DOI: 10.13376/j.cbls/2024067
文章编号：1004-0374(2024)05-0658-11

瘦素-脂联素比值：代谢健康中的可靠指标

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摘 要：瘦素 - 脂联素比值 (leptin-adiponectin ratio, LAR) 将瘦素的促炎和胰岛素抵抗作用与脂联素的抗炎和胰岛素增敏特性相结合，是一种可以反映有关胰岛素敏感性、脂肪组织功能障碍和心血管健康的可靠指标。在临床应用中，LAR 表现出在评估胰岛素抵抗、诊断代谢综合征、衡量心血管风险方面的潜力，与多种疾病密切相关。它的应用范围涵盖了从儿童、青年到老年人的多个年龄段及孕妇等特殊生理状态。该文提供了 LAR 作为评估代谢健康的新兴生物标志物的强有力证据，同时指出了当前的挑战和限制，旨在为相关疾病的病情评估、疾病进展、疗效观察以及临床预后的判断等提供科学依据。

关键词：瘦素；脂联素；瘦素脂联素比值；胰岛素抵抗；脂肪组织功能障碍；代谢健康
中图分类号：Q493 **文献标志码：**A

Leptin-adiponectin ratio: a reliable indicator in metabolic health

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Abstract: The leptin-adiponectin ratio (LAR) integrates the contrasting roles of leptin and adiponectin in metabolic health, combining the pro-inflammatory and insulin-resistance properties of leptin with the anti-inflammatory and insulin-sensitizing characteristics of adiponectin. This offers a comprehensive and reliable indicator for assessing insulin sensitivity, adipose tissue dysfunction, and cardiovascular health. In clinical applications, LAR has demonstrated potential in diagnosing and evaluating a range of metabolic disorders, including insulin resistance, metabolic syndrome, and cardiovascular diseases, across diverse age groups from children to the elderly, and in special physiological conditions such as pregnancy. This paper provides robust evidence supporting LAR as an emerging biomarker in metabolic health assessment and discusses its current challenges and limitations, aiming to establish a scientific basis for disease status assessment, progression monitoring, efficacy observation, and clinical prognosis determination.

Key words: leptin; adiponectin; leptin-adiponectin ratio; insulin resistance; adipose tissue dysfunction; metabolic health

瘦素和脂联素是 20 世纪 90 年代发现的脂肪因子 [1-2]，由于它们在食欲调节、能量平衡和胰岛素敏感性方面发挥着不可或缺的作用而迅速跻身代谢研究的前沿。它们的发现挑战了脂肪组织仅作为脂肪储存库的传统观点，并强调了其作为内分泌和炎症器官的重要性，以此为契机开启了研究脂肪组织介导的代谢串扰新局面。

瘦素是调控食欲和能量代谢的重要细胞因子，然而当过量存在时，它会促进炎症和胰岛素抵抗 [3]。与之相对的是脂联素，另一种脂肪组织分泌的细胞因子，它在血液循环中更丰富，具有抗炎和胰岛素

收稿日期：2023-10-24；**修回日期：**2023-12-05
基金项目：厦门市自然科学基金项目(3502Z202374077)
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增敏作用[4]。在许多生理环境下，特别是与胰岛素敏感性和炎症反应相关时，这两种脂肪因子表现出不同的调节模式。考虑到这种相互关系，瘦素 - 脂联素比值 (leptin-adiponectin ratio, LAR) 的概念作为衡量这两种关键脂肪因子之间平衡的整体指标而被关注。最新的证据表明，LAR 可能有超越传统标记物的潜力，在预测和诊断一系列代谢和心血管疾病方面提供更高的敏感性。此外，LAR 因其广泛的临床适用性以及与不同人群 (涵盖了从孕妇、儿童青少年到成人和老人) 的广泛相关性而得到重视，逐步展现出其不容忽视的临床应用价值。

1　瘦素

瘦素是由脂肪组织分泌的 16 kD 大小的非糖基化蛋白[5]，它往往与身体脂肪组织质量呈显著的正相关关系[6]，与内脏脂肪相比，皮下脂肪会表达更多的瘦素[7]。瘦素参与调节许多生理过程，包括但不限于食物摄入、非颤抖产热、生殖、止血、血管生成、动脉压控制以及神经内分泌和免疫功能[8]。它对胰岛素敏感性和炎症途径的影响是复杂的，究竟产生积极还是消极的影响取决于不同的生理环境，这也意味着它在代谢健康方面可能既是朋友又是敌人。

1.1　瘦素在调节胰岛素敏感性中的作用

在促进胰岛素敏感性方面，瘦素表现出多种作用机制，主要体现在：(1) 细胞内脂质调节：胰岛素抵抗的一个关键驱动因素是异常的细胞内脂质积累[9]，瘦素被认为可以刺激脂肪酸氧化，从而减少特别是肌肉和肝脏等关键组织中的脂质堆积，瘦素这种降脂作用改善了胰岛素信号转导途径从而增强了胰岛素在这些组织中的作用[10-11]；(2) 葡萄糖摄取和代谢：瘦素增加了骨骼肌对葡萄糖的摄取和利用，促进肝糖原的储存并抑制了肝脏葡萄糖的输出[12-14]，这些作用共同维持了机体葡萄糖稳态；(3) 在中枢神经系统中的作用：相对于外周组织，在中枢神经系统中能够产生完整信号转导的长亚型瘦素受体 (LepRb)，尤其是下丘脑表达更高[15]。瘦素可以通过其受体 (LepRb) 作用于中枢神经系统，增强胰岛素在中枢的作用，同时瘦素可以调节交感神经活性，从而影响骨骼肌和肝脏等外周组织的胰岛素敏感性，并且有效地降低胰岛素水平[16-17]。

在某些生理条件下，瘦素会抑制胰岛素的敏感性。在肥胖等营养过剩的情况下，瘦素水平升高与细胞对瘦素的反应减弱矛盾地共存，这种现象被称为“瘦素抵抗”，即身体无法对瘦素信号做出反应[18]。值得注意的是，瘦素抵抗通常与胰岛素抵抗同时发生，有报道称胰岛素抵抗与血浆瘦素水平升高之间存在独立关联[19]。在正常生理条件下，胰岛素能够刺激脂肪细胞分泌和产生瘦素[20]，同时瘦素通过作用于中枢神经系统和直接刺激 β 细胞来抑制胰岛素的分泌[17, 21]。然而在肥胖症中，瘦素水平持续升高以及随之而来的瘦素抵抗会损害这种调节反馈[18]。升高的瘦素水平并不能有效抑制胰岛素分泌，最终促进高胰岛素血症的发展，加剧胰岛素抵抗[22]。这种高胰岛素血症反过来会刺激脂质生成，进而促进肥胖和瘦素的产生，形成代谢反馈的恶性循环。

1.2　瘦素在炎症发展中的作用

瘦素在炎症中的作用具有双重性质，身体的代谢状态、涉及的细胞类型和其他背景因素都会改变瘦素的炎症作用。肥胖被视为是一种慢性低度炎症[23]，这种炎症环境的核心介质便是瘦素。在急性炎症 (如感染或受伤) 的情况下，瘦素可以作为促炎介质，激活一系列免疫细胞，特别是巨噬细胞和 T 细胞，导致 TNF-α、IL-6 和 IFN-γ 等促炎细胞因子的分泌增加[24-25]。急性炎症期间瘦素水平的增加可能是增强免疫系统对抗病原体或组织修复能力的适应性反应[26]。而在如肥胖这类慢性炎症或营养过剩的情况下[23]，瘦素的慢性升高持续刺激促炎细胞因子产生的同时长期激活免疫细胞，使得炎症持续存在[27]。而在饥饿或营养不足的状态下，适应性降低的瘦素水平会使免疫应答减弱而减轻炎症反应以节省能量[28]。在某些维持生理稳态 (如妊娠) 至关重要的情况下，瘦素可能会调节免疫反应，平衡促炎和抗炎信号，以保持组织功能的完整性[29]。

