WCJD 世界华人消化杂志®

在线投稿: https://www.baishideng.com

世界华人消化杂志 2023年12月8日; 31(23): 953-959

DOI: 10.11569/wcjd.v31.i23.953

ISSN 1009-3079 (print) ISSN 2219-2859 (online)

述评 EDITORIAL

肥胖在急性胰腺炎中的作用研究进展

李壮丽, 孙 昀

李壮丽, 中国人民解放军联勤保障部队第901医院(安徽医科大学临床学院)重症医学科 安徽省合肥市 230031

孙昀, 安徽医科大学第二附属医院重症医学一科 安徽省合肥市 230601

李壮丽, 主治医师, 研究方向为脓毒症和急性胰腺炎相关方向.

基金项目: 安徽医科大学第二附属医院国家自然科学基金孵育项目(面上), No. 2022GMFY09; 皖南医学院教学医院自然科学基金项目, No. JXYY202109.

作者贡献分布: 论文撰写由李壮丽完成; 论文审阅修改由孙昀完成.

通讯作者: 孙昀, 主任医师, 副教授, 博士研究生导师, 230601, 合肥市经济技术开发区芙蓉路678号, 安徽医科大学第二附属医院. sunyun15@163.com

收稿日期: 2023-10-22
修回日期: 2023-11-10
接受日期: 2023-11-18
在线出版日期: 2023-12-08

Role of obesity in pathogenesis of acute pancreatitis

Zhuang-Li Li, Yun Sun

Zhuang-Li Li, Department of Critical Care Medicine, The 901 Hospital of The Joint Logistic Support Force of the Chinese People`s Liberation Army, Clinic College, Anhui Medical University, Hefei 230031, Anhui Province, China

Yun Sun, The First Department of Critical Care Medicine, The Second Affiliated Hospital of Anhui Medical University, Hefei 230601, Anhui Province, China

Supported by: National Natural Science Foundation Incubation Plan of Second Affiliated Hospital of Anhui Medical University, No. 2022GMFY09; The Scientific Research Fund of Wannan Medical College, No. JXYY202109.

Corresponding author: Yun Sun, Chief Physician, Associate Professor, Doctoral Supervisor, The First Department of Critical Care Medicine, The Second Affiliated Hospital of Anhui Medical University, No. 678 Furong Road, Hefei Economic and Technological Development Zone, Hefei 230601, Anhui Province, China. sunyun15@163.com

Received: 2023-10-22
Revised: 2023-11-10
Accepted: 2023-11-18
Published online: 2023-12-08

Abstract

Acute pancreatitis (AP) is one of the most common digestive disorders that cause hospitalization. While most of patients with AP have a mild to moderate disease and recover rapidly, about 20% of patients with AP have a severe disease and experience substantial morbidity and mortality from local and/or systemic compli-cations. The incidence of obesity has increased worldwide, and its epidemiological characteristics and rising trend are consistent with those of AP. Therefore, obesity has probably contributed to the increase in the incidence and severity of AP. However, previous studies have generated conflicting results, and some studies demonstrated that obesity is a protective factor in patients with AP. Here we discuss the role of obesity in the pathogenesis of AP and the underlying mechanisms based on clinically relevant studies.

Key Words: Obesity; Acute pancreatitis; Obesity paradox

Citation: Li ZL, Sun Y. Role of obesity in pathogenesis of acute pancreatitis. Shijie Huaren Xiaohua Zazhi 2023; 31(23): 953-959
URL: https://www.wjgnet.com/1009-3079/full/v31/i23/953.htm
DOI: https://dx.doi.org/10.11569/wcjd.v31.i23.953

摘要

急性胰腺炎是导致患者住院的一种最常见消化疾病之一, 多数患者为轻中度, 恢复较快, 临床约20%患者因局部和/或全身并发症而发展为重症, 发病率和死亡率较高. 肥胖在全球范围内发病率日益增多, 其流行病学特点和升高趋势与急性胰腺炎一致, 肥胖可能增加

了急性胰腺炎的发病率和严重程度. 然而, 也有研究得出了相互矛盾的结果, 即肥胖对急性胰腺炎患者有保护作用. 本综述结合临床相关研究, 探讨肥胖在急性胰腺炎发病中的作用及其潜在机制.

关键词: 肥胖; 急性胰腺炎; 肥胖悖论

核心提要: 急性胰腺炎以局部炎性反应为主, 而重症患者以全身炎症反应, 多器官功能障碍和胰腺局部坏死为特征. 肥胖患者全身脂肪量增加, 基础代谢率增高, 可能对急性胰腺炎病情严重程度产生不利影响; 但同时肥胖患者由于脂肪代偿能力较正常体重者更高, 重症时可能起到延迟病程发展的作用. 目前对于肥胖在急性胰腺炎发病中的作用争议较大, 有待大样本前瞻性临床试验进一步研究.

文献来源: 李壮丽, 孙昀. 肥胖在急性胰腺炎中的作用研究进展. 世界华人消化杂志 2023; 31(23): 953-959
URL: https://www.wjgnet.com/1009-3079/full/v31/i23/953.htm
DOI: https://dx.doi.org/10.11569/wcjd.v31.i23.953

0 引言

急性胰腺炎(acute pancreatitis, AP)是由多种原因致胰酶异常激活消化自身胰腺组织及周围器官引起胰腺局部炎症反应, 甚至多器官功能障碍为特征的疾病, 是临床上最常见的消化系统疾病之一. 发病率约为每10万人中110-140人, 多数患者为轻症, 自限性. 临床上约20%的患者因合并胰腺或胰腺周围组织坏死和器官功能功能衰竭而发展为中度甚至重症急性胰腺炎(severe acute pancreatitis, SAP), 死亡率约20%[1]. 这类患者多需要入住重症监护室治疗. AP常见病因有胆源性, 酒精性胰腺炎等, 近年来随着人们生活水平提高, 高脂血症性胰腺炎明显增加, 在中国, 甚至已成为继胆石症之后的第二大病因[2]; 其他病因还包括自身免疫性, 创伤性, 药物性等; 临床上导致AP加重的危险因素较多, 如并发急性呼吸窘迫综合征(acute respiratory distress syndrome, ARDS), 脓毒症等全身并发症, 大面积胰腺坏死等局部并发症. 近年来研究发现, AP患者中肥胖人群占比越来越多, 且肥胖的AP患者易进展为SAP, 易并发ARDS及器官功能衰竭等, 预后较非肥胖患者更差[3].

