

甘油三酯 - 葡萄糖体重指数的相关研究进展

曹 亮*, 孙洪涛#

内蒙古民族大学附属医院心血管内科, 内蒙古 通辽

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摘 要

甘油三酯 - 葡萄糖体重指数(TyG-BMI指数)是最新研究发现的一种联合性指标, 通过简单计算空腹甘油三酯、血糖及BMI的数值即可快捷地评估胰岛素功能。既往研究表明胰岛素抵抗通过各种病理生理机制引起临床众多代谢性疾病, 同时TyG-BMI指数在识别和诊断常见疾病方面, 也有极高的临床价值。本文通过探讨临床常见疾病与甘油三酯 - 葡萄糖体重指数以及胰岛素抵抗的相关研究进展进行进一步的探讨和总结, 从多方面分析胰岛素抵抗导致机体疾病发生的协同作用, 帮助临床医生对病情发展进行更好和更早的评估, 帮助患者提升远期生活质量。

关键词

甘油三酯 - 葡萄糖体重指数, 胰岛素抵抗, 肥胖, 心血管疾病

Research Progress on Triglycerides-Glucose Body Mass Index

Liang Cao*, Hongtao Sun#

Department of Cardiovascular Medicine, Affiliated Hospital of Inner Mongolia Minzu University, Tongliao Inner Mongolia

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Abstract

The Triglyceride-Glucose Body Mass Index (TyG-BMI) is a composite measure identified in recent research. A simple calculation involving fasting triglyceride levels, blood glucose, and BMI allows for a quick assessment of insulin function. Prior investigations have demonstrated that insulin resistance

*第一作者。

#通讯作者。

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contributes to a variety of clinical metabolic disorders through different pathophysiological pathways, with the TyG-BMI index proving to be highly valuable for the identification and diagnosis of prevalent diseases. This paper further explores and synthesizes the latest research developments related to common clinical conditions, triglyceride-glucose BMI, and insulin resistance. It examines the combined effects of insulin resistance on the emergence of body disorders from multiple perspectives, aiming to assist clinicians in improving their assessments of disease progression, and enhance patients' long-term quality of life.

Keywords

Triglyceride-Glucose Body Mass Index, Insulin Resistance, Obesity, Cardiovascular Disease

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1. 引言

即使全世界的医疗技术水平在不断提高和进步, 经调查心血管疾病仍然是世界范围内负担最大的主要疾病之一。机体代谢、生活习惯、环境和社会风险等因素均是导致心血管疾病发生的主要驱动因素[1]。与此同时, 罹患糖尿病(DM)的风险也在全球范围内急剧上升, 使得全球预期的寿命值降低。众所周知, 糖尿病患者的病程进展会引起心脏疾病的加重, 还会影响冠心病患者的预后。Wang 等人于 2021 年通过对人群的调查研究发现: BMI 水平从 2014 年的 22.7 kg/m^2 , 四年期间上升至 24.4 kg/m^2 , 与此同时肥胖患病率从 3.1% 上升到 8.1%。从 2010 年起, 八年期间, 中国人群平均每年 BMI 增加 0.09 kg/m^2 [2]。人们不健康的生活方式日益流行致使人群肥胖率日益升高, 所以心血管疾病的发病率和死亡率下降的拐点仍然没有出现。既往研究多次证实: 胰岛素抵抗(Insulin resistance, IR)被认为是导致机体发生糖尿病和代谢性疾病不可忽视的病理原因, 同时也是重要机制[3]-[5]。因此临床诊疗中尽早评估和治疗 IR 是必不可少的, 目前主要检测方法有: 作为金标准的高胰岛素-正葡萄糖钳夹法(Hyper-insulinemic euglycemic clamp, HIEC)、胰岛素抑制试验(Insulin suppression test, IST)和稳态模型评估法(HOMA-IR)等, 但过程复杂且费用昂贵, 在临床实际工作中未能普及[6]。既往研究发现机体发生 IR 的原因尚不清楚, 但它与肥胖有着密切的关系[7], 尤其是脂肪分布在腹部区域(腹型肥胖)与 IR 的严重程度紧密相连[8]-[11]。其原理: 机体的内分泌器官之一就是脂肪组织, 它可以分泌脂肪细胞因子(肿瘤坏死因子、游离脂肪酸和瘦素等)扰乱胰岛素信号传导通路系统, 是 IR 发生的重要诱因[12]。

