Advances in Clinical Medicine 临床医学进展, 2026, 16(5), 292-300
Published Online May 2026 in Hans. https://www.hanspub.org/journal/acm
https://doi.org/10.12677/acm.2026.1651818

TyG-VAI与代谢功能障碍相关脂肪性肝病患病风险关系的研究进展

何秋霞，吴　蓉*

重庆医科大学附属第二医院消化内科，重庆

收稿日期：2026年4月7日；录用日期：2026年4月28日；发布日期：2026年5月7日

摘　要

代谢功能障碍相关脂肪性肝病(metabolic dysfunction-associated steatotic liver disease, MASLD)是目前最常见的慢性肝病之一，其患病率持续上升，并与2型糖尿病、心血管疾病、慢性肾脏病及肝细胞癌等多种不良结局密切相关。由于MASLD的发生发展与胰岛素抵抗、糖脂代谢紊乱、内脏脂肪堆积及脂肪组织功能异常密切相关，寻找简便、经济、稳定的无创指标，对疾病的早期识别和风险分层具有重要意义。甘油三酯－葡萄糖指数(triglyceride-glucose index, TyG)是反映胰岛素抵抗的常用替代指标，内脏脂肪指数(visceral adiposity index, VAI)主要用于反映内脏脂肪分布及脂肪组织功能异常。二者分别从糖脂代谢异常和内脏脂肪功能失衡两个方面反映MASLD的核心代谢特征。近年来，越来越多研究表明，TyG、VAI及其相关衍生指标与脂肪肝或MASLD风险密切相关，但单一指标对疾病复杂代谢背景的反映仍然有限。甘油三酯－葡萄糖－内脏脂肪指数(triglyceride glucose-visceral adiposity index, TyG-VAI)作为进一步整合胰岛素抵抗和内脏脂肪异常信息的复合指标，理论上可能更全面地反映MASLD的代谢特征，并在风险识别中具有潜在优势。本文对MASLD的代谢基础、TyG与VAI在脂肪肝风险评估中的研究进展，以及TyG-VAI用于MASLD风险评估的理论依据和潜在价值进行了综述，以期为后续相关研究和临床无创筛查提供参考。

关键词

代谢功能障碍相关脂肪性肝病，甘油三酯－葡萄糖指数，内脏脂肪指数，TyG-VAI

Research Progress on the Association of TyG-VAI with the Risk of Metabolic Dysfunction-Associated Steatotic Liver Disease

Qiuxia He, Rong Wu*

Department of Gastroenterology, The Second Affiliated Hospital of Chongqing Medical University, Chongqing

*通讯作者。

文章引用: 何秋霞, 吴蓉. TyG-VAI 与代谢功能障碍相关脂肪性肝病患病风险关系的研究进展[J]. 临床医学进展, 2026, 16(5): 292-300. DOI: 10.12677/acm.2026.1651818

Received: April 7, 2026; accepted: April 28, 2026; published: May 7, 2026

Abstract

Metabolic dysfunction-associated steatotic liver disease (MASLD) is one of the most common chronic liver diseases worldwide. Its prevalence continues to rise, and it is closely associated with multiple adverse outcomes, including type 2 diabetes, cardiovascular disease, chronic kidney disease, and hepatocellular carcinoma. Because the development of MASLD is closely linked to insulin resistance, disordered glucose and lipid metabolism, visceral fat accumulation, and adipose tissue dysfunction, the identification of simple, affordable, and reliable non-invasive indicators is of great importance for early detection and risk stratification. The triglyceride-glucose (TyG) index is widely used as a surrogate marker of insulin resistance, whereas the visceral adiposity index (VAI) is mainly used to reflect visceral fat distribution and adipose tissue dysfunction. These two indices capture key metabolic features of MASLD from the perspectives of glucose-lipid metabolic disturbance and visceral adipose dysfunction, respectively. In recent years, growing evidence has shown that TyG, VAI, and their related derivatives are closely associated with the risk of fatty liver disease or MASLD; however, single indicators may not fully reflect the complex metabolic background of the disease. As a composite index that further integrates information on insulin resistance and visceral adiposity abnormality, triglyceride glucose-visceral adiposity index (TyG-VAI) may provide a more comprehensive assessment of the metabolic characteristics of MASLD and may offer potential advantages in risk identification. This review summarizes the metabolic basis of MASLD, the research progress on TyG and VAI in fatty liver risk assessment, and the theoretical rationale and potential value of TyG-VAI in MASLD risk evaluation, with the aim of providing a reference for future studies and non-invasive clinical screening.

Keywords

Metabolic Dysfunction-Associated Steatotic Liver Disease, Triglyceride-Glucose Index, Visceral Adiposity Index, TyG-VAI

1. 引言

代谢功能障碍相关脂肪性肝病(metabolic dysfunction-associated steatotic liver disease, MASLD)是现在最常见的慢性肝病之一[1]。2023 年，多学会 Delphi 共识提出用 MASLD 代替过去的非酒精性脂肪性肝病(non-alcoholic fatty liver disease, NAFLD) [2]。这一变化更强调代谢异常在脂肪性肝病发生和发展中的重要作用，也让这种病的定义从过去的“排除性诊断”转向以代谢功能障碍为基础的诊断方式[3]。现有研究显示，MASLD 已影响全球 30%以上的成年人，并且和 2 型糖尿病、心血管疾病、慢性肾脏病、肝细胞癌等多种不良结局关系密切，已经成为一个重要的公共卫生问题[4]-[8]。

MASLD 不是由单一因素引起的，而是胰岛素抵抗、脂质代谢紊乱、内脏脂肪堆积、慢性低度炎症、氧化应激以及遗传和环境因素一起作用的结果[9]-[13]。在这个过程中，肝脏不只是脂质沉积的主要器官，也是全身代谢异常的重要反映部位[14]-[18]。所以，寻找简单、便宜、可重复、适合大样本人群筛查的代谢指标，对 MASLD 的早期识别和风险分层很重要。

