

肌肉、脂肪与不良肝脏结局的研究进展

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摘要

全球肝病发病率以及因肝病导致的死亡率上升, 是全球医疗保健的一个重大负担, 肝病已成为世界范围内的一个主要公共卫生问题。越来越多的证据表明, 肌肉质量和功能、脂肪组织含量和肌肉与脂肪质量的比率与肝脏不良结局的发生和进展密切相关。随着临床研究的进展, 大量研究证实了身体成分(特别是肌肉和脂肪含量)与肝脏疾病之间存在双向和病理生理上的复杂关系。本文系统地回顾了肌肉组织、脂肪组织和肝脏不良结局之间的关系。此外, 它还讨论了肌肉、脂肪和肝脏健康受损之间关联的病理生理机制。最后, 总结了目前该领域面临的挑战, 提出了未来肝脏疾病与肌肉、脂肪组织相互关系研究的新方向, 为肝脏相关疾病的预防和临床管理提供了新的视角。

关键词

肌肉, 脂肪, 肌肉与脂肪质量的比率, 不良肝脏结局

Research Progress on Muscle, Fat and Adverse Liver Outcomes

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Abstract

The rising global incidence of liver diseases and the increasing mortality attributable to these conditions constitute a major burden on healthcare systems worldwide. Liver disease has emerged as a critical public health problem with significant global ramifications. Accumulating evidence indicates that muscle mass and function, adipose tissue content, and the ratio of muscle-to-fat mass are closely associated with the development and progression of adverse hepatic outcomes. As clinical research advances, numerous studies have corroborated the existence of a bidirectional and path-

ophysiologically complex relationship between body composition (specifically muscle and fat content) and liver diseases. This article systematically reviews the relationships between muscle tissue, adipose tissue, and adverse hepatic outcomes. Furthermore, it discusses the pathophysiological mechanisms underlying the associations between muscle, fat, and compromised liver health. The paper concludes by summarizing the current challenges in this field, proposing novel research directions for future investigations into the interconnections between liver diseases, muscle, and adipose tissue, and offering a new perspective for the prevention and clinical management of liver-related pathologies.

Keywords

Muscle, Fat, The Ratio of Muscle-to-Fat Mass, Adverse Liver Outcomes

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1. 肝脏疾病的流行现状

肝脏疾病代表了多种疾病，其特征是肝细胞损伤、炎症细胞浸润和造血干细胞激活，这些疾病累积地损害肝功能并破坏其结构[1]。肝病的范围从非酒精性脂肪性肝病等轻度、可逆性疾病到肝硬化和肝癌等严重且危及生命的疾病。全球肝病发病率呈上升趋势，同时肝病也是全球死亡的主要原因，每年，肝病与约 200 万人死亡有关，占全球死亡率的 4% [2]。尽管全球公共卫生干预措施不断加强，但肝病仍然占全球疾病负担的很大一部分，这凸显了肝病流行病学的复杂性和多维性，肝病已成为世界范围内的一个主要公共卫生问题，给医疗保健系统和社会带来沉重负担[3] [4]。

1.1. 酒精性肝病及其流行情况

酒精相关性肝病(Alcohol related liver disease, ALD)是指由于长期过量饮酒导致的肝脏结构和功能损伤的一系列疾病。它是全球范围内肝病发病和死亡的主要原因之一。2019 年，ALD 造成全球 1100 万人寿命损失，5 年病死率超过 50%。ALD 是一种复杂的，涉及多系统的疾病，其发病率和死亡率在全球范围内持续上升，已成为危害经济发展、社会稳定及民众健康的重大公共卫生负担。大量证据表明，ALD 不仅仅由过量饮酒造成，其发病机制还涉及消化及免疫等多个器官系统[5] [6]，遗传因素表观遗传修饰[7] [8]等机制的相互作用。ALD 的分子机制尚不完全清楚，这导致 ALD 治疗的有效性受到限制。在疾病早期，大多数患者缺乏特异性症状，这使得疾病的早期识别极为困难。因此，识别导致该疾病的新风险因素可能有助于识别高危人群并制定预防或治疗策略。