肥胖是目前全球突出的公共卫生问题和疾病负担, 一项纳入了195个国家的人口统计数据显示, 2015年全球约有6亿成人肥胖人群和1亿儿童肥胖人群, 成人超重人口约占总人口的35%, 肥胖者达10%以上, 且这一数字仍在上升趋势[4]. 在中国, 肥胖患病率自2004年的3.1%升高到2018年的8.1%, 人数迅速上升[5]. 肥胖可导致患代谢相关疾病的风险增加, 如心血管疾病, 2型糖尿病, 高血压及慢性肾病等[6], 并可致AP发病率增加和病情加重[7,8]. 然而, 近年来也有研究发现, 肥胖在心血管疾病[9], 慢性阻塞性肺疾病[10]和慢性肾病中[11], 不仅不会加重病情, 反而可以起到保护作用, 即肥胖患者相较于正常体重患者而言, 这些疾病的病死率反而降低, 即“肥胖悖论”. 这种现象在AP患者中亦有发现[12]. 本文就肥胖的定义, 肥胖对AP患者可能的发病机制进一步探讨.

1 肥胖的定义及分级

世界卫生组织[13]将肥胖定义为危害健康的过量或异常脂肪堆积, 人体脂肪含量的测量可通过水下称重法及核磁共振成像(MRI)检查法等. 临床上普遍采用简便易行的体重指数(body mass index, BMI)[体重(Kg)/身高(m)^2]来估计体脂量, 并依据BMI将体重分为四级, 分别为, 低于正常体重者: BMI≤18.5 kg/m^2; 正常体重: 18.6-25 kg/m^2; 超重: 25-30 kg/m^2; 肥胖: BMI≥30 kg/m^2. 但这一标准主要是针对欧美人群, 由于种族差异, 这一分级标准并不适应于中国乃至亚洲人群[14], 故而中国肥胖工作组提出了针对中国成年人群的BMI分级标准, BMI≤18.5 kg/m^{2}为低体重, 18.5-24 kg/m^{2}正常, 24-28 kg/m^{2}超重, ≥28 kg/m^{2}为肥胖[15]. 这一分级标准同世界卫生组织对于亚洲人群的BMI分级标准一致.

BMI作为反应肥胖程度的人体计量学指标, 虽简便易行, 临床易获取, 但不能反应全身脂肪分布情况, 如皮下脂肪分布、内脏脂肪组织分布及内脏脂肪与肌肉的比例等. 而腹部肥胖和内脏脂肪/肌肉比值被认为与心血管疾病和重症急性胰腺炎发病成正相关[16,17]. 目前评估腹部脂肪量的方法有腰围(waist circumference, WC), 腰臀比(waist hip rate, WHR)等. 男女由于体型差异, 采用腰围判断肥胖的标准亦不同, 对于男性而言, 腰围≥102 cm为肥胖; 而对于女性而言, 腰围≥88 cm为肥胖. 同样, 腰臀比在男女之间亦存在差异, 男性腰臀比≥0.95为肥胖, 而女性肥胖者腰臀比≥0.80. 腰围和腰臀比被认为比BMI更能反应内脏脂肪组织分布情况, 是腹部肥胖常用的评估手段[18,19].

2 肥胖加重急性胰腺炎

AP作为一种炎症性疾病, 其进展趋势和临床预后取决于疾病严重程度. 鉴于目前对于SAP有限的治疗手段及高死亡率形势下, 对危险因素的干预就显得至关重要. 前已述及, AP常见病因为胆石症及酒精性, 高甘油三酯性胰腺炎占比越来越高, 且高甘油三酯性胰腺炎相较于其他病因更严重[22], 高甘油三酯血症患者发生局部并

发症的频次和程度随着甘油三酯水平的增加而显著增加[23]. 这些引起胰腺炎最常见的病因均与肥胖相关. 研究显示[24], 年轻人群出现胆石症与个体超重或肥胖相关, 肥胖患者体内胆固醇晶体生长过快导致胆汁中胆固醇结石形成, 导致胆石症, 继发胰腺炎, 提示肥胖可能是影响AP发病的一个重要因素. 有研究显示, BMI在23-28 kg/m^{2}范围内AP发病风险显著增加[25]. 而Dobszai的研究指出[26], BMI大于25 kg/m^{2}的AP患者更易进展成SAP, 而BMI大于30 kg/m^{2}的AP患者死亡风险明显增加. Blaszczak的研究也表明[27], 肥胖是AP的独立危险因素, 可加重AP病情及导致死亡率增加. 目前对于肥胖导致胰腺炎病情加重及死亡率增加的机制尚不完全明确, 常见的假说有以下几种.

2.1 脂质介质 肥胖者体内脂肪组织超过体重的30%, 而甘油三酯占脂肪组织的80%以上. 高甘油三酯使得肥胖的胰腺炎患者病情更重, 死亡率增加, 提示甘油三酯在肥胖导致急性胰腺炎过程中可能起到介导作用[25], 血甘油三酯越高, 胰腺坏死越严重[28]. 有研究认为[29], 体内多余的甘油三酯被胰脂肪酶分解为游离脂肪酸, 其对胰腺腺泡细胞和胰腺血管内皮均具有脂毒性, 导致胰腺微循环障碍, 进而致多器官功能损伤, 加重病情. 另外, 高甘油三酯血症使血液粘度增加, 血流减慢, 胰腺导管和腺泡细胞缺血, 导致胰腺自身消化和细胞损伤, 使病情加重[30]. 再次, 胰腺腺泡细胞的体外实验研究表明, 在SAP患者的血清及坏死脂肪组织中, 游离脂肪酸浓度显著升高, 它与钙结合后导致脂肪组织皂化和坏死, 这也是SAP常合并低钙血症的原因; 而未与钙结合的游离脂肪酸则通过促进炎症因子释放, 抑制线粒体复合物I和V, 降低ATP水平, 导致胰腺坏死; 通过抑制肥胖胰腺炎动物模型中脂肪组织分解, 防止游离脂肪酸增加, 可防止全身炎症反应、减少胰腺坏死和降低死亡率[31].

