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评 述

生活习惯对非酒精性脂肪肝病的影响

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摘要 近年来, 社会经济蓬勃发展, 人们的生活方式也相应发生了一些改变. 经过科学研究和医学实践证实, 人们在饮食结构、身体活动、睡眠模式以及心理状态等各方面的改变, 均会对个体的身体健康产生深远影响. 这些改变, 尤其是不良的身体活动方式和饮食习惯, 已经逐渐威胁到人们的身体健康. 非酒精性脂肪肝病, 作为一种慢性肝病, 其发病率正逐年上升, 与这些不健康的生活方式密切相关. 久坐不动、膳食中脂质和胆固醇含量过高等均与非酒精性脂肪肝病的发病率呈现出高度的相关性. 值得注意的是, 迄今为止, 在美国和欧盟尚无药物获批用于治疗该病. 因此, 我们更需要关注非药物治疗策略, 特别是通过改变不良的身体活动方式和饮食模式来预防和缓解这一疾病. 为此, 本文将深入讨论不同饮食模式和身体活动方式对肝脏物质代谢的影响, 阐明其分子机制, 以期为非酒精性脂肪肝病提供切实有效的非药物治疗策略.

关键词 非酒精性脂肪肝病, 有氧运动, 抗阻训练, 高强度间歇性训练, 地中海饮食, 生酮饮食, 间歇性能量限制饮食

肝脏是人体内脏最大的器官, 在维持脂质代谢中起着关键作用. 肝脏中的脂质代谢包括胆固醇代谢、脂肪酸氧化、脂蛋白代谢和甘油三酯代谢. 其中肝脏脂肪代谢紊乱可使脂肪堆积于肝脏内形成脂肪肝, 导致非酒精性脂肪肝病(non-alcohol fatty liver disease, NAFLD)和肥胖症的发生[1]. 非酒精性脂肪肝病已经成为欧美最流行的慢性肝病, 其患病速率正快速地向全球蔓延[2]. 非酒精性脂肪肝病并不是一种单一的疾病, 而是一系列疾病, 其范围包括从单一的肝脏脂肪变性到伴有不同程度的纤维化和肝硬化[3]. 2023年, 专家建议将NAFLD更名为代谢功能障碍相关脂肪性肝病(metabolic dysfunction associated steatotic liver disease, MASLD), 并进一步赋予MASLD诊断标准全新而详尽的定义. MASLD的新定义强调了体重超标、胰岛素抵抗、血脂异常、2型糖尿病和代谢性炎症等在脂肪性肝病发病过程中的重要作用以及干预这些代谢心血管危险因素防治肝病及其合并症的重要性(图1). 非酒精性脂肪肝炎(Nonalcoholic Steatohepatitis, NASH)是NAFLD的进展阶段[4], 除了肝中有脂肪堆积外, 常伴有肝脏肿胀或发炎以及肝细胞受损等症状, 炎症和肝细胞受损往往导致肝纤维化或瘢痕生成[5,6]. 鉴于目前尚无治疗非酒精性脂肪肝的有效药物, 人们越来越关注生活方式干预对NAFLD的治疗效果[7].

许多研究发现健康的生活方式因素(包括正常体重指数、戒烟、坚持地中海饮食和充足的睡眠时间等)均与降低肝细胞癌风险相关; 而不健康的生活方式

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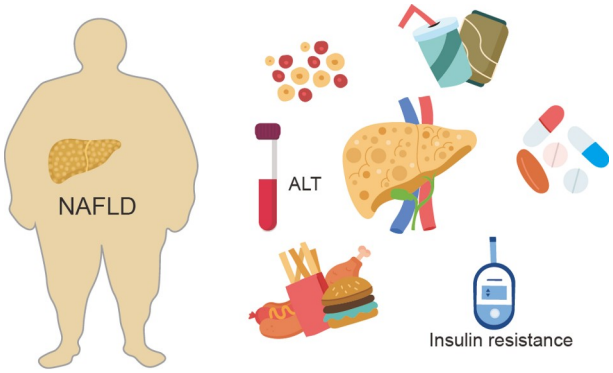

图 1 (网络版彩图)非酒精性脂肪肝病的致病因素. 超重和肥胖症、胰岛素抵抗以及血糖含量过高均会导致甘油三酯在肝脏中蓄积, 从而引发非酒精性脂肪肝病的发生. 持续的丙氨酸氨基转移酶含量的升高常与疾病的进展风险增加有关