1.2. 非酒精性脂肪性肝病及其流行情况

非酒精性脂肪性肝病(Non-alcoholic Fatty Liver Disease, NAFLD)是一种非传染性疾病，其特征是在没有其他病因(如肝炎(病毒性和自身免疫性)、药物、药物和过量饮酒)的情况下肝脏中脂肪堆积过多[9] [10]。疾病谱包括非酒精性单纯性肝脂肪变(Non-alcoholic Fatty Liver, NAFL)、非酒精性脂肪性肝炎(Non-alcoholic Steatohepatitis, NASH)，严重者可能发展为 NASH 相关肝硬化和肝癌。NAFLD 已被公认为最常见的慢性肝病形式之一。在全球范围内，每 4 名成年人中就有 1 名被诊断出患有 NAFLD (25.2%) [9]。根据最近的一项系统评价和荟萃分析，全球非酒精性脂肪肝患病率从 1990~2006 年的 25.3% 上升到 2016~2019 年的 38.0% [11]。与此同时，非酒精性脂肪性肝炎(NASH)是 NAFLD 的一种更活跃的形式，其特征是存

在肝脂肪变性、炎症和肝细胞气球膨胀,正在成为肝硬化、肝硬化并发症、肝细胞癌(HCC)和肝脏相关死亡的主要原因之一[12]。过去几年,NAFLD的患病率迅速上升,这与过去几年呈指数级增长的其他慢性疾病(如2型糖尿病、肥胖症和高血压)密切相关[13]。此外,年轻人群肥胖患病率的增加表明,许多患者从更早的时间点患NAFLD,从而具有更长的病程。因此,更多的人可能会发展为进行性纤维化,最终导致肝硬化,而不会首先死于心血管疾病等竞争性原因。生命早期肥胖而导致的NAFLD,是晚年进展为肝硬化和肝癌的独立危险因素[14]-[17]。NAFLD与健康相关生活质量下降、工作效率下降、疲劳、医疗资源利用率增加和巨大的经济负担都有关联,鉴于NAFLD是肝脏健康早期损害的标志,早期识别NAFLD可改变风险因素并加以干预,对防止、延缓NAFLD进展为更为严重的肝脏疾病具有重要公共卫生意义。

1.3. 肝纤维化和肝硬化及其流行现状

肝纤维化和肝硬化是慢性肝病的终末期后果,源于慢性炎症导致肝实质中纤维组织(主要是胶原蛋白)积聚,作为对肝损伤的反应[18][19]。肝硬化是一种不可逆转的疾病,由于门静脉高压症、食管静脉曲张、腹水、肝性脑病和肝细胞癌风险增加等并发症,发病率和死亡率很高[20][21]。一项荟萃研究显示在全球范围内,晚期肝纤维化和肝硬化在一般人群中的合并患病率分别为3.3%和1.3%。2016年后,晚期纤维化和肝硬化的患病率呈上升趋势[22]。一项中国的横断面研究显示在5,757,335名受试者中,晚期纤维化和肝硬化的患病率分别为2.85%和0.87%[23]。肝纤维化和肝硬化导致肝脏相关死亡,肝硬化是慢性肝病患者死亡的重要原因之一,2019年,肝硬化死亡人数约为150万人,占全球死亡人数的2.6%[24],这凸显了了解其流行病学和相关危险因素的必要性。鉴于病因多样且进展缓慢,早期发现和干预对于减轻不可逆转的损害和改善患者的预后至关重要[4][25]-[27]。