瘦素对特定的免疫细胞会产生不同的影响。瘦素促进促炎性的 Th1 细胞免疫反应[28]，但对该通路的促进可能会加剧如系统性红斑狼疮、多发性硬化症、类风湿性关节炎等自身免疫性疾病的发生发展[30-32]。但在营养不足的情况下，瘦素则支持调节性 T 细胞的抗炎作用，以维持免疫耐受和限制炎症反应[33]。

瘦素在不同组织中对炎症的调节方式会受到组织类型的影响。对于血管细胞来说，一氧化氮 (NO) 是维持内皮健康和功能的关键分子。在正常生理环境下，瘦素可以刺激内皮细胞产生 NO，从而调节血管张力。然而当身体出现瘦素抵抗时，瘦素刺激 NO 产生的作用会减弱，进而加剧血管炎症和内皮功能障碍，这是动脉粥样硬化的早期信号[34]。在中

枢神经系统中，瘦素主要在小胶质细胞和星形胶质细胞上展现出其抗炎作用，它能够抑制促炎细胞因子如 TNF-α 释放，并促进抗炎细胞因子如 IL-1β 的分泌 [35-36]，从而对神经系统提供保护作用。而在瘦素抵抗的情况下，这种保护或抗炎作用可能会被削弱，而促炎途径持续活跃，导致神经炎症的加重 [37]。

2 脂联素

脂联素是另一种脂肪细胞因子，其单体相对分子质量约为 30 kD，它以各种多聚体形式在血液中循环：低分子量 (LMW) 三聚体、中等分子量 (MMW) 六聚体和高分子量 (HMW) 多聚体，其中以 HMW 脂联素最为活跃 [38-39]。在肥胖和胰岛素抵抗状态下，瘦素水平通常会升高，而脂联素水平则往往会下降 [40]。值得注意的是，身体不同部位的脂肪组织对脂联素水平有不同的影响。内脏脂肪组织质量与脂联素浓度呈负相关，而皮下脂肪组织与血浆脂联素浓度可能呈正相关，或至少不像内脏脂肪组织那样与其呈负相关 [40-43]。减肥手术能够有效地减少内脏脂肪，手术后循环脂联素水平显著增加支持了这一观点 [44]。脂联素以胰岛素增敏作用而闻名，可以提前 10 年预测糖尿病的发病风险 [45]；除此之外，它还具有抗炎、抗动脉粥样硬化、抗细胞凋亡、促血管生成和促脂肪生成的特性 [46]。

2.1 脂联素在调节胰岛素敏感性中的作用

在脂肪组织中，脂联素的基因表达、血浆浓度都与胰岛素敏感性指标密切相关 [47]。肥胖个体的体重减轻通常伴随着脂联素的升高以及胰岛素敏感性的改善 [46]。从机制上讲，脂联素可以通过降低肌肉和肝脏中的甘油三酯含量，增加骨骼肌中的脂肪酸 β 氧化，减少与胰岛素抵抗发展有关的脂质代谢物的细胞内积累来改善胰岛素敏感性 [48-49]。AMP 激活蛋白激酶 (AMPK) 途径是代谢调节和胰岛素信号转导的重要途径，也是脂联素激活的主要细胞内途径之一 [50]。脂联素直接激活该信号通路，放大胰岛素介导的骨骼肌等外周组织对葡萄糖摄取、维持整体葡萄糖稳态并改善胰岛素敏感性 [51-52]。此外，它可以通过与胰岛素受体的相互作用以及增强神经酰胺酶活性来保护和刺激胰腺细胞 [53-54]。胰岛素抵抗的另一个常见现象是肝脏糖异生的上调导致的高血糖，脂联素已经被证明可以抑制肝脏糖异生，改善血糖 [55]。脂肪组织的分布与个体的代谢健康和各种疾病的风险相关，异位脂质沉积能够导致胰岛素抵抗 [56-57]。脂联素可以帮助脂肪组织进行再分布，优先促进皮下脂肪，而不是内脏脂肪、肝脏或骨骼肌的脂肪储存 [58]，以此减少内脏脂肪组织质量，减轻全身炎症，提高葡萄糖和脂肪代谢，增强胰岛素敏感性 [58]。除了胰岛素增敏作用外，脂联素还可以保护胰腺 β 细胞免于凋亡并延长其寿命 [59-60]。脂联素的三聚体和六聚体形式可以从血清转运到脑脊液，从而调节大脑的各种生理功能 [61]，这使得脂联素有激活下丘脑胰岛素信号通路的能力，而下丘脑胰岛素信号通路调节着肝脏胰岛素抵抗和肝脏葡萄糖生成 [62-63]。

2.2 脂联素在炎症发展中的作用

大量研究表明，脂联素在多种疾病状态下具有抗炎特性，包括 2 型糖尿病、非酒精性脂肪性肝病和心血管疾病 [64-66]。例如，在冠状动脉疾病患者中，脂联素浓度与炎症急性期标志物 C 反应蛋白 (CRP) 呈负相关 [47]。体重减轻期间脂联素浓度往往会增加，同时 CRP 和 IL-6 水平则降低 [67]。从作用机制上看，脂联素抗炎作用的主要靶点是巨噬细胞。脂联素引导巨噬细胞极化为抗炎选择性活化状态 M2，而不是促炎经典活化状态 M1[68]。极化为 M2 状态的巨噬细胞会释放白介素 10 等抗炎细胞因子，有助于减轻炎症 [69]。此外，脂联素可以直接抑制炎症趋化因子的产生 [70-71]。在血管系统中，脂联素增加内皮细胞 NO 的释放，促进血管舒张，减轻血管炎症 [72]。脂联素能够降低黏附分子的表达，减少白细胞与血管内皮细胞的粘连而减缓该炎症过程 [73]。在心肌细胞和成纤维细胞中，脂联素可以通过抑制 TNF-α 表达和细胞凋亡减轻炎症 [74]。

大多数研究表明脂联素是一种经典的抗炎细胞因子，但部分关于脂联素促炎作用的研究提示着脂联素在炎症环境中作用的复杂性。例如，分离的原代人类巨噬细胞的转录组分析表明脂联素既没有促进巨噬细胞极化为经典状态 (M1) 也没有促进其活化为抗炎状态 (M2)，而是引发了与 M1 更加相似的促炎反应 [75]。然而这种促炎作用可能是急性且短暂的，被认为是脂联素先诱导有限的炎症激活程序，从而使这些细胞对进一步的促炎刺激产生抵抗力 [76-78]。