甘油三酯－葡萄糖指数(triglyceride-glucose index, TyG)由空腹血糖和甘油三酯组成，已经被广泛用作胰岛素抵抗的替代指标[19]-[21]。内脏脂肪指数(visceral adiposity index, VAI)则把体重指数、腰围、甘油三酯和高密度脂蛋白胆固醇放在一起，主要用来反映内脏脂肪分布和脂肪组织功能异常[22] [23]。两者分别从糖脂代谢异常和内脏脂肪功能失衡两个方面反映 MASLD 的核心代谢特点。在这个基础上，甘油三酯－葡萄糖－内脏脂肪指数(triglyceride glucose-visceral adiposity index, TyG-VAI)作为一个进一步整合胰岛素抵抗和内脏脂肪异常信息的复合指标，具有较强的理论基础，可能比单一指标更接近 MASLD 的病理生理本质。

2. MASLD 的代谢本质与无创风险评估需求

MASLD 的核心病理基础是在代谢功能障碍背景下出现的肝细胞脂质沉积[9] [24]。胰岛素抵抗会促进脂肪组织脂解，使大量游离脂肪酸进入肝脏。同时，肝脏脂质从头合成增加，而脂肪酸氧化和输出能力下降，最后造成肝脂肪堆积[25]-[27]。随着病情发展，单纯脂肪变性还可以进一步发展为脂肪性肝炎、纤维化、肝硬化，甚至肝细胞癌[28]-[31]。正因为这样，围绕胰岛素抵抗和脂肪分布建立无创风险评估指标，已经成为 MASLD 研究的重要方向。

目前，肝活检仍然是评估脂肪性肝炎和纤维化的参考标准，但它有创伤性，患者依从性也较差，不适合一般人群筛查。影像学方法虽然更实用，但在设备可及性、成本和检测一致性方面仍然有一些限制。所以，基于常规体检和实验室检查数据建立无创代谢指标，对基层筛查和大规模流行病学研究尤其重要。TyG 和 VAI 都有计算简单、数据容易获得、成本较低等优点，因此在脂肪肝相关研究中受到广泛关注

3. TyG 指数与 MASLD/脂肪肝风险的研究进展

TyG 指数最早由 Simental-Mendía 等提出，用来识别胰岛素抵抗。这个指标只需要空腹血糖和甘油三酯两个参数，计算简单，而且和经典胰岛素抵抗指标有较好的一致性[32]。随着研究不断增加，TyG 已经广泛应用于代谢综合征、糖尿病、心血管疾病和脂肪肝等多个领域[33]-[36]。

现有证据显示，TyG 和脂肪肝风险之间存在稳定的正相关关系。Kitae 等在日本人群中做的一项队列研究纳入了 16,093 名表面健康成年人，结果发现，较高的 TyG 水平和新发 NAFLD 风险明显升高有关，而且这种关系在男性和女性中都存在[37]。这个研究提示，TyG 不只和脂肪肝患病状态有关，也和脂肪肝发生风险密切相关。

后续的系统评价和 Meta 分析进一步支持了这一结果。Beran 等纳入 17 项观察性研究、共 121,975 名受试者后发现，不管把 TyG 作为分类变量还是连续变量分析，它的升高都和 NAFLD 风险增加明显相关[38]。Ling 等的剂量－反应 Meta 分析进一步显示，TyG 每增加 1 个单位，NAFLD 风险明显上升，而且这种关系整体上呈线性趋势[36]。还有系统评价提示，TyG 在代谢相关脂肪性肝病(metabolic associated fatty liver disease, MAFLD)和 MASLD 的诊断和预测中有中等偏上的准确性，合并 AUC 约为 0.75 [39]。

从机制上看，TyG 和 MASLD 关系密切，主要是因为它能较好反映胰岛素抵抗这一 MASLD 的核心病理环节。空腹血糖升高提示葡萄糖代谢失衡，甘油三酯升高提示脂质代谢异常[40]-[42]。这两个指标一起升高，通常说明机体已经处于明显的代谢紊乱状态，而这正是肝脏脂质沉积和炎症激活的重要基础[43]-[46]。所以，TyG 可以看作一个既有代谢敏感性、又有临床实用性的早期风险指标。

不过，TyG 也有一定局限。它主要反映糖脂代谢异常和胰岛素抵抗状态，但对脂肪分布，尤其是内脏脂肪功能异常的反映还不够[40] [47] [48]。MASLD 的发生不只和代谢紊乱有关，也和内脏脂肪堆积及脂肪组织功能失衡密切相关，所以单独使用 TyG 可能难以完整反映疾病的代谢全貌[41] [42] [46] [49]。

4. VAI 与 MASLD/脂肪肝风险的研究进展

VAI 由 Amato 等于 2010 年提出，目的是通过腰围、体重指数(body mass index, BMI)、甘油三酯(triglyceride, TG)和高密度脂蛋白胆固醇(high-density lipoprotein cholesterol, HDL-C)间接反映内脏脂肪功能[50]-[53]。和单纯 BMI 或腰围相比，VAI 的优点在于同时纳入了人体测量指标和血脂信息，所以它不只反映脂肪负荷，也在一定程度上反映脂肪组织功能状态[54] [55]。

关于 VAI 和脂肪肝风险的研究也比较充分。Xu 等开展的前瞻性研究显示，较高的 VAI 水平是新发 NAFLD 的独立危险因素，而且存在比较清楚的剂量–反应关系[56]。随着基线 VAI 四分位数升高，后续发生 NAFLD 的风险逐步增加，这提示 VAI 能较好反映未来脂肪肝发生的倾向。