1.4. 肝癌及其流行现状

肝癌是肝病的终末结局,肝癌是全球第6位较常见的恶性肿瘤,也是导致人类死亡的第3位恶性肿瘤死因。据WHO国际癌症研究中心估计,2022年全球新发肝癌病例约87万例,死亡病例约76万例[28]。在肝癌发病中,肝细胞癌(HCC)是肝癌最常见的类型,约占全部肝癌发病的80%;肝内胆管细胞癌(ICC)次之,约占全部发病的15%;其他罕见类型的肝癌约占5%[29]。在过去的几十年里,随着人类社会经济的发展和肝癌防控的进展,肝癌的发病率和死亡率在传统意义的高发国家呈下降趋势,如中国和日本;但随着肥胖和代谢性疾病的增加,肝癌在以往低发国家如美国、澳大利亚和多数欧洲国家等的疾病负担却呈升高趋势。肝癌是一种与多种因素密切相关的多因素疾病。尽管过去十年在肝细胞癌治疗方面取得了重大进展,但其总体预后仍然很差,5年生存率为<20%。作为全球常见且致死性较强的恶性肿瘤之一,肝癌过去几十年在预防、筛查和治疗方面取得了进展,传统高发国家的发病率和死亡率有所下降。但随着很多国家和地区的超重、肥胖和糖尿病患病率的增加,全球肝癌疾病负担的下降趋势有可能被减缓甚至逆转。因此,肝癌在未来很长一段时间内仍是需要全球重点关注的公共卫生问题之一,了解肝癌的危险因素、识别高危人群和早期预防对于肝癌的防控仍然十分重要。

2. 肌肉、脂肪与不良肝脏结局之间关联的研究进展

2.1. 肌肉质量和功能与不良肝脏结局的研究进展

肌肉是运动的“发动机”。强壮的肌肉以及其所带来的力量自然也是人类生存以及健康最基本的保障,骨骼肌是一种组织,占健康人总体重的30%~40%,含有高达75%的全身蛋白质。因此,它是非肥胖受试者中最大的器官。肌肉蛋白对全身代谢起积极作用。对许多身体器官(如脑、心脏和肝脏)而言,保障其蛋白质的稳定性是人赖以生存的最基本的条件。当营养缺乏时,肌肉蛋白可以转换为血氨基酸保证其

他重要器官的稳定性。骨骼肌作为人体的重要组成成分,可一定程度反映机体的营养健康状况[30]。当个体处于慢性疾病状态时,其机体炎症因子分泌增加、氧化应激损伤加剧、线粒体功能异常,这些因素共同作用可能导致肌肉结构和功能减退[31]。肌肉重量(skeletal muscle mass, SMM)和肌肉力量(skeletal muscle strength, SMS)常用于反映骨骼肌的结构功能。SMM 和 SMS 低下可以导致多种疾病预后不良,如慢性肝病、糖尿病、心血管疾病、癌症等[32] [33],甚至增加死亡风险[34]。二者形成恶性循环,进一步加重健康负担。过去几年,人们越来越意识到骨骼肌的质量和在各种慢性疾病预后评价中的作用。大量证据将慢性肝病(CLD)的严重程度、并发症和死亡率与骨骼肌耗竭联系起来。一些横断面研究强调,低肌肉质量、身体机能或肌肉脂肪浸润增加与肝病严重程度和生存率低之间存在联系[35]-[39]。前瞻性的研究也表明较低的肌肉质量和握力与患严重 NAFLD 的风险较高相关[40],不良肌肉成分与 NAFLD 的不良功能表现和代谢合并症有关,是 NAFLD 患者全因死亡率的有力预测因子[41] [42],测量肌肉健康状况(患者的肌肉体积和肌肉中的脂肪量)可以帮助识别更脆弱的患者,并能够及早预防严重肝病。目前大部分研究聚焦在肌肉质量和 NAFLD 的关联上,较少研究肌肉质量对后续严重肝病(比如肝硬化、肝衰竭以及肝癌等)的影响,并且有关肌肉功能对肝脏疾病研究也较少,仅有部分研究探索了握力与肝脏疾病的关联,肌肉和肝脏疾病关联的病理生理学机制还需要进一步探讨。

