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载脂蛋白B/载脂蛋白A1的临床研究进展

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摘　要

载脂蛋白(Apolipoprotein)是与脂质结合，形成脂蛋白的蛋白质分子，它主要负责脂质的运输和代谢，根据其功能和结构特性，载脂蛋白可分为A类、B类、C类、E类以及脂蛋白(a)，其主要的载脂蛋白如ApoA1、ApoB和ApoE各自承担着独特的职能，影响着人体的脂质代谢和心血管健康。既往研究表明，Apolipoprotein异常表达与多种疾病的发生和发展密切相关，本文将从载脂蛋白A1 (ApoA1)、载脂蛋白B (ApoB)及两者比值(ApoB/ApoA1)的研究进展入手进行概述。

关键词

载脂蛋白，冠心病，高血压，心力衰竭，糖尿病

Clinical Research Progress of Apolipoprotein B/Apolipoprotein A1

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Abstract

Apolipoproteins are protein molecules that bind with lipids to form lipoproteins. It is mainly responsible for the transportation and metabolism of lipids. They can be classified into various classes based on their functional and structural characteristics, including apolipoprotein A, B, C, E, and lipoprotein (a). Key proteins, such as ApoA1, ApoB, and ApoE each have unique functions that impact lipid metabolism and cardiovascular health in the human body. Research conducted in the past indicates that unusual levels of apolipoproteins are strongly linked to the onset and progression of multiple diseases. This article will summarize the research progress of apolipoprotein A1 (ApoA1),

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apolipoprotein B (ApoB), and their ratio (ApoB/ApoA1).

Keywords

Apolipoprotein, Coronary Heart Disease, Hypertension, Heart Failure, Diabetes

1. 引言

载脂蛋白是一类与脂蛋白颗粒内部脂质结合的蛋白质，已经被证实在脂质代谢过程中具有重要的作用，其功能不仅包括脂质的转运、储存和利用，还具有激活或抑制与脂质代谢相关的酶的能力，从而在脂质代谢调节方面发挥着关键作用[1]，载脂蛋白与多种代谢状态及心血管疾病的发生密切相关，本文将从主要载脂蛋白如 ApoA、ApoB、ApoB/ApoA1 的生理作用及其与多种疾病的影响进展进行综述。

2. ApoB、ApoA1、ApoB/ApoA1 生理作用

ApoB 是低密度脂蛋白胆固醇(LDL-C)的主要载脂蛋白，能够更准确地反映脂蛋白致动脉粥样硬化负荷，并参与血清胆固醇(CH)的运输，并介导 CH 在外周组织的摄取和利用，被证明是比总胆固醇或低密度脂蛋白胆固醇更准确的心血管风险指标[2] [3]。ApoB 携带的脂蛋白(如 LDL-C)在内皮细胞下沉积，触发炎症因子，如白细胞介素-6 (IL-6)和肿瘤坏死因子 α (TNF-α)释放，导致内皮细胞激活和炎症反应[4]，激活的内皮细胞表达黏附分子(如 VCAM-1、ICAM-1)，促进单核细胞浸润并转化为巨噬细胞，进一步释放炎症因子，加剧炎症。ApoB 携带的 LDL 在血管壁内易被氧化，形成氧化低密度脂蛋白(ox-LDL)，触发氧化应激反应，损伤内皮细胞。ox-LDL 通过 LOX-1 受体促进活性氧(ROS)生成，进一步损伤细胞，形成恶性循环。ox-LDL 和炎症因子可诱导内皮细胞和平滑肌细胞凋亡，加速斑块形成和不稳定。ApoA1 是由肝脏分泌的蛋白质，是高密度脂蛋白(HDL-C)颗粒的最主要成分，具有重要的生物学作用[5]。ApoA1 不仅具有重要的免疫功能，还负责胆固醇逆向转运[6]，具有抗氧化作用，还可直接清除自由基，抑制脂质过氧化，保护内皮细胞免受氧化损伤。ApoB/ApoA1 比值升高可能削弱 ApoA1 的抗氧化功能，导致氧化应激加剧；也可通过炎症和氧化应激导致内皮细胞损伤，降低一氧化氮(NO)的生物利用度，引发内皮功能障碍，促进血管病变。根据报道，ApoA1 与许多疾病有关，包括动脉粥样硬化[6]，冠状动脉疾病[7]，神经系统疾病[8]，肝炎[9]，糖尿病心肌病[10]等。因此，ApoB 具有致动脉粥样硬化能力，ApoA1 能够有效反映出机体抵御动脉粥样硬化的能力。与此相对，ApoB/ApoA1 的比值代表了促动脉粥样硬化因素与抗动脉粥样硬化作用之间的动态平衡状态。因此，许多研究认为 ApoB/ApoA1 比值是评估动脉粥样硬化风险的更为优越的预测指标[11]-[13]。在临床实践中，ApoB/ApoA1 的应用前景正在受到越来越多的关注。