Figure 1 (color online) Pathogenic factors of NAFLD. Overweight and obesity, insulin resistance, and high blood glucose levels all contribute to the accumulation of triglycerides in the liver, which triggers the development of NAFLD. Persistent elevated levels of alanine aminotransferase are often associated with an increased risk of disease progression

(如大量摄入精制碳水化合物、饱和脂肪酸和添加果糖的饮料以及缺乏体育锻炼), 会诱发和促进非酒精性脂肪肝发展为非酒精性脂肪性肝炎、肝纤维化和肝细胞癌[8~11]. 在众多针对NAFLD的干预措施中, 饮食调控和运动锻炼饱受期待[12], 其不仅是NAFLD发病机理中的关键因素, 且干预的效果较为直观和可视化, 并易于在实践过程中推广实施. 运动对非酒精性脂肪肝患者的益处机制仍不明确, 但运用代谢组学的方法分析不同类型的患者脂肪组织、血浆、尿液和粪便样本能够帮助确定运动干预(不改变饮食)后与人类NAFLD相关的代谢变化[13]. 而膳食结构的改变不仅涉及调整个别营养元素, 还要改变整体的营养成分和比例[14]. 本文旨在总结NAFLD在饮食和运动方面的最新科学发现, 期冀在未来为防治NAFLD提供可参考的建议.

1 运动方式对非酒精性脂肪肝病的影响

运动过程中, 身体需要燃烧卡路里以提供能量, 从而消耗能量. 当消耗的热量超过摄入的热量时, 就会发生减重[15]. 坚持运动可以提高身体的代谢率, 使得机体即使在安静状态下也会消耗更多的卡路里[16]. 力量训练能够增加肌肉量, 而肌肉组织往往比脂肪组织更易消耗能量[17]. 减重可以有效改善代谢状态, 减少脂肪在肝脏中的积累, 从而降低非酒精性脂肪肝病的患病风险[18]. 常见的影响肝脏脂质代谢的运动方式有以下几种:

1.1 有氧运动

20世纪80年代, 美国的内科医生库泊博士经多年的探索, 率先提出闻名世界的有氧运动的概念. 所谓的有氧运动, 就是以糖和脂肪的有氧代谢提供能量的运动. 常见的有氧运动项目有步行、慢跑、游泳、骑自行车、跳健身操等. 有氧运动的特点是强度低、有节奏、不中断和持续、时间长. 有氧运动对不同年龄段人群的多个组织和器官系统均能产生正向影响, 其中, 脑组织是受体育活动和锻炼影响最为显著的组织和器官[19]. 在神经退行性疾病中, 运动训练通过参与行为、感觉和认知模式, 驱动和增强神经可塑性, 帮助受损的大脑进行技能再学习[20]. 在多种神经退行性变模型中, 有氧运动能够提高神经元存活率, 促进突触可塑性、神经发生、血管生成和自噬等许多过程, 并减缓疾病发生进程[21].

除了上述发现, 越来越多的研究证明有氧运动与改善代谢性脂肪肝病的发生密切相关. Chun-Sheng Hsu等人[22]通过获得2008年至2016年间招募的7532名参与者的数据, 经过多元逻辑分析比较发现有氧运动对于代谢综合征有保护作用. 此外, Yasser Nassef等人[23]采用方差分析法证明了对于成年人, 有氧运动和羽毛球通常与较高的高密度脂蛋白胆固醇水平有关. 同时, Ryuki Hashida等人[24]对24个有氧运动方案进行总结, 分析代谢当量, 发现有氧运动能减轻非酒精性脂肪肝患者的肝脏脂肪变性. 在一项关于有氧运动改善非酒精性脂肪肝的机制研究中, Junhan Li等人[25]发现, CNPY2-PERK通路参与了非酒精性脂肪肝的形成, 而有氧运动能通过下调CNPY2-PERK通路的蛋白表达改善非酒精性脂肪肝.

