·脂肪性肝病·

DOI：10.12449/JCH250914

非酒精性脂肪性肝病与抑郁症关系的系统评价及Meta分析

李淑娣[1a]，曹帅兵[1a]，巴明玉[2a]，李素领[2b]，段　飞[2b]，禄保平[1b]

1 河南中医药大学 a.研究生院，b.教务部，郑州 450000

2 河南中医药大学第一附属医院 a.内分泌科，b.脾胃肝胆病科，郑州 450000

通信作者：禄保平，lbp1921@sohu.com（ORCID：0000-0002-3707-2185）

摘要：目的　系统评价非酒精性脂肪性肝病（NAFLD）与抑郁症的关联性，为临床协同管理提供依据。**方法**　本研究根据PRISMA指南完成，PROSPERO注册号：CRD42023482013。检索PubMed、Embase、Cochrane Library、Web of Science、中国知网、万方、维普、CBM数据库建库至2024年11月1日公开发表的NAFLD和抑郁症二者相关性的研究文献，根据纳入和排除标准筛选文献并提取数据。采用RevMan 5.3进行Meta分析。**结果**　共纳入18项研究，涉及396 793例参与者。12项研究探讨NAFLD对抑郁症的影响，共涉及224 269例参与者，其中包含75 574例NAFLD患者。Meta分析显示，NAFLD显著增加抑郁症发生风险（*OR*=1.21，95%*CI*：1.12～1.30，*P*<0.001）。6项研究分析抑郁症对NAFLD的影响，共涉及172 524例参与者，其中包含29 368例抑郁症患者。Meta分析显示，抑郁症导致NAFLD风险显著增加（*OR*=1.13，95%*CI*：1.05～1.22，*P*=0.001）。**结论**　NAFLD与抑郁症存在显著的双向关联。在初诊和随访时，建议对NAFLD患者行抑郁症筛查并加强心理健康监测；对抑郁症患者需重视代谢功能评估并实施运动干预。

关键词：非酒精性脂肪性肝病；抑郁症；Meta分析

基金项目：第七批全国老中医药专家学术经验继承项目（国家中医药人教函〔2022〕76号）；河南省省级科技研发计划联合基金（242301420081）

Association between non-alcoholic fatty liver disease and depression: A systematic review and Meta-analysis

LI Shudi[1a], *CAO Shuaibing*[1a], *BA Mingyu*[2a], *LI Suling*[2b], *DUAN Fei*[2b], *LU Baoping*[1b]

1. a. Graduate School, b. Academic Affairs Department, Henan University of Chinese Medicine, Zhengzhou 450000, China; 2. a. Department of Endocrinology, b. Department of Hepatology and Spleen-Stomach, The First Affiliated Hospital of Henan University of Chinese Medicine, Zhengzhou 450000, China

Corresponding author: LU Baoping, lbp1921@sohu.com (ORCID: 0000-0002-3707-2185)

Abstract: Objective　To systematically review the association between non-alcoholic fatty liver disease (NAFLD) and depression, and to provide a basis for synergistic management in clinical practice. **Methods**　This study was conducted according to the PRISMA guidelines, with the PROSPERO registration number of CRD42023482013. PubMed, Embase, the Cochrane Library, Web of Science, CNKI, Wanfang Data, VIP, and CBM were searched for articles on the association between NAFLD and depression published up to November 1, 2024. The articles were screened according to the inclusion and exclusion criteria, and related data were extracted. RevMan 5.3 was used to perform the Meta-analysis. **Results**　A total of 18 studies were included, involving 396 793 participants. Among these studies, 12 discussed the influence of NAFLD on depression, involving 224 269 participants, among whom there were 75 574 patients with NAFLD. The Meta-analysis showed that NAFLD was significantly associated with the risk of depression (odds ratio [*OR*]=1.21, 95% confidence interval [*CI*]: 1.12—1.30, *P*<0.001). Six studies examined the influence of depression on NAFLD, involving 172 524 participants, among whom there were 29 368 patients with depression. The meta-analysis showed that depression caused a significant increase in the risk of NAFLD (*OR*=1.13, 95%*CI*: 1.05—1.22, *P*=0.001). **Conclusion**　There is a significant bidirectional association between NAFLD and depression. It is recommended to perform the screening for depression and enhance mental health monitoring in patients with NAFLD, and

metabolic function assessment and exercise intervention should be performed for patients with depression.

Key words: Non-Alcoholic Fatty Liver Disease; Depressive Disorder; Meta-Analysis

Research funding: The 7th Batch of National Traditional Chinese Medicine Experts Academic Experience Inheritance Project (National Traditional Chinese Medicine Education Letter [2022] No. 76); Henan Provincial Science and Technology Research and Development Joint Fund Project (242301420081)

非酒精性脂肪性肝病(non-alcoholic fatty liver disease, NAFLD)是一种与胰岛素抵抗和遗传易感性密切相关的代谢应激性肝损伤[1],其患病率呈逐年上升趋势。据估算,至2030年NAFLD的全球疾病负担将增加2~3倍[2]。目前尚无针对NAFLD的治疗方法,因此明确NAFLD及其进展的可调控危险因素至关重要[3]。抑郁症是一种常见的致残性情绪障碍,可导致认知、情绪和躯体功能受损[4]。全球疾病负担研究显示,2030年抑郁症的年龄标准化发病率预计将达到男性2 519.88/10万、女性3 835.11/10万[5]。尽管现有多种治疗手段,抑郁症患者仍面临症状反复发作的困扰,严重影响生活质量[6]。