2.2. 脂肪含量与肝脏疾病之间的研究进展

导致不良肝脏结局的病因多种多样。脂肪组织与健康之间有着复杂而微妙的关系,有流行病学研究表明,过多的脂肪量与较高的代谢性疾病发病率密切相关[43]。脂肪组织和肝脏是全身能量代谢的核心组织,目前,多项研究将不良肝脏结局与脂肪堆积联系起来[44]-[46]。肥胖流行与 NAFLD 的患病率和严重程度密切相关[47]-[49],肥胖的存在会使肝酶升高的风险增加两到三倍,超声检查脂肪变性的风险在肥胖的情况下约为 15 倍,肝硬化和肝细胞癌也与普通人群的肥胖有关,观察到的 NAFLD 患者中,肥胖与晚期纤维化和纤维化进展系统相关[50]。缺乏运动和暴饮暴食会增加脂肪量,尤其是内脏脂肪组织(VAT)的含量。VAT 积累会诱导胰岛素抵抗并加剧肝损伤[51]。有一项日本横断面研究表明,肝纤维化与脂肪量、脂肪量/身高平方、内脏脂肪面积、腰臀比呈显著正相关[52]。还有一项美国的横断面调查显示,脂肪量指数与肝脂肪变性和纤维化成正相关[53]。目前大多数研究都聚焦在 BMI、腰围等传统描述身体肥胖的指标和肝脏疾病的关联上,有关于各部位身体脂肪含量与肝脏疾病关联的研究较少,仅有部分研究关注内脏脂肪含量与肝脏疾病之间的关联。未来需要进一步探讨身体各部位脂肪含量对肝脏健康以及肝脏不良结局的影响。

2.3. 肌肉含量与脂肪含量的比值与肝脏疾病的研究进展

BMI 和四肢骨骼肌质量(ASM)等指标在肥胖和肌少症的诊断中被广泛应用,但它们忽略了肌肉与脂肪之间的平衡,例如, BMI 无法区分体重的减轻是源于肌肉质量减少还是脂肪量的减少,且相同 BMI 个体的体成分可能存在显著差异,这突出了寻找替代指标的必要性。腰围、腰臀比、脂肪质量等虽用于评估中心性肥胖,却无法区分皮下与内脏脂肪,且易受肌肉量影响产生误导。因此,肌脂比作为一种新兴的生物标志物应运而生。它直接反映肌肉与脂肪在总体重中比例,能精准揭示肌肉减少与脂肪增多状况,尤其适用于揭示老年人群及慢性病患者体内肌肉与脂肪的不平衡状态。肌肉质量减少时体重可能仍保持正常甚至增加,因此肌脂比异常可能早于传统指标揭示疾病状态。其在精准评估健康风险及潜在疾病预防与健康管理价值方面的优势,使其成为未来研究与临床实践的重要关注点。身体分为脂肪、骨骼和软组织三个组成部分,这些组成部分之间的不平衡会导致生活方式相关疾病和慢性疾病相关症状,如肥胖、糖尿病、高血脂、骨质疏松、水肿、营养不良、身体功能障碍和跌倒等[54]。来自中国的回顾性横断

面研究也发现无脂肪质量(FFM)与脂肪量(FM)比值(FFM/FM)和四肢骨骼肌质量指数(ASMI)水平与 NAFLD 患病率呈负相关(OR: 0.553 和 0.850), FFM/FM 与肝损伤指标呈负相关, 包括与丙氨酸转氨酶呈负相关($\text{Beta} \pm \text{SE}: -1.00 \pm 0.17, p < 0.001$) [55]。在一项美国横断面调查(NHANES)中也发现骨骼肌质量与内脏脂肪面积比与 NAFLD 之间存在显著关联[56]。在一项中国的前瞻性队列研究表明在中老年人群中, 全身的脂肪和肌肉的比值与 NAFLD 和 NAFLD 相关肝纤维化风险呈正相关, 肌肉质量和握力与 NAFLD 呈负相关, 但与 NAFLD 相关肝纤维化无关[57]。目前仍缺乏相关大型前瞻性研究来阐明肌肉脂肪比值对不良肝脏结局的影响。