关于运动降血脂的机制, 目前研究认为机体进行有氧运动训练时, 骨骼肌以游离脂肪酸氧化作为主要能量来源[26]. 随着游离脂肪酸的大量利用, 很大程度减少了脂肪在肝脏中的积累, 进一步预防脂肪肝的发生. 另外, 运动也增加了脂蛋白脂酶(lipoprotein lipase, LPL)活性. LPL是甘油三酯(triglyceride, TG)水解的关键酶, 其活性升高可以有效地降低血浆中的TG水平[27]

(图2). LPL活性的增加能使运动中和运动后体内脂肪的分解增加. 同时运动过程中脂蛋白合成和分泌的增加使得其与低密度脂蛋白(low density lipoprotein, LDL)更好地结合, 促进TG的表面成分向LDL转移[28], 这种转移的过程有利于脂肪的运输和代谢, 维持身体的能量平衡和健康. 运动也会使肝脏低密度脂蛋白受体(low-density lipoprotein receptor, LDLR)的基因表达量增多[29], 随着LDLR蛋白含量的增加, 促进LDL体内的自清除. 此外, 2023年上海体育大学运动健康学院郭亮教授研究团队发现, 有氧运动(8周跑台锻炼)能促进肝脏1型半胱氨酸双加氧酶(cysteine dioxygenase 1, Cdo1)的基因和蛋白表达, 且伴随着小鼠肝脏环磷酸腺苷(cyclic adenosine monophosphate, cAMP)水平的升高和环磷腺苷效应元件结合蛋白(cAMP-response element binding protein, CREB)磷酸化的激活[30](图2). Cdo1能够将半胱氨酸氧化为半胱氨酸亚磺酸, 后者又进一步代谢为牛磺酸或硫酸盐[31]. 小鼠脂肪细胞特异性敲除Cdo1会抑制脂肪组织脂解基因的表达, 削弱小鼠能量消耗和寒冷耐受能力, 加剧高脂饮食诱导的肥胖、糖耐量受损和胰岛素抵抗[32]. 肝细胞Cdo1作为运动的潜在下游效应分子, 通过Cdo1-Camkk2-AMPK轴抑制肝细胞脂肪变性, 为运动干预脂肪肝进展、精准运动防治脂肪肝提供理论依据和新的分子靶点.

1.2　抗阻训练

美国运动医学学会(American College of Sports Medicine, ACSM) 2021年在《运动指南: 抗阻训练》(Exercise Guide: Resistance Training)发布了关于抗阻训练的描述. 该指南指出, 抗阻运动可以增加肌肉力量, 改变身体构成, 提高代谢率, 并有助于改善和维护关节稳定性. 这些益处可以帮助人们保持健康, 预防和管理许多慢性病.

抗阻运动通常涉及使用自身重量或外部设备(如哑铃、杠铃等健身器械)进行力量训练, 提升肌肉质量. 成年人的肌肉质量往往随着年龄的增长而下降. 30岁以后, 肌肉质量每10年下降大约3%~8%[33], 平均每年体重减轻约0.2 kg[34]. 50岁以后, 肌肉质量损失增加至每10年大约5%~10%[35], 此后每年减重大约0.4 kg[36]. 骨骼肌占身体总体重的40%, 主要影响包括肥胖、血脂异常、2型糖尿病和心血管疾病在内的多种代谢相关型疾病[37]. 肌肉组织是葡萄糖和甘油三酯代谢的主要场所, 因此, 肌肉损失增加了和脂质代谢异常相关健康问题的患病风险[33,37,38]. 许多研究表明, 定期进行常规抗阻训练(如每周进行2~3次的抗阻训练, 总持续时间10~26周不等)可以增加不同年龄段成年人的肌肉质量[39~44](图2). 大约进行3个月的抗阻训练后, 肌肉重量增加1.35 kg, 脂肪重量减少1.7 kg, 并在任何年龄组之间肌肉发育状况无明显差异[44].

进行抗阻训练时, 肌肉接收到刺激或指令, 从静息态变为收缩态, 可能增加成年人的能量消耗和脂质氧化率[42], 减少脂肪在肝脏内的堆积, 从而预防非酒精性脂肪肝的发生. 事实上, 抗阻训练通过增加收缩蛋白含量, 提高肌肉的蛋白质周转速率[45], 对于静息代谢率起着双重作用. 一方面, 作为一种慢性反应, 抗阻训练往往导致肌肉质量的提升, 因此在静息状态下往往需要更多的能量进行组织维护. 有研究支持, 训练后肌肉质量每增加1 kg, 静息态代谢速率会提升21 kcal[37]. 另一方面, 作为一种急性反应, 抗阻训练可能会导致组织微损伤[46], 这需要相对较多的能量用于肌肉重塑过程, 该过程大约持续72 h[47]. 更值得惊喜的是, 研究人员通过对8名受试者按照ACSM关于静息能量消耗的指南分别进行中等强度的抗阻训练(10次练习, 每3次为一组)、低强度抗阻训练(10次练习, 单次即为一组), 两种方案在全身抗阻训练结束24、48、72 h后静息态能量消耗有明显地升高(约5%或400 kJ/d)[48]. 基于这些发现, 不难得出, 定期的抗阻训练会加快静息态能量消耗速率, 改善肝脏脂肪代谢(图2).