图 1 和图 2 分别总结了瘦素和脂联素在胰岛素抵抗和炎症发展中的作用。

3 瘦素脂联素比值的临床应用证据

如上所述，瘦素和脂联素在代谢过程中发挥着相反又互补的生理作用，瘦素 - 脂联素比值 (LAR) 囊括了瘦素的促炎、胰岛素抵抗作用和脂联素的抗

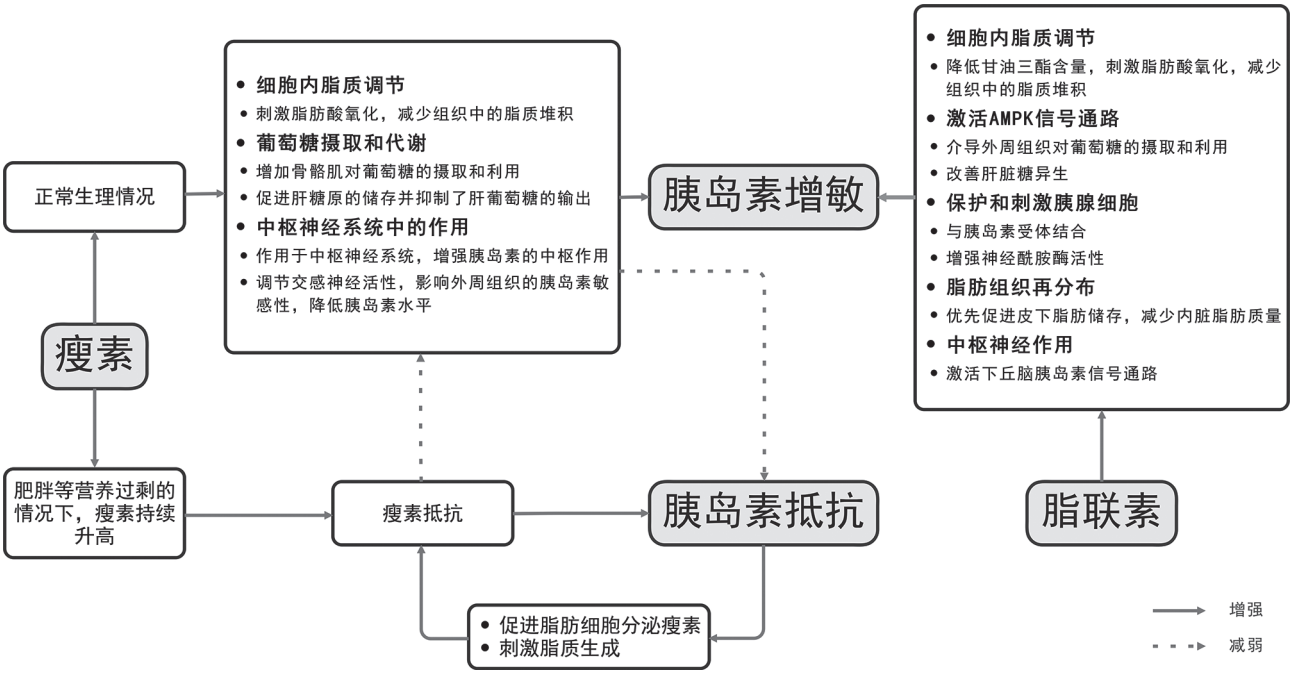

图1　瘦素和脂联素在调节胰岛素敏感性中的作用

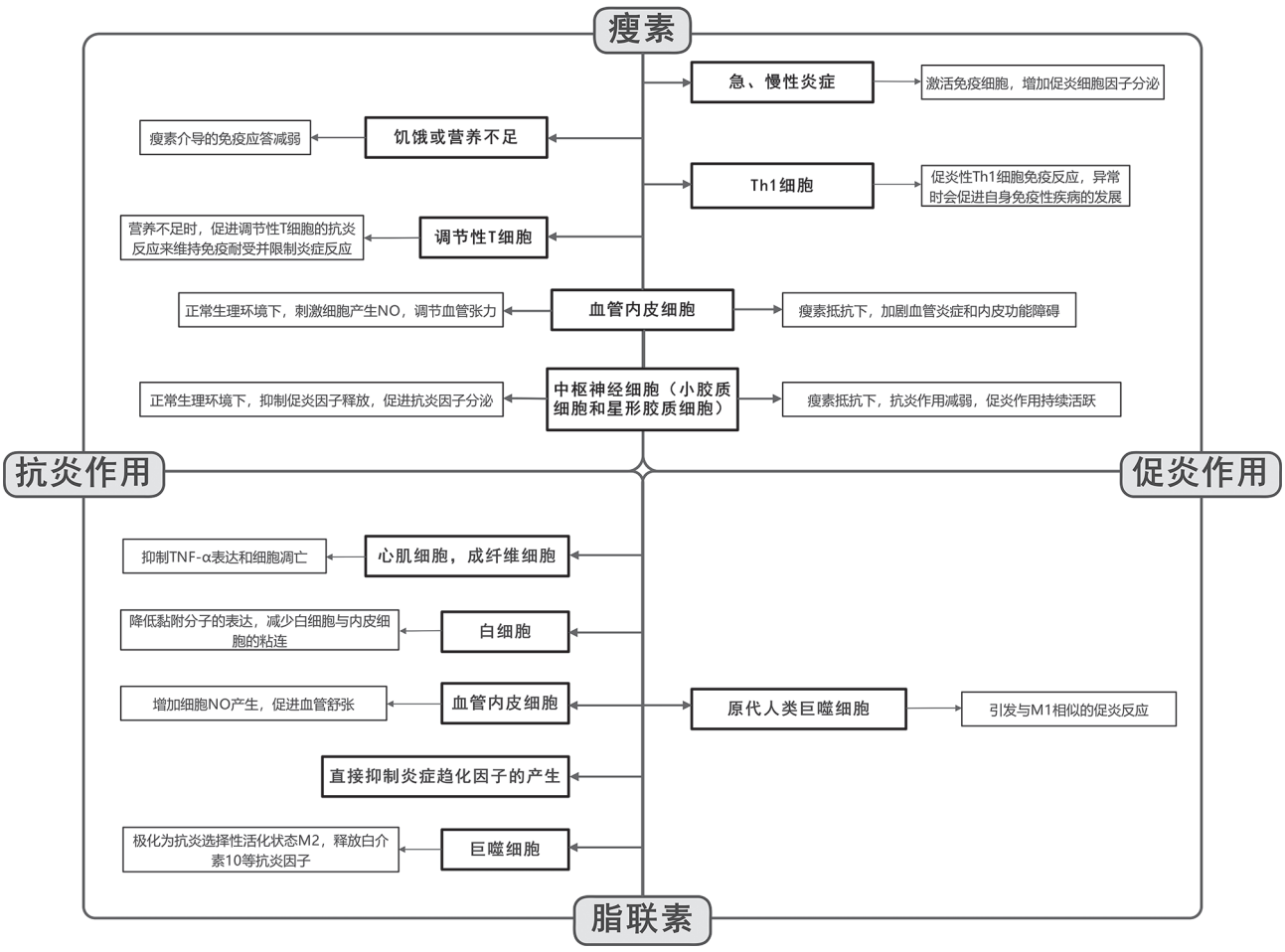

图2　瘦素和脂联素在炎症发展中的作用

炎、胰岛素增敏作用，提供了更全面的代谢状态视图。因此，相较于使用单独的瘦素或单独的脂联素，该比值能够增强在相关代谢疾病中的预测和诊断价值，成为代谢和心血管健康的新兴生物标志物[79-81]。