已有大量研究证实 TyG 指数是胰岛素抵抗的可靠指标。而甘油三酯-葡萄糖体重指数(TyG-BMI 指数)是最新研究发现的联合性指标, 由 TyG 和 BMI 相乘而得。在 2016 年由 Er 首次提出, 通过计算空腹甘油三酯、空腹血糖及 BMI 的数值而来, 其计算公式为 $\text{Ln}[\text{TG} (\text{mg/dL}) \times \text{FPG} (\text{mg/dL})/2] * \text{BMI} (\text{kg/m}^2)$ 。同时 Er 等人通过研究证实与传统脂质参数、血糖参数、血脂比率以及肥胖相关指标进行统计分析对比后发现: TyG-BMI 用于鉴别胰岛素抵抗的 AUC 曲线下面积最大, 具有更高的临床诊断价值。证明它是一种简单、有效、可使用的替代标志物, 便于临床早期识别 IR [13]。

2. 胰岛素抵抗在动脉粥样硬化中的作用与机制

IR 导致动脉粥样硬化的机制涉及内皮细胞的两个特性: 抑制 eNOS 活性和触发白细胞粘附。目前许多体外研究已经证实了血液中高葡萄糖浓度对内皮细胞有直接影响, 同时通过动物和人类的体内研究也

有间接证据说明: 内皮细胞对人体葡萄糖浓度的变化特别敏感, 内皮细胞导致血糖升高的机制可能是: 蛋白激酶介导的细胞间黏附分子-1、粘附分子-选择素、血管细胞黏附因子-1 的表达增加和机体氧化应激增多。同时机体高血糖状态促进白细胞粘附也是导致动脉粥样硬化的第一步[14]。

Moore 等人发现巨噬细胞在动脉粥样硬化的各个阶段都起着关键作用。在病变早期, 覆盖载脂蛋白活化区域的内皮细胞会将单核细胞招募到内膜, 分化后成为巨噬细胞, 巨噬细胞进一步摄取脂蛋白成为胆固醇负载的泡沫细胞。内膜巨噬细胞参与许多促动脉粥样硬化过程, 包括炎症介质、蛋白酶和促凝因子的分泌[15]。当机体发生胰岛素抵抗时巨噬细胞会使内质网保持较长时间的应激状态, 加速巨噬细胞凋亡, 从而引起机体发生动脉粥样硬化, 甚至硬化斑块的坏死[16]。

3. TyG-BMI 与临床常见疾病的相关研究进展

3.1. TyG-BMI 指数与冠状动脉粥样硬化性心脏病的相关研究

随着全球生活质量的好转, 糖尿病、高血压、血脂异常、超重和久坐不动的生活方式被认为是导致动脉粥样硬化性心血管疾病的关键因素[17][18]。胰岛素抵抗(IR)是机体自身分泌的胰岛素敏感性和反应性降低的状态, 在心血管疾病中发挥重要作用[19]。逐渐增多的研究事实表明, IR 不仅与糖尿病的发生密切相连, 也是非糖尿病患者发生心血管疾病的危险因素之一[20]。并且通过研究发现即使在正常血糖的情况下, 胰岛素抵抗也会导致人们发生冠状动脉粥样硬化性心脏病[21]。Huang 等人通过纳入一项 3143 名患者的研究发现, 创新型指标 TyG-BMI 在 ASCVD 和 2 型糖尿病发病率方面优于传统的人体测量指标。在中国男性和女性成人中, 与冠心病风险升高显著相关[22]。与 BMI 相关的腹型肥胖(中心性肥胖)通过胰岛素抵抗、分泌脂肪因子和炎症蛋白增加心血管风险, 导致动脉粥样硬化内皮功能障碍[23]-[25]。对于我们个人而言, 腹型肥胖和 BMI 是可以通过自身锻炼改善的, 因此也是临床上降低 ASCVD 负担的潜在治疗靶点[26]。