3. ApoB/ApoA1 临床应用

3.1. ApoB/ApoA1 与冠心病

冠状动脉粥样硬化性心脏病(coronary heart disease, CHD)是一种较为常见的心血管疾病，它是由冠状动脉的狭窄或阻塞所致，也是全球最常见的慢性疾病之一，冠心病依据其发病特点和治疗原则，可分为两大类：慢性冠状动脉疾病(CAD)、急性冠状动脉综合征(ACS)。研究表明，新的血脂指标，如 ApoB 与 ApoA1

的比值，与冠心病的发生、发展及其风险有较强的关联性[11] [14] [15]。高 ApoB/ApoA1 比值通常表明低密度脂蛋白的增加和高密度脂蛋白的减少，这种失衡会加重动脉粥样硬化的发展，从而加重冠心病的严重程度。研究表明，ApoB/ApoA1 比率在预测心血管事件(如心肌梗死和中风)时，具有独立于年龄、性别和其他传统风险因素的能力[16]。尽管 LDL-C 长期以来一直是心血管疾病风险评估的标准指标，但越来越多的研究显示，ApoA1、ApoB 和 ApoB/ApoA1 比值比 LDL-C 更能预测冠状动脉疾病[17]-[19]。另外有一项涉及全球 52 个国家的研究显示，与吸烟、高血压、糖尿病、腹部肥胖等因素相比，ApoB/ApoA1 比值是心血管不良事件最重要的影响因素[20]。此外，Bodde 等人[21]认为 ApoB/ApoA1 是比总胆固醇与高密度脂蛋白胆固醇(TC/HDL-C)比值更可靠的急性心肌梗死(Acute myocardial infarction, AMI)风险预测因子，INTERHEART 研究的研究者也得出了一致的结论[22]，即 ApoB/ApoA1 是比 TC/HDL-C 更好的 AMI 风险标志物。Galal 等人[23]研究发现 ApoB/ApoA1 可作为评估非 ST 段抬高急性冠状动脉综合征(NSTE-ACS)患者风险的有效预测因子，较高的 ApoB/ApoA1 与冠状动脉多支血管病变以及复杂病变之间存在显著关联。除此之外，ApoB/ApoA1 可能作为不稳定型心绞痛的早期生物标志物，提供临床诊断和风险评估的参考依据[24]。Florvall 等人发现 ApoB/ApoA1 是老年男性心血管疾病和死亡率的预测因子[25]。三项大规模队列研究也呈现出一致的结果，即 ApoB 和 ApoA1 都是独立、相同的预测值，并且 ApoB/ApoA1 是心血管疾病最强且最具体的指标[22] [26] [27]。总之，ApoB/ApoA1 在冠心病的筛查和早期诊断中具有重要的临床价值，随着进一步的研究，ApoB/ApoA1 有望在心血管疾病的早期发现和干预中发挥更大的作用，从而提高了整体病人的心血管健康状况和生活质量。

3.2. ApoB/ApoA1 与高血压

高血压通常被定义为系统性动脉压力的慢性升高，根据世界卫生组织(WHO)的定义，收缩压达到 140 mmHg (18.7 kPa)或以上，或舒张压达到 90 mmHg (12.0 kPa)或以上可被定义为高血压。高血压是心血管疾病中较为常见的一种，它的发展受到多种因素的影响，其中包括遗传因素、环境因素以及生活方式等方面。这些因素相互作用，共同塑造了其发展过程。脂质代谢异常，特别是 ApoB/ApoA1 的增加与高血压的发生有显著关联，高比值不仅反映了不良的脂质代谢状态，还可能通过促进炎症、氧化应激及内皮功能障碍等途径，加快发展动脉硬化和血压升高[28]。Pietri 等人[29]的研究提示 ApoB/ApoA1 与高血压患者的靶器官损伤(如心脏、肾脏等)有独立关系，即使不存在其他风险因素，ApoB/ApoA1 也能有效预测高血压患者的健康状况和可能出现的并发症。Han 等人[28]的研究表明，ApoB 浓度较高与未来高血压的风险增加相关，这一发现独立于腹部内脏脂肪面积和胰岛素敏感性。此外，ApoB/ApoA1 的升高与代谢综合征成分恶化、胰岛素抵抗加重以及激素水平升高之间存在显著关联[30]，这些因素都是与高血压发病有很大关系的。随着相关研究的不断深入，ApoB 和 ApoA1 有望在未来成为高血压管理中不可或缺的生物标志物。

3.3. ApoB/ApoA1 与心力衰竭

心力衰竭(heart failure, HF)是一种常见的致命性疾病，可由冠心病、高血压、瓣膜性心脏病和特发性扩张型心肌病[31]等多种因素引起。尽管慢性心力衰竭的诊断和治疗已取得显著进展，但病死率和再住院率仍保持高位[32]。Li 等人[33]随机将 2400 例心衰患者分为训练组(n = 1400)和验证组(n = 1000)，通过受试者的工作特征曲线，确定训练队列中 ApoB/ApoA1 的最佳临界值为 0.69，并在验证队列中进一步验证。即使消除了高、低 ApoB/ApoA1 组基线特征的不平衡。最终得出结论，一致认为 ApoB/ApoA1 ≥ 0.69 是心力衰竭患者死亡风险增加的独立预测因子，调整传统风险因素后，其重要性仍然存在。在一项大型人群研究中，ApoB/ApoA1 的增加与 HF 的发生显著相关[34]。此外，Fu 等人[16]认为 ApoB/ApoA1 比值升