3.1 LAR与体内的代谢活动

3.1.1 LAR与胰岛素敏感性

LAR 与胰岛素敏感性密切相关，能够有效诊断或预测以胰岛素抵抗为基本病理特征的相关疾病。早在 2003 年，Vigouroux 等[82]就首次提出了使用脂联素 - 瘦素比值去评估感染 HIV 的脂肪营养不良和代谢障碍患者的胰岛素敏感性，且该评估能力不受身体脂肪含量的影响。Zaletel 等[79]通过正常血糖高胰岛素钳夹测量，比较了脂联素 - 瘦素比值和其他胰岛素抵抗替代指标与钳夹测量之间的相关性，结果发现该指标不仅优于单独脂联素或瘦素，并且与钳形衍生敏感性指数相关性最好 (r = 0.553, P < 0.001)，强于 HOMA、QUICKI、空腹葡萄糖 / 胰岛素比值或 McAuley 指数，同时这种相关性不会受到 BMI 和血糖的影响。多项临床观察性研究也指出，LAR 可以有效评估胰岛素抵抗，并且其价值优于单独脂联素和瘦素，甚至会优于临床常用的 HOMA-IR 指数[83-87]。即使是在血糖控制不佳或糖耐量受损的群体中，LAR 也能与胰岛素抵抗表现出良好的相关性[88-89]。有趣的是，被认为是脂联素最具活性形式的高分子量脂联素所产生的瘦素 /HMW 脂联素比值与瘦素 / 总脂联素比值相比，在评估代谢综合征和 2 型糖尿病的胰岛素抵抗上，没有体现出任何优势[90-91]。

3.1.2 LAR与脂肪组织功能

脂肪组织是一个高度活跃的内分泌器官，其功能障碍是一系列肥胖相关疾病发展前期的关键事件，也是肥胖和胰岛素抵抗病理生理学的核心特征[85, 92]。持续存在的炎症被认为是导致脂肪组织功能障碍的主要因素之一[92]。高 LAR 可能与脂肪组织的炎症和功能降低相关，被认为能够作为脂肪组织功能障碍的生物标志物[85, 93-94]。LAR 在体重下降后有所降低，可能提示着脂肪组织功能有所改善[95]。因此，可以通过 LAR 来评估脂肪组织功能障碍，帮助早期识别发生代谢并发症风险较高的个体，及时调整相关的治疗方案和干预措施。

3.2 LAR与代谢性疾病

3.2.1 代谢综合征

代谢综合征是以胰岛素抵抗和肥胖为核心特征的代谢紊乱疾病，它与心血管疾病和 2 型糖尿病的风险增加有关[96]。LAR 在预测和诊断代谢综合征方面表现出极大的优势。一项涉及 2 691 名参与者的前瞻性研究发现 LAR 与代谢综合征的发生风险呈正相关，LAR 高的人出现代谢综合征的风险大概是普通人的 3 倍[97]。LAR 判别代谢综合征的 ROC 曲线下面积在不同研究和不同人群中有所不同，其最高的 AUC 甚至可以达到 0.960[98-100]。

3.2.2 心血管疾病

瘦素和脂联素在心血管系统的炎症和动脉粥样硬化中表现出的生理作用让它们的比率能够体现这些相反效应之间的平衡，因此 LAR 还可以作为心血管疾病的潜在生物标志物[101]。我们的前期研究发现，相较于被广泛应用于诊断急性心衰的标志物氨基末端脑利钠肽前体 (amino-terminal pro-brain natriuretic peptide, NT-proBNP)，脂联素可以更好地识别肾功能不全患者的急性心衰 (AUC，0.872 vs 0.828)[102]。尽管当时没有比较 LAR 在该人群中的诊断价值，但在其他的临床研究中发现，LAR 可以作为颈总动脉内膜中层厚度的预测指标，并且其相关性优于单独的脂联素或者瘦素[103]；较高的 LAR 与冠状动脉粥样硬化的存在相关，该比值与受累的血管数呈正相关，可以提示冠状动脉病变的范围和严重程度[104]；在一项回顾性队列研究中还发现 LAR 或许与新发阵发性心房颤动患者的心脏自主神经功能相关[105]。LAR 还能够预测如 2 型糖尿病、多囊卵巢综合征等患者发生心血管并发症的风险[106-107]。

3.2.3 其他代谢疾病

多囊卵巢综合征是一种常见的内分泌疾病，患者常常存在胰岛素抵抗[108]，能够反映这种潜在的胰岛素抵抗以及慢性低度炎症状态的 LAR 在多囊卵巢综合征患者中显著升高[109]，可以强有力地预测多囊卵巢综合征，其 ROC 曲线下面积可以达到 0.867[110-111]。此外，LAR 还能有效预测与多囊卵巢综合征相关的代谢并发症，如 2 型糖尿病和心血管疾病，从而实现早期干预[107, 112]，其比值变化还能有助于评估治疗干预措施的效果[113]。非酒精性脂肪性肝病 (nonalcoholic fatty liver disease, NAFLD) 是一类与代谢功能障碍相关的肝脏疾病，与健康对照组相比，LAR 在 NAFLD 患者中显著升高[114]，进一步的分析揭示，LAR 随着脂肪变性的严重程度的增加而增加[115]，提示 LAR 作为预测 NAFLD 严重程度的生物标志物的可能性。在某些存在代谢功能障碍，炎症或胰岛素抵抗的癌症如子宫内膜癌、乳腺癌和卵巢癌中，也发现了 LAR 的升高[116-118]。这

表1 LAR的临床应用证据

	参考文献	结论	临床应用
体内代谢活动			
胰岛素敏感性	[82]	评估感染HIV的脂肪营养不良和代谢障碍患者的胰岛素敏感性，且不受身体脂肪含量的影响	评估不同人群的胰岛素敏感性或胰岛素抵抗
	[79, 83-87]	该指标与钳形衍生敏感性指数相关性最好，强于其他胰岛素抵抗替代指数，优于单独脂联素和瘦素，且不受到BMI和血糖的影响	
	[88-89]	在血糖控制不佳或糖耐量受损的群体中，LAR与胰岛素抵抗也有良好的相关性	
脂肪组织功能	[85, 93-95]	高LAR与脂肪组织的炎症和功能降低相关，LAR在体重下降后降低	评估脂肪组织功能障碍
代谢性疾病			
代谢综合征	[97]	LAR高的人出现代谢综合征的风险大概是普通人的3倍	预测和诊断代谢综合征
	[98-100]	LAR判别代谢综合征的AUC最高可以达到0.960	
心血管疾病	[103]	LAR与颈总动脉内膜中层厚度呈正相关	预测心血管疾病的病变范围和严重程度，以及发生心血管并发症的风险
	[104]	LAR与冠状动脉粥样硬化受累的血管数呈正相关	
	[106-107]	LAR能够预测如2型糖尿病、多囊卵巢综合征等患者发生心血管并发症的风险	
多囊卵巢综合征	[109-111]	LAR在多囊卵巢综合征患者中升高，识别多囊卵巢综合征的AUC可达到0.867	预测和诊断多囊卵巢综合征，预测其发生代谢并发症的风险，评估预后
	[107, 112-113]	预测与多囊卵巢综合征相关的代谢并发症，如2型糖尿病和心血管疾病 评估多囊卵巢综合征治疗的效果	
非酒精性脂肪性肝病	[114-115]	LAR在NAFLD患者中显著升高，且与脂肪变性的严重程度相关	预测NAFLD严重程度
癌症	[116-118]	在某些存在代谢功能障碍、炎症或胰岛素抵抗的癌症如子宫内膜癌、乳腺癌和卵巢癌中，发现LAR升高	潜在临床应用价值
特殊群体			
母婴	[120]	高LAR孕妇的妊娠期糖尿病发生风险是对照组的2.72倍	预测妊娠期糖尿病及其病后心血管并发症发生风险，识别先兆子痫
	[80]	较高的LAR会增加妊娠期糖尿病后的心血管风险	
	[121]	能够判别先兆子痫，其AUC为0.712	
	[121]	婴儿的相对出生体重与LAR之间存在正相关关系	
青少年	[122]	LAR可以预测青春期前非肥胖儿童的肥胖风险	预测青少年肥胖风险，评估青少年的代谢综合征及心血管疾病
	[86-87, 123]	LAR能够评估儿童青少年的胰岛素抵抗，诊断其代谢综合征，与其他的心脏代谢并发症相关	
老年人	[84, 124]	LAR可评估老年人的胰岛素抵抗，在不同血糖水平老年人中与胰岛素抵抗依旧能保持较好的相关性	评估老年人的胰岛素抵抗和脂肪组织功能障碍
	[125]	LAR作为衡量老年人组织功能障碍的指标	