2.2 炎症介质 正常情况下, 脂肪组织主要由前脂肪细胞和脂肪细胞组成, 白细胞较少. 肥胖的过程中, 体内营养物质过度积累, 脂肪组织的组成和功能发生了改变. 有储存能力的脂肪组织被脂肪饱和, 导致脂肪细胞肥大, 进而导致缺氧、脂肪细胞坏死、趋化因子分泌、脂肪酸不规则流动等并发症[32]. 而脂肪细胞的缺氧和坏死导致巨噬细胞浸润, 促进炎症介质的分泌和释放, 炎症介质包括白介素-6、白介素1β、肿瘤坏死因子-α和单核细胞趋化蛋白-1等, 从而使得肥胖患者炎症程度较非肥胖患者更重; 另一方面, 肥大的脂肪细胞干扰了脂肪组织来源的细胞因子和脂肪因子的平衡, 导致前炎症状态, 继而导致脂肪细胞功能障碍, 抑制脂联素mRNA的表达, 脂联素浓度降低, 内皮细胞进入促炎状态, 炎症发生[33]. 实际上, 肥胖期间促炎细胞因子的过度表达被认为是肥胖和炎症之间的联系[34]. 也因此肥胖又被认为是一种慢性低级别炎症的代谢状态. 肥胖患者炎症反应升高, 局部和全身并发症发生风险均增大, 是AP死亡的预后因素[35].

2.3 脂肪因子 脂肪因子是由脂肪组织分泌的具有生物活性的细胞因子及激素, 参与肥胖过程的重要脂肪因子有瘦素和脂联素等. 瘦素是脂肪细胞分泌的一种肽类激素, 在循环中通过与受体结合而发挥作用, 瘦素可抑制食欲并诱导能量消耗[36], 如机体处于饥饿状态, 血清瘦素浓度下降, 降低机体能量消耗; 反之, 营养过剩所致的体脂量累积, 可使循环中瘦素浓度增加, 加速能量消耗, 以此达到减少食物摄入, 调节能量代谢的目的. 研究表明, 肥胖患者中血清瘦素水平各不相同, 可能是由瘦素抵抗或瘦素表达减少引起的[37]. 而在对缺血再灌注AP模型的动物实验研究中发现, 预先注射瘦素可减轻AP大鼠模型的胰腺组织损伤[38]. 瘦素对AP患者的胰腺保护机制可能与其可调节细胞因子的产生、刺激热休克蛋白和改变腺泡细胞的凋亡过程以及激活胰腺组织的抗氧化系统有关[39]. 一项比较了瘦素基因缺陷的肥胖小鼠及瘦素受体缺陷的肥胖小鼠和野生型小鼠AP模型的研究观察到, 前两者AP严重程度较野生型更重, 并且瘦素基因缺陷的肥胖小鼠体内白介素-1和白介素-6浓度增加[40].

我们知道, 脂肪组织除具有储存能量的功能外, 还具有内分泌功能, 脂联素是脂肪组织分泌的另外一种重要脂肪因子, 它通过下调核转录因子-κB(nuclear factor kappa B, NF-κB)通路, 抑制NF-κB的表达, 降低NF-κB的活性, 降低促炎因子的反应性发挥抗炎作用, 减轻胰腺炎症损伤, 保护胰腺组织[41]. 除此之外, 脂联素参与调节人体外周神经系统, 加速脂肪组织氧化和提升胰岛素敏感性, 降低循环中脂肪酸水平, 降低肝脏组织中甘油三酯水平, 参与肥胖代谢相关疾病, 脂联素水平与肥胖呈负相关关系[42,43]. 肥胖基因小鼠的AP模型中观察到, 先天性肥胖的小鼠, 不仅胰腺炎症程度更重, 且其严重程度与循环中脂联素浓度负相关, 即脂联素浓度越低, 先天性肥胖小鼠的AP严重程度越重[40]. 因此, 相对于高瘦素和低脂联素水平的慢性有害后果, 肥胖患者在危重症的急性应激期可能受益于他们的内分泌状况[44].

除瘦素和脂联素外, 抵抗素也参与炎症过程. 抵抗素是脂肪细胞和巨噬细胞分泌的一种富含半胱氨酸的脂肪因子, 与肥胖和糖尿病的发生发展有关[45]. 抵抗素通过激活NF-κB在肝星状细胞和胰腺腺泡细胞中的表达, 增加促炎趋化因子的表达. 肥胖急性胰腺炎患者胰腺组织中抵抗素水平升高, 且抵抗素表达升高与急性胰

腺炎的严重程度相关[46].

3 关于“肥胖悖论”

在对普通人群的大型队列研究中发现, 超重和肥胖个体的死亡风险增加[47]. 而在ICU和患慢性疾病的患者中研究显示, BMI与死亡率成“J”型或“U”型关系[6,48], 即超重和中度肥胖患者相比于正常体重或重度肥胖而言, 死亡率更低. 这种肥胖增加了患相关慢性疾病的风险, 但同时肥胖患者较正常体重患者死亡率反而下降的现象, 即“肥胖悖论”[6]. 关于“肥胖悖论”的研究不仅存在于心血管疾病[49], 糖尿病[50]及慢性肾脏病[51]等代谢性疾病中, 在脓毒症及SAP患者中也存在“肥胖悖论”现象[12,52]. 如Dahiya的研究指出[53], 肥胖AP患者的住院死亡率和并发症小于正常体重患者. Bala[54]的研究支持AP患者中存在“肥胖悖论”. 产生“肥胖悖论”现象可能及假说有几下几种.