系统评价和 Meta 分析也支持这一结论。Ismaiel 等纳入 24 项研究后发现，VAI 在成人 NAFLD 和非酒精性脂肪性肝炎(non-alcoholic steatohepatitis, NASH)患者中明显升高，对 NAFLD 和 NASH 都有一定预测价值，合并 AUC 分别约为 0.767 和 0.732 [57]。也就是说，VAI 在脂肪肝识别方面有中等以上的诊断效能。

VAI 和 MASLD 关系密切，主要是因为内脏脂肪在 MASLD 发病中有关键作用。内脏脂肪不是单纯的储能组织，而是一个有活跃内分泌和炎症调节功能的代谢器官。它分泌的游离脂肪酸、炎症因子和脂肪因子可以通过门静脉直接进入肝脏，进而影响肝细胞脂质代谢、炎症反应和胰岛素敏感性[17] [58]-[61]。所以，VAI 升高本质上提示的是一种更高风险的脂肪分布模式和脂肪组织功能异常状态。

但 VAI 也不是没有不足。它的计算里已经包括 TG 和 HDL-C，所以在一定程度上容易受到血脂状态影响。同时，VAI 更强调脂肪分布和脂肪功能，对高血糖和胰岛素抵抗本身的直接反映不如 TyG 敏感。也就是说，VAI 更偏向脂肪组织这一方面，而不是糖脂代谢这一方面[23] [62]-[64]。

5. TyG-VAI 的理论基础及其在 MASLD 风险评估中的潜在优势

TyG 能较好反映胰岛素抵抗和糖脂代谢异常，VAI 则更能反映内脏脂肪负荷和脂肪组织功能紊乱[20] [46] [58] [65]。两者结合后，理论上比单独使用任何一个指标都更能全面反映 MASLD 的核心代谢背景。

近几年，越来越多研究开始关注 TyG 的衍生指标，比如甘油三酯–葡萄糖–体重指数(TyG-BMI)、甘油三酯–葡萄糖–腰围指数(TyG-WC)等。这些研究表现出比较一致的趋势，即将 TyG 与肥胖或脂肪分布指标结合后，对脂肪肝的识别能力优于单一 TyG [40] [66]。2025 年一项研究在比较多种 TyG 相关指标后发现，TyG-BMI 在识别 MASLD 方面的表现优于 TyG、VAI 和肝脂肪变性指数(hepatic steatosis index, HSI)等传统指标[40]。另有 2024 年研究在墨西哥人群中比较 16 种生物标志物后指出，TyG-WC 的诊断表现最好[67]。虽然这些研究并不直接等同于 TyG-VAI，但它们共同提示，“TyG+脂肪分布/肥胖信息”的联合建模可能是提高 MASLD 风险识别能力的重要方向。

和 TyG-BMI 或 TyG-WC 相比，TyG-VAI 的潜在优势在于，VAI 不是简单的体型指标，而是同时纳入了腰围、BMI、TG 和 HDL-C，更强调内脏脂肪功能状态[42] [49]。所以，TyG-VAI 可能不只整合了糖脂代谢异常信息，也整合了脂肪组织功能失衡信息，从而更接近 MASLD 的“代谢–脂肪”双通路特征。对于 BMI 并不明显升高、但已经存在明显内脏脂肪异常或代谢失衡的人群，TyG-VAI 可能有更高的敏感性。

然而，到目前为止，直接把 TyG-VAI 作为核心暴露指标用于 MASLD 的研究仍然比较少，特别是基于统一 MASLD 定义的高质量人群研究还不够。因此，未来需要在大规模、具有人群代表性的样本中进一步验证 TyG-VAI 与 MASLD 风险之间的独立关联、剂量–反应关系及潜在阈值效应，并明确不同人群中的适宜截断值。以 TyG-VAI 为例，TyG 由空腹血糖与 TG 计算得出，VAI 则包含 TG、HDL-C、BMI

及腰围，二者均涉及 TG。若将 TyG 与 VAI 直接纳入多因素回归模型，TG 的重复出现可能导致估计系数的方差膨胀(即共线性)，降低统计效能并增加假阴性风险。此外，若复合指标的权重或组合方式基于特定探索性数据集确定，则存在过拟合风险，即在推导队列中表现优异，但在外部验证队列中效能下降。

针对上述问题，可采用以下解决策略。在共线性处理方面，可采用方差膨胀因子(VIF)进行诊断，通常认为 VIF > 5 或 10 提示存在显著共线性，此时可考虑对变量进行中心化、主成分提取或采用正则化回归(如 Lasso 回归)。Lasso 回归通过引入 L1 惩罚项，可将部分变量系数压缩至零，从而实现变量筛选并缓解过拟合。在模型验证方面，应优先采用交叉验证或独立外部队列验证，以评估复合指标的可泛化性。

与常见的 TyG 衍生指标(如 TyG-BMI)相比，TyG-VAI 在理论上可能具有更低的信息冗余和更高的病理生理针对性。TyG-BMI 虽计算简便，但 BMI 作为总肥胖指标无法区分皮下脂肪与内脏脂肪，且与 TyG 中的代谢信息(尤其是 TG)可能存在较强的线性相关性，共线性风险较高[40]。相比之下，VAI 通过纳入腰围(反映中心性肥胖)和 HDL-C (反映脂代谢功能)，更精准地指向“功能失调的内脏脂肪”这一 MASLD 关键驱动因素。因此，TyG-VAI 的组分分工更为清晰：TyG 侧重胰岛素抵抗驱动的糖脂代谢紊乱，VAI 侧重内脏脂肪分布与功能异常，二者在生物学意义上互补大于重叠，理论上共线性程度较低。当然，这一理论优势仍需通过实证研究(如计算 VIF、比较不同复合指标的 AUC 及净重分类改善指数)予以验证。