也为临床疗效的评估提供了一个新思路：让机体达到低水平瘦素和高水平脂联素的平衡，而不是单纯追求较低的瘦素或较高的脂联素水平。

3.3 LAR在特殊群体中的应用

3.3.1 母婴

妊娠期需要强大的代谢适应，以确保胎儿有足够的营养供应，其中一个重要方面是由一系列母体、胎盘和胎儿激素介导的不同程度的进行性胰岛素抵抗[119]。孕妇的LAR升高可能提示着妊娠相关疾病风险增加。在一项前瞻性嵌套病例对照研究中，LAR预测妊娠期糖尿病风险的比值比(OR)可达到2.72[120]。此外，与正常妊娠相比，较高的LAR会增加妊娠期糖尿病后的心血管风险[80]。除妊娠期糖尿病外，有研究还发现尽管单独的瘦素和脂联素与先兆子痫没有相关性，但二者比值可以判别先兆子痫，其AUC为0.712[121]。LAR还与胎儿的生长发育相关，相对出生体重与LAR之间存在正相关关系[121]。

3.3.2 儿童青少年

近年来，儿童青少年的肥胖率逐渐上升，该群体发生代谢综合征及其相关疾病的风险也在增加。LAR可以预测青春期前非肥胖儿童的肥胖风险[122]。与成人相似，LAR能够评估儿童青少年的胰岛素抵抗，Agostinis-Sobrinho等[87]提出胰岛素抵抗发生风险的最佳LAR临界值在男孩中为>0.35，在女孩中为>0.97，认为LAR似乎比脂联素或瘦素具有更高的诊断价值，它可作为一项反映儿童青少年胰岛素抵抗的新指标，对肥胖相关代谢紊乱的预测具有参考价值。LAR也能诊断其代谢综合征，同时该比值与其他的心脏代谢并发症相关[86-87, 123]。

3.3.3 老年人

随着年龄增长，机体更易出现多种代谢疾病，LAR在老年群体中也有其应用价值。Biercewicz等[84]建议将LAR作为老年人胰岛素抵抗和营养状况的标志。与在高血糖人群中与胰岛素抵抗相关性降低的HOMA-IR指数不同，LAR在不同血糖水平老年人中与胰岛素抵抗依旧能保持较好的相关性[124]。一项随机对照试验表明运动和饮食干预可以帮助改善老年人群的LAR，支持将LAR作为衡量老年人组织功能障碍的指标[125]。

4 结语

瘦素-脂联素比值(LAR)将瘦素和脂联素在炎症和胰岛素敏感性中错综复杂的生理作用相结合，提供了更全面的代谢状态视角。LAR在评估胰岛素抵抗、诊断代谢综合征、评估心血管风险方面具有潜在的临床应用价值，并且在不同人群和多种特定疾病的相关研究中得以应用(表1)。尽管LAR可以在特定疾病症状出现之前作为代谢或心血管健康的预测指标，并且展现出较高的敏感性，但同时它可能面临着特异性不够高和难以标准化的挑战。高LAR与多种疾病状态相关，可能导致诊断不够明确而需要结合其他方法加以鉴别。不同的研究和检测方法可能会得到不同的结果，同时瘦素和脂联素的浓度可能受性别、营养状态和昼夜节律等多种因素影响，因此为不同的人群和不同的临床条件确定统一的“正常”范围是另一大难题。

为了克服这些挑战，未来的研究重点应该集中在标准化的测定技术统一溯源上以减少测量的变异性，并进行纵向研究以确定适合特定人群或临床条件的医学决定水平。LAR在临床诊断中的潜力是显而易见的，随着深入的研究和标准化，它有望成为评估代谢和心血管健康的关键指标。

[参 考 文 献]

[1] Zhang Y, Proenca R, Maffei M, et al. Positional cloning of the mouse obese gene and its human homologue. Nature, 1994, 372: 425-32

[2] Scherer PE, Williams S, Fogliano M, et al. A novel serum protein similar to C1q, produced exclusively in adipocytes. J Biol Chem, 1995, 270: 26746-9

[3] Gruzdeva O, Borodkina D, Uchasova E, et al. Leptin resistance: underlying mechanisms and diagnosis. Diabetes Metab Syndr Obes, 2019, 12: 191-8

[4] Straub LG, Scherer PE. Metabolic messengers: adiponectin. Nat Metab, 2019, 1: 334-9

[5] Zhang F, Basinski MB, Beals JM, et al. Crystal structure of the obese protein leptin-E100. Nature, 1997, 387: 206-9

[6] Considine RV, Sinha MK, Heiman ML, et al. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. N Engl J Med, 1996, 334: 292-5

[7] Hube F, Lietz U, Igel M, et al. Difference in leptin mRNA levels between omental and subcutaneous abdominal adipose tissue from obese humans. Horm Metab Res, 1996, 28: 690-3

[8] Zhang Y, Chua S Jr. Leptin function and regulation. Compr Physiol, 2017, 8: 351-69

[9] Krebs M, Roden M. Molecular mechanisms of lipid-induced insulin resistance in muscle, liver and vasculature. Diabetes Obes Metab, 2005, 7: 621-32

[10] Metlakunta A, Huang W, Stefanovic-Racic M, et al. Kupffer cells facilitate the acute effects of leptin on hepatic lipid metabolism. Am J Physiol Endocrinol Metab, 2017, 312: E11-8