3.1 肥胖患者可能有更强的抗炎性反应 肥胖患者体内的脂蛋白水平较高, 而脂蛋白与脂多糖结合可中和炎症内毒素, 减轻神经内分泌应激反应[55]; 其次, 肥胖患者不仅炎性因子水平升高, 白介素-10和可溶性肿瘤坏死因子α受体水平也升高, 它们具有免疫调节作用, 并可减弱炎症反应[55,56]. 除此之外, 肥胖患者体内脂肪组织增加, 新生分化的小脂肪细胞数量增多, 随后被活化的M2巨噬细胞浸润, 这些M2巨噬细胞具有抗炎和胰岛素增敏特性, 在病情加重时起保护作用[57].

3.2 药物干预更早 肥胖患者由于心输出量及心肌耗氧增加以及胰岛素抵抗的发生, 易合并心血管疾病和糖尿病等代谢相关疾病, 但同时由于肥胖患者症状出现较早, 也促使患者及早接受治疗, 改善临床预后. 其次, 由于人们对肥胖的担忧, 不仅使患者更早就医, 也使得医护人员更重视, 从而得到更积极的干预和更密切的监测[58].

3.3 对代谢障碍的代偿能力更强 肥胖者的代谢储备能力较正常体重和偏瘦者更高, 丢失蛋白质的速度也慢很多, 发生严重高分解代谢的风险较小, 脂肪组织可作为燃料来源, 可提供能量和脂溶性营养物质[44]. 另外, 脂肪细胞分泌的免疫调节物质, 如瘦素、白细胞介素-10和可溶性肿瘤坏死因子-α受体具有免疫调节作用, 减弱炎症反应, 提高重症患者的生存[59]; 不仅如此, 瘦素还具有保护肠粘膜屏障的作用, 减弱胰腺组织的损伤. 前已述及, 肥胖患者体内多伴高瘦素血症, 这也可能是肥胖AP患者预后更好的原因之一.

然而, “肥胖悖论”现象近年来备受质疑, 可能的原因有: 第一, 样本选择的偏差[60]; 第二, 流行病学中观察到的危险因素与死亡率之间的关联与临床研究的不同, 导致因果关系的不成立, 反向因果可能会消弱真正的关联性; 第三, 先前体重降低或低体重的其它决定因素(如患慢性消耗性疾病, 营养不良)造成的混淆, 会高估这类正常体重患者的死亡风险, 从而误认为肥胖具有保护作用[61]; 第四, 采用BMI作为肥胖判断标准的局限性, 如在一些个体中的高BMI可能与肌肉质量增加有关, 或者说这些个体中的脂肪分布更合理, 而与代谢综合征无关, 被称为“代谢健康肥胖”[59,62], 这种情况与较弱的肥胖相关炎症和较低的死亡风险相关. 它会混淆肥胖悖论的研究结果. 事实上, BMI本身作为肥胖的一个判断指标, 不仅未反映脂肪和肌肉比例, 也不能反映脂肪分布情况, 因而评价指标的缺陷使得肥胖悖论现象仍存在质疑. 如针对肥胖与AP患者的相关性研究中, 更多的研究均倾向于腹型肥胖, 而非全身肥胖, 与AP的严重程度和死亡率相关[17,18,63], 而腹型肥胖并不能用BMI指标代替. 因此, 对于肥胖悖论仍需进一步研究.

4 结论

综上, 肥胖可通过促进炎症反应, 影响脂肪因子的分泌及调节, 在一定程度上影响AP的发病过程. 肥胖悖论现象虽在多种疾病中发现, 但缺乏强有力证据支持, 质疑较多, 未来仍需大样本前瞻性临床试验研究验证.

5 参考文献

1 Boxhoorn L, Voermans RP, Bouwense SA, Bruno MJ, Verdonk RC, Boermeester MA, van Santvoort HC, Besselink MG. Acute pancreatitis. *Lancet* 2020; 396: 726-734 [PMID: 32891214 DOI: 10.1016/s0140-6736(20)31310-6]

2 Zhu Y, Pan X, Zeng H, He W, Xia L, Liu P, Zhu Y, Chen Y, Lv N. A Study on the Etiology, Severity, and Mortality of 3260 Patients With Acute Pancreatitis According to the Revised Atlanta Classification in Jiangxi, China Over an 8-Year Period. *Pancreas* 2017; 46: 504-509 [PMID: 28196012 DOI: 10.1097/mpa.0000000000000776]

3 Lee PJ, Lahooti A, Culp S, Boutsicaris A, Holovach P, Wozniak K, Lahooti I, Paragomi P, Hinton A, Pothoulakis I, Talukdar R, Kochhar R, Goenka MK, Gulla A, Gonzalez JA, Singh V, Bogado MF, Stevens T, Babu ST, Nawaz H, Gutierrez SC, Zarnescu N, Capurso G, Easler J, Triantafyllou K, Peláez Luna M, Thakkar S, Ocampo C, de-Madaria E, Cote GA, Wu BU, Hart PA, Krishna SG, Lara L, Han S, Papachristou GI. Obesity and alcoholic etiology as risk factors for multisystem organ failure in acute pancreatitis: Multinational study. *United European Gastroenterol J* 2023; 11: 383-391 [PMID: 37096304 DOI: 10.1002/ueg2.12390]

4 GBD 2015 Obesity Collaborators, Afshin A, Forouzanfar MH, Reitsma MB, Sur P, Estep K, Lee A, Marczak L, Mokdad AH, Moradi-Lakeh M, Naghavi M, Salama JS, Vos T, Abate KH, Abbafati C, Ahmed MB, Al-Aly Z, Alkerwi A, Al-Raddadi R, Amare AT, Amberbir A, Amegah AK, Amini E, Amrock SM, Anjana RM, Ärnlöv J, Asayesh H, Banerjee A, Barac A, Baye E, Bennett DA, Beyene AS, Biadgilign S, Biryukov S, Bjertness E, Boneya DJ, Campos-Nonato I, Carrero JJ, Cecilio P, Cercy K, Ciobanu LG, Cornaby L, Damtew SA, Dandona L, Dandona R, Dharmaratne SD, Duncan BB, Eshrati B, Esteghamati A, Feigin VL, Fernandes JC, Fürst T, Gebrehiwot TT, Gold A, Gona PN, Goto A, Habtewold TD, Hadush KT, Hafezi-Nejad N, Hay SI, Horino M, Islami F, Kamal R, Kasaeian A, Katikireddi SV,