3.2. TyG-BMI 指数与缺血性脑卒中的研究

尽管全球脑卒中的年龄标准化死亡率有所下降, 但中国脑卒中的发病率和患病率仍呈爆炸性增长[27]-[29]据研究所知长期吸烟、高血压和糖尿病是导致脑卒中发生的主要风险因素[29][30]。Tatjana 等人通过研究证实: 尽早识别和治疗胰岛素抵抗可成为预防脑卒中发作的新靶点[31]。众所周知 TyG-BMI 指数由三个心血管疾病标志物运算得到, 综合了血脂、血糖及肥胖的相关指标数值被认为是评估 IR 的有效指标。Du 等人通过调查中国正常人群研究发现: TyG-BMI 与缺血性卒中之间存在明显的正相关性且线性相关(无饱和或阈值), 使用标准差转换的 TyG-BMI 作为连续变量的回归分析表明, 进行调整校对后发现: 缺血性卒中的发生率会随着 TyG-BMI 数值的增加而增加(1:20%)。同时, 随着 TyG-BMI 降低, 可显著降低缺血性脑卒中的危险分层。缺血性脑卒中的始发病理生理机制即动脉粥样硬化。既往实验研究已经确定其机制: IR 会降低 eNOS 的活性、增加内皮细胞中的血管细胞黏附因子-1 的表达、促使平滑肌细胞迁移和增殖来加速动脉粥样硬化的进展, 甚至导致晚期动脉粥样硬化中斑块坏死凋亡[32]。

3.3. TyG-BMI 指数与高血压的研究

大量研究表明, 内脏脂肪过多是机体代谢异常的原因之一会导致机体发生胰岛素抵抗和心脏代谢性疾病的风险, 同时增加高血压风险[33]。IR 导致高血压的机制包括: 胰岛素抵抗和高胰岛素血症会通过抑制钠钾 ATP 酶和钠氢泵的活性从而导致高血压, 而后进一步引起动脉抵抗和交感神经活动增加[34]。Shimamoto 等人认为通过使用血管紧张素 II 的 I 型受体拮抗剂可减轻原发性高血压患者发生胰岛素抵抗的概率[35][36]。2020 年的一项研究分析共纳入了 105,070 名无高血压的非肥胖的成年人。根据相应公式

计算体重指数(BMI)、腰围(WC)、腰围身高比(WtHR)和 TyG。通过乘以相应的两个参数计算得到 TyG-BMI、TyG-WC 和 TyG-WtHR, 结果发现: TyG-BMI 和 TyG-WC 与机体发生高血压前期改变显著相关, 其中 TyG-BMI 对高血压前期的诊断价值最高, 可作为临床监测的指标用来分层管理非肥胖的高血压前期患者[37], 这一发现对于临床工作来说, 是一项极具诊疗效能的发现。

3.4. TyG-BMI 指数与代谢相关脂肪性肝病的研究

非酒精性脂肪性肝病(nonalcoholic fatty liver disease, NAFLD)是一种常见的较重要的慢性肝病, 在全球范围内影响成人和儿童[38]。正常人摄取热量和食物后, 胰岛素便开始发挥作用: 通过抑制糖原分解和限制餐后血糖升高来减少肝糖原的产生。然而在糖尿病患者中, 这种反馈机制会受损: 机体会增加脂肪组织的分解, 使机体内游离脂肪酸(FFA)增加, 加快脂肪变性, 会进一步加重 IR。同时在超重及肥胖相关疾病中, 促炎因子和转录因子在脂肪和肝脏组织中高度表达[39]。Zhang 等人通过研究发现在中国患者群体中 TyG-BMI 在识别和诊断非肥胖患者的 NAFLD 方面效能优于 TyG。其原因可能是: BMI 在非肥胖者的 NAFLD 的发展中起着至关重要的作用(BMI < 23 kg/m² 的受试者中 NAFLD 的患病率为 11.7%)。通过统计分析证明了非肥胖型 NAFLD 的风险随着 BMI 水平的升高而增加, 这支持了 BMI 与非肥胖型 NAFLD 之间的密切关系。这一发现具有特殊的临床意义, 因为 TyG-BMI 的数值可基于标准化测量即可计算出来[40]。