NAFLD与抑郁症共享肥胖、代谢综合征、2型糖尿病及心血管疾病等危险因素,这些因素可协同增加NAFLD的患病风险[7-9]。多项研究表明,抑郁症患者发生代谢综合征的风险是普通人群的2倍[10-12]。因此,相关指南推荐对所有抑郁症患者常规筛查超重/肥胖[13]。同时,NAFLD患者中抑郁症的患病率亦显著升高[14]。胰岛素抵抗既是NAFLD的核心病理特征,也是抑郁症患者常见的状态依赖性代谢异常[15],其可能通过干扰抑郁相关脑区功能,成为二者关联的潜在机制[16]。尽管现有证据提示NAFLD与抑郁症密切相关,但尚缺乏系统评价研究。本研究采用Meta分析方法,系统评价NAFLD与抑郁症的关联性,旨在为临床协同防治提供循证依据。

1 资料与方法

1.1 规程与注册 本研究严格遵循系统评价和Meta分析优先报告条目(PRISMA)声明[17]。研究方案已于PROSPERO国际前瞻性系统评价注册平台完成注册,注册号:CRD42023482013。

1.2 文献检索策略 检索PubMed、Embase、Cochrane Library、Web of Science、中国知网、万方、维普、CBM数据库建库至2024年11月1日公开发表的NAFLD和抑郁症二者相关性的研究文献。使用与“非酒精性脂肪性肝病”和“抑郁症”相关的中英文搜索词,采用主题词与自由词相结合的检索方法。中文检索主题词分别为非酒精性脂肪性肝病和抑郁症,自由词为:非酒精性脂肪肝、非酒性脂肪肝、非酒精性脂肪肝病、单纯性脂肪肝、非乙醇性脂肪肝、非乙醇性脂肪性肝病、非酒精性脂肪性肝病、非酒精性肝病;抑郁症、抑郁性神经症、神经症性抑郁、抑郁性障碍、抑郁障碍、抑郁障碍症。英文检索主题词分别为nonalcoholic fatty liver disease、depression。自由词为:nonalcoholic fatty liver、NAFLD、nonalcoholic fatty liver disease、non alcoholic fatty liver disease、non alcoholic hepato-steatosis、non alcoholic hepatosteatosis、non alcoholic liver steatosis、non alcoholic steatotic hepatopathy、non-alcoholic fatty liver、non-alcoholic fatty liver disease等;clinical depression、depressive disease、depressive disorder、depressive episode、depressive illness等。

1.3 纳入标准 (1)研究类型:前瞻性或回顾性的观察性研究;(2)抑郁症诊断:符合《美国精神病学会精神障碍诊断与统计手册》(DSM)标准或《国际疾病和相关健康问题统计分类(第十版)》疾病代码F32~F33或抑郁症筛查工具报告标准;(3)NAFLD诊断:符合肝活检或放射学、腹部超声等影像学检查诊断标准。

1.4 排除标准 (1)重复发表或无法获取全文的文献;(2)非中或英文文献;(3)会议摘要、病例报告、综述、信函、评论及临床指南类文献;(4)无法提取有效数据的文献。

1.5 文献筛选与数据提取 研究由3位研究者独立检索和筛选。首先根据标题和摘要进行初筛,再依据纳入标准对潜在研究进行全文评估。研究者对筛选结果进行交叉核对,通过讨论和投票解决分歧。数据提取内容包括:第一作者、发表年份、国家、样本量、研究对象特征、年龄分布、研究设计类型、效应量指标[优势比(*OR*)、风险比(*HR*)、相对风险(*RR*)及其95%可信区间(95%*CI*)]、校正变量等关键信息。

1.6 文献质量评价 采用纽卡斯尔-渥太华量表(NOS)评估纳入研究的质量[18],该量表满分为9分,评分≥6分视为高质量研究,<6分为低质量研究。3位研究者独立完成质量评价后,通过讨论协商解决评分差异。

1.7 统计学方法 使用RevMan 5.3软件进行Meta分析。基于NAFLD和抑郁症的全球患病率(分别为25%和

4.4%)[19-20]，选择*OR*作为主要效应量指标。对于以抑郁症为结局的研究直接采用*OR*值；对于以NAFLD为结局的研究，采用公式*OR*=(1-P0)×*RR*/(1-P0×*RR*)将*RR*/*HR*转换为*OR*[21]，其中P0为结局事件发生率。多因素分析中优先选择校正最充分的模型。根据数据可获得性，按亚洲和欧美地区进行亚组分析。采用Q检验和I^2统计量评估异质性：I^2<50%时选用固定效应模型，I^2≥50%时选用随机效应模型。通过敏感性分析探讨异质性来源，当纳入研究超过10项时采用漏斗图评估发表偏倚。*P*<0.05为差异有统计学意义。