1.3　高强度间歇训练

近年来, 高强度间歇训练(high-intensity interval training, HIIT)在健身行业饱受关注. 这种训练方法包括反复进行5 s到8 min不等的高强度训练, 然后进行时间长短不一的恢复训练[49]. 这种“爆发-恢复”循环式训练, 被认为是替代传统有氧健身的一种可行方法[50~52]. 其优点体现在: (1) 有氧能力: 有学者通过文献荟萃分析出HIIT比长时间中等强度训练(moderate-intensity continuous training, MICT)的最大摄氧量明显升高[53]; (2) 体重控制: 高强度间歇训练法比其他的训练方法能更有效地减少脂肪百分比和脂质沉积量[54~56]; (3) 血管功能: 高强度训练法可以有效地保护心血管并提高其功能[57]; (4) 肌肉爆发力: 高强度训练法能够更有效地

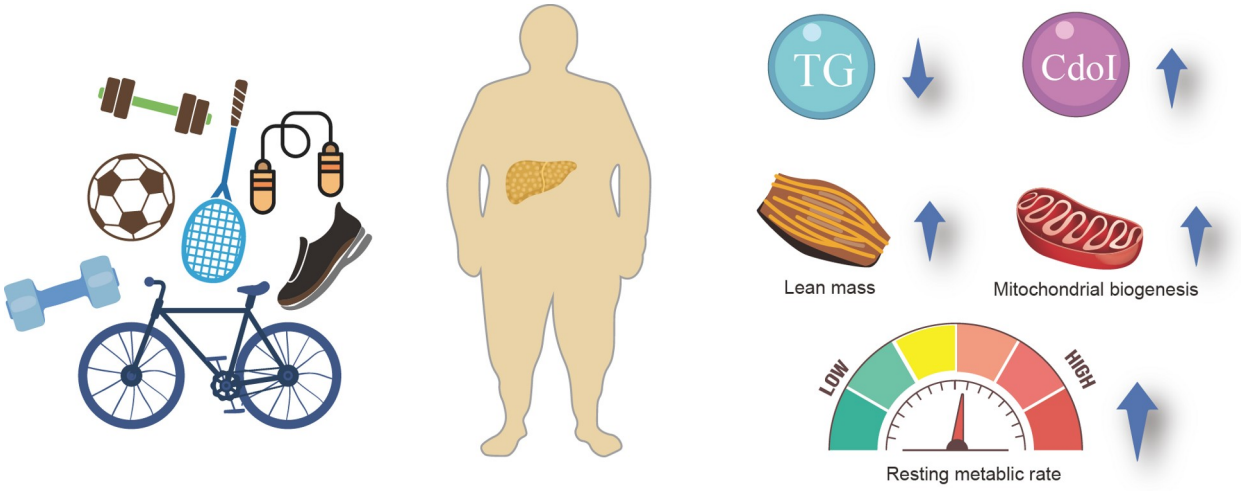

图 2 (网络版彩图)运动改善非酒精性脂肪肝的机制. 坚持运动均能够减少甘油三酯的含量. 有氧运动能够促进肝脏I型半胱氨酸双加氧酶基因的表达. 抗阻训练能够有效提升肌肉质量, 加快静息态能量消耗速率. 高强度间歇训练通过增加肝脏线粒体生物合成相关基因改善线粒体生物合成

Figure 2 (color online) Mechanisms by which exercise improves NAFLD. Adherence to exercise are able to reduce triglyceride levels. Aerobic exercise promotes hepatic type I cysteine dioxygenase gene expression. Resistance training effectively improves muscle mass and accelerates the rate of resting-state energy expenditure. High-intensity interval training improves mitochondrial biosynthesis by increasing hepatic mitochondrial biosynthesis-related genes

激发更多的肌肉组织运动并提高爆发力[58,59].