[11] Minokoshi Y, Kim YB, Peroni OD, et al. Leptin stimulates

fatty-acid oxidation by activating AMP-activated protein kinase. Nature, 2002, 415: 339-43
[12] Nicholson T, Church C, Baker DJ, et al. The role of adipokines in skeletal muscle inflammation and insulin sensitivity. J Inflamm (Lond), 2018, 15: 9
[13] Anderwald C, Müller G, Koca G, et al. Short-term leptin-dependent inhibition of hepatic gluconeogenesis is mediated by insulin receptor substrate-2. Mol Endocrinol, 2002, 16: 1612-28
[14] Pereira S, Cline DL, Glavas MM, et al. Tissue-specific effects of leptin on glucose and lipid metabolism. Endocr Rev, 2021, 42: 1-28
[15] Leshan RL, Bjornholm M, Munzberg H, et al. Leptin receptor signaling and action in the central nervous system. Obesity, 2006, 14: 208-12
[16] Shiuchi T, Toda C, Okamoto S, et al. Induction of glucose uptake in skeletal muscle by central leptin is mediated by muscle β(2)-adrenergic receptor but not by AMPK. Sci Rep, 2017, 7: 15141
[17] Morton G, Schwartz MW. Leptin and the central nervous system control of glucose metabolism. Physiol Rev, 2011, 91: 389-411
[18] Myers MG, Cowley MA, Munzberg H. Mechanisms of leptin action and leptin resistance. Annu Rev Physiol, 2008, 70: 537-56
[19] Kumar R, Mal K, Razaq MK, et al. Association of leptin with obesity and insulin resistance. Cureus, 2020, 12: e12178
[20] Marques-Oliveira GH, Silva TM, Lima WG, et al. Insulin as a hormone regulator of the synthesis and release of leptin by white adipose tissue. Peptides, 2018, 106: 49-58
[21] Kieffer TJ, Keller RS, Leech CA, et al. Leptin suppression of insulin secretion by the activation of ATP-sensitive K^+ channels in pancreatic β-cells. Diabetes, 1997, 46: 1087-93
[22] Seufert J, Kieffer TJ, Habener JF. Leptin inhibits insulin gene transcription and reverses hyperinsulinemia in leptin-deficient ob/ob mice. Proc Natl Acad Sci U S A, 1999, 96: 674-9
[23] Kawai T, Autieri MV, Scalia R. Adipose tissue inflammation and metabolic dysfunction in obesity. Am J Physiol Cell Physiol, 2021, 320: C375-91
[24] Monteiro LB, Prodonoff JS, Favero de Aguiar C, et al. Leptin signaling suppression in macrophages improves immunometabolic outcomes in obesity. Diabetes, 2022, 71: 1546-61
[25] Saucillo DC, Gerriets VA, Sheng J, et al. Leptin metabolically licenses T cells for activation to link nutrition and immunity. J Immunol, 2014, 192: 136-44
[26] Kratofil RM, Shim HB, Shim R, et al. A monocyte-leptin-angiogenesis pathway critical for repair post-infection. Nature, 2022, 609: 166-73
[27] Mancuso P. The role of adipokines in chronic inflammation. Immunotargets Ther, 2016, 5: 47-56
[28] Lord GM, Matarese G, Howard JK, et al. Leptin modulates the T-cell immune response and reverses starvation-induced immunosuppression. Nature, 1998, 394: 897-901
[29] Pérez-Pérez A, Vilariño-García T, Guadix P, et al. Leptin and nutrition in gestational diabetes. Nutrients, 2020, 12: 1970
[30] Wang M, Wei J, Li H, et al. Leptin upregulates peripheral $CD4^+CXCR5^+ICOS^+$ T cells via increased IL-6 in rheumatoid arthritis patients. J Interferon Cytokine Res, 2018, 38: 86-92
[31] Xu WD, Zhang M, Zhang YJ, et al. Association between leptin and systemic lupus erythematosus. Rheumatol Int, 2014, 34: 559-63
[32] Han H, Zhou W. Leptin and its derivatives: a potential target for autoimmune diseases. Curr Drug Targets, 2019, 20: 1563-71
[33] Matarese G, Procaccini C, De Rosa V, et al. Regulatory T cells in obesity: the leptin connection. Trends Mol Med, 2010, 16: 247-56
[34] Becerril S, Rodríguez A, Catalán V, et al. Functional relationship between leptin and nitric oxide in metabolism. Nutrients, 2019, 11: 2129
[35] Lafrance V, Inoue W, Kan B, et al. Leptin modulates cell morphology and cytokine release in microglia. Brain Behav Immun, 2010, 24: 358-65
[36] Santos CL, Bobermin LD, Souza DO, et al. Leptin stimulates the release of pro-inflammatory cytokines in hypothalamic astrocyte cultures from adult and aged rats. Metab Brain Dis, 2018, 33: 2059-63
[37] Dragano NR, Haddad-Tovolli R, Velloso LA. Leptin, neuroinflammation and obesity. Front Horm Res, 2017, 48: 84-96
[38] Berg AH, Combs TP, Scherer PE. ACRP30/adiponectin: an adipokine regulating glucose and lipid metabolism. Trend Endocrinol Metab, 2002, 13: 84-9
[39] Schraw T, Wang ZV, Halberg N, et al. Plasma adiponectin complexes have distinct biochemical characteristics. Endocrinology, 2008, 149: 2270-82
[40] Arita Y, Kihara S, Ouchi N, et al. Paradoxical decrease of an adipose-specific protein, adiponectin, in obesity. Biochem Biophys Res Commun, 1999, 257: 79-83
[41] Manolopoulos KN, Karpe F, Frayn KN. Gluteofemoral body fat as a determinant of metabolic health. Int J Obes (Lond), 2010, 34: 949-59
[42] Turer AT, Khera A, Ayers CR, et al. Adipose tissue mass and location affect circulating adiponectin levels. Diabetologia, 2011, 54: 2515-24
[43] Lee MJ, Wu Y, Fried SK. Adipose tissue heterogeneity: implication of depot differences in adipose tissue for obesity complications. Mol Aspects Med, 2013, 34: 1-11
[44] Valenzano A, Tartaglia N, Ambrosi A, et al. The metabolic rearrangements of bariatric surgery: focus on orexin-A and the adiponectin system. J Clin Med, 2020, 9: 3327
[45] Tabák AG, Carstensen M, Witte DR, et al. Adiponectin trajectories before type 2 diabetes diagnosis: Whitehall Ⅱ study. Diabetes Care, 2012, 35: 2540-7
[46] Fang H, Judd RL. Adiponectin regulation and function. Compr Physiol, 2018, 8: 1031-63
[47] Xu W, Tian M, Zhou Y. The relationship between insulin resistance, adiponectin and C-reactive protein and vascular

