉衰退现象^[99]。

4.3 蛋白质与维生素 D 的联合作用

维生素 D 不足会导致老年人肌力下降增大患肌少症的风险,摄入足够的维生素 D 是预防和治疗肌少病的办法^[100]。维生素 D 可以影响蛋白质的合成和调节钙转运,进而影响肌肉力量^[101]。国外研究显示^[102]三周的维生素 D 补充对预防耐力训练跑步者的骨骼肌损伤有积极影响。一项 Meta 分析^[103]结果说明补充维生素 D(100~1600 IU/d)并同时补充蛋白质(10~44 g/d)对肌肉力量有好处。研究发现对于患肌少症人群口服补充维生素 D 和蛋白质可以有效增强老年患病者肌肉质量和身体活动能力^[104]。结果表明补充维生素 D 再加以结合蛋白质,可提高肌肉减少症患者的肌力。

5 结论与展望

肌少症作为一种在随着年龄增长而易发的身体疾病,目前已经成为社会中被逐渐重视起来的疾病,其发病可能性强,易病人群广,治疗这种疾病对提高老年人生活质量有很重要的意义。

各种疾病和营养缺乏都会导致肌少症的发生,在不同种肌少症的预防治疗方法中营养补充对于肌少症的治疗效果更加显著、安全。大量研究表明补充蛋白质是预防老年人肌肉萎缩的一个有效方法。而在不同蛋白质当中因乳清蛋白必需氨基酸含量较高,可以认为其抗肌肉衰减效果最好。为预防肌少症可以提高乳清蛋白利用率,或利用乳清蛋白为基础进行类蛋白反应使其具有更全面的功效,建议进行蛋白质补充时辅以运动对于肌少症的治疗效果将会更加显著。市面上蛋白质补充产品种类繁多,但大多针对于健身人群设计,老年人与健身人群不同,运动量较小,建议对于患肌少症老年人的蛋白质补充策略加以调整。未来,对于使用蛋白质治疗肌少症的产品应更多的在功能性上作出创新。例如增加蛋白质中必需氨基酸含量、将蛋白质与维生素相结合等综合性功能产品。在蛋白质抗肌肉衰减作用研究上侧重于预防肌少症的发生的方面,建立补充标准,针对不同时期肌少症的特点针对性进行蛋白质补充。

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