

代谢相关性脂肪性肝病的相关影响因素

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摘 要

随着医疗技术的不断进步以及人民生活方式的改变, 全球慢性肝病的病因谱已经发生了巨大变化。脂肪肝已然成为全球最常见的慢性肝病, 其中非酒精性脂肪性肝病(nonalcoholic fatty liver disease, NAFLD) 占据比例更大。目前非酒精性脂肪性肝病已被多位专家更名为代谢相关性脂肪性肝病(metabolic associated fatty liver disease, MAFLD)。MAFLD已成为全世界最主要的非传染性肝病, 严重威胁着人类的生命健康。本综述旨在介绍代谢相关性脂肪性肝病的几大影响因素, 从而为更好地预防和控制疾病起到指导作用。

关键词

非酒精性脂肪性肝病, 代谢相关性脂肪性肝病, 影响因素

Related Factors of Metabolic Associated Fatty Liver Disease

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Abstract

With the continuous progress of medical technology and the change of people's lifestyle, the etiological spectrum of chronic liver disease in the world has changed greatly. Fatty liver has become the most common chronic liver disease in the world, among which nonalcoholic fatty liver disease (NAFLD) occupies a larger proportion. At present, nonalcoholic fatty liver disease has been re-named as metabolic associated fatty liver disease (MAFLD) by many experts. MAFLD has become the most important non-infectious liver disease in the world, seriously threatening human life and health. This review aims to introduce several influential factors of metabolic associated fatty liver

disease, so as to provide guidance for better prevention and control of the disease.

Keywords

Nonalcoholic Fatty Liver Disease, Metabolic Associated Fatty Liver Disease, Influencing Factors

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1. 引言

近 20 余年,全世界慢性肝病的病因谱发生了巨大变化[1]。一方面是由于病毒性肝炎现已成为可以有效预防和控制的疾病[2],另一方面是因为随着生活方式的改变、人口老龄化,以及肥胖和酒精滥用的流行,脂肪肝正成为全球越来越常见的慢性非传染性疾病[3]。目前已有研究统计结果显示,脂肪肝已取代病毒性肝炎成为主要的慢性肝病[4]。随着全世界范围内肥胖和 2 型糖尿病的流行,脂肪肝中非酒精性脂肪性肝病(NAFLD)的患病率增加的比例更高[5]。目前国际专家已达成共识,将非酒精性脂肪性肝病(NAFLD)更名为代谢相关性脂肪性肝病(MAFLD) [6] [7] [8] [9]。代谢相关性脂肪性肝病是西方国家最常见的原发性肝病,其影响着全球约四分之一的人口[10]。可以预见的是 MAFLD 必将成为一个很严重的公共卫生问题[11] [12]。目前我国成人代谢相关性脂肪性肝病的患病率已超过 29.2%,在中国,MAFLD 已成为第一大非传染性慢性肝病,而且患病率也在不断上升[13]。影响 MAFLD 发病的相关因素有很多,比如糖脂代谢紊乱、高尿酸血症、胆汁酸代谢紊乱、肠道菌群紊乱、胰岛素抵抗等代谢综合征表现[14]。除此之外,还有年龄、性别[15] [16]以及种族、家族遗传等因素[17] [18]。相关研究报道 MAFLD 与血红蛋白、白细胞计数还有相关性[19] [20]。目前 MAFLD 具体影响因素尚未完全明确,研究其相关影响因素对临床有效的干预、治疗有很重要的意义。

2. MAFLD

代谢相关性脂肪性肝病是一种非常复杂的疾病,由遗传易感性、环境因素和代谢综合征组成的,由动态交互作用形成。MAFLD 的诊断主要靠影像学诊断出肝脏脂肪变性,且合并以下任何一种:超重/肥胖,糖尿病,或代谢失调[9]。

3. MAFLD 的影响因素

3.1. 年龄和性别

随着年龄的增长,人体器官功能呈衰减状态,肝脏中的血流量及肝脏功能下降,胆汁酸合成减少和胆固醇代谢减慢,肝脏中线粒体数量的减少[21],肝脏细胞也在逐渐衰老[22]。另外,衰老的同时身体还会出现组成的变化,其中包括肌肉含量的减少,腹部脂肪的增多以及异位脂肪的沉积,胰岛素的抵抗和代谢综合征的发生等等[15]。性别在 MAFLD 发病的流行中也有不同的显现。有研究发现相对于男性来说,女性脂肪肝的发病率较低,尤其是初潮后绝经前女性[16] [23],这可能与女性体内的激素变化有很大关系。

3.2. 种族和家族遗传

有统计数据显示脂肪肝的患病率有种族差异:一项荟萃分析表明,NAFLD 的患病率在西班牙人中最

高,在白种人居中,在黑人中最低[17]。MAFLD 在亚洲人群中的患病率也呈递增状态[24]。代谢相关性脂肪性肝病发生风险的种族差异原因可能与遗传易感性、群体代谢、文化和社会经济因素、饮食和锻炼习惯、医疗保健条件以及环境风险的差异有关[25] [26] [27]。有回顾性研究表明, MAFLD 的发生有家族聚集现象[18]。