6. 现有研究的不足与本研究的意义

虽然 TyG 和 VAI 分别和脂肪肝/MASLD 风险关系密切，但现有证据仍有几个明显不足。多数研究沿用 NAFLD 或 MAFLD 旧定义，与新 MASLD 框架存在差异；横断面研究居多，前瞻性证据有限；不同人群中截断值异质性大；直接针对 TyG-VAI 的研究匮乏。基于上述局限，未来研究可优先围绕以下具体问题展开：

第一，针对跨种族、跨人群的最佳截断值验证与校准。不同种族、人群的体脂分布、代谢特征及 MASLD 患病率存在显著差异。如，亚洲人群常表现为正常体重代谢性肥胖，即 BMI 正常但已存在内脏脂肪堆积，其 TyG-VAI 的适宜筛查阈值可能低于美国人群。未来需在东亚、欧洲、拉美等不同人群中开展多中心横断面研究，采用统一的 MASLD 诊断标准，通过约登指数确定各人群的最佳截断值，并采用 DeLong 检验比较 TyG-VAI 与 TyG-BMI、VAI、FLI 等指标的 AUC 差异，同时计算净重分类改善指数(NRI)和综合判别改善指数(IDI)以评估其增量预测价值。

第二，在大型前瞻性队列中评估 TyG-VAI 对 MASLD 远期结局的预测能力。当前证据多为横断面关联分析，TyG-VAI 能否独立预测 MASLD 的疾病进展尚不清楚。未来应利用已建立的大规模前瞻性队列(如 UK Biobank、开滦研究、Rotterdam 研究等)，检验基线 TyG-VAI 水平与 MASLD 患者远期发生显著肝纤维化($F \geq 2$)、肝硬化失代偿、肝细胞癌及主要心血管不良事件之间的关联。可采用时间依赖的 ROC 曲线和 Cox 比例风险模型，评估 TyG-VAI 在传统危险因素(年龄、性别、血压、血糖、血脂等)基础上的增量预测价值，并通过决策曲线分析(DCA)评估其临床净获益。

第三，借助孟德尔随机化等方法探究 TyG-VAI 与 MASLD 之间的因果关系。观察性研究难以完全排除残余混杂和反向因果偏倚。未来可采用两样本孟德尔随机化(two-sample MR)设计，筛选与 TyG 组分(空腹血糖、TG)和 VAI 组分(腰围、HDL-C)相关的独立遗传变异作为工具变量，评估 TyG-VAI 所代表的“胰岛素抵抗–内脏脂肪功能异常”联合表型与 MASLD 风险之间是否存在因果关联[44]。若 MR 分析结果与观察性研究一致，将为 TyG-VAI 作为 MASLD 风险因子的临床推广提供更高级别的证据支持。此外，可进一步采用非线性孟德尔随机化方法探索是否存在阈值效应，以验证观察性研究中发现的拐点是否具有因果解释。

第四，评估 TyG-VAI 与 MASLD 之间是否存在关联及其可能的剂量–反应模式。当前关于 TyG-VAI

与 MASLD 的研究尚处于起步阶段，二者之间是否存在独立关联，以及如果存在，该关联呈现何种剂量–反应模式(线性或非线性)，均有待阐明。TyG 指数和 VAI 均被证实与 MASLD 风险存在显著正相关[36] [56]。考虑到胰岛素抵抗与内脏脂肪功能异常是 MASLD 的两大核心驱动因素，且二者之间存在复杂的交互作用[26] [28]，TyG-VAI 与 MASLD 之间的关联可能并非简单的线性关系。因此，未来研究应首先采用多因素回归分析验证二者之间的独立关联，在此基础上进一步采用限制性立方样条、分段回归及阈值效应分析等方法，评估是否存在非线性剂量–反应关系，并探索潜在的拐点。若非线性关系得以确认，则需进一步从脂肪组织扩增能力、肝脏脂质储存饱和阈值及胰岛素抵抗代偿机制等角度探讨其生物学基础。

参考文献

[1] Zhao, J., Liu, L., Cao, Y., Gao, X., Targher, G., Byrne, C.D., *et al*. (2024) MAFLD as Part of Systemic Metabolic Dysregulation. *Hepatology International*, **18**, 834-847. https://doi.org/10.1007/s12072-024-10660-y

[2] Rinella, M.E. and Sookoian, S. (2024) From NAFLD to MASLD: Updated Naming and Diagnosis Criteria for Fatty Liver Disease. *Journal of Lipid Research*, **65**, Article ID: 100485. https://doi.org/10.1016/j.jlr.2023.100485

[3] Lu, Z., Shao, W. and Song, J. (2024) The Transition from NAFLD to MASLD and Its Impact on Clinical Practice and Outcomes. *Journal of Hepatology*, **81**, e155-e156. https://doi.org/10.1016/j.jhep.2024.02.021

[4] Das, S., Agarwal, K., Kapoor, N., Lakhani, O.J. and Das Gupta, A. (2025) Emerging Concepts in the Diagnosis and Management of Metabolically Associated Steatotic Liver Disease. *Current Opinion in Endocrinology, Diabetes & Obesity*, **32**, 269-278. https://doi.org/10.1097/med.0000000000000935

[5] Bilson, J., Mantovani, A., Byrne, C.D. and Targher, G. (2024) Steatotic Liver Disease, MASLD and Risk of Chronic Kidney Disease. *Diabetes & Metabolism*, **50**, Article ID: 101506. https://doi.org/10.1016/j.diabet.2023.101506

[6] Kim, G., Moon, J.H. and Kim, W. (2023) Critical Appraisal of Metabolic Dysfunction-Associated Steatotic Liver Disease: Implication of Janus-Faced Modernity. *Clinical and Molecular Hepatology*, **29**, 831-843. https://doi.org/10.3350/cmh.2023.0277