Kengne AP, Kesavachandran CN, Khader YS, Khang YH, Khubchandani J, Kim D, Kim YJ, Kinfu Y, Kosen S, Ku T, Defo BK, Kumar GA, Larson HJ, Leinsalu M, Liang X, Lim SS, Liu P, Lopez AD, Lozano R, Majeed A, Malekzadeh R, Malta DC, Mazidi M, McAlinden C, McGarvey ST, Mengistu DT, Mensah GA, Mensink GBM, Mezgebe HB, Mirrakhimov EM, Mueller UO, Noubiap JJ, Obermeyer CM, Ogbo FA, Owolabi MO, Patton GC, Pourmalek F, Qorbani M, Rafay A, Rai RK, Ranabhat CL, Reinig N, Safiri S, Salomon JA, Sanabria JR, Santos IS, Sartorius B, Sawhney M, Schmidhuber J, Schutte AE, Schmidt MI, Sepanlou SG, Shamsizadeh M, Sheikhbahaei S, Shin MJ, Shiri R, Shiue I, Roba HS, Silva DAS, Silverberg JI, Singh JA, Stranges S, Swaminathan S, Tabarés-Seisdedos R, Tadese F, Tedla BA, Tegegne BS, Terkawi AS, Thakur JS, Tonelli M, Topor-Madry R, Tyrovolas S, Ukwaja KN, Uthman OA, Vaezghasemi M, Vasankari T, Vlassov VV, Vollset SE, Weiderpass E, Werdecker A, Wesana J, Westerman R, Yano Y, Yonemoto N, Yonga G, Zaidi Z, Zenebe ZM, Zipkin B, Murray CJL. Health Effects of Overweight and Obesity in 195 Countries over 25 Years. *N Engl J Med* 2017; 377: 13-27 [PMID: 28604169 DOI: 10.1056/NEJMoa1614362]

5 Wang L, Zhou B, Zhao Z, Yang L, Zhang M, Jiang Y, Li Y, Zhou M, Wang L, Huang Z, Zhang X, Zhao L, Yu D, Li C, Ezzati M, Chen Z, Wu J, Ding G, Li X. Body-mass index and obesity in urban and rural China: findings from consecutive nationally representative surveys during 2004-18. *Lancet* 2021; 398: 53-63 [PMID: 34217401 DOI: 10.1016/s0140-6736(21)00798-4]

6 Schetz M, De Jong A, Deane AM, Druml W, Hemelaar P, Pelosi P, Pickkers P, Reintam-Blaser A, Roberts J, Sakr Y, Jaber S. Obesity in the critically ill: a narrative review. *Intensive Care Med* 2019; 45: 757-769 [PMID: 30888440 DOI: 10.1007/s00134-019-05594-1]

7 Peery AF, Crockett SD, Murphy CC, Jensen ET, Kim HP, Egberg MD, Lund JL, Moon AM, Pate V, Barnes EL, Schlusser CL, Baron TH, Shaheen NJ, Sandler RS. Burden and Cost of Gastrointestinal, Liver, and Pancreatic Diseases in the United States: Update 2021. *Gastroenterology* 2022; 162: 621-644 [PMID: 34678215 DOI: 10.1053/j.gastro.2021.10.017]

8 McGuire SP, Keller SL, Maatman TK, Lewellen KA, Ceppa EP, House MG, Nakeeb A, Nguyen TK, Quigley SN, Schmidt CM, Zyromski NJ. Obesity Worsens Local and Systemic Complications of Necrotizing Pancreatitis and Prolongs Disease Course. *J Gastrointest Surg* 2022; 26: 2128-2135 [PMID: 35960426 DOI: 10.1007/s11605-022-05383-0]

9 Sharma A, Lavie CJ, Borer JS, Vallakati A, Goel S, Lopez-Jimenez F, Arbab-Zadeh A, Mukherjee D, Lazar JM. Meta-analysis of the relation of body mass index to all-cause and cardiovascular mortality and hospitalization in patients with chronic heart failure. *Am J Cardiol* 2015; 115: 1428-1434 [PMID: 25772740 DOI: 10.1016/j.amjcard.2015.02.024]

10 Yamauchi Y, Hasegawa W, Yasunaga H, Sunohara M, Jo T, Takami K, Matsui H, Fushimi K, Nagase T. Paradoxical association between body mass index and in-hospital mortality in elderly patients with chronic obstructive pulmonary disease in Japan. *Int J Chron Obstruct Pulmon Dis* 2014; 9: 1337-1346 [PMID: 25525351 DOI: 10.2147/copd.S75175]

11 Stenvinkel P, Gillespie IA, Tunks J, Addison J, Kronenberg F, Drueke TB, Marcelli D, Schernthaner G, Eckardt KU, Floege J, Froissart M, Anker SD; ARO Steering Committee. Inflammation Modifies the Paradoxical Association between Body Mass Index and Mortality in Hemodialysis Patients. *J Am Soc Nephrol* 2016; 27: 1479-1486 [PMID: 26567245 DOI: 10.1681/asn.2015030252]

12 Davis PJ, Eltawil KM, Abu-Wasel B, Walsh MJ, Topp T, Molinari M. Effect of obesity and decompressive laparotomy on mortality in acute pancreatitis requiring intensive care unit admission. *World J Surg* 2013; 37: 318-332 [PMID: 23052814 DOI: 10.1007/s00268-012-1821-8]

13 Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser* 2000; 894: i-xii, 1-253 [PMID: 11234459]

14 He W, Li Q, Yang M, Jiao J, Ma X, Zhou Y, Song A, Heymsfield SB, Zhang S, Zhu S. Lower BMI cutoffs to define overweight and obesity in China. *Obesity (Silver Spring)* 2015; 23: 684-691 [PMID: 25645003 DOI: 10.1002/oby.20995]

15 Pan XF, Wang L, Pan A. Epidemiology and determinants of obesity in China. *Lancet Diabetes Endocrinol* 2021; 9: 373-392 [PMID: 34022156 DOI: 10.1016/s2213-8587(21)00045-0]