高与首发急性心肌梗死患者经皮冠状动脉介入术(Percutaneous Coronary Intervention, PCI)术后发生心力衰竭有关，且较高的 ApoB/ApoA1 与接受 PCI 的急性冠脉综合征患者发生主要不良心血管事件(MACE)显著相关[35]。但 ApoB/ApoA1 是如何直接影响心力衰竭的预后尚不清楚，猜测炎症可能是 ApoB/ApoA1 与心力衰竭预后之间的联系[21]。ApoB/ApoA1 对心力衰竭的预后价值值得在更大规模的前瞻性和多中心研究中进一步验证。

3.4. ApoB/ApoA1 与糖尿病

糖尿病(diabetes mellitus, DM)是一种代谢性疾病，其主要特征是高血糖，其发生往往与多种病因密切相关。糖尿病的慢性高血糖与不同器官的长期损伤、功能障碍和衰竭有关，特别是眼睛、肾脏、神经、心脏和血管等[36]。DM 患者常伴有脂质代谢障碍，ApoB 和 ApoA1 在糖尿病的发病机制中扮演着重要角色。它们的水平和比值不仅反映了脂质代谢的状态，还与胰岛素抵抗、炎症反应和氧化应激等多种病理生理过程密切相关。研究发现[37]，ApoB/ApoA1 比值与 2 型糖尿病发病率以及空腹血糖(FBG)之间存在正相关关系。进一步的研究表明，ApoB/ApoA1 比值与中国女性的糖尿病及前糖尿病期风险之间存在正相关性，这凸显了该比值在不同人群中的普遍适用性[38]。另有一些研究提出，ApoB/ApoA1 比值与 2 型糖尿病之间的关系可能不是简单的线性关系，而是还存在阈值效应或非线性的相关性[39]。一项韩国的观察性研究表明，ApoB/ApoA1 比值升高与 2 型糖尿病的患病率增加相关，即 ApoB 水平较高(≥87.0 mg/dL)的个体，其新发糖尿病的风险约为 ApoB 水平较低个体的两倍[40]。此外，大规模前瞻性调研显示，ApoB/A1 比值可以作为代谢综合征定义之外的潜在预测糖尿病风险的标志物[41]。ApoB/ApoA1 比值作为一项有潜力的生物标志物，显示出在评估和管理 2 型糖尿病方面的巨大潜力。尽管已有研究显示出 ApoB/ApoA1 比值在糖尿病预测中的潜力，但大规模的前瞻性研究仍有待开展，以进一步验证其作为临床标志物的有效性并明确其机制。

3.5. ApoB/ApoA1 与非酒精性脂肪肝病

非酒精性脂肪肝病(non-alcoholic fatty liver disease, NAFLD)是指在不饮酒或少饮酒的情况下，肝脏中的脂肪累积超过 5%。这种脂肪的存储可以通过组织学检查(如肝活检)或磁共振成像(MRI)来确认，后者的标准是肝脏脂肪含量超过 5.6% [42]。NAFLD 的发生通常与多种因素有关，如肥胖、糖尿病、高血压和高血脂等，脂质的合成和分解失衡可能导致肝脏内脂肪的异常累积。在一项对韩国人群的研究中，Choe 等人[43]纳入 9162 名受试者，应用回归分析来评估 ApoB/ApoA1 与 NAFLD 之间的关联，研究发现，较高的血清 ApoB 水平、较低的 ApoA1 水平以及较高的 ApoB/ApoA1 比值与 NAFLD 的风险显著相关，提示对于识别高危人群，该比值可能是一个有用的生物标志物，Zhao 等人也得到了相同的结论[44]。ApoB/ApoA1 比值在非酒精性肝病发展中起着重要的生物学作用，通过深入研究这一比值及其相关机制，能为 NAFLD 提供早期诊断和治疗的新思路。

3.6. ApoB/ApoA1 与急性胰腺炎

急性胰腺炎(acute pancreatitis, AP)是一种消化系统的急腹症，其主要特征为胰腺局部炎症反应，且可能导致多脏器功能衰竭。在急性胰腺炎研究中[45] [46]，研究者发现 ApoB/ApoA1 的变化与急性胰腺炎的严重程度及其并发症之间存在相关性，其升高反映了体内促炎与抗炎因子的失衡，这种失衡可能导致胰腺组织的进一步损伤和炎症反应的加剧，从而增加并发症的发生率。同时，Wu 等人[47]的研究认为，入院时的血清 ApoB/ApoA1 与 AP 患者的疾病严重程度独立相关，ApoB/ApoA1 预测急性重症胰腺炎(SAP)的预测临界值为 0.88，敏感性 83.08%，而特异性则为 69.03%。Fan 等人[48]认为，较高的 ApoB/ApoA1 比值与多脏器功能不全的发生风险显著相关。这是由于系统性炎症反应综合症(SIRS)导致的血流动力学