2 结果

2.1 文献筛选结果 通过系统检索共获得1 546篇文献（截至2024年11月1日），经筛选后最终纳入18项研究（图1）。

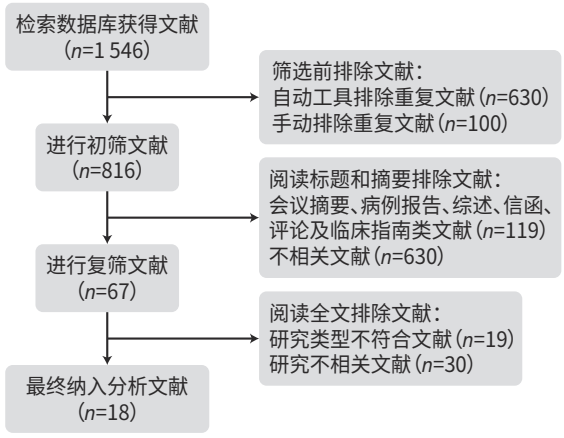

图1 文献筛选流程

Figure 1 Document screening flow chart

2.2 纳入文献基本特征及质量评价 18项研究共纳入396 793例研究对象，其中12项研究[22-33]探讨NAFLD对抑郁症的影响，6项研究[34-39]分析抑郁症对NAFLD的影响（表1）。质量评价显示纳入研究总体质量中等至较高。多数研究未明确说明随访方法，导致该方面证据质量有所降低。

2.3 NAFLD对抑郁症风险的影响 12项研究[22-33]纳入224 269例研究对象（NAFLD患者75 574例）分析NAFLD与抑郁症的关联。异质性检验（I^2=65%）提示采用随机效应模型。Meta分析显示，NAFLD显著增加抑郁症风险（*OR*=1.21，95%*CI*：1.12～1.30，*P*<0.001）（图2）。排除研究[28]后进行亚组分析，亚洲地区（*OR*=1.21，95%*CI*：1.05～1.40）与欧美地区（*OR*=1.22，95%*CI*：1.10～1.36）差异无统计学意义（*P*=0.96）（图3）。

2.4 抑郁症对NAFLD风险的影响 6项研究[34-39]纳入172 524例研究对象（抑郁症患者29 368例）。异质性检验（I^2=75%）提示采用随机效应模型。Meta分析显示，抑郁症显著增加NAFLD风险（*OR*=1.13，95%*CI*：1.05～1.22，*P*=0.001）（图4）。亚组分析显示，亚洲地区（*OR*=1.24，95%*CI*：1.06～1.45）与欧美地区（*OR*=1.22，95%*CI*：0.87～1.71）差异无统计学意义（*P*=0.94）（图5）。

2.5 敏感性分析与发表偏倚分析 采用逐一剔除研究法进行敏感性分析，结果显示合并效应量保持稳定，提示结果稳健。异质性可能源于各研究采用的诊断和评估方法不同。由于抑郁症对NAFLD影响的研究不足10项，未进行发表偏倚评估。NAFLD对抑郁症影响的漏斗图对称性良好，提示无明显发表偏倚（图6）。

3 讨论

本研究通过系统评价证实NAFLD与抑郁症存在显著的双向关联。Meta分析结果显示，NAFLD患者发生抑郁症的风险增加21%，而抑郁症患者发生NAFLD的风险增加13%。既往研究结果与本研究结论一致。NAFLD作为代谢综合征在肝脏的表现，与抑郁症存在共同的病理生理基础。现有证据表明，代谢综合征与抑郁、焦虑等精神障碍具有直接相关性[40-42]。其中，肥胖等代谢异常因素可通过诱发体像障碍和社会歧视增加抑郁风险[43]。从机制上而言，NAFLD进展过程中释放的促炎细胞因子和趋化因子可能通过干扰神经递质合成和信号传导促进抑郁行为[44-45]。

全球疾病负担数据显示，精神-躯体共病现象日益突出[46-47]，NAFLD/NASH（非酒精性脂肪性肝炎）与精神障碍共病尤为显著[48]。抑郁症可使代谢综合征风险增加1倍，这与抑郁相关的不良健康行为（如运动减少、情绪化饮食）密切相关[49-50]。此外，精神科药物（抗抑郁药、抗精神病药等）对体质量和能量代谢的影响可能加重NAFLD/NASH的发生发展，在儿童患者中的表现尤为明显[51-54]。抑郁症相关的慢性炎症状态（表现为CRP、TNF-α、IL-6等炎症标志物升高）也被认为参与肝损伤进程[55]。

本研究存在以下局限性：（1）纳入研究采用的诊断标准和评估工具存在差异，可能是异质性的主要来源；（2）受研究数量限制，仅完成地域亚组分析（亚洲vs欧美），未能进行年龄、性别等分层分析，其中两项研究提示性别可能是重要影响因素[32, 37]；（3）部分研究随访资料不完整，影响证据质量。未来研究需采用标准化诊断方法、延长随访时间，并加强人口学特征的分层分析。