16 Arderiu G, Lambert C, Ballesta C, Moscatiello F, Vilahur G, Badimon L. Cardiovascular Risk Factors and Differential Transcriptomic Profile of the Subcutaneous and Visceral Adipose Tissue and Their Resident Stem Cells. *Cells* 2020; 9 [PMID: 33022994 DOI: 10.3390/cells9102235]

17 Yoon SB, Choi MH, Lee IS, Lim CH, Kim JS, Cho YK, Park JM, Lee BI, Cho YS, Choi MG. Impact of body fat and muscle distribution on severity of acute pancreatitis. *Pancreatology* 2017; 17: 188-193 [PMID: 28190685 DOI: 10.1016/j.pan.2017.02.002]

18 Wang Z, Xu Y, Yang K, Zhou M, Huang D, Luo L. Early evaluation of waist-to-height ratio for the prediction of worsening acute pancreatitis. *Medicine (Baltimore)* 2023; 102: e34515 [PMID: 37543804 DOI: 10.1097/md.0000000000034515]

19 Ping Z, Pei X, Xia P, Chen Y, Guo R, Hu C, Imam MU, Chen Y, Sun P, Liu L. Anthropometric indices as surrogates for estimating abdominal visceral and subcutaneous adipose tissue: A meta-analysis with 16,129 participants. *Diabetes Res Clin Pract* 2018; 143: 310-319 [PMID: 30086371 DOI: 10.1016/j.diabres.2018.08.005]

20 Blüher M. Obesity: global epidemiology and pathogenesis. *Nat Rev Endocrinol* 2019; 15: 288-298 [PMID: 30814686 DOI: 10.1038/s41574-019-0176-8]

21 Hebebrand J, Holm JC, Woodward E, Baker JL, Blaak E, Durrer Schutz D, Farpour-Lambert NJ, Frühbeck G, Halford JGC, Lissner L, Micic D, Mullerova D, Roman G, Schindler K, Toplak H, Visscher TLS, Yumuk V. A Proposal of the European Association for the Study of Obesity to Improve the ICD-11 Diagnostic Criteria for Obesity Based on the Three Dimensions Etiology, Degree of Adiposity and Health Risk. *Obes Facts* 2017; 10: 284-307 [PMID: 28738325 DOI: 10.1159/000479208]

22 Khatua B, El-Kurdi B, Singh VP. Obesity and pancreatitis. *Curr Opin Gastroenterol* 2017; 33: 374-382 [PMID: 28719397 DOI: 10.1097/mog.0000000000000386]

23 Pascual I, Sanahuja A, García N, Vázquez P, Moreno O, Tosca J, Peña A, Garayoa A, Lluch P, Mora F. Association of elevated serum triglyceride levels with a more severe course of acute pancreatitis: Cohort analysis of 1457 patients. *Pancreatology* 2019; 19: 623-629 [PMID: 31229460 DOI: 10.1016/j.pan.2019.06.006]

24 Zhang J, Chen L, Shen K, Zhang J, Zhu Y, Qiao Q, Chen L. Association between metabolically healthy overweight/obesity and gallstones in Chinese adults. *Nutr Metab (Lond)* 2023; 20: 20 [PMID: 37004051 DOI: 10.1186/s12986-023-00741-4]

25 Hansen SEJ, Madsen CM, Varbo A, Nordestgaard BG. Body Mass Index, Triglycerides, and Risk of Acute Pancreatitis: A Population-Based Study of 118 000 Individuals. *J Clin Endocrinol Metab* 2020; 105 [PMID: 31588492 DOI: 10.1210/clinem/dgz059]

26 Dobszai D, Mátrai P, Gyöngyi Z, Csupor D, Bajor J, Erőss B, Mikó A, Szakó L, Meczker Á, Hágendorn R, Márta K, Szentesi A, Hegyi P; Hungarian Pancreatic Study Group. Body-mass index correlates with severity and mortality in acute pancreatitis: A meta-analysis. *World J Gastroenterol* 2019; 25: 729-743 [PMID: 30783376 DOI: 10.3748/wjg.v25.i6.729]

27 Blaszczak AM, Krishna SG, Hart PA, Bradley D, Hsueh W, Lara LF, Hussan H, Hinton A, Conwell DL, Cruz-Monserrate Z. Class III obesity rather than metabolic syndrome impacts clinical outcomes of acute pancreatitis: A propensity score weighted analysis. *Pancreatology* 2020; 20: 1287-1295 [PMID: 32891531 DOI: 10.1016/j.pan.2020.08.011]

28 Hidalgo NJ, Pando E, Alberti P, Mata R, Fernandes N, Adell M, Villasante S, Blanco L, Balsells J, Charco R. The role of high serum triglyceride levels on pancreatic necrosis development and related complications. *BMC Gastroenterol* 2023; 23: 51 [PMID: 36829113 DOI: 10.1186/s12876-023-02684-9]

29 Valdivielso P, Ramírez-Bueno A, Ewald N. Current knowledge of hypertriglyceridemic pancreatitis. *Eur J Intern Med* 2014; 25: 689-694 [PMID: 25269432 DOI: 10.1016/j.ejim.2014.08.008]

30 Adiamah A, Psaltis E, Crook M, Lobo DN. A systematic review of the epidemiology, pathophysiology and current management of hyperlipidaemic pancreatitis. *Clin Nutr* 2018; 37: 1810-1822 [PMID: 29056284 DOI: 10.1016/j.clnu.2017.09.028]

31 Navina S, Acharya C, DeLany JP, Orlichenko LS, Baty CJ, Shiva SS, Durgampudi C, Karlsson JM, Lee K, Bae KT, Furlan A, Behari J, Liu S, McHale T, Nichols L, Papachristou GI, Yadav D, Singh VP. Lipotoxicity causes multisystem organ failure and exacerbates acute pancreatitis in obesity. *Sci Transl Med* 2011; 3: 107ra110 [PMID: 22049070 DOI: 10.1126/scitranslmed.3002573]

32 Kwaifa IK, Bahari H, Yong YK, Noor SM. Endothelial Dysfunction in Obesity-Induced Inflammation: Molecular Mechanisms and Clinical Implications. *Biomolecules* 2020; 10 [PMID: 32069832 DOI: 10.3390/biom10020291]