[7] Portincasa, P. and Baffy, G. (2024) Metabolic Dysfunction-Associated Steatotic Liver Disease: Evolution of the Final Terminology. *European Journal of Internal Medicine*, **124**, 35-39. https://doi.org/10.1016/j.ejim.2024.04.013

[8] Targher, G., Byrne, C.D. and Tilg, H. (2024) MASLD: A Systemic Metabolic Disorder with Cardiovascular and Malignant Complications. *Gut*, **73**, 691-702. https://doi.org/10.1136/gutjnl-2023-330595

[9] Basil, B., Myke-Mbata, B.K., Eze, O.E. and Akubue, A.U. (2024) From Adiposity to Steatosis: Metabolic Dysfunction-Associated Steatotic Liver Disease, a Hepatic Expression of Metabolic Syndrome—Current Insights and Future Directions. *Clinical Diabetes and Endocrinology*, **10**, Article No. 39. https://doi.org/10.1186/s40842-024-00187-4

[10] Chen, H., Chen, Z., Bai, X., Li, Z., Huang, S., Lu, D., *et al*. (2025) Metabolic and Hepatic Biomarkers Associated with MASLD in the Chinese Population. *Scientific Reports*, **15**, Article No. 31593. https://doi.org/10.1038/s41598-025-17219-3

[11] Chen, H., Zhang, J., Chen, X., Luo, L., Dong, W., Wang, Y., *et al*. (2025) Development and Validation of Machine Learning Models for MASLD: Based on Multiple Potential Screening Indicators. *Frontiers in Endocrinology*, **15**, Article 1449064. https://doi.org/10.3389/fendo.2024.1449064

[12] Feng, G., Targher, G., Byrne, C.D., He, N., Mi, M., Liu, Y., *et al*. (2025) Biomarker Discovery for Metabolic Dysfunction-Associated Steatotic Liver Disease Utilizing Mendelian Randomization, Machine Learning, and External Validation. *Journal of Clinical and Translational Hepatology*, **13**, 723-733. https://doi.org/10.14218/jcth.2025.00270

[13] Iwaszko-Sochal, K., Kasztelan-Szczerbińska, B. and Cichoż-Lach, H. (2025) Is There a Diagnostic Miracle on the Horizon? Emerging Biomarkers in MASLD. *Journal of Clinical Medicine*, **14**, Article 6148. https://doi.org/10.3390/jcm14176148

[14] Jain, P., Jain, A., Deshmukh, R., Samal, P., Satapathy, T. and Ajazuddin, (2025) Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD): Exploring Systemic Impacts and Innovative Therapies. *Clinics and Research in Hepatology and Gastroenterology*, **49**, Article ID: 102584. https://doi.org/10.1016/j.clinre.2025.102584

[15] Liu, X., Yin, S., Chen, Y. and Lee, M. (2025) Metabolic Dysfunction-Associated Steatotic Liver Disease and Its Associated Health Risks. *Journal of the Chinese Medical Association*, **88**, 343-351. https://doi.org/10.1097/jcma.0000000000001230

[16] Naja, K., Anwardeen, N. and Elrayess, M.A. (2025) Metabolomic Signatures of MASLD Identified by the Fatty Liver Index Reveal Gamma-Glutamyl Cycle Disruption and Lipid Remodeling. *Metabolites*, **15**, Article 687. https://doi.org/10.3390/metabo15110687

[17] Bharaj, I.S., Brar, A.S., Kahlon, J., Singh, A., Hotwani, P., Kumar, V., *et al*. (2025) Metabolic-Dysfunction Associated Steatotic Liver Disease and Atrial Fibrillation: A Review of Pathogenesis. *World Journal of Cardiology*, **17**, Article ID: 106147. https://doi.org/10.4330/wjc.v17.i6.106147

[18] Zou, H., Ma, X., Pan, W. and Xie, Y. (2025) The Association of the Metabolic Score for Insulin Resistance and Metabolic Dysfunction-Related Steatosis Liver Disease: A Population-Based Observational Study. *European Journal of Medical Research*, **30**, Article No. 657. https://doi.org/10.1186/s40001-025-02936-2

[19] Er, L., Wu, S., Chou, H., Hsu, L., Teng, M., Sun, Y., *et al*. (2016) Triglyceride Glucose-Body Mass Index Is a Simple and Clinically Useful Surrogate Marker for Insulin Resistance in Nondiabetic Individuals. *PLOS ONE*, **11**, e0149731. https://doi.org/10.1371/journal.pone.0149731

[20] Gao, X., Chen, T., Zhou, F., Sun, Y., Zhang, J., Li, X., *et al*. (2025) The Association between Different Insulin Resistance Surrogates and All-Cause Mortality and Cardiovascular Mortality in Patients with Metabolic Dysfunction-Associated Steatotic Liver Disease. *Cardiovascular Diabetology*, **24**, Article No. 200. https://doi.org/10.1186/s12933-025-02758-w

[21] Kurniawan, L.B. (2024) Triglyceride-Glucose Index as a Biomarker of Insulin Resistance, Diabetes Mellitus, Metabolic Syndrome, and Cardiovascular Disease: A Review. *EJIFCC*, **35**, 44-51.