HIIT对肝脏脂质代谢产生重要的影响. Gavin Fredrickson等人[60]发现HIIT通过降低肝脏TG水平、炎症和纤维化来改善非酒精性脂肪肝炎的恶化(图2). 一项随机对照试验对28名2型糖尿病患者开展为期12周的HIIT训练, 通过^{1}H-磁共振光谱测定肝脏脂肪含量、口服葡萄糖耐量试验测定葡萄糖耐量, 发现HIIT能够有效改善2型糖尿病患者的心脏结构功能并减少肝脏脂肪含量[61].

更进一步地, 有学者发现, HIIT通过提高脂肪酸氧化相关基团(如PPARα、CPT1α、ACOX1) mRNAs水平、降低脂肪生成相关基因(PPARγ) mRNA水平, 改善由高脂饮食联合链脲佐菌素诱导的2型糖尿病小鼠肝脏代谢紊乱[62]. 同时, 当机体脂质堆积过多时, 线粒体的结构和功能异常, 导致线粒体融合减少、分裂增加、生物合成下调、自噬抑制等效应[63]. 线粒体功能障碍可降低呼吸链复合物活性和线粒体脂肪酸β氧化, 促进活性氧的过量产生和脂质过氧化, 进一步加重肝脏脂肪堆积, 引起炎症, 导致肝脏胰岛素抵抗[64~67], 这也是导致非酒精性脂肪肝病发生和发展的主要机制之一. HIIT则能通过增加肝脏线粒体生物合成相关基因(PGC-1α和TFAM)和恢复线粒体动力学相关基因(MFN2和DRP1)的mRNA水平改善线粒体生物合成与动力学[62], 从而预防NAFLD的发生(图2).

2 饮食模式对非酒精性脂肪肝病的影响

众所周知, 不良的饮食行为习惯, 如高糖、高脂、高盐饮食, 可能导致中心性肥胖、胰岛素抵抗和NAFLD的患病率增加[68~70], 并发展为肥胖、代谢综合征和糖尿病等[71]. 西式饮食和肠道微生物群相互作用产生的代谢物可能与NAFLD的加重有关[72]. 因此, 本文将回顾3种当下较为热门的饮食模式在非酒精性脂肪肝病发生发展过程中的影响:

2.1 地中海饮食

地中海饮食(Mediterranean diet, MD)起源于希腊、意大利等地中海沿岸的国家, 最先由Ancel Keys和Francisco Grande提出[73], 被认为是世界上最健康的饮食模式之一, 这主要归功于其富含抗氧化剂和抗炎营养素的食物组合. 它包含每天3~9份蔬菜、0.5~2份水果、1~13份谷物和最多八份橄榄油, 为人体提供约9300 kJ的热量、37%的总脂肪、18%的单不饱和脂肪和9%的饱和脂肪, 以及每天33 g的膳食纤维[74]. 大量

的研究表明，坚持地中海饮食能够预防某些慢性疾病(如心血管疾病、糖尿病等)和癌症的发生[75~77]. 除了上述发现，越来越多的研究证明地中海饮食与肝脏脂质代谢有关. 地中海饮食干预一定时间能够降低肝脏脂肪含量、肝脏硬度和TG水平[78,79]，并与NASH发病率降低密切相关[80].

橄榄油是地中海饮食中一种非常有特色的食物，地中海饮食中强调橄榄油是“初榨橄榄油”而不是普通的橄榄油. 初榨橄榄油和普通橄榄油之间的主要区别在于其高含量的抗氧化剂，包括胡萝卜素和生物活性酚[81]，两者都富含单不饱和脂肪酸，具有抗氧化和抗炎活性[82]. 氧化应激被视作NAFLD多种致病因素中的一种[83]，活性氧水平的升高可调节胰岛素信号通路活性，影响脂质代谢相关酶的活性，最终导致肝脏脂质代谢的氧化还原性失衡[84](图3). 一些研究肝脏转录组中脂肪变化的研究显示，橄榄油能够降低SREBP-1c的表达，降低了肝TG含量与脂肪生成[85,86].

各种饮食模式都能对肠道微生物的种类和功能产生一定的影响，反过来肠道微生物又影响器官代谢[87,88] (图3). 地中海饮食中，消耗特级初榨橄榄油能够促进乳酸菌(主要是双歧杆菌和乳酸杆菌)的生长并增加它们在肠相关淋巴组织中的生物代谢物，导致IL-6、IL-17A、TNF-α、IL-1β、COX-2、LDL-c、oxLDL-c和血压的降低[89]. 此外，一项随机对照试验显示，MD通过增加与丁酸代谢相关的普氏粪杆菌和微生物碳水化合物降解基因的水平，降低血清胆固醇含量并增加胰岛素敏感性[90]. 遗憾的是，目前尚没有将地中海饮食对肠道微生物的影响以及肠道微生物与NAFLD之间，三者系统相关联的直接研究.