endothelial injury in diabetic patients with coronary heart disease. Exp Ther Med, 2018, 16: 2022-6
[48] Yamauchi T, Kamon J, Waki H, et al. The fat-derived hormone adiponectin reverses insulin resistance associated with both lipoatrophy and obesity. Nat Med, 2001, 7: 941-6
[49] Fruebis J, Tsao TS, Javorschi S, et al. Proteolytic cleavage product of 30-kDa adipocyte complement-related protein increases fatty acid oxidation in muscle and causes weight loss in mice. Proc Natl Acad Sci U S A, 2001, 98: 2005-10
[50] Wang Y, Zhang J, Zhang L, et al. Adiponectin attenuates high glucose-induced apoptosis through the AMPK/p38 MAPK signaling pathway in NRK-52E cells. PLoS One, 2017, 12: e0178215
[51] Martinez-Huenchullan SF, Tam CS, Ban LA, et al. Skeletal muscle adiponectin induction in obesity and exercise. Metabolism, 2020, 102: 154008
[52] Yamauchi T, Kamon J, Minokoshi Y, et al. Adiponectin stimulates glucose utilization and fatty-acid oxidation by activating AMP-activated protein kinase. Nat Med, 2002, 8: 1288-95
[53] Holland WL, Xia JY, Johnson JA, et al. Inducible overexpression of adiponectin receptors highlight the roles of adiponectin-induced ceramidase signaling in lipid and glucose homeostasis. Mol Metab, 2017, 6: 267-75
[54] Vasiliauskaité-Brooks I, Sounier R, Rochaix P, et al. Structural insights into adiponectin receptors suggest ceramidase activity. Nature, 2017, 544: 120-3
[55] Berg AH, Combs TP, Du X, et al. The adipocyte-secreted protein Acrp30 enhances hepatic insulin action. Nat Med, 2001, 7: 947-53
[56] Petersen MC, Shulman GI. Mechanisms of insulin action and insulin resistance. Physiol Rev, 2018, 98: 2133-223
[57] Tchernof A, Després JP. Pathophysiology of human visceral obesity: an update. Physiol Rev, 2013, 93: 359-404
[58] Kim JY, van de Wall E, Laplante M, et al. Obesity-associated improvements in metabolic profile through expansion of adipose tissue. J Clin Invest, 2007, 117: 2621-37
[59] Brown JE, Conner AC, Digby JE, et al. Regulation of β-cell viability and gene expression by distinct agonist fragments of adiponectin. Peptides, 2010, 31: 944-9
[60] Patane G, Caporarello N, Marchetti P, et al. Adiponectin increases glucose-induced insulin secretion through the activation of lipid oxidation. Acta Diabetol, 2013, 50: 851-7
[61] Qi Y, Takahashi N, Hileman SM, et al. Adiponectin acts in the brain to decrease body weight. Nat Med, 2004, 10: 524-9
[62] Muse ED, Obici S, Bhanot S, et al. Role of resistin in diet-induced hepatic insulin resistance. J Clin Invest, 2004, 114: 232-9
[63] Obici S, Zhang BB, Karkanias G, et al. Hypothalamic insulin signaling is required for inhibition of glucose production. Nat Med, 2002, 8: 1376-82
[64] Ohashi K, Ouchi N, Matsuzawa Y. Anti-inflammatory and anti-atherogenic properties of adiponectin. Biochimie, 2012, 94: 2137-42
[65] Choi HM, Doss HM, Kim KS. Multifaceted physiological roles of adiponectin in inflammation and diseases. Int J Mol Sci, 2020, 21: 1219
[66] Shabalala SC, Dludla PV, Mabasa L, et al. The effect of adiponectin in the pathogenesis of non-alcoholic fatty liver disease (NAFLD) and the potential role of polyphenols in the modulation of adiponectin signaling. Biomed Pharmacother, 2020, 131: 110785
[67] Illan-Gomez F, Gonzalvez-Ortega M, Orea-Soler I, et al. Obesity and inflammation: change in adiponectin, C-reactive protein, tumour necrosis factor-α and interleukin-6 after bariatric surgery. Obes Surg, 2012, 22: 950-5
[68] Ohashi K, Parker JL, Ouchi N, et al. Adiponectin promotes macrophage polarization toward an anti-inflammatory phenotype. J Biol Chem, 2010, 285: 6153-60
[69] Bartosh TJ, Ylostalo JH. Macrophage inflammatory assay. Bio Protoc, 2014, 4: e1180
[70] Ajuwon KM, Spurlock ME. Adiponectin inhibits LPS-induced NF-κB activation and IL-6 production and increases PPARγ2 expression in adipocytes. Am J Physiol Regul Integr Comp Physiol, 2005, 288: R1220-5
[71] Okamoto Y, Folco EJ, Minami M, et al. Adiponectin inhibits the production of CXC receptor 3 chemokine ligands in macrophages and reduces T-lymphocyte recruitment in atherogenesis. Circ Res, 2008, 102: 218-25
[72] Chen H, Montagnani M, Funahashi T, et al. Adiponectin stimulates production of nitric oxide in vascular endothelial cells. J Biol Chem, 2003, 278: 45021-6
[73] Ouchi N, Kihara S, Arita Y, et al. Novel modulator for endothelial adhesion molecules: adipocyte-derived plasma protein adiponectin. Circulation, 1999, 100: 2473-6
[74] Peng J, Chen Q, Wu C. The role of adiponectin in cardiovascular disease. Cardiovasc Pathol, 2023, 64: 107514
[75] Cheng X, Folco EJ, Shimizu K, et al. Adiponectin induces pro-inflammatory programs in human macrophages and $CD4^+$ T cells. J Biol Chem, 2012, 287: 36896-904
[76] Tsatsanis C, Zacharioudaki V, Androulidaki A, et al. Adiponectin induces TNF-α and IL-6 in macrophages and promotes tolerance to itself and other pro-inflammatory stimuli. Biochem Biophys Res Commun, 2005, 335: 1254-63
[77] Park PH, McMullen MR, Huang H, et al. Short-term treatment of RAW264.7 macrophages with adiponectin increases tumor necrosis factor-alpha (TNF-α) expression via ERK1/2 activation and Egr-1 expression: role of TNF-α in adiponectin-stimulated interleukin-10 production. J Biol Chem, 2007, 282: 21695-703
[78] Zhang Y, Aldridge J, Vasileiadis GK, et al. Recombinant adiponectin induces the production of pro-inflammatory chemokines and cytokines in circulating mononuclear cells and fibroblast-like synoviocytes from non-inflamed subjects. Front Immunol, 2020, 11: 569883
[79] Zaletel J, Barlovic DP, Prezelj J. Adiponectin-leptin ratio: a useful estimate of insulin resistance in patients with type 2 diabetes. J Endocrinol Invest, 2010, 33: 514-8
[80] Lekva T, Michelsen AE, Aukrust P, et al. Leptin and

adiponectin as predictors of cardiovascular risk after gestational diabetes mellitus. Cardiovasc Diabetol, 2017, 16: 5

[81] Agostinis-Sobrinho CA, Lacerda Mendes E, Moreira C, et al. Association between leptin, adiponectin, and leptin/adiponectin ratio with clustered metabolic risk factors in portuguese adolescents: the LabMed physical activity study. Ann Nutr Metab, 2017, 70: 321-8

[82] Vigouroux C, Maachi M, Nguyen TH, et al. Serum adipocytokines are related to lipodystrophy and metabolic disorders in HIV-infected men under antiretroviral therapy. AIDS, 2003, 17: 1503-11

[83] Oda K, Kawate H, Ishibashi A, et al. Insulin resistance and the adiponectin/leptin ratio as a surrogate measure of insulin resistance in Japanese collegiate baseball players. J Sports Med Phys Fitness, 2021, 61: 1661-7

[84] Biercewicz M, Slusarz R, Kedziora-Kornatowska K, et al. Assessment of leptin-to-adiponectin ratio in prediction of insulin resistance and nutrition status in a geriatric female population. J Physiol Pharmacol, 2020, 71: 35-46

[85] Castela I, Morais J, Barreiros-Mota I, et al. Decreased adiponectin/leptin ratio relates to insulin resistance in adults with obesity. Am J Physiol Endocrinol Metab, 2023, 324: E115-9

[86] Frithioff-Bojsoe C, Lund MAV, Lausten-Thomsen U, et al. Leptin, adiponectin, and their ratio as markers of insulin resistance and cardiometabolic risk in childhood obesity. Pediatr Diabetes, 2020, 21: 194-202

[87] Agostinis-Sobrinho C, Vicente S, Norkiene S, et al. Is the leptin/adiponectin ratio a better diagnostic biomarker for insulin resistance than leptin or adiponectin alone in adolescents? Children (Basel), 2022, 9: 1193

[88] Inoue M, Maehata E, Yano M, et al. Correlation between the adiponectin-leptin ratio and parameters of insulin resistance in patients with type 2 diabetes. Metabolism, 2005, 54: 281-6

[89] 刘师伟, 杨静. 脂联素与瘦素的比值和2型糖尿病胰岛素抵抗的相关性. 中华内分泌代谢杂志, 2008, 24: 21-2

[90] Yun JE, Won S, Mok Y, et al. Association of the leptin to high-molecular-weight adiponectin ratio with metabolic syndrome. Endocr J, 2011, 58: 807-15

[91] Bravo C, Cataldo LR, Galgani J, et al. Leptin/adiponectin ratios using either total or high-molecular-weight adiponectin as biomarkers of systemic insulin sensitivity in normoglycemic women. J Diabetes Res, 2017, 2017: 9031079