3. 肌肉、脂肪和不良肝脏结局关联的生物学机制

3.1. 肌肉与不良肝脏结局关联的生物学机制

肌肉减少和不良肝脏结局之间的关联是复杂且多因素的, 涉及共同的病理生理机制, 包括胰岛素抵抗、炎症、细胞因子失衡、代谢失调、维生素 D 缺乏以及肠道微生态失衡等, 引起机体肌肉-肝脏轴的细胞和分子协调机制受损并形成恶性循环, 从而影响肝脏疾病的发生和进展。

胰岛素抵抗(insulin resistance, IR)是肌肉减少症和肝脏疾病的主要病理生理机制。IR 由骨骼肌质量损失引起, 降低机体组织正常摄取和利用葡萄糖的能力, 胰岛素敏感性下降[58]。IR 不仅导致肝脏脂肪生成的增加, 而且还抑制了脂肪的分解, 从而加重肝脏内脂肪酸的堆积[59]。IR 可引起代偿性高胰岛素血症, 促进糖异生、上调固醇调节元件结合蛋白 1c、抑制 β -氧化、增加 FFA 输送和改变甘油三酯转运, 从而加重甘油三酯在骨骼肌和肝脏中的累积, 导致肝脏脂肪变性。另一方面, IR 可减少蛋白质合成、促进分解代谢[60]以及肌因子的变化来加剧肌肉损失[61] [62]。在 NAFLD 患者中, 经常观察到肌肉胰岛素抵抗, 这可能先于肝胰岛素抵抗, 这表明肌肉功能障碍加重肝脏病变的顺序关系[63] [64]。此外, NAFLD 中还经常观察到促炎细胞因子水平升高, 如白细胞介素-6 (IL-6)和肿瘤坏死因子- α (TNF- α), 会促进肌肉退化[65] [66]。这种炎症环境可能导致肌肉减少症恶性循环, 使肝功能恶化, 进一步增强胰岛素抵抗和炎症[67]。维生素 D 缺乏也与肌肉减少和肝脏疾病之间的关联有关, 维生素 D 是一种参与钙稳态、骨代谢和肌肉生长的激素, 维生素 D 受体可在包括肝脏和骨骼肌在内的维生素 D 水平低在肝脏疾病患者中很常见, 并且与肌肉质量加速损失有关[68]。肠道微生态失衡促进慢性炎症和 IR, 至少部分是通过调节骨骼肌的组成和功能而实现的, 但至今没有直接证据表明人类肠道菌群组成与肌肉减少症有关[69]。肌肉对肝脏不良结局发生风险的作用可能涉及其他潜在机制, 仍需进一步探索。

3.2. 脂肪与不良肝脏结局关联的生物学机制

肝脏中脂质过度沉积会引起一系列肝脏病理学, 包括脂肪性肝炎、纤维化/肝硬化和肝细胞癌等不良肝脏结局。当脂肪在肝脏中积聚时, 它会引发肝细胞损伤并随后激活炎症反应。这种炎症涉及免疫细胞浸润肝脏。如果不加以解决, 持续的炎症会导致进一步的肝损伤、纤维化, 并最终发展为肝硬化和肝细胞癌等更严重的疾病, 从而导致全因死亡率和肝脏相关死亡率升高[70]-[72]。大量证据表明, 肝脏脂质代谢的改变是主要驱动力(14)。脂质代谢紊乱是 NAFLD 的基本标志, 推动了该疾病的进展。NAFLD 是由肝细胞中脂质的异常积累发展而来的, 肝细胞是肝脏中的一种实质细胞。超过 5%的肝细胞中脂质[70]。细胞内脂质的异常升高会引发线粒体功能障碍并加剧氧化应激, 通常伴随着从头脂肪生成(DNL)增加和脂肪酸氧化减少。肝细胞长期暴露于高水平的脂质过氧化和氧化应激, 最终导致脂毒性细胞死亡。另一方面, 受损肝细胞释放危险信号后, 组织中的巨噬细胞和浸润性炎症细胞被激活, 导致促炎细胞因子的分泌, 进一步加剧肝细胞的损伤和死亡, 导致脂肪性肝炎[70]。由于肝脏脂质代谢在身体整体能量平衡中起着重要作用, 肝脏利用各种分子机制, 如脂肪酸的摄取、运输、输出、DNL 和脂肪酸(FA)氧化, 来调