33 Mongraw-Chaffin M, Foster MC, Kalyani RR, Vaidya D, Burke GL, Woodward M, Anderson CA. Obesity Severity and Duration Are Associated With Incident Metabolic Syndrome: Evidence Against Metabolically Healthy Obesity From the Multi-Ethnic Study of Atherosclerosis. *J Clin Endocrinol Metab* 2016; 101: 4117-4124 [PMID: 27552544 DOI: 10.1210/jc.2016-2460]

34 Ellulu MS, Patimah I, Khaza'ai H, Rahmat A, Abed Y. Obesity and inflammation: the linking mechanism and the complications. *Arch Med Sci* 2017; 13: 851-863 [PMID: 28721154 DOI: 10.5114/aoms.2016.58928]

35 US Preventive Services Task Force, Curry SJ, Krist AH, Owens DK, Barry MJ, Caughey AB, Davidson KW, Doubeni CA, Epling JW Jr, Grossman DC, Kemper AR, Kubik M, Landefeld CS, Mangione CM, Phipps MG, Silverstein M, Simon MA, Tseng CW, Wong JB. Behavioral Weight Loss Interventions to Prevent Obesity-Related Morbidity and Mortality in Adults: US Preventive Services Task Force Recommendation Statement. *JAMA* 2018; 320: 1163-1171 [PMID: 30326502 DOI: 10.1001/jama.2018.13022]

36 Myers MG Jr, Olson DP. Central nervous system control of metabolism. *Nature* 2012; 491: 357-363 [PMID: 23151578 DOI: 10.1038/nature11705]

37 Dallner OS, Marinis JM, Lu YH, Birsoy K, Werner E, Fayzikhodjaeva G, Dill BD, Molina H, Moscati A, Kutalik Z, Marques-Vidal P, Kilpeläinen TO, Grarup N, Linneberg A, Zhang Y, Vaughan R, Loos RJF, Lazar MA, Friedman JM. Dysregulation of a long noncoding RNA reduces leptin leading to a leptin-responsive form of obesity. *Nat Med* 2019; 25: 507-516 [PMID: 30842678 DOI: 10.1038/s41591-019-0370-1]

38 Kosacka J, Woidt K, Toyka KV, Paeschke S, Klöting N, Bechmann I, Blüher M, Thiery J, Ossmann S, Baum P, Nowicki M. The role of dietary non-heme iron load and peripheral nerve inflammation in the development of peripheral neuropathy (PN) in obese non-diabetic leptin-deficient ob/ob mice. *Neurol Res* 2019; 41: 341-353 [PMID: 30638160 DOI: 10.1080/01616412.2018.1564191]

39 Jaworek J, Konturek SJ. Hormonal protection in acute pancreatitis by ghrelin, leptin and melatonin. *World J Gastroenterol* 2014; 20: 16902-16912 [PMID: 25493003 DOI: 10.3748/wjg.v20.i45.16902]

40 Zyromski NJ, Mathur A, Pitt HA, Lu D, Gripe JT, Walker JJ, Yancey K, Wade TE, Swartz-Basile DA. A murine model of obesity implicates the adipokine milieu in the pathogenesis of severe acute pancreatitis. *Am J Physiol Gastrointest Liver Physiol* 2008; 295: G552-G558 [PMID: 18583460 DOI: 10.1152/ajpgi.90278.2008]

41 Dikmen K, Bostanci H, Gobut H, Yavuz A, Alper M, Kerem M. Recombinant adiponectin inhibits inflammation processes via NF-kB pathway in acute pancreatitis. *Bratisl Lek Listy* 2018; 119: 619-624 [PMID: 30345768 DOI: 10.4149/bll_2018_110]

42 Anandaraj AA, Syed Ismail PM, Namis SM, Bajnaid YJ, Shetty SB, Almutairi KM. Association of Selected Adipocytokines and Inflammatory Markers on Body Mass Index in Type 2 Diabetes Patients in Saudi Arabia and as Risk Factors to Cardiovascular Disease. *Curr Diabetes Rev* 2017; 13: 330-335 [PMID: 27296168 DOI: 10.2174/1573399812666160614014254]

43 陈倩楠, 伍丽, 朱益民, 张旭慧. 肥胖者血清脂联素水平与代谢状况的关系. 华中科技大学学报(医学版) 2021; 50: 778-782

44 Marques MB, Langouche L. Endocrine, metabolic, and morphologic alterations of adipose tissue during critical illness. *Crit Care Med* 2013; 41: 317-325 [PMID: 23135416 DOI: 10.1097/CCM.0b013e318265f21c]

45 Taouis M, Benomar Y. Is resistin the master link between inflammation and inflammation-related chronic diseases? *Mol Cell Endocrinol* 2021; 533: 111341 [PMID: 34082045 DOI: 10.1016/j.mce.2021.111341]

46 Kwak MS, Lim JW, Kim H. Astaxanthin Inhibits Interleukin-6 Expression in Cerulein/Resistin-Stimulated Pancreatic Acinar Cells. *Mediators Inflamm* 2021; 2021: 5587297 [PMID: 34349610 DOI: 10.1155/2021/5587297]

47 Heymsfield SB, Wadden TA. Mechanisms, Pathophysiology, and Management of Obesity. *N Engl J Med* 2017; 376: 254-266 [PMID: 28099824 DOI: 10.1056/NEJMra1514009]

48 Li S, Zhang W, Fu Z, Liu H. Impact of obesity on all-cause and cause-specific mortality among critically ill men and women: a cohort study on the eICU database. *Front Nutr* 2023; 10: 1143404 [PMID: 37153915 DOI: 10.3389/fnut.2023.1143404]

49 Fröhlich H, Bossmeyer A, Kazmi S, Goode KM, Agewall S, Atar D, Grundtvig M, Frey N, Cleland JGF, Frankenstein L, Clark AL, Täger T. Glycaemic control and insulin therapy are significant confounders of the obesity paradox in patients with heart failure and diabetes mellitus. *Clin Res Cardiol* 2023 [PMID: 37608126 DOI: 10.1007/s00392-023-02268-3]