[92] Crewe C, An YA, Scherer PE. The ominous triad of adipose tissue dysfunction: inflammation, fibrosis, and impaired angiogenesis. J Clin Invest, 2017, 127: 74-82

[93] Fruhbeck G, Catalan V, Rodriguez A, et al. Adiponectin-leptin ratio is a functional biomarker of adipose tissue inflammation. Nutrients, 2019, 11: 454

[94] 翁晓峰, 朱燕忠, 宋成, 等. 脂联素与瘦素比值作为脂肪组织功能障碍生物标志物的应用. 实用检验医师杂志, 2022, 14: 407-11

[95] Rafey MF, Abdalgwad R, O'Shea PM, et al. Changes in the leptin to adiponectin ratio are proportional to weight loss after meal replacement in adults with severe obesity. Front Nutr, 2022, 9: 845574

[96] Saklayen MG. The global epidemic of the metabolic syndrome. Curr Hypertens Rep, 2018, 20: 12

[97] Lee KW, Shin D. Prospective associations of serum adiponectin, leptin, and leptin-adiponectin ratio with incidence of metabolic syndrome: the Korean genome and epidemiology study. Int J Environ Res Public Health, 2020, 17: 3287

[98] Chen VC, Chen CH, Chiu YH, et al. Leptin/adiponectin ratio as a potential biomarker for metabolic syndrome in patients with schizophrenia. Psychoneuroendocrinology, 2018, 92: 34-40

[99] Adejumo EN, Adejumo OA, Azenabor A, et al. Leptin:adiponectin ratio discriminated the risk of metabolic syndrome better than adiponectin and leptin in Southwest Nigeria. Diabetes Metab Syndr, 2019, 13: 1845-9

[100] de Dios O, Vales-Villamarín C, Herrero L, et al. Analysis of leptin-adiponectin ratio and C-reactive protein as potential biomarkers of metabolic syndrome in adolescents. Clin Chem Lab Med, 2021, 59: e382-5

[101] Zhao S, Kusminski CM, Scherer PE. Adiponectin, leptin and cardiovascular disorders. Circ Res, 2021, 128: 136-49

[102] Dai Z, Zhang Y, Ye H, et al. Adiponectin is valuable in the diagnosis of acute heart failure with renal insufficiency. Exp Ther Med, 2018, 16: 2725-34

[103] Norata GD, Raselli S, Grigore L, et al. Leptin: adiponectin ratio is an independent predictor of intima media thickness of the common carotid artery. Stroke, 2007, 38: 2844-6

[104] Rahmani A, Toloueitabar Y, Mohsenzadeh Y, et al. Association between plasma leptin/adiponectin ratios with the extent and severity of coronary artery disease. BMC Cardiovasc Disord, 2020, 20: 474

[105] Zhu T, Chen M, Wang M, et al. Association between adiponectin-to-leptin ratio and heart rate variability in new-onset paroxysmal atrial fibrillation: a retrospective cohort study. Ann Noninvasive Electrocardiol, 2022, 27: e12896

[106] Mohammed Saeed W, Nasser Binjawhar D. Association of serum leptin and adiponectin concentrations with type 2 diabetes biomarkers and complications among Saudi women. Diabetes Metab Syndr Obes, 2023, 16: 2129-40

[107] Gupta V, Mishra S, Mishra S, et al. L: A ratio, insulin resistance and metabolic risk in women with polycystic ovarian syndrome. Diabetes Metab Syndr, 2017, 11 Suppl 2: S697-701

[108] Meier RK. Polycystic ovary syndrome. Nurs Clin North Am, 2018, 53: 407-20

[109] Mishra P, Mittal P, Rani A, et al. Adiponectin to leptin ratio and its association with insulin resistance in women with polycystic ovarian syndrome. Indian J Endocrinol Metab, 2022, 26: 239-44

[110] Vatannejad A, Kheirollahi A. Adiponectin/leptin and HOMA/adiponectin ratios in Iranian women with polycystic ovary syndrome. Ir J Med Sci, 2023, 192: 1793-9

[111] Golbahar J, Das NM, Al-Ayadhi MA, et al. Leptin-to-adiponectin, adiponectin-to-leptin ratios, and insulin are specific and sensitive markers associated with polycystic ovary syndrome: a case-control study from Bahrain. Metab Syndr Relat Disord, 2012, 10: 98-102

[112] López-Jaramillo P, Gómez-Arbeláez D, López-López J, et al. The role of leptin/adiponectin ratio in metabolic syndrome and diabetes. Horm Mol Biol Clin Investig, 2014, 18: 37-45

[113] Vatier C, Antuna-Puente B, Fellahi S, et al. The adiponectin to leptin ratio, a still unrecognized biomarker of insulin resistance and cardiometabolic risk. Ann Biol Clin (Paris), 2020, 78: 265-8

[114] Angın Y, Arslan N, Kuralay F. Leptin-to-adiponectin ratio in obese adolescents with nonalcoholic fatty liver disease. Turk J Pediatr, 2014, 56: 259-66

[115] Mikami K, Endo T, Sawada N, et al. Leptin/adiponectin ratio correlates with hepatic steatosis but not arterial stiffness in nonalcoholic fatty liver disease in Japanese population. Cytokine, 2020, 126: 154927

[116] Gong TT, Wu QJ, Wang YL, et al. Circulating adiponectin, leptin and adiponectin-leptin ratio and endometrial cancer risk: evidence from a meta-analysis of epidemiologic studies. Int J Cancer, 2015, 137: 1967-78

[117] Słomian GJ, Nowak D, Buczkowska M, et al. The role of adiponectin and leptin in the treatment of ovarian cancer patients. Endokrynol Pol, 2019, 70: 57-63

[118] Cairat M, Rinaldi S, Navionis AS, et al. Circulating inflammatory biomarkers, adipokines and breast cancer risk-a case-control study nested within the EPIC cohort. BMC Med, 2022, 20: 118

[119] Barbour LA, McCurdy CE, Hernandez TL, et al. Cellular mechanisms for insulin resistance in normal pregnancy and gestational diabetes. Diabetes Care, 2007, 30 Suppl 2: S112-9

[120] Ye Y, Wu P, Wang Y, et al. Adiponectin, leptin, and leptin/adiponectin ratio with risk of gestational diabetes mellitus: a prospective nested case-control study among Chinese women. Diabetes Res Clin Pract, 2022, 191: 110039

[121] de Knegt VE, Hedley PL, Eltvedt AK, et al. First-trimester maternal serum adiponectin/leptin ratio in pre-eclampsia and fetal growth. Life (Basel), 2023, 13: 130

[122] Zhang M, Cheng H, Zhao X, et al. Leptin and leptin-to-adiponectin ratio predict adiposity gain in nonobese children over a six-year period. Child Obes, 2017, 13: 213-21

[123] Li G, Xu L, Zhao Y, et al. Leptin-adiponectin imbalance as a marker of metabolic syndrome among Chinese children and adolescents: the BCAMS study. PLoS One, 2017, 12: e0186222

[124] 倪一虹, 庄向华, 黄建安. 不同血糖水平老年人脂联素, 瘦素水平及其比值与胰岛素抵抗的相关性. 中国老年学杂志, 2012, 32: 2008-10

[125] Senkus KE, Crowe-White KM, Bolland AC, et al. Changes in adiponectin: leptin ratio among older adults with obesity following a 12-month exercise and diet intervention. Nutr Diabetes, 2022, 12: 30