3.5. TyG-BMI 指数与高尿酸血症的研究

高尿酸血症的定义通常为血清尿酸浓度 > 7 mg/dl [41], 但 2023 年的 URRAH 研究, 重新定义高尿酸血症为女性 5.1 mg/dl, 男性 5.6 mg/dl [42]。高尿酸血症的临床后果包括痛风性关节炎和慢性肌肉骨骼疼痛。既往研究证明即使是无症状的高尿酸血症也会增加各种心脏代谢性疾病的风险, 包括顽固性高血压、高脂血症、代谢综合征、II 型糖尿病、慢性肾脏疾病、心血管事件和缺血性心脏病等[43]。Seifi 等人研究发现胰岛素抵抗的作用, 无论是作为一个原因或作为一个介质, 都会导致高尿酸血症的后果[44]。先前的研究表明, 肥胖标志物(BMI、WC 和 WHtR)与高尿酸血症显著相关[45], 而脂肪组织释放促炎细胞因子也可加重 IR [46] [47]。一项以学生为对象的研究证明了 TyG 与肥胖指标结合的优越性, 指出 TyG 及其衍生物可能会增加特定人群中高尿酸血症的患病风险[45]。另一项针对中国老年人的横断面研究中 TyG 和 TyG-BMI 指数被用作 IR 生物标志物, 研究发现这些标志物单独或联合使用, 均与 HUA 或高血压风险有显著关联[48]。据估计, 血尿酸每升高 1 毫克/分升, 成人患 2 型糖尿病的风险增加 20%, 儿童增加 15% [49]。高尿酸血症患者, 内皮细胞的功能会降低, 发生障碍, 同时一氧化氮释放减少, 进一步引起机体发生胰岛素抵抗和糖尿病。肾小管的尿酸转运蛋白(URAT1)在机体发生胰岛素抵抗时被刺激, 使尿酸重吸收增加, 通过肾脏的排泄减少, 从而引起高尿酸血症[50]。

这些尿酸转运蛋白(UT)是基因编码的蛋白质。若外界因素导致基因突变也会引起尿酸重吸收紊乱, 并导致高尿酸血症、胰岛素抵抗、内皮功能障碍、糖尿病和其他代谢疾病的发生[51]。

3.6. TyG-BMI 指数与代谢综合征的相关研究

代谢综合征的定义是根据国际糖尿病联合会的标准确定[52]: 腰围 ≥ 94 cm (男性)或 ≥ 80 cm (女性)。同时满足以下至少两个标准: (1)血糖水平 ≥ 5.6 mmol/L 或诊断为糖尿病; (2) 低高密度脂蛋白胆固醇(HDL-C)水平 < 1.0 mmol/L (男性), < 1.3 mmol/L (女性), 或接受低 HDL-C 药物治疗; (3) 甘油三酯(TG)水平 ≥ 1.7 mmol/L 或接受高 TG 药物治疗; (4) 血压 ≥ 130/85 mmHg 或正在接受高血压药物治疗。Gallagher 等人[53]讨论了正常人的胰岛素信号传导生理过程和胰岛素抵抗后诱发代谢综合征的机制: 正常情况下胰岛素刺激骨骼肌对葡萄糖的摄取, 减少肝脏糖异生, 脂肪组织分解进一步降低和抑制低密度脂蛋

白的产生。胰岛素信号传递到大脑抑制人的食欲后通过下丘脑的神经元信号传导通路阻止肝脏减少葡萄糖的产生。因此当机体发生胰岛素抵抗时低密度脂蛋白的产生增加, 高密度脂蛋白的产生减少, 线粒体功能发生障碍导致骨骼肌对葡萄糖摄取减少, 增加了肝脏糖异生引起机体高血糖状态。此外, 发生胰岛素抵抗时, 一氧化氮诱导血管舒张的机制被损害导致高血压的发生。目前一项研究证实: 在女性方面, TyG 指数和肥胖指数的组合, 在代谢综合征的临床识别和预测方面优于单独的 TyG 指数[54]。流行病学研究证实, 胰岛素抵抗可能是代谢综合征各个组成部分的共同病因, 单独发生时, 每一种成分都会增加心血管疾病的风险, 但合并发作时, 它们会有更加强大的关联性。这意味着在临床工作中对高血糖和其他代谢综合征患者的管理不仅应关注血糖控制, 还应包括降低其他心血管疾病危险因素(如肥胖), 代谢综合征的特征可能出现在人体血糖紊乱之前(长达 10 年之久)这对于高血糖的病因治疗和预防相关的 CVD 风险具有重要的临床治疗潜力。因此, 对代谢综合征进行规范化的早期管理可能对预防糖尿病和心血管疾病产生重大影响[55]。

4. 结语

综合以上研究我们可知, 计算甘油三酯-葡萄糖体重指数(TyG-BMI)的数据通过实验室化验及进行身体测量即可得到, 计算方便, 实用性强, 具有较高的成本效益。大量研究也证实 TyG-BMI 与心脏疾病、血管疾病和代谢性疾病等密切相关, 这为临床工作提供了一种可靠、灵敏、方便的评估工具。胰岛素抵抗(IR)一直被认为是一系列代谢性疾病的“共同根基”, 尽早识别并治疗胰岛素抵抗, 可以减少诸多代谢性疾病的发生和进展, 减轻患者预后不良的可能。

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