表1 纳入研究的基本特征

Table 1 Basic features of the included study

作者及发表年份	国家或地区	总样本量（例）	研究对象数量（例）	研究对象年龄（岁）	研究类型	*OR*/*RR*/*HR*（95%*CI*）	调整的变量	NOS评分（分）
NAFLD对抑郁症的影响								
Choi，2021[22]	韩国	25 333	7 846 NAFLD	48.4±10.1	回顾性研究	1.09（0.95～1.26）	年龄、性别、糖尿病、血压、吸烟	7
Elwing，2006[23]	美国	72	36 NASH	51.4±2.0	前瞻性研究	3.8（1.40～10.20）	年龄	7
Filipovic，2018[24]	塞尔维亚	283	40 NAFLD	47.88±6.07	前瞻性研究	1.65（1.16～2.36）	BMI、高血压、代谢综合征	8
Goulart，2023[25]	巴西	7 241	2 223 NAFLD	49.0	前瞻性研究	1.17（1.00～1.38）	年龄、性别	7
Jung，2019[26]	韩国	112 797	31 635 NAFLD		前瞻性研究	1.32（1.17～1.48）	年龄、性别、家庭月收入、婚姻状况、工作、平均饮酒量、吸烟、收缩压、TC、HDL-C、糖尿病、体力活动、BMI、HOMA-IR	7
Labenz，2020[27]	德国	39 742	19 871 NAFLD	58.5±14.2	回顾性研究	1.21（1.14～1.26）	糖尿病、心血管疾病、哮喘、慢性阻塞性肺病、癌症	6
Lee，2013[28]	美国	10 231	497 NAFLD	49.62±0.72	回顾性研究	0.92（0.68～1.24）	性别、家庭收入、吸烟、BMI、血脂异常、心脏病、慢性肝病、药物使用史	6
Ng，2022[29]	美国	21 414	6 726 NAFLD	52.16	回顾性研究	1.12（1.00～1.26）	年龄、性别、种族、糖尿病、超重	7
Noon，2021[30]	美国	160	160 NAFLD	15±1.8	前瞻性研究	1.60（1.11～2.52）	BMI、ALT、AST、GGT	9
Younossi，2022[31]	18个国家或地区[1)]	5 691	5 691 NAFLD	51	回顾性研究	1.94（1.41～2.67）	年龄、性别、肥胖、焦虑、2型糖尿病、高脂血症、高血压、心肌梗死、中风、充血性心力衰竭	6
Youssef，2013[32]	美国	567	567 NAFLD	49±1.0	回顾性研究	1.30（0.80～2.11）	年龄、性别、种族、BMI、糖尿病、高血压	7
杨旭瑶，2022[33]	中国	738	282 NAFLD	41.17±11.57	回顾性研究	1.10（1.03～1.16）	性别、BMI、TC、TG	6
抑郁症对NAFLD的影响								
Cai，2023[34]	美国	3 263	3 263抑郁症	48.0	回顾性研究	1.05（1.02～1.08）	年龄、性别、种族/民族、教育水平、家庭贫困收入比、婚姻状况、体力活动、过度饮酒、吸烟、BMI、乙型/丙型肝炎、糖尿病、高血压、心血管疾病	6
Cho，2021[35]	韩国	142 005	16 961抑郁症	34.8	回顾性研究	1.07（1.03～1.11）	年龄、性别、教育水平、BMI、吸烟、体力活动、总能量摄入、糖尿病、高血压、心血管疾病、收缩压、血糖、TC、TG、HDL-C、HOMA-IR、Hs-CRP	8
Kamari，2023[36]	印度	7 114	7 114抑郁症	45.78±7.80	回顾性研究	1.30（0.72～2.35）	年龄、婚姻状况、居住地、饮酒情况	6
Kim，2019[37]	美国	10 484	1 162抑郁症	49.5±0.6	回顾性研究	1.48（1.17～1.87）	年龄、性别、种族/民族、教育水平、婚姻状况、经济状况、吸烟、高血压、体力活动、TC、糖尿病、腰围、BMI	7
Lee，2021[38]	韩国	4 688	422抑郁症	50.1	回顾性分析	1.63（1.26～2.10）	年龄、性别、婚姻状况、个人收入、吸烟、糖尿病、高血压、心血管疾病	7
廖倩，2017[39]	中国	4 970	446抑郁症	46	前瞻性研究	1.11（0.95～1.31）	年龄、性别、教育水平、现在或既往吸烟和饮酒、打鼾、收缩压、舒张压、睡眠持续时间、糖尿病、BMI、步行时间、血脂	6

注：HDL-C，高密度脂蛋白胆固醇；HOMA-IR，稳态模型的胰岛素抵抗指数；Hs-CRP，超敏C反应蛋白。1）包括中国内地、中国香港、中国台湾、澳大利亚、古巴、埃及、希腊、印度、意大利、日本、沙特阿拉伯、马来西亚、墨西哥、巴基斯坦、俄罗斯、西班牙、土耳其和美国。

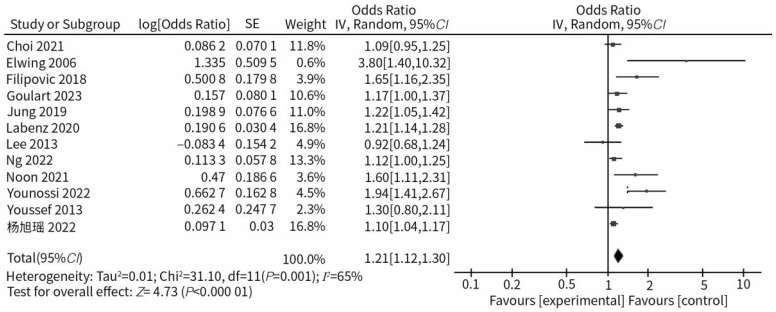

图2 NAFLD对抑郁症风险的影响

Figure 2 The effect of non-alcoholic fatty liver disease on the risk of depression