不稳定和器官灌注不足所致。目前关于 ApoB/ApoA1 比值预测 AP 严重程度的医学证据仍不充分，需要进行更多研究以进一步证实其优势。

3.7. ApoB/ApoA1 与缺血性脑卒中

缺血性脑卒中(ischemic stroke)是由于脑动脉狭窄或堵塞导致脑部血流不足，从而产生突发的神经功能缺损和脑组织的永久性损伤[49]。近来，在缺血性中风的研究中，ApoB/ApoA1 比值逐渐受到关注。几项研究表明[16] [50]，ApoB/ApoA1 比值是有效预测急性缺血性脑卒中发生的一个指标，其比值增加与中风的发生率正相关，在初次中风发作后的急性期所测定的 ApoB/ApoA1 比值与一年内中风再次发作的风险呈现正比关系，这提示，早期对这一比值的评估可能对预测患者的长期健康结果具有指导意义[51]。Kalani 等人[52]的研究也揭示了血清 ApoB/ApoA1 比值的增加与缺血性中风发生之间存在密切关联。此外，在一个纵向研究中：升高的 ApoB/ApoA1 不仅与中风的风险紧密相连，还与后续的缺血性脑损伤(脑梗塞)的发展有密切关系[53]。更有研究者认为[54] ApoB/ApoA1 比值可以作为脑动脉狭窄的可靠生物标志物，帮助医生在临床上早期识别这些患者，除了 ApoB/ApoA1 比值外，ApoA1 的水平本身也被认为是缺血性中风的一个预测因子；Eldeeb 等人[55]前瞻性地纳入了 60 名首次脑血管缺血性卒中患者，在中风发作的最初 24 小时内采集静脉血样测量 ApoA1 水平，结果发现 ApoA1 水平低的患者在缺血性中风后可能面临更差的预后。Kostapanos 等[56]研究认为 ApoB/ApoA1 对老年急性缺血性卒中有较高预测价值。

ApoB/ApoA1 比值与缺血性卒中相关，监控此比值有助于评估风险，制定预防和治疗策略。研究需进一步探索其在人群中的表现及机制，以便早期识别和干预。

3.8. ApoB/ApoA1 与肾病综合征

肾病综合征(nephrotic syndrome, NS)是一种由肾小球滤过屏障障碍引起的临床综合征，表现为大量尿蛋白、低白蛋白血症、浮肿、高脂血症。在肾脏中，ApoB 和 ApoA1 的表达与肾脏功能的维护以及肾脏疾病的发生发展密切相关。有研究表明[57]，ApoB 与肾脏的损伤和慢性肾病的进展相关，ApoB 的增加可能会导致肾小管间质的病理变化，加重肾脏的损伤。ApoA1 在肾脏中的表达同样重要，其水平与肾脏的健康状况相关。ApoA1 在脂质代谢过程中扮演着关键角色，它有助于清除肾脏内的多余脂质，进而减轻氧化应激和炎症反应。Pan 等人[58]认为较高的 ApoB/ApoA1 比率与较低的肾小管滤过率(eGFR)相关，并且该比值可以作为肾病患者的预后指标之一。ApoB 和 ApoA1 在脂质代谢的调节中参与作用，还通过影响炎症反应和氧化应激等机制直接参与肾小管和肾小球的损伤。进一步的研究有助于深入理解这些脂蛋白在肾脏疾病中的作用，也许能为开发新的治疗策略提供理论基础。

4. ApoB/ApoA1 比值的临床应用前景

ApoA1 和 ApoB 是入院常规血液检查的关键组成部分之一，其测量简便、快捷且成本效益高，使其成为大多数医院的最佳选择，并广泛应用于临床实践。ApoB/ApoA1 比率在临床实践中的应用受到一些限制。例如，代谢综合症、糖尿病及其他心血管疾病的患者，其 ApoB 和 ApoA1 水平可能会受到疾病状态的显著影响[59]，不同年龄、性别和种族的个体在 ApoB 和 ApoA1 水平上可能存在显著差异[60]，从而导致 ApoB/ApoA1 比率的解读变得复杂。ApoB/ApoA1 比值通过炎症、氧化应激等机制影响疾病的发生发展，具体机制包括 ApoB 的促炎和促氧化作用、ApoA1 的抗炎和抗氧化作用，以及两者失衡导致的慢性炎症和氧化应激状态。总体而言，随着对 ApoB/A1 比值的深入研究，其在多种疾病的预测和评估中展现了良好的前景，临床应用愈发广阔。未来的研究应进一步集中在 ApoB/ApoA1 比值如何通过核因子 κB (NF-κB)、核苷酸结合寡聚化结构域样受体蛋白 3 (NLRP3)炎症小体等信号通路调控炎症和氧化应激，为相关疾病的防治提供理论依据。

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基于 Akt-GSK3β-mPTP 信号通路探究 SGLT-2 抑制剂防治急性心肌梗死缺血灌注损伤 I/R 作用机制。

参考文献

[1] Beisiegel, U. (1998) Lipoprotein Metabolism. *European Heart Journal*, **19**, A20-A23.

[2] Behbodikhah, J., Ahmed, S., Elyasi, A., Kasselman, L.J., De Leon, J., Glass, A.D., *et al*. (2021) Apolipoprotein B and Cardiovascular Disease: Biomarker and Potential Therapeutic Target. *Metabolites*, **11**, Article 690. https://doi.org/10.3390/metabo11100690

[3] Linton, M.F., Yancey, P.G., Davies, S.S., *et al*. (2019) The Role of Lipids and Lipoproteins in Atherosclerosis. Endotext.