2.2　生酮饮食

生酮饮食(ketogenic diet，KD)是一种高脂肪、富含蛋白质和极低碳水化合物(或无碳水化合物)的饮食[90]，已经成为体重管理的有效方式之一[91]. 生酮饮食的历史可以追溯到1921年[92]，当时禁食最初被发现对治疗癫痫有效. 在小鼠体内，KD已被证明可以降低血糖，增加胰岛素敏感性，甚至延长寿命[93,94]. 近年来，在人体内，KD由于其在癌症治疗等其他疾病中的潜在功效[95]以及作为普通人或运动员提高训练能力的营养方法[96]而重新受到研究人员的关注.

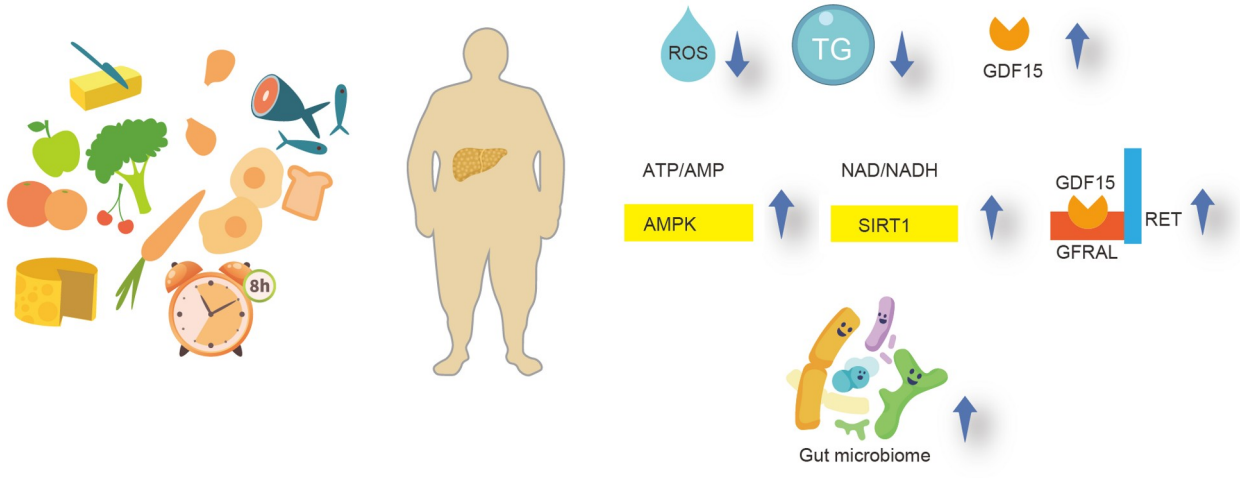

图 3　(网络版彩图)饮食改善非酒精性脂肪肝的机制. 3种饮食模式都会降低肝脏表面甘油三酯的水平，影响肠道微生物的种类和功能，反过来肠道微生物又影响着器官代谢. 初榨橄榄油中高含量的抗氧化剂抑制活性氧水平的升高，维持肝脏氧化还原性的平衡. 生酮饮食能使肝脏中GDF15的表达增加，GDF15与其受体GFRAL以及神经元表面的受体酪氨酸激酶RET形成三元复合物，打开身体能量代谢通路. 同时生酮饮食也能通过提高ATP/AMP、NAD/NADH的比值激活AMPK、SIRT1信号通路

Figure 3　(color online) Mechanisms by which diet improves NAFLD. All three dietary patterns in the text reduce liver surface triglyceride levels, affecting the type and function of gut microbes, which in turn influence organ metabolism. The high content of antioxidants in virgin olive oil inhibits the elevation of reactive oxygen species levels and maintains the balance of redox properties in the liver. The ketogenic diet increases the expression of GDF15 in the liver, which forms a ternary complex with its receptor GFRAL and the receptor tyrosine kinase RET on the surface of neurons, opening up the body′s energy metabolic pathways. The ketogenic diet also activates the AMPK and SIRT1 signaling pathways by increasing the ATP/AMP and NAD/NADH ratios