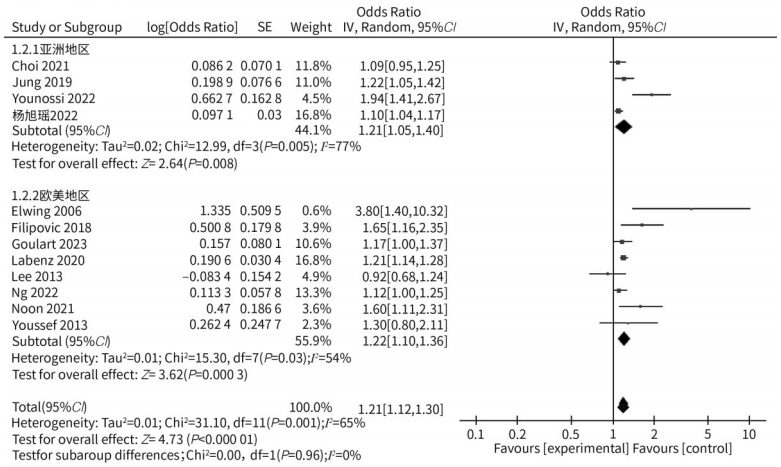

图3 NAFLD对抑郁症风险影响的亚组分析

Figure 3 Subgroup analysis of the effect of non-alcoholic fatty liver disease on the risk of depression

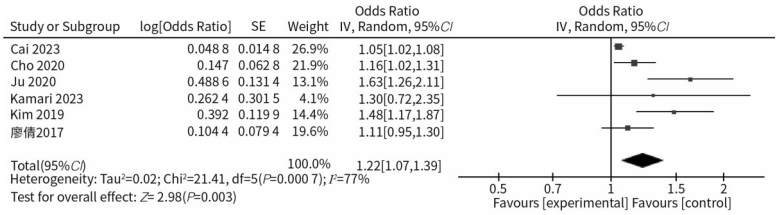

图4 抑郁症对NAFLD风险的影响

Figure 4 The effect of depression on the risk of non-alcoholic fatty liver disease

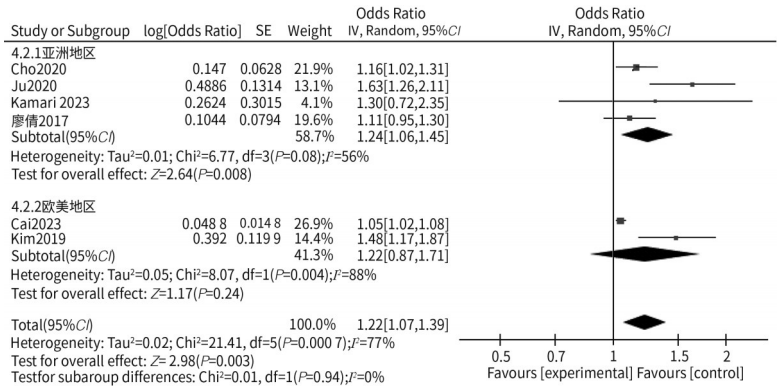

图5 抑郁症对NAFLD风险的影响

Figure 5 Subgroup analysis of the effects of depression on the risk of non-alcoholic fatty liver disease

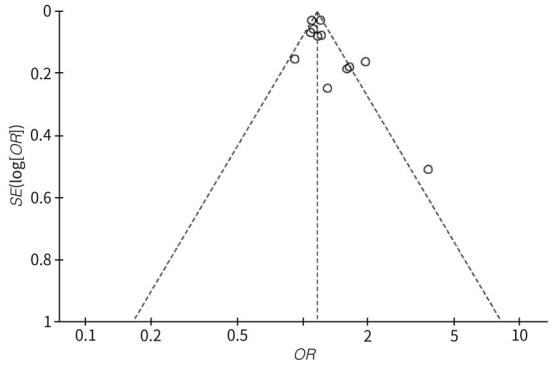

图6 发表偏倚风险漏斗图

Figure 6 Funnel plot of publication bias risk

本研究在临床层面证实了NAFLD与抑郁症之间存在双向关联。NAFLD患者发生抑郁症的风险显著增加，同时抑郁症也是NAFLD发生的重要危险因素。基于上述结论，建议临床实践中对NAFLD患者在初诊和随访时进行抑郁症筛查，加强心理健康监测；对抑郁症患者应重视代谢指标评估和运动干预。未来研究可进一步深入探讨NAFLD与抑郁症发生发展的共同病理生理机制。

利益冲突声明：本文不存在任何利益冲突。

作者贡献声明：李淑娣负责设计论文框架，起草论文；李淑娣、曹帅兵、巴明玉负责操作及研究过程的实施；李淑娣负责数据收集，统计学分析，绘制图表；李素领、段飞负责论文修改；禄保平负责拟定写作思路，指导撰写文章并最后定稿。

参考文献：

[1] ANSTEE QM, DARLAY R, COCKELL S, et al. Genome-wide association study of non-alcoholic fatty liver and steatohepatitis in a histologically characterised cohort[J]. J Hepatol, 2020, 73(3): 505-515. DOI: 10.1016/j.jhep.2020.04.003.

[2] ESTES C, ANSTEE QM, ARIAS-LOSTE MT, et al. Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016-2030[J]. J Hepatol, 2018, 69(4): 896-904. DOI: 10.1016/j.jhep.2018.05.036.