[4] Borén, J. and Williams, K.J. (2016) The Central Role of Arterial Retention of Cholesterol-Rich Apolipoprotein-B-Containing Lipoproteins in the Pathogenesis of Atherosclerosis: A Triumph of Simplicity. *Current Opinion in Lipidology*, **27**, 473-483. https://doi.org/10.1097/mol.0000000000000330

[5] Frank, P.G. and Marcel, Y.L. (2000) Apolipoprotein A-I: Structure-Function Relationships. *Journal of Lipid Research*, **41**, 853-872. https://doi.org/10.1016/s0022-2275(20)32028-9

[6] Cochran, B.J., Ong, K., Manandhar, B. and Rye, K. (2021) ApoA1: A Protein with Multiple Therapeutic Functions. *Current Atherosclerosis Reports*, **23**, Article No. 11. https://doi.org/10.1007/s11883-021-00906-7

[7] Chistiakov, D.A., Orekhov, A.N. and Bobryshev, Y.V. (2016) ApoA1 and ApoA1-Specific Self-Antibodies in Cardiovascular Disease. *Laboratory Investigation*, **96**, 708-718. https://doi.org/10.1038/labinvest.2016.56

[8] Button, E.B., Boyce, G.K., Wilkinson, A., Stukas, S., Hayat, A., Fan, J., *et al*. (2019) ApoA-I Deficiency Increases Cortical Amyloid Deposition, Cerebral Amyloid Angiopathy, Cortical and Hippocampal Astrogliosis, and Amyloid-Associated Astrocyte Reactivity in APP/PS1 Mice. *Alzheimer's Research & Therapy*, **11**, Article No. 44. https://doi.org/10.1186/s13195-019-0497-9

[9] Wang, X., Gong, Y., Deng, T., Zhang, L., Liao, X., Han, C., *et al*. (2019) Diagnostic and Prognostic Significance of mRNA Expressions of Apolipoprotein A and C Family Genes in Hepatitis B Virus-Related Hepatocellular Carcinoma. *Journal of Cellular Biochemistry*, **120**, 18246-18265. https://doi.org/10.1002/jcb.29131

[10] Hughes, T.A., Calderon, R.M., Diaz, S., Mendez, A.J. and Goldberg, R.B. (2016) Lipoprotein Composition in Patients with Type 1 Diabetes Mellitus: Impact of Lipases and Adipokines. *Journal of Diabetes and Its Complications*, **30**, 657-668. https://doi.org/10.1016/j.jdiacomp.2016.01.018

[11] Tian, M., Li, R., Shan, Z., Wang, D.W., Jiang, J. and Cui, G. (2019) Comparison of Apolipoprotein B/A1 Ratio, Framingham Risk Score and TC/HDL-C for Predicting Clinical Outcomes in Patients Undergoing Percutaneous Coronary Intervention. *Lipids in Health and Disease*, **18**, Article No. 202. https://doi.org/10.1186/s12944-019-1144-y

[12] Ljungberg, J., Holmgren, A., Bergdahl, I.A., Hultdin, J., Norberg, M., Näslund, U., *et al*. (2017) Lipoprotein(a) and the Apolipoprotein B/A1 Ratio Independently Associate with Surgery for Aortic Stenosis Only in Patients with Concomitant Coronary Artery Disease. *Journal of the American Heart Association*, **6**, e007160. https://doi.org/10.1161/jaha.117.007160

[13] Tani, S., Nagao, K., Anazawa, T., Kawamata, H., Furuya, S., Takahashi, H., *et al*. (2010) Relation of Change in Apolipoprotein B/Apolipoprotein A-I Ratio to Coronary Plaque Regression after Pravastatin Treatment in Patients with Coronary Artery Disease. *The American Journal of Cardiology*, **105**, 144-148. https://doi.org/10.1016/j.amjcard.2009.08.670

[14] Kim, J.H., Jeong, M.H., Hong, Y.J., Lee, K.H., Kim, I.S., Choi, Y.H., *et al*. (2012) Low Density Lipoprotein-Cholesterol/High Density Lipoprotein-Cholesterol Ratio Predicts Plaque Vulnerability in Patients with Stable Angina. *Korean Circulation Journal*, **42**, 246-251. https://doi.org/10.4070/kcj.2012.42.4.246

[15] Hua, R., Li, Y., Li, W., Wei, Z., Yuan, Z. and Zhou, J. (2021) Apolipoprotein B/A1 Ratio Is Associated with Severity of Coronary Artery Stenosis in CAD Patients but Not in Non-Cad Patients Undergoing Percutaneous Coronary Intervention. *Disease Markers*, **2021**, 1-10. https://doi.org/10.1155/2021/8959019

[16] Fu, C., Liu, D., Liu, Q., Wang, X., Ma, X., Pan, H., *et al*. (2024) Revisiting an Old Relationship: The Causal Associations of the ApoB/ApoA1 Ratio with Cardiometabolic Diseases and Relative Risk Factors—A Mendelian Randomization Analysis. *Cardiovascular Diabetology*, **23**, Article No. 51. https://doi.org/10.1186/s12933-024-02140-2