[22] Lee, J., Kim, B., Kim, W., Ahn, C., Choi, H.Y., Kim, J.G., *et al*. (2021) Lipid Indices as Simple and Clinically Useful Surrogate Markers for Insulin Resistance in the U.S. Population. *Scientific Reports*, **11**, Article No. 2366. https://doi.org/10.1038/s41598-021-82053-2

[23] Mazidi, M., Kengne, A., Katsiki, N., Mikhailidis, D.P. and Banach, M. (2018) Lipid Accumulation Product and Triglycerides/Glucose Index Are Useful Predictors of Insulin Resistance. *Journal of Diabetes and Its Complications*, **32**, 266-270. https://doi.org/10.1016/j.jdiacomp.2017.10.007

[24] Alpízar Salazar, M., Olguín Reyes, S.E., Medina Estévez, A., Saturno Lobos, J.A., De Aldecoa Castillo, J.M., Carrera Aguas, J.C., *et al*. (2025) Natural History of Metabolic Dysfunction-Associated Steatotic Liver Disease: From Metabolic Syndrome to Hepatocellular Carcinoma. *Medicina*, **61**, Article 88. https://doi.org/10.3390/medicina61010088

[25] Feng, X., Zhang, R., Yang, Z., Zhang, K. and Xing, J. (2024) Mechanism of Metabolic Dysfunction-Associated Steatotic Liver Disease: Important Role of Lipid Metabolism. *Journal of Clinical and Translational Hepatology*, **12**, 815-826. https://doi.org/10.14218/jcth.2024.00019

[26] Kuchay, M.S., Choudhary, N.S. and Ramos-Molina, B. (2025) Pathophysiological Underpinnings of Metabolic Dysfunction-Associated Steatotic Liver Disease. *American Journal of Physiology-Cell Physiology*, **328**, C1637-C1666. https://doi.org/10.1152/ajpcell.00951.2024

[27] Lee, W., Kipp, Z.A., Bates, E.A., Pauss, S.N., Martinez, G.J. and Hinds, T.D. (2025) The Physiology of MASLD: Molecular Pathways between Liver and Adipose Tissues. *Clinical Science*, **139**, 1015-1046. https://doi.org/10.1042/cs20257571

[28] Steinberg, G.R., Valvano, C.M., De Nardo, W. and Watt, M.J. (2025) Integrative Metabolism in MASLD and MASH: Pathophysiology and Emerging Mechanisms. *Journal of Hepatology*, **83**, 584-595. https://doi.org/10.1016/j.jhep.2025.02.033

[29] Samanta, A. and Sen Sarma, M. (2024) Metabolic Dysfunction-Associated Steatotic Liver Disease: A Silent Pandemic. *World Journal of Hepatology*, **16**, 511-516. https://doi.org/10.4254/wjh.v16.i4.511

[30] Truong, X.T. and Lee, D.H. (2025) Hepatic Insulin Resistance and Steatosis in Metabolic Dysfunction-Associated Steatotic Liver Disease: New Insights into Mechanisms and Clinical Implications. *Diabetes & Metabolism Journal*, **49**, 964-986. https://doi.org/10.4093/dmj.2025.0644

[31] Wang, S., Yin, J., Liu, Z., Liu, X., Tian, G., Xin, X., *et al*. (2024) Metabolic Disorders, Inter-Organ Crosstalk, and Inflammation in the Progression of Metabolic Dysfunction-Associated Steatotic Liver Disease. *Life Sciences*, **359**, Article ID: 123211. https://doi.org/10.1016/j.lfs.2024.123211

[32] Simental-Mendía, L.E., Rodríguez-Morán, M. and Guerrero-Romero, F. (2008) The Product of Fasting Glucose and Triglycerides as Surrogate for Identifying Insulin Resistance in Apparently Healthy Subjects. *Metabolic Syndrome and Related Disorders*, **6**, 299-304. https://doi.org/10.1089/met.2008.0034

[33] Cao, T., Ni, X., Halengbieke, A., Tang, J., Han, Y., Sun, F., *et al*. (2025) Effects of the Triglyceride-Glucose Index on Non-Alcoholic Fatty Liver Disease: Causal Evidence from Longitudinal Cohort Studies. *Archives of Gerontology and Geriatrics*, **133**, Article ID: 105813. https://doi.org/10.1016/j.archger.2025.105813

[34] Correa, T.L., Guelli, M.S.T.C. and de Oliveira, I.O. (2021) Triglyceride-glucose Index (tyg) Is Positively Associated with Nonalcoholic Fatty Liver Disease. *American Heart Journal*, **242**, 158-159. https://doi.org/10.1016/j.ahj.2021.10.035

[35] Lee, S.B., Kim, M.K., Kang, S., Park, K., Kim, J.H., Baik, S.J., *et al*. (2019) Triglyceride Glucose Index Is Superior to the Homeostasis Model Assessment of Insulin Resistance for Predicting Nonalcoholic Fatty Liver Disease in Korean Adults. *Endocrinology and Metabolism*, **34**, 179-186. https://doi.org/10.3803/enm.2019.34.2.179

[36] Ling, Q., Chen, J., Liu, X., Xu, Y., Ma, J., Yu, P., *et al*. (2023) The Triglyceride and Glucose Index and Risk of Nonalcoholic Fatty Liver Disease: A Dose-Response Meta-Analysis. *Frontiers in Endocrinology*, **13**, Article 1043169. https://doi.org/10.3389/fendo.2022.1043169

[37] Kitae, A., Hashimoto, Y., Hamaguchi, M., Obora, A., Kojima, T. and Fukui, M. (2019) The Triglyceride and Glucose Index Is a Predictor of Incident Nonalcoholic Fatty Liver Disease: A Population-Based Cohort Study. *Canadian Journal of Gastroenterology and Hepatology*, **2019**, Article ID: 5121574. https://doi.org/10.1155/2019/5121574

[38] Beran, A., Ayesh, H., Mhanna, M., Wahood, W., Ghazaleh, S., Abuhelwa, Z., *et al*. (2022) Triglyceride-Glucose Index for Early Prediction of Nonalcoholic Fatty Liver Disease: A Meta-Analysis of 121,975 Individuals. *Journal of Clinical Medicine*, **11**, Article 2666. https://doi.org/10.3390/jcm11092666