[3] LI F, LI MW, WANG YS. Therapeutic paradigms and potential therapies for nonalcoholic steatohepatitis[J]. J Clin Hepatol, 2024, 40(10): 2082-2086. DOI: 10.12449/JCH241025.
李凤, 李茂微, 王雨杉. 非酒精性脂肪肝病的治疗模式和潜在疗法[J]. 临床肝胆病杂志, 2024, 40(10): 2082-2086. DOI: 10.12449/JCH241025.

[4] BATTLE DE. Diagnostic and statistical manual of mental disorders (DSM)[J]. Codas, 2013, 25(2): 191-192. DOI: 10.1590/s2317-17822-013000200017.

[5] ZHANG Y, JIA XC, YANG YL, et al. Change in the global burden of depression from 1990-2019 and its prediction for 2030[J]. J Psychiatr Res, 2024, 178: 16-22. DOI: 10.1016/j.jpsychires.2024.07.054.

[6] BERGFELD IO, MANTIONE M, FIGEE M, et al. Treatment-resistant depression and suicidality[J]. J Affect Disord, 2018, 235: 362-367. DOI: 10.1016/j.jad.2018.04.016.

[7] PARK SJ, ROH S, HWANG J, et al. Association between depression and metabolic syndrome in Korean women: Results from the Korean national health and nutrition examination survey (2007-2013)[J]. J Affect Disord, 2016, 205: 393-399. DOI: 10.1016/j.jad.2016.08.022.

[8] WANG L, GUO JH, LU JP. Risk factor compositions of nonalcoholic fatty liver disease change with body mass index in males and females[J]. Oncotarget, 2016, 7(24): 35632-35642. DOI: 10.18632/oncotarget.9691.

[9] CHEN ZB, HUANG LY, WANG BY, et al. Research advances in the association between metabolic associated fatty liver and type 2 diabetes mellitus and the mechanism of comorbidity[J]. J Clin Hepatol, 2023, 39(10): 2454-2459. DOI: 10. 3969/j.issn.1001-5256.2023.10.025.
陈兆斌, 黄丽媛, 王炳元, 等. 代谢相关脂肪性肝病与2型糖尿病的关系及共病机制研究进展[J]. 临床肝胆病杂志, 2023, 39(10): 2454-2459. DOI: 10. 3969/j.issn.1001-5256.2023.10.025.

[10] GOLDBACHER EM, BROMBERGER J, MATTHEWS KA. Lifetime history of major depression predicts the development of the metabolic syndrome in middle-aged women[J]. Psychosom Med, 2009, 71(3): 266-272. DOI: 10.1097/PSY.0b013e318197a4d5.

[11] KINDER LS, CARNETHON MR, PALANIAPPAN LP, et al. Depression and the metabolic syndrome in young adults: Findings from the Third National Health and Nutrition Examination Survey[J]. Psychosom Med, 2004, 66(3): 316-322. DOI: 10.1097/01.psy.0000124755.91880.f4.

[12] RORIZ-CRUZ M, ROSSET I, WADA T, et al. Stroke-independent association between metabolic syndrome and functional dependence, depression, and low quality of life in elderly community-dwelling Brazilian people [J]. J Am Geriatr Soc, 2007, 55(3): 374-382. DOI: 10.1111/j.1532-5415.2007.01068.x.

[13] GARVEY WT, MECHANICK JI, BRETT EM, et al. American association of clinical endocrinologists and American college of endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity[J]. Endocr Pract, 2016, 22(Suppl 3): 1-203. DOI: 10.4158/EP1-61365.GL.

[14] SINGH MK, LESLIE SM, PACKER MM, et al. Brain and behavioral correlates of insulin resistance in youth with depression and obesity[J]. Horm Behav, 2019, 108: 73-83. DOI: 10.1016/j.yhbeh.2018.03.009.

[15] WATSON K, NASCA C, AASLY L, et al. Insulin resistance, an unmasked culprit in depressive disorders: Promises for interventions[J]. Neuropharmacology, 2018, 136(Pt B): 327-334. DOI: 10.1016/j.neuropharm.2017.11.038.

[16] LYRA E SILVA NM, LAM MP, SOARES CN, et al. Insulin resistance as a shared pathogenic mechanism between depression and type 2 diabetes [J]. Front Psychiatry, 2019, 10: 57. DOI: 10.3389/fpsyt.2019.00057.

[17] PAGE MJ, MCKENZIE JE, BOSSUYT PM, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews[J]. BMJ, 2021, 372: n71. DOI: 10.1136/bmj.n71.

[18] STANG A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses[J]. Eur J Epidemiol, 2010, 25(9): 603-605. DOI: 10.1007/s10654-010-9491-z.

[19] MAURICE J, MANOUSOU P. Non-alcoholic fatty liver disease[J]. Clin Med, 2018, 18(3): 245-250. DOI: 10.7861/clinmedicine.18-3-245.

[20] FRIEDRICH MJ. Depression is the leading cause of disability around the world[J]. JAMA, 2017, 317(15): 1517. DOI: 10.1001/jama.2017.3826.

[21] VIERA AJ. Odds ratios and risk ratios: What's the difference and why does it matter?[J]. South Med J, 2008, 101(7): 730-734. DOI: 10.1097/SMJ.0b013e31817a7ee4.