生酮饮食对肝脏脂质代谢的影响主要通过限制碳水化合物摄入和酮体来实现[97]. 限制碳水化合物的摄入, 一方面能够有效管理体重. 2023年, 研究人员揭示了在生酮饮食的条件下, 肝脏的过氧化物酶体增殖物激活受体(peroxisome proliferator-activated receptor, PPAR)信号通路, 尤其是PPARγ及其靶标在内的靶基因显著上调, 肝脏中生长分化因子15(Growth differentiation factor 15, GDF15)的表达与分泌增加, 升高血液循环GDF15水平[98] (图3). 2017年以来, 先后有研究人员报道GDF15通过受体GFRAL抑制食欲发挥其生物学作用[98~101], 能够作为二甲双胍药物减肥的主要调节因子[102,103]. 另一方面, 限制碳水化合物的摄入能够激活SIRT1和AMPK经典信号通路. (图3)AMPK信号通路被认为是细胞能量状态的传感器, 能够对ATP低水平做出反应[104], 在其激活后, 可对补充细胞ATP供应的信号转导通路做出正向反馈, 减轻脂肪变性[105]和胰岛素抵抗[106]. SIRT1能够使SREBP-1c脱乙酰基, 从而抑制脂肪生成并改善肝脏脂肪变性[107], 还可通过PPARα/PGC-1α促进脂肪酸β氧化, 提高脂质利用率[108]. 酮体包括β-羟基丁酸酯、乙酰乙酸酯和丙酮, 可以作为G蛋白偶联受体的配体[109]. GPR 109 A是一种在脂肪细胞、巨噬细胞和中性粒细胞中大量表达的G蛋白偶联受体[110]. 最近的一项研究表明, β-羟基丁酸酯可通过GPR 109 A/AMPK途径抑制老年大鼠的肝脏脂质积累[111]. 上述实验和理论基础支持均表明在NAFLD患者的饮食管理中使用生酮饮食能够缓解相应的症状.

2.3 间歇性能量限制饮食

为了控制肥胖者的体重, 能量的摄入应该小于能量的消耗[112]. 限制能量摄入可对胰岛素抵抗、血压和血脂等代谢指标产生积极影响[113]. 间歇性能量限制饮食(intermittent energy restriction, IER)就是限制能量摄入的方法之一, 这种方法的前提是: 人在进食期间无法完全补偿在两餐之间长时间禁食所产生的能量不足, 又称“轻断食”.

常见的间歇性饮食方式主要分为3种: (1) 隔日禁食, 即一天进食与一天禁食交替进行, 该方法可能是NAFLD患者的最有效饮食减肥疗法[114,115]; (2) 5:2断食法, 即每周5天进食, 2天断食; (3) 16:8限时进食, 即每天的进食时间限制在特定的时间内(通常是4~8 h), 剩余时间禁食[116].

IER能够帮助肥胖者有效减肥, 并有助于减少与肥胖相关的并发症, 而这种体重减轻同时也会显著改变肠道菌群和大脑活动(图3). 近来, 来自中国的研究人员使用粪便样本宏基因组学、血液检测和功能磁共振成像, 研究了25名IER饮食肥胖的男女性志愿者肠道微生物组组成、生理参数和血清组成以及大脑活动的变化, 揭示了间歇性能量限制(IER)饮食改变了人类的大脑-肠道-微生物轴[117]. 中枢神经系统通过脑-肠-微生物组轴与肠道微生物相互作用. 食物摄入影响控制能量平衡的大脑回路活动, 大脑回路对营养信号的异常反应改变了饮食模式, 进而导致肥胖的发展, 肠道微生物则通过多种机制调节大脑活动和饮食行为. IER干预减少了与饮食行为相关的大脑区域的活动, 增加肠道微生物多样性[117].

然而, 有关IER对非酒精性脂肪肝患者影响的证据却很少, 研究人员普遍接受IER是一种间歇性肝糖原消耗和补充的状态, 脂质在此种饮食模式中扮演的角色超越了碳水化合物[118]. 更进一步的机制研究仍有待发现与确定.

3 不同方式的组合和比较

鉴于单独的运动和饮食干预都能在一定程度上缓解非酒精性脂肪肝病的发生, 不少研究人员开始评估饮食与运动结合是否会在NAFLD的发展过程中产生更好的改善效果.