节 FA 代谢。改变这些途径的平衡会导致肝脏中脂质的积累，导致细胞器功能障碍、细胞损伤、细胞凋亡、炎症和纤维化途径的持续激活，所有这些都会加剧肝功能损伤并促进肝脏疾病的进展[70] [73] [74]。

4. 肌肉脂肪指标的评估对临床实践的指导意义

4.1. 临床上测量身体成分的常用方法及其优缺点比较

肌肉质量和脂肪质量的测量主要有以下几种方法：双能 X 线吸收测定法(DXA)、生物电阻抗分析(BIA)、磁共振成像(MRI)、计算机断层扫描(CT)。通常，MRI 和 CT 因为其测量的精确性被认为是金标准，但由于成本高、缺乏便携性和需要专业的影像学医务人员等原因，在初级临床实践中并不普遍使用。而 DXA 和 BIA 是更为普遍和实用的测量技术，特别是 BIA 相对便宜，便携，易于使用，是 CT 的有效替代物[75]。近几年，有研究使用超声来估计肌肉量，为肌肉质量估计提供了新的更易解决方案。几种肌脂比测量方法的特点见表 1。

Table 1. Summary of the characteristics of several muscle fat ratio measurement methods
表 1. 几种肌脂比测量方法的特点总结

项目	DXA	BIA	MRI	CT
定义	采用两种不同能量 X 射线来测肌肉质量及脂肪含量	利用电流通过人体时的电阻抗变化来估计身体组成	利用强磁场和无线电波形成身体内部结构图像	利用 X 射线束围绕身体旋转并生成连续的横断面图像来观察内部结构
适用范围	适用于全面的身体成分分析，尤其适用于骨质疏松和肌肉减少症评估	便捷、快速的初步筛查工具	在医学研究和特定临床条件下的精细分析	不主要用于肌肉脂肪比的测量，但在某些特定研究中可间接评估
精确度	高	中等至高	非常高	非常高
安全性	较低剂量的辐射	安全无辐射	安全无辐射	辐射剂量高于 MRI，但低于多次常规 X 线检查
便利性	需要专门设备，操作较耗时	便携式设备较多，操作快捷，可在短时间内完成	设备昂贵，操作复杂且耗时较长	操作迅速，尤其在急诊场景下可快速诊断
成本	较高	中等	非常高	较高
是否量化肌肉脂肪比	是	是，准确性相对 DXA 略低	可以精确测量肌肉与脂肪分布	可以间接评估
优点	准确可靠，可测量多个身体成分	无创、便捷	无辐射，软组织分辨率极高	成像速度快，对骨性结构敏感
缺点	辐射暴露、设备昂贵	结果受身体水分状态、食物摄入等因素影响	检查时间长、费用高昂	辐射暴露，不适合频繁重复检查

注：DXA：双能 X 线吸收测定法，BIA：生物电阻抗分析，MRI：磁共振成像，CT：计算机断层扫描。

4.2. 改善身体成分来干预肝病的临床研究证据

目前改变饮食、生活方式及运动干预仍是代谢相关脂肪性肝脏疾病的一线治疗方法，其能减少肝脏脂肪含量，减轻肝脏炎症和纤维化，改善胰岛素抵抗，提高患者的生活质量。研究表明减重 ≥ 10%几乎可逆转 MASH，或使肝纤维化程度降低至少一个等级[76]。通过人体成分分析可全面评估人体水分含量、肌肉容积和脂肪储备的分布等，指导调整膳食摄入和制订运动干预方案来进行科学的体质量管理，避免

大幅度减重导致脂肪代谢紊乱,进而加重肝损伤。有研究根据患者人体成分和饮食习惯等制定合理的食谱,控制能量摄入,结果显示,与治疗前比较,观察组体质量、BMI、体脂百分比、骨骼肌百分比、腰臀比、基础代谢率等指标均改善。