[39] Wang, J., Yan, S., Cui, Y., Chen, F., Piao, M. and Cui, W. (2022) The Diagnostic and Prognostic Value of the Triglyceride-Glucose Index in Metabolic Dysfunction-Associated Fatty Liver Disease (MAFLD): A Systematic Review and Meta-Analysis. *Nutrients*, **14**, Article 4969. https://doi.org/10.3390/nu14234969

[40] Boushehri, Y.G., Meymanatabadi, Z., Tanha, A.E., Azami, P., Alaei, M., Alamdari, A.A., *et al*. (2025) Association of Triglyceride Glucose-Body Mass Index (TyG-BMI) with Metabolic Dysfunction-Associated Steatotic Liver Disease: A Systematic Review and Meta-Analysis. *PLOS One*, **20**, e0324483. https://doi.org/10.1371/journal.pone.0324483

[41] Mondal, S., Pattnaik, S.S., Mohanty, N.R., Nayak, S., Mohanty, A. and Patro, S. (2026) Association of the Triglyceride-Glucose Index with Established Cardiovascular Disease in Adults with Metabolic Dysfunction-Associated Steatotic Liver Disease: A Cross-Sectional Study. *Cureus*, **18**, e103062. https://doi.org/10.7759/cureus.103062

[42] Qiao, Y., Wang, Y., Chen, C., Huang, Y. and Zhao, C. (2025) Association between Triglyceride-Glucose (TyG) Related Indices and Cardiovascular Diseases and Mortality among Individuals with Metabolic Dysfunction-Associated Steatotic Liver Disease: A Cohort Study of UK Biobank. *Cardiovascular Diabetology*, **24**, Article No. 12. https://doi.org/10.1186/s12933-024-02572-w

[43] Su, Z., Xue, J., Sun, J., Ding, Y. and Ji, C. (2025) Triglyceride Glucose Index as a Causal Risk Factor for Metabolic Dysfunction-Associated Fatty Liver Disease: Evidence from the National Health and Nutrition Examination Survey 2017-2020 and Mendelian Randomization. *European Journal of Gastroenterology & Hepatology*, **37**, 1292-1301. https://doi.org/10.1097/meg.0000000000003033

[44] Wei, S., He, L., Zhang, Y., Li, X., Zhong, S., Xiao, L., *et al*. (2025) Decoding the Triglyceride-Glucose Index in Metabolic Dysfunction-Associated Steatotic Liver Disease: Integrative Insights from Mendelian Randomization, Cross-Tissue Transcriptomics, and Spatial Multi-omics. *International Journal of Surgery*, **112**, 94-109. https://doi.org/10.1097/js9.0000000000003576

[45] Xiao, W., Sun, X., Lv, H., Liu, X. and Zhu, J. (2025) Association of Lipid and Blood Glucose Profiles with MASLD among Young Adults. *Diabetes, Metabolic Syndrome and Obesity*, **18**, 4009-4019. https://doi.org/10.2147/dmso.s547717

[46] Yilmaz, Y., Saeedian, B., Babajani, N., Ashtari, S., Ghorat, F. and Taheri, E. (2025) Novel Surrogate Markers of Insulin Resistance in Patients with Metabolic Dysfunction-Associated Steatosis Liver Disease: Associations with Dietary and Lifestyle Inflammatory Scores in the Large Cross-Sectional Study. *Clinical Nutrition ESPEN*, **70**, 204-217. https://doi.org/10.1016/j.clnesp.2025.09.021

[47] Abdallah, H., Khalil, M., Awada, E., Lanza, E., Di Ciaula, A. and Portincasa, P. (2025) Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). Assessing Metabolic Dysfunction, Cardiovascular Risk Factors, and Lifestyle Habits. *European Journal of Internal Medicine*, **138**, 101-111. https://doi.org/10.1016/j.ejim.2025.05.018

[48] Du, K., Huang, Y., Yu, Y., Guo, J., Feng, J. and Jiang, F. (2026) Diagnosis of Metabolic Dysfunction-Associated Steatotic Liver Disease by Triglyceride Glucose-Body Mass Index: A Systematic Review and Meta-Analysis. *Annals of Hepatology*, **31**, Article ID: 102122. https://doi.org/10.1016/j.aohep.2025.102122

[49] Tamini, S., Bondesan, A., Caroli, D., Marazzi, N. and Sartorio, A. (2025) The Ability of the Triglyceride-Glucose (TyG) Index and Modified Tyg Indexes to Predict the Presence of Metabolic-Associated Fatty Liver Disease and Metabolic Syndrome in a Pediatric Population with Obesity. *Journal of Clinical Medicine*, **14**, Article 2341. https://doi.org/10.3390/jcm14072341

[50] Amato, M.C. and Giordano, C. (2013) Clinical Indications and Proper Use of Visceral Adiposity Index. *Nutrition, Metabolism and Cardiovascular Diseases*, **23**, e31-e32. https://doi.org/10.1016/j.numecd.2013.04.006

[51] Amato, M.C., Giordano, C., Pitrone, M. and Galluzzo, A. (2011) Cut-Off Points of the Visceral Adiposity Index (VAI) Identifying a Visceral Adipose Dysfunction Associated with Cardiometabolic Risk in a Caucasian Sicilian Population. *Lipids in Health and Disease*, **10**, Article No. 183. https://doi.org/10.1186/1476-511x-10-183

[52] Amato, M.C. and Giordano, C. (2014) Visceral Adiposity Index: An Indicator of Adipose Tissue Dysfunction. *International Journal of Endocrinology*, **2014**, Article ID: 730827. https://doi.org/10.1155/2014/730827

[53] Amato, M.C., Giordano, C., Galia, M., Criscimanna, A., Vitabile, S., Midiri, M., *et al*. (2010) Visceral Adiposity Index.