[22] CHOI JM, CHUNG GE, KANG SJ, et al. Association between anxiety and depression and nonalcoholic fatty liver disease[J]. Front Med (Lausanne), 2021, 7: 585618. DOI: 10.3389/fmed.2020.585618.

[23] ELWING JE, LUSTMAN PJ, WANG HL, et al. Depression, anxiety, and nonalcoholic steatohepatitis[J]. Psychosom Med, 2006, 68(4): 563-569. DOI: 10.1097/01.psy.0000221276.17823.df.

[24] FILIPOVIĆ B, MARKOVIĆ O, ĐURIĆ V, et al. Cognitive changes and brain volume reduction in patients with nonalcoholic fatty liver disease [J]. Can J Gastroenterol Hepatol, 2018, 2018: 9638797. DOI: 10.1155/2018/9638797.

[25] GOULART AC, BIANCHI LLT, BISMARCHI D, et al. Sex differences in the relationship between hepatic steatosis, mood and anxiety disorders [J]. J Psychosom Res, 2023, 168: 111216. DOI: 10.1016/j.jpsychores.2023.111216.
[26] JUNG JY, PARK SK, OH CM, et al. Non-alcoholic fatty liver disease and its association with depression in Korean general population[J]. J Korean Med Sci, 2019, 34(30): e199. DOI: 10.3346/jkms.2019.34.e199.
[27] LABENZ C, HUBER Y, MICHEL M, et al. Nonalcoholic fatty liver disease increases the risk of anxiety and depression[J]. Hepatol Commun, 2020, 4(9): 1293-1301. DOI: 10.1002/hep4.1541.
[28] LEE K, OTGONSUREN M, YOUNOSZAI Z, et al. Association of chronic liver disease with depression: A population-based study[J]. Psychosomatics, 2013, 54(1): 52-59. DOI: 10.1016/j.psym.2012.09.005.
[29] NG CH, XIAO JL, CHEW NWS, et al. Depression in non-alcoholic fatty liver disease is associated with an increased risk of complications and mortality[J]. Front Med (Lausanne), 2022, 9: 985803. DOI: 10.3389/fmed.2022.985803.
[30] NOON SL, D'ANNIBALE DA, SCHWIMMER MH, et al. Incidence of depression and anxiety in a cohort of adolescents with nonalcoholic fatty liver disease[J]. J Pediatr Gastroenterol Nutr, 2021, 72(4): 579-583. DOI: 10.1097/MPG.0000000000003024.
[31] YOUNOSSI ZM, YILMAZ Y, YU ML, et al. Clinical and patient-reported outcomes from patients with nonalcoholic fatty liver disease across the world: Data from the global non-alcoholic steatohepatitis (NASH)/non-alcoholic fatty liver disease (NAFLD) registry[J]. Clin Gastroenterol Hepatol, 2022, 20(10): 2296-2306.e6. DOI: 10.1016/j.cgh.2021.11.004.
[32] YOUSSEF NA, ABDELMALEK MF, BINKS M, et al. Associations of depression, anxiety and antidepressants with histological severity of nonalcoholic fatty liver disease[J]. Liver Int, 2013, 33(7): 1062-1070. DOI: 10.1111/liv.12165.
[33] YANG XY, CHANG J, YU D, et al. The correlation between depression and non-alcoholic fatty liver disease[J]. J Int Psychiatry, 2022, 49(5): 840-845. DOI: 10.13479/j.cnki.jip.2022.05.018.
杨旭瑶, 常江, 余荻, 等. 抑郁症与非酒精性脂肪性肝病的相关性分析[J]. 国际精神病学杂志, 2022, 49(5): 840-845. DOI: 10.13479/j.cnki.jip.2022.05.018.
[34] CAI HW, ZHANG R, ZHAO CH, et al. Associations of depression score with metabolic dysfunction-associated fatty liver disease and liver fibrosis [J]. J Affect Disord, 2023, 334: 332-336. DOI: 10.1016/j.jad.2023.04.093.
[35] CHO IY, CHANG Y, SUNG E, et al. Depression and increased risk of non-alcoholic fatty liver disease in individuals with obesity[J]. Epidemiol Psychiatr Sci, 2021, 30: e23. DOI: 10.1017/S204579602000116X.
[36] KAMARI N, FATEH HL, DARBANDI M, et al. Fatty liver index relationship with biomarkers and lifestyle: Result from RaNCD cohort study[J]. BMC Gastroenterol, 2023, 23(1): 172. DOI: 10.1186/s12876-023-02785-5.
[37] KIM D, YOO ER, LI AA, et al. Depression is associated with non-alcoholic fatty liver disease among adults in the United States[J]. Aliment Pharmacol Ther, 2019, 50(5): 590-598. DOI: 10.1111/apt.15395.
[38] LEE JW, PARK SH. Association between depression and nonalcoholic fatty liver disease: Contributions of insulin resistance and inflammation [J]. J Affect Disord, 2021, 278: 259-263. DOI: 10.1016/j.jad.2020.09.073.
[39] LIAO Q, ZHENG Y, LIU XF, et al. Correlation of non-alcoholic fatty liver disease and depression in an elderly Chinese population[J]. J Third Mil Med Univ, 2017, 39(19): 1954-1959. DOI: 10.16016/j.1000-5404.2017-04136.