[17] Pencina, M.J., D'Agostino, R.B., Zdrojewski, T., Williams, K., Thanassoulis, G., Furberg, C.D., *et al*. (2015) Apolipoprotein B Improves Risk Assessment of Future Coronary Heart Disease in the Framingham Heart Study Beyond LDL-C and Non-HDL-C. *European Journal of Preventive Cardiology*, **22**, 1321-1327. https://doi.org/10.1177/2047487315569411

[18] Sniderman, A.D., Islam, S., McQueen, M., Pencina, M., Furberg, C.D., Thanassoulis, G., *et al*. (2016) Age and Cardiovascular Risk Attributable to Apolipoprotein B, Low-Density Lipoprotein Cholesterol or Non-High-Density Lipoprotein

Cholesterol. *Journal of the American Heart Association*, **5**, e003665. https://doi.org/10.1161/jaha.116.003665

[19] Thanassoulis, G., Williams, K., Ye, K., Brook, R., Couture, P., Lawler, P.R., *et al*. (2014) Relations of Change in Plasma Levels of LDL-C, Non-HDL-C and ApoB with Risk Reduction from Statin Therapy: A Meta-Analysis of Randomized Trials. *Journal of the American Heart Association*, **3**, e000759. https://doi.org/10.1161/jaha.113.000759

[20] Yusuf, S., Hawken, S., Ôunpuu, S., Dans, T., Avezum, A., Lanas, F., *et al*. (2004) Effect of Potentially Modifiable Risk Factors Associated with Myocardial Infarction in 52 Countries (the INTERHEART Study): Case-Control Study. *The Lancet*, **364**, 937-952. https://doi.org/10.1016/s0140-6736(04)17018-9

[21] Bodde, M.C., Hermans, M.P.J., Jukema, J.W., Schalij, M.J., Lijfering, W.M., Rosendaal, F.R., *et al*. (2018) Apolipoproteins A1, B, and ApoB/ApoA1 Ratio Are Associated with First St-Segment Elevation Myocardial Infarction but Not with Recurrent Events during Long-Term Follow-Up. *Clinical Research in Cardiology*, **108**, 520-538. https://doi.org/10.1007/s00392-018-1381-5

[22] McQueen, M.J., Hawken, S., Wang, X., Ounpuu, S., Sniderman, A., Probstfield, J., *et al*. (2008) Lipids, Lipoproteins, and Apolipoproteins as Risk Markers of Myocardial Infarction in 52 Countries (The Interheart Study): A Case-Control Study. *The Lancet*, **372**, 224-233. https://doi.org/10.1016/s0140-6736(08)61076-4

[23] Galal, H., Samir, A. and Shehata, M. (2020) Assessment of Apolipoprotein B/Apolipoprotein A-I Ratio in Non-ST Segment Elevation Acute Coronary Syndrome Patients. *The Egyptian Heart Journal*, **72**, Article No. 27. https://doi.org/10.1186/s43044-020-00057-1

[24] Liu, Y., Jia, S., Yuan, D., Xu, N., Jiang, L., Gao, Z., *et al*. (2020) Apolipoprotein B/A-I Ratio Predicts Lesion Severity and Clinical Outcomes in Diabetic Patients with Acute Coronary Syndrome. *Circulation Journal*, **84**, 1132-1139. https://doi.org/10.1253/circj.cj-19-1097

[25] Florvall, G., Basu, S. and Larsson, A. (2006) Apolipoprotein A1 Is a Stronger Prognostic Marker than Are HDL and LDL Cholesterol for Cardiovascular Disease and Mortality in Elderly Men. *The Journals of Gerontology Series A*: *Biological Sciences and Medical Sciences*, **61**, 1262-1266. https://doi.org/10.1093/gerona/61.12.1262

[26] Walldius, G., Jungner, I., Aastveit, A.H., Holme, I., Furberg, C.D. and Sniderman, A.D. (2004) The ApoB/ApoA-I Ratio Is Better than the Cholesterol Ratios to Estimate the Balance between Plasma Proatherogenic and Antiatherogenic Lipoproteins and to Predict Coronary Risk. *Clinical Chemistry and Laboratory Medicine* (*CCLM*), **42**, 1355-1363. https://doi.org/10.1515/cclm.2004.254

[27] Canouï-Poitrine, F., Luc, G., Bard, J., Ferrieres, J., Yarnell, J., Arveiler, D., *et al*. (2010) Relative Contribution of Lipids and Apolipoproteins to Incident Coronary Heart Disease and Ischemic Stroke: The PRIME Study. *Cerebrovascular Diseases*, **30**, 252-259. https://doi.org/10.1159/000319067

[28] Han, S.J., Fujimoto, W.Y., Kahn, S.E., Leonetti, D.L. and Boyko, E.J. (2020) Apolipoprotein B Levels Predict Future Development of Hypertension Independent of Visceral Adiposity and Insulin Sensitivity. *Endocrinology and Metabolism*, **35**, 351-358. https://doi.org/10.3803/enm.2020.35.2.351