一项关于NAFLD与近期指南的更新提示我们通过每天摄入500~1000 cal热量和中等强度的运动能够更有效帮助人们减肥[119]. 对18项试验进行的汇总分析中, 研究人员发现联合饮食+运动比单纯节食多减轻1.14 kg体重[120]. 伊利诺伊大学芝加哥分校的研究人员通过一项随机对照临床试验, 比较了隔日禁食+中等强度的有氧训练、只进行隔日禁食、只进行运动这3种非药物干预方式对肝内TG水平的影响, 在第3个月时, 相比开始干预前, 隔日禁食+有氧运动组的肝内甘油三酯水平下降了5.48%, 隔日禁食组下降了2.25%, 有氧运动组下降1.30%[121], 这提示我们隔日禁食+有氧运动能够更好地降低肥胖和NAFLD患者的肝脏脂肪变性.

此外, 不少科学家认为自噬也参与肝脏的脂质代

谢, 并在NAFLD发病机制中起作用[122,123]. 在大鼠的肝细胞系中, 用3-甲基腺嘌呤或利用小分子干扰RNA敲除自噬相关蛋白atg5抑制自噬, 均能够观察到TG水平和脂滴数目大小的增加[124], 这提示我们诱导自噬可能是治疗NAFLD的有效方法. 单独的运动或饮食并未在降低肝脏TG水平中呈现出差异, 但是将两种方式结合起来更有效[125]. 运动和饮食干预分别通过激活AMPK/ULK1和抑制Akt/mTOR/ULK1途径来增强脂质吞噬功能[125]. 考虑其抑脂机制的不同, 将两种方式结合起来可能具有协同作用, 使得干预效果更为显著.

运动能够增加能量消耗, 促进脂肪代谢, 提高身体机能, 而饮食则是调节能量摄入和营养素平衡的重要手段. 运动结合饮食干预能够更全面地改善身体机能和代谢状态. 这种联合干预方式可能会产生协同效应, 更有助于患者养成健康的生活方式, 从而有效地控制疾病的发展.

临床上, 对于无 NASH 无纤维化的NAFLD人群, 仅需要提供健康饮食及运动的建议. 长期的生酮饮食、间歇性能量限制饮食均会导致相应疾病的发生. 地中海饮食被认为是最合适的饮食模式之一, 其通过氧化应激、自噬和肠道微生物群调节等机制发挥作用. 而运动方式的选择则是在患者能够长期坚持的前提下根据患者情况来决定. 通常情况下, 有氧运动以及耐力训练都可以有效地减少肝脏脂肪蓄积. 尽管运动和饮食干预在改善NAFLD方面展现出显著效果, 但这并不意味着其他因素(如睡眠、心理状况)对NAFLD无影响. 实际上, 这些因素之间可能存在相互关联, 共同对非酒精性脂肪性肝病的发生和发展产生影响. 运动联合饮食的非药物疗法目前的相关研究相对较少. 因此, 未来的研究应进一步深入探讨这些因素之间的相互作用关系, 以更全面地理解NAFLD的发病机理, 并制定更加完善的治疗方案.

本文总结了几种常见的运动方式和饮食模式在非酒精性脂肪肝病发生发展进程中发挥作用的证据与机制, 阐明它们在肝脏脂质代谢过程中的影响, 期冀为非酒精性脂肪肝患者提供可参考的非药物治疗策略.

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Influence of lifestyle habits on nonalcoholic fatty liver disease

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In recent years, there has been a booming social and economic development, and people's lifestyles have also undergone some changes accordingly. Scientific research and medical practice have confirmed that changes in people's dietary structure, physical activity, sleep patterns and psychological state have far-reaching effects on individual health. These changes, especially poor physical activity and dietary habits, have gradually threatened people's health. Non-alcoholic fatty liver disease (NAFLD), a chronic liver disease whose incidence is increasing year by year, is closely related to these unhealthy lifestyles. Sedentary lifestyle, excessive dietary fat and cholesterol content, etc. all show a high correlation with the incidence of NAFLD. It is worth noting that, to date, no drugs have been approved for the treatment of this disease in the United States and the European Union. Therefore, there is a greater need to focus on non-pharmacological treatment strategies, especially to prevent and alleviate this disease by modifying poor physical activity patterns and dietary patterns. To this end, this article will discuss in depth the effects of different dietary and physical activity patterns on hepatic substance metabolism and elucidate their molecular mechanisms, with a view to providing effective non-pharmacological therapeutic strategies for non-alcoholic fatty liver disease.

non-alcoholic fatty liver disease, aerobic exercise, resistance training, high-intensity interval training, Mediterranean diet, ketogenic diet, intermittent energy-restricted diet

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