50 Cheung YM, Joham A, Marks S, Teede H. The obesity paradox: an endocrine perspective. *Intern Med J* 2017; 47: 727-733 [PMID: 27643504 DOI: 10.1111/imj.13257]

51 Naderi N, Kleine CE, Park C, Hsiung JT, Soohoo M, Tantisattamo E, Streja E, Kalantar-Zadeh K, Moradi H. Obesity Paradox in Advanced Kidney Disease: From Bedside to the Bench. *Prog Cardiovasc Dis* 2018; 61: 168-181 [PMID: 29981348 DOI: 10.1016/j.pcad.2018.07.001]

52 Pepper DJ, Demirkale CY, Sun J, Rhee C, Fram D, Eichacker P, Klompas M, Suffredini AF, Kadri SS. Does Obesity Protect Against Death in Sepsis? A Retrospective Cohort Study of 55,038 Adult Patients. *Crit Care Med* 2019; 47: 643-650 [PMID: 30789403 DOI: 10.1097/ccm.0000000000003692]

53 Dahiya DS, Sharma NR, Perisetti A, Singh A, Chandan S, Pisipati S, Gangwani MK, Garg R, Aggarwal M, Vennikandam M, Cheng CI, Ali H, Inamdar S, Sanaka M, Al-Haddad M. The Influence of Obesity on Acute Pancreatitis Hospitalizations: Does Body Mass Index Matter? *Pancreas* 2023; 52: e171-e178 [PMID: 37716011 DOI: 10.1097/mpa.0000000000002243]

54 Bala S, Alkhayro A, Hila A. Obesity Paradox in Acute Pancreatitis: 76. *Am J Gastroenterol* 2016; 111: S36-S37

55 Kalantar-Zadeh K, Rhee CM, Chou J, Ahmadi SF, Park J, Chen JL, Amin AN. The Obesity Paradox in Kidney Disease: How to Reconcile it with Obesity Management. *Kidney Int Rep* 2017; 2: 271-281 [PMID: 28439569 DOI: 10.1016/j.ekir.2017.01.009]

56 Alipoor E, Mohammad Hosseinzadeh F, Hosseinzadeh-Attar MJ. Adipokines in critical illness: A review of the evidence and knowledge gaps. *Biomed Pharmacother* 2018; 108: 1739-1750 [PMID: 30372877 DOI: 10.1016/j.biopha.2018.09.165]

57 Trivedi V, Jean RE, Genese F, Fuhrmann KA, Saini AK, Mangulabnan VD, Bavishi C. Impact of Obesity on Outcomes

in a Multiethnic Cohort of Medical Intensive Care Unit Patients. *J Intensive Care Med* 2018; 33: 97-103 [PMID: 27139008 DOI: 10.1177/0885066616646099]
58 O'Brien JM Jr, Philips GS, Ali NA, Aberegg SK, Marsh CB, Lemeshow S. The association between body mass index, processes of care, and outcomes from mechanical ventilation: a prospective cohort study. *Crit Care Med* 2012; 40: 1456-1463 [PMID: 22430246 DOI: 10.1097/CCM.0b013e31823e9a80]
59 Acharya P, Upadhyay L, Qavi A, Naaraayan A, Jesmajian S, Acharya S, Bharati R. The paradox prevails: Outcomes are better in critically ill obese patients regardless of the comorbidity burden. *J Crit Care* 2019; 53: 25-31 [PMID: 31174173 DOI: 10.1016/j.jcrc.2019.05.004]
60 Elagizi A, Kachur S, Lavie CJ, Carbone S, Pandey A, Ortega FB, Milani RV. An Overview and Update on Obesity and the Obesity Paradox in Cardiovascular Diseases. *Prog Cardiovasc Dis* 2018; 61: 142-150 [PMID: 29981771 DOI: 10.1016/j.pcad.2018.07.003]
61 Tobias DK. Addressing Reverse Causation Bias in the Obesity Paradox Is Not "One Size Fits All". *Diabetes Care* 2017; 40: 1000-1001 [PMID: 28733375 DOI: 10.2337/dci17-0010]
62 Cheng FW, Gao X, Mitchell DC, Wood C, Rolston DD, Still CD, Jensen GL. Metabolic Health Status and the Obesity Paradox in Older Adults. *J Nutr Gerontol Geriatr* 2016; 35: 161-176 [PMID: 27559852 DOI: 10.1080/21551197.2016.1199004]
63 Chung KH, Choi YH, Cho IR, Son BK, Ryu JK, Kim YT, Lee SH, Han K. Hypertriglyceridaemic waist phenotype and waist circumference triglyceride index are associated with higher incidence of acute pancreatitis: a nationwide population-based retrospective cohort study. *BMJ Open* 2023; 13: e071213 [PMID: 37643853 DOI: 10.1136/bmjopen-2022-071213]

科学编辑: 张砚梁 制作编辑: 张砚梁

ISSN 1009-3079 (print) ISSN 2219-2859 (online) DOI: 10.11569

• 消息 •

书讯

本刊讯 由池肇春教授等主编的《代谢相关脂肪性肝病肝外并发症》已由天津科学技术出版社出版发行.

本书的出版为国内首创, 填补了国内有关这方面的空白, 拓宽了对《代谢相关脂肪性肝病》认识的高度和深度. 《代谢相关脂肪性肝病肝外并发症》分总论和各论两部分. 1-4章为总论, 分别介绍代谢相关脂肪性肝病肝外并发症研究现状与进展, 包括发病风险、发病机制和治疗近展; 脂肪代谢生物化学和分子生物学; 代谢相关脂肪性肝病肝外并发病免疫学; 肠道微生物生态失衡与代谢相关脂肪性肝病肝外并发病. 5-18章为各论, 分别介绍代谢相关脂肪性肝病肝外并发症与机体各系统疾病的相关性. 可为消化科、肝病科、内分泌代谢科、普外科、肿瘤科、影像科、其他相关科临床医师和从事MAFLD研究的人员学习和参考.

全书71万余字, 精装、图文并茂. 每册定价188元, 可根据购书数量给予优惠, 欢迎选购. 购书联系电话022-23332390(发行部何老师).

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton,
CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

ISSN 1009-3079
23>
9 771009 307056