[29] Pietri, P., Vlachopoulos, C., Vyssoulis, G., Ioakeimidis, N., Terentes-Printzios, D., Skoumas, J., *et al*. (2016) [OP.1B.08] Association of ApoB/ApoA 1 Ratio with Target Organ Damage in Hypertensive Patients. *Journal of Hypertension*, **34**, e7. https://doi.org/10.1097/01.hjh.0000491343.04581.f3

[30] He, H., Feng, J., Zhang, S., Wang, Y., Li, J., Gao, J., *et al*. (2022) The Apolipoprotein B/A1 Ratio Is Associated with Metabolic Syndrome Components, Insulin Resistance, Androgen Hormones, and Liver Enzymes in Women with Polycystic Ovary Syndrome. *Frontiers in Endocrinology*, **12**, Article 773781. https://doi.org/10.3389/fendo.2021.773781

[31] Sun, Q., Jiang, S., Wang, X., Zhang, J., Li, Y., Tian, J., *et al*. (2022) A Prediction Model for Major Adverse Cardiovascular Events in Patients with Heart Failure Based on High-Throughput Echocardiographic Data. *Frontiers in Cardiovascular Medicine*, **9**, Article 1022658. https://doi.org/10.3389/fcvm.2022.1022658

[32] Smadja, D.M. (2022) Stem Cell Therapy, Artificial Heart or Xenotransplantation: What Will Be New "Regenerative" Strategies in Heart Failure during the Next Decade? *Stem Cell Reviews and Reports*, **19**, 694-699. https://doi.org/10.1007/s12015-022-10476-z

[33] Li, S., Xie, X., Zeng, X., Wang, S. and Lan, J. (2023) Serum Apolipoprotein B to Apolipoprotein A-I Ratio Predicts Mortality in Patients with Heart Failure. *ESC Heart Failure*, **11**, 99-111. https://doi.org/10.1002/ehf2.14547

[34] Holme, I., Aastveit, A.H., Hammar, N., Jungner, I. and Walldius, G. (2009) Lipoprotein Components and Risk of Congestive Heart Failure in 84 740 Men and Women in the Apolipoprotein Mortality Risk Study (AMORIS). *European Journal of Heart Failure*, **11**, 1036-1042. https://doi.org/10.1093/eurjhf/hfp129

[35] Zhou, Y., Liu, H., Yang, H., Zhao, X. and Jiao, Y. (2023) The Value of the Apolipoprotein B/Apolipoprotein A1 Ratio in Predicting the Rapid Progression of Non-Culprit Coronary Lesions in Acute Coronary Syndrome in Patients with Diabetes Mellitus after Percutaneous Coronary Intervention. *International Heart Journal*, **64**, 562-569. https://doi.org/10.1536/ihj.22-676

[36] American Diabetes Association (2013) Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*, **37**, S81-S90.

https://doi.org/10.2337/dc14-s081

[37] Gao, L., Zhang, Y., Wang, X. and Dong, H. (2021) Association of Apolipoproteins A1 and B with Type 2 Diabetes and Fasting Blood Glucose: A Cross-Sectional Study. *BMC Endocrine Disorders*, **21**, Article No. 59. https://doi.org/10.1186/s12902-021-00726-5

[38] Zheng, S., Han, T., Xu, H., Zhou, H., Ren, X., Wu, P., *et al*. (2017) Associations of Apolipoprotein B/Apolipoprotein A-I Ratio with Pre-Diabetes and Diabetes Risks: A Cross-Sectional Study in Chinese Adults. *BMJ Open*, **7**, e014038. https://doi.org/10.1136/bmjopen-2016-014038

[39] Mao, Y., Xu, Y. and Lu, L. (2017) The Nonlinear Association between Apolipoprotein B to Apolipoprotein A1 Ratio and Type 2 Diabetes. *Medicine*, **96**, e5834. https://doi.org/10.1097/md.0000000000005834

[40] Lim, H.H. and Kim, O.Y. (2016) Association of Serum Apolipoprotein B with the Increased Risk of Diabetes in Korean Men. *Clinical Nutrition Research*, **5**, 204-212. https://doi.org/10.7762/cnr.2016.5.3.204

[41] Malyala, R., Rapi, L., Nash, M.M. and Prasad, G.V.R. (2019) Serum Apolipoprotein B and A1 Concentrations Predict Late-Onset Posttransplant Diabetes Mellitus in Prevalent Adult Kidney Transplant Recipients. *Canadian Journal of Kidney Health and Disease*, **6**, Article 2054358119850536. https://doi.org/10.1177/2054358119850536

[42] Han, S.K., Baik, S.K. and Kim, M.Y. (2023) Non-Alcoholic Fatty Liver Disease: Definition and Subtypes. *Clinical and Molecular Hepatology*, **29**, S5-S16. https://doi.org/10.3350/cmh.2022.0424

[43] Choe, Y.G., Jin, W., Cho, Y.K., Chung, W.G., Kim, H.J., Jeon, W.K., *et al*. (2013) Apolipoprotein B/AI Ratio Is Independently Associated with Non-Alcoholic Fatty Liver Disease in Nondiabetic Subjects. *Journal of Gastroenterology and Hepatology*, **28**, 678-683. https://doi.org/10.1111/jgh.12077