4.3. 将身体成分指标纳入现有肝病风险分层和预后评估模型的可行性

基于计算机断层扫描(CT)的身体成分测量可以为慢性病患者提供预后价值,并在心血管疾病和肝脏疾病方面显示出预测能力[77][78]。身体成分可以通过影像学检查,依据多种因素进行量化,如脂肪组织、肌肉质量和器官体积等[79][80]。无论采用何种影像学检查方式,先前的研究都表明,一些身体成分测量指标可以预测肝移植受者的生存率,其中肌肉相关指标的测量尤其具有价值[81]-[84]。有一项研究报告了基于完全自动化 CT 的身体成分指标和临床衰弱数据在预测肝移植受者术后预后方面的潜力[85]。然而,关于肌肉密度(肌肉脂肪变性)和肌肉面积的影响,有研究报告了相互矛盾的结果[83][86]。回顾性研究还发现,基于脂肪的测量指标,如内脏脂肪组织(VAT)和皮下脂肪组织(SAT)面积,对死亡率和移植术衰竭具有预测价值[86][87]。未来,还需要进一步探索有关肌肉和脂肪的身体测量指标在肝脏疾病分层和预后模型中的应用。

5. 总结与展望

5.1. 总结

肌肉质量低、肌肉功能低,脂肪质量高以及肌肉脂肪比值低与不良肝脏结局的发生风险增加相关,并且潜在机制具有生物学合理性,但仍存在诸多待深入探索的领域。现有资料表明,肌肉和脂肪可能通过多重生物学机制影响肝脏健康,如肌肉通过胰岛素抵抗、炎症、代谢失调等机制导致肝功能恶化,肝脏中脂肪的蓄积则会导致脂质代谢紊乱,从而导致细胞器功能障碍、细胞损伤、细胞凋亡、炎症和纤维化途径的持续激活损伤肝脏健康。

然而,现有研究结果仍存在局限性。尽管横断面与观察性研究普遍支持肌肉质量功能低、脂肪质量高对肝脏健康的损害作用,但是目前缺乏大型的前瞻性研究来验证此关系,并且大部分研究聚焦在对肌肉、脂肪含量对 NAFLD 发生风险的影响上,较少的研究探索了与更严重的肝脏不良结局的关联,比如肝纤维化、肝硬化、肝癌等。此外,鉴于肌肉和脂肪分布的可变性,目前缺乏对于不同身体部位肌肉和脂肪含量与不良肝脏结局之间关联的研究,检查手臂、腿部和躯干等区域的肌肉和脂肪含量与不良肝脏结局之间的关系可以提高我们对区域身体成分临床意义的理解。

5.2. 未来发展方向

目前肌肉、脂肪与肝脏疾病关联的研究多为横断面及队列研究等观察性研究,未来研究应侧重于大规模前瞻性队列研究,以明确肌肉、脂肪以及肌肉脂肪比值与多种肝脏疾病间的因果关联,提升其在疾病预测与进展监控中的效能。研究应致力于确立不同人群的肌肉、脂肪以及肌肉脂肪比值正常范围和异常标准,以便更准确地识别高风险个体。后续还需要精密设计的自然试验或社区干预实验研究,更加精确地评估肌肉、脂肪与不良肝脏结局发生以及后续相关疾病进展关联,并结合成本效益分析为政策制定提供依据。

未来还应探索肌肉脂肪比值与其他生物标志物的相互作用,如血液生化指标、基因表达和肠道菌群,以构建一个多维生物标志物网络。这将有助于全面评估肌肉、脂肪与肝脏健康的关联,并指导个性化的诊疗方案。目标是将这些研究成果转化为实用的临床决策工具,以改善患者的治疗效果和生活质量。

综上,肌肉、脂肪与不良肝脏结局的关联研究为肝脏相关疾病的防治提供了新视角,但其转化应用

仍需克服方法论与实施层面的多重障碍。未来需强化跨学科合作,整合不同领域的知识和资源,推动从“相关性”到“因果性”的研究发展。未来需结合纵向追踪、多维度身体成分指标与肝脏疾病的关联,以明确主导机制并优化干预策略。

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