3.3. 肠道菌群结构、胆汁酸、饮食结构

有研究表明,肠道菌群及其代谢物对 NAFLD 的晚期纤维化和肝硬化有预测作用[28] [29]。肠道菌群还参与了胆汁酸及其代谢产物的调节,而胆汁酸及其代谢产物又反过来可以调节葡萄糖、脂质等的代谢[30]。国外的饮食模式以高糖、高脂为主,导致了人群肥胖和脂肪肝的增加,其与多种代谢功能障碍有关,包括胰岛素抵抗和血脂异常[31]。相反,改变高糖、高脂的饮食模式后,多食蔬菜、水果等, MAFLD 患者肝脂肪明显减少,患病率大大地降低[32]。

3.4. 葡萄糖、高血脂、高血压、胰岛素抵抗、肥胖

有研究表明,葡萄糖、血脂、胰岛素抵抗可增加肝脏脂肪变性,且其有互相促进作用,其中胰岛素抵抗对肝脏脂肪变的影响相对更大[33]。在 MAFLD 患者组中糖尿病、高血压、高脂血症的患病率明显高于非 MAFLD 组[34]。BMI 越大的人群中,患 MAFLD 的比例更大[35]。较高的体重指数、腰围、血脂、血糖与 MAFLD 独立且呈正相关,它们是患 MAFLD 的危险因素[36] [37]。多元 logistic 回归分析显示 HGB、TG、FPG 水平与 MAFLD 严重程度独立且呈正相关。肝脏在脂质和葡萄糖的代谢中起着巨大作用。大量研究发现 MAFLD 患者的 TC、TG、LDL-C 水平升高, HDL-C 水平降低[38]。MAFLD 发病的主要过程是脂质代谢紊乱和胰岛素抵抗,胰岛素抵抗的程度不同,均可以加重 MAFLD 的病理生理过程。人体内脂质代谢紊乱又可进一步加剧胰岛素抵抗,它们是一种互相影响的动态演变过程。过多的高脂类食物摄入使体内产生大量的游离脂肪酸,这些脂肪酸可使肝细胞内的线粒体氧化功能出现障碍,能量摄入和消耗之间的不平衡,进而出现机体出现胰岛素抵抗和肠道菌群失调。细胞中过量的游离脂肪酸可导致肝细胞出现不同程度的代谢紊乱,而肝脏脂肪含量、胰岛素抵抗又密切相关[39]。

3.5. 血红蛋白、白细胞计数

血红蛋白水平与 MAFLD 之间存在独立的关系,血红蛋白水平越高, MAFLD 的患病率越高,血红蛋白与 MAFLD 的发病率独立相关[19] [40] [41] [42]。另外,血红蛋白水平可作为 MAFLD 一个简单且可靠的生物标志物[43]。在王[44]的一项基于健康评估的大规模城市汉族人群纵向队列研究中,结果显示 MAFLD 组的白细胞计数明显高于对照组。一项针对韩国人群的研究显示白细胞计数与 MAFLD 的发生率有显著的相关性[20]。白细胞水平的变化可能与脂肪肝的慢性炎症有关。

3.6. 尿酸

尿酸是氢、碳、氧、氮等的杂环化合物。尿酸是嘌呤代谢的最终产物。高尿酸血症也是一种代谢功能障碍,它被认为与代谢综合征产生的原因有关。它可引起痛风、肾功能受损、高血压、高血脂、肥胖和糖尿病等疾病。一项前瞻性队列研究发现,血清尿酸水平是脂肪肝发病的独立危险因素[45]。研究还发现血尿酸水平与 MAFLD 之间存在独立的正相关关系。血尿酸水平与 MAFLD 之间除了可能通过提高空腹胰岛素水平、血压、TC 水平和降低 HDL-C 水平,还可直接增加 MAFLD 的风险[46]。一项前瞻性队列研究,将 2832 名随访对象入组研究,研究结果 Kaplan-Meier 生存曲线显示,与较低血清尿酸水平的个体相比,较高血清尿酸水平的个体发生 MAFLD 的风险增加。血清尿酸水平与 MAFLD 呈正相关,其水平升高可作为 MAFLD 的独立预测指标[47]。

4. 结论与展望

MAFLD 是一种全身多系统受累的代谢性疾病,它与代谢综合征、2 型糖尿病等相互影响、互为因果。MAFLD 是目前肝脏疾病与代谢疾病共同的新挑战。对这些 MAFLD 相关影响因素早干预、早处理,可以大大地减轻 MAFLD 患者的负担,降低代谢性疾病与肝脏疾病的发生率,改善患者的不良结局与预后。MAFLD 的相关影响因素还有很多,需要我们不断探索与发现,本综述只选了其中的一部分,其余相关影响因素需要我们继续积极探索与发现。

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