Diabetes Care, **33**, 920-922. https://doi.org/10.2337/dc09-1825

[54] Bozorgmanesh, M., Hadaegh, F. and Azizi, F. (2011) Predictive Performance of the Visceral Adiposity Index for a Visceral Adiposity-Related Risk: Type 2 Diabetes. *Lipids in Health and Disease*, **10**, Article No. 88. https://doi.org/10.1186/1476-511x-10-88

[55] Elisha, B., Messier, V., Karelis, A., Coderre, L., Bernard, S., Prud'homme, D., *et al*. (2013) The Visceral Adiposity Index: Relationship with Cardiometabolic Risk Factors in Obese and Overweight Postmenopausal Women—A MONET Group Study. *Applied Physiology*, *Nutrition*, *and Metabolism*, **38**, 892-899. https://doi.org/10.1139/apnm-2012-0307

[56] Xu, C., Ma, Z., Wang, Y., Liu, X., Tao, L., Zheng, D., *et al*. (2018) Visceral Adiposity Index as a Predictor of NAFLD: A Prospective Study with 4-Year Follow-Up. *Liver International*, **38**, 2294-2300. https://doi.org/10.1111/liv.13941

[57] Ismaiel, A., Jaaouani, A., Leucuta, D., Popa, S. and Dumitrascu, D.L. (2021) The Visceral Adiposity Index in Non-Alcoholic Fatty Liver Disease and Liver Fibrosis—Systematic Review and Meta-Analysis. *Biomedicines*, **9**, Article 1890. https://doi.org/10.3390/biomedicines9121890

[58] Bende, R., Heredea, D., Rațiu, I., Sporea, I., Dănilă, M., Șirli, R., *et al*. (2025) Association between Visceral Adiposity and the Prediction of Hepatic Steatosis and Fibrosis in Patients with Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). *Journal of Clinical Medicine*, **14**, Article 3405. https://doi.org/10.3390/jcm14103405

[59] Ercin, C.N., Dogru, T., Genc, H., Celebi, G., Aslan, F., Gurel, H., *et al*. (2015) Insulin Resistance but Not Visceral Adiposity Index Is Associated with Liver Fibrosis in Nondiabetic Subjects with Nonalcoholic Fatty Liver Disease. *Metabolic Syndrome and Related Disorders*, **13**, 319-325. https://doi.org/10.1089/met.2015.0018

[60] Flagiello, V., Gallo, P., Terracciani, F., Falcomatà, A., De Vincentis, A., Pasquale, G.D., *et al*. (2026) Ultrasound-derived Visceral Adipose Tissue as a Reliable Marker of Hepato-Metabolic Risk in Patients with MASLD. *Digestive and Liver Disease*, **58**, 113-118. https://doi.org/10.1016/j.dld.2025.11.008

[61] Zhou, T., Ding, X., Chen, L., Huang, Q. and He, L. (2025) Visceral Adiposity Index as a Predictor of Metabolic Dysfunction-Associated Steatotic Liver Disease: A Cross-Sectional Study. *BMC Gastroenterology*, **25**, Article No. 326. https://doi.org/10.1186/s12876-025-03957-1

[62] Ahn, N., Baumeister, S.E., Amann, U., Rathmann, W., Peters, A., Huth, C., *et al*. (2019) Visceral Adiposity Index (VAI), Lipid Accumulation Product (LAP), and Product of Triglycerides and Glucose (TyG) to Discriminate Prediabetes and Diabetes. *Scientific Reports*, **9**, Article No. 9693. https://doi.org/10.1038/s41598-019-46187-8

[63] Jakubiak, G.K., Badicu, G., Surma, S., Waluga-Kozłowska, E., Chwalba, A. and Pawlas, N. (2025) The Visceral Adiposity Index and Its Usefulness in the Prediction of Cardiometabolic Disorders. *Nutrients*, **17**, Article 2374. https://doi.org/10.3390/nu17142374

[64] Martínez-Sánchez, F.D., Vargas-Abonce, V.P., Rocha-Haro, A., Flores-Cardenas, R., Fernández-Barrio, M., Guerrero-Castillo, A.P., *et al*. (2021) Visceral Adiposity Index Is Associated with Insulin Resistance, Impaired Insulin Secretion, and β-Cell Dysfunction in Subjects at Risk for Type 2 Diabetes. *Diabetes Epidemiology and Management*, **2**, Article ID；100013. https://doi.org/10.1016/j.deman.2021.100013

[65] Colantoni, A., Bucci, T., Cocomello, N., Angelico, F., Ettorre, E., Pastori, D., *et al*. (2024) Lipid-Based Insulin-Resistance Markers Predict Cardiovascular Events in Metabolic Dysfunction Associated Steatotic Liver Disease. *Cardiovascular Diabetology*, **23**, Article No. 175. https://doi.org/10.1186/s12933-024-02263-6

[66] Zou, H., Xie, J., Ma, X. and Xie, Y. (2025) The Value of Tyg-Related Indices in Evaluating MASLD and Significant Liver Fibrosis in MASLD. *Canadian Journal of Gastroenterology and Hepatology*, **2025**, Article ID: 5871321. https://doi.org/10.1155/cjgh/5871321

[67] Priego-Parra, B.A., Reyes-Diaz, S.A., Ordaz-Alvarez, H.R., Bernal-Reyes, R., Icaza-Chávez, M.E., Martínez-Vázquez, S.E., *et al*. (2024) Diagnostic Performance of Sixteen Biomarkers for MASLD: A Study in a Mexican Cohort. *Clinics and Research in Hepatology and Gastroenterology*, **48**, Article ID: 102400. https://doi.org/10.1016/j.clinre.2024.102400