廖倩, 郑怡, 刘羞菲, 等. 中老年人群非酒精性脂肪肝与抑郁症的相关性研究[J]. 第三军医大学学报, 2017, 39(19): 1954-1959. DOI: 10.16016/j.1000-5404.201704136.
[40] KAČAVENDA-BABOVIĆ D, ĐURIĆ P, BABOVIĆ R, et al. Depression, anxiety and quality of life in patients with chronic hepatitis c virus infection in Vojvodina[J]. Acta Clin Croat, 2021, 60(4): 579-589. DOI: 10.20471/acc.2021.60.04.03.
[41] LI SD, LI SL, DUAN F, et al. Depression and NAFLD risk: A meta-analysis and Mendelian randomization study[J]. J Affect Disord, 2024, 352: 379-385. DOI: 10.1016/j.jad.2024.02.074.
[42] LIANG YJ, ZOU LL, TIAN YL, et al. Dietary and metabolic risk of neuropsychiatric disorders: Insights from animal models[J]. Br J Nutr, 2021, 126(12): 1771-1787. DOI: 10.1017/S0007114521000659.
[43] LUPPINO FS, DE WIT LM, BOUVY PF, et al. Overweight, obesity, and depression: A systematic review and meta-analysis of longitudinal studies[J]. Arch Gen Psychiatry, 2010, 67(3): 220-229. DOI: 10.1001/archgenpsychiatry.2010.2.
[44] LI W, LIU JY, CAI JJ, et al. NAFLD as a continuous driver in the whole spectrum of vascular disease[J]. J Mol Cell Cardiol, 2022, 163: 118-132. DOI: 10.1016/j.yjmcc.2021.10.007.
[45] CHAN KL, CATHOMAS F, RUSSO SJ. Central and peripheral inflammation link metabolic syndrome and major depressive disorder[J]. Physiology (Bethesda), 2019, 34(2): 123-133. DOI: 10.1152/physiol.00047.2018.
[46] MARRIE RA, WALLD R, BOLTON JM, et al. Psychiatric comorbidity increases mortality in immune-mediated inflammatory diseases[J]. Gen Hosp Psychiatry, 2018, 53: 65-72. DOI: 10.1016/j.genhosppsych.2018.06.001.
[47] van der FELTZ-CORNELIS CM, VAN OS J, KNAPPE S, et al. Towards Horizon 2020: Challenges and advances for clinical mental health research-outcome of an expert survey[J]. Neuropsychiatr Dis Treat, 2014, 10: 1057-1068. DOI: 10.2147/NDT.S59958.
[48] SOTO-ANGONA Ó, ANMELLA G, VALDÉS-FLORIDO MJ, et al. Non-alcoholic fatty liver disease (NAFLD) as a neglected metabolic companion of psychiatric disorders: Common pathways and future approaches [J]. BMC Med, 2020, 18(1): 261. DOI: 10.1186/s12916-020-01713-8.
[49] GHANEI GHESHLAGH R, PARIZAD N, SAYEHMIRI K. The relationship between depression and metabolic syndrome: Systematic review and meta-analysis study[J]. Iran Red Crescent Med J, 2016, 18(6): e26523. DOI: 10.5812/ircmj.26523.
[50] KONTTINEN H, SILVENTOINEN K, SARLIO-LÄHTEENKORVA S, et al. Emotional eating and physical activity self-efficacy as pathways in the association between depressive symptoms and adiposity indicators[J]. Am J Clin Nutr, 2010, 92(5): 1031-1039. DOI: 10.3945/ajcn.2010.29732.
[51] DAYABANDARA M, HANWELLA R, RATNATUNGA S, et al. Antipsychotic-associated weight gain: Management strategies and impact on treatment adherence[J]. Neuropsychiatr Dis Treat, 2017, 13: 2231-2241. DOI: 10.2147/NDT.S113099.
[52] GRACIOUS BL, BHATT R, POTTER C. Nonalcoholic fatty liver disease and fibrosis in youth taking psychotropic medications: Literature review, case reports, and management[J]. J Child Adolesc Psychopharmacol, 2015, 25(8): 602-610. DOI: 10.1089/cap.2015.0007.
[53] MOUZAKI M, YODOSHI T, ARCE-CLACHAR AC, et al. Psychotropic medications are associated with increased liver disease severity in pediatric nonalcoholic fatty liver disease[J]. J Pediatr Gastroenterol Nutr, 2019, 69(3): 339-343. DOI: 10.1097/MPG.0000000000002401.
[54] CARRIER P, DEBETTE-GRATIEN M, GIRARD M, et al. Liver illness and psychiatric patients[J]. Hepat Mon, 2016, 16(12): e41564. DOI: 10.5812/hepatmon.41564.
[55] MILLER AH, RAISON CL. The role of inflammation in depression: From evolutionary imperative to modern treatment target[J]. Nat Rev Immunol, 2016, 16(1): 22-34. DOI: 10.1038/nri.2015.5.

收稿日期：2024-12-15；**录用日期：**2025-01-16
本文编辑：邢翔宇

引证本文：LI SD, CAO SB, BA MY, et al. Association between non-alcoholic fatty liver disease and depression: A systematic review and Meta-analysis[J]. J Clin Hepatol, 2025, 41(9): 1795-1801.
李淑娣, 曹帅兵, 巴明玉, 等. 非酒精性脂肪性肝病与抑郁症关系的系统评价及Meta分析[J]. 临床肝胆病杂志, 2025, 41(9): 1795-1801.