[44] Zhao, Y. (2022) Association between Apolipoprotein B/A1 and the Risk of Metabolic Dysfunction Associated Fatty Liver Disease According to Different Lipid Profiles in a Chinese Population: A Cross-Sectional Study. *Clinica Chimica Acta*, **534**, 138-145. https://doi.org/10.1016/j.cca.2022.07.014

[45] Huh, J.H., Jung, S., Cho, S.K., Lee, K.J. and Kim, J.W. (2018) Predictive Value of Apolipoprotein B and A-I Ratio in Severe Acute Pancreatitis. *Journal of Gastroenterology and Hepatology*, **33**, 548-553. https://doi.org/10.1111/jgh.13860

[46] 钟瑞, 徐欢, 彭燕, 等. 血清载脂蛋白 A1 和载脂蛋白 B/A1 比值对重型急性胰腺炎的预测价值[J]. 临床肝胆病杂志, 2020, 36(3): 631-635.

[47] Wu, J., Wang, Y., Li, H., Tan, W., Chen, X. and Ye, S. (2019) Serum Apolipoprotein B-to-Apolipoprotein A1 Ratio Is Independently Associated with Disease Severity in Patients with Acute Pancreatitis. *Scientific Reports*, **9**, Article No. 7764. https://doi.org/10.1038/s41598-019-44244-w

[48] Fan, S., Lai, E.C.S., Mok, F.P.T., Lo, C., Zheng, S. and Wong, J. (1993) Prediction of the Severity of Acute Pancreatitis. *The American Journal of Surgery*, **166**, 262-269. https://doi.org/10.1016/s0002-9610(05)80970-5

[49] Woodruff, T.M., Thundyil, J., Tang, S., Sobey, C.G., Taylor, S.M. and Arumugam, T.V. (2011) Pathophysiology, Treatment, and Animal and Cellular Models of Human Ischemic Stroke. *Molecular Neurodegeneration*, **6**, Article No. 11. https://doi.org/10.1186/1750-1326-6-11

[50] Hahm, C. and Hong, K. (2012) Apolipoprotein B/A1 Ratio as Risk Factor for Cerebral Ischemic Stroke. *The Ewha Medical Journal*, **35**, 21-25. https://doi.org/10.12771/emj.2012.35.1.21

[51] Lin, J., Si, Z. and Wang, A. (2024) Predictive Value of ApoB/ApoA-I for Recurrence within 1 Year after First Incident Stroke. *Frontiers in Neurology*, **14**, Article 1308442. https://doi.org/10.3389/fneur.2023.1308442

[52] Kalani, R., Krishnamoorthy, S., Deepa, D., Gopala, S., Prabhakaran, D., Tirschwell, D., *et al*. (2020) Apolipoproteins B and A1 in Ischemic Stroke Subtypes. *Journal of Stroke and Cerebrovascular Diseases*, **29**, Article 104670. https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.104670

[53] Lee, M., Lim, J., Kim, Y., Park, S.H., Lee, S., Kim, C., *et al*. (2023) High ApoB/ApoA-I Ratio Predicts Post-Stroke Cognitive Impairment in Acute Ischemic Stroke Patients with Large Artery Atherosclerosis. *Nutrients*, **15**, Article 4670. https://doi.org/10.3390/nu15214670

[54] Fahmy, E.M., El Awady, M.A.E.S., Sharaf, S.A., Selim, N.M., Abdo, H.E.S. and Mohammed, S.S. (2020) Apolipoproteins A1 and B and Their Ratio in Acute Ischemic Stroke Patients with Intracranial and Extracranial Arterial Stenosis: An Egyptian Study. *The Egyptian Journal of Neurology, Psychiatry and Neurosurgery*, **56**, Article No. 115. https://doi.org/10.1186/s41983-020-00245-5

[55] Eldeeb, M.A., Zaki, A.S., Ashour, S., Abdel Nasser, A., El Bassiouny, A. and Abdulghani, K.O. (2019) Serum Apolipoprotein A1: A Predictor and Prognostic Biomarker in Acute Ischemic Stroke. *The Egyptian Journal of Neurology, Psychiatry and Neurosurgery*, **56**, Article No. 3. https://doi.org/10.1186/s41983-019-0138-z

[56] Kostapanos, M.S., Christogiannis, L.G., Bika, E., Bairaktari, E.T., Goudevenos, J.A., Elisaf, M.S., *et al*. (2010) Apolipoprotein B-to-A1 Ratio as a Predictor of Acute Ischemic Nonembolic Stroke in Elderly Subjects. *Journal of Stroke and Cerebrovascular Diseases*, **19**, 497-502. https://doi.org/10.1016/j.jstrokecerebrovasdis.2009.09.010

[57] Daneshpajouhnejad, P., Kopp, J.B., Winkler, C.A. and Rosenberg, A.Z. (2022) The Evolving Story of Apolipoprotein L1 Nephropathy: The End of the Beginning. *Nature Reviews Nephrology*, **18**, 307-320. https://doi.org/10.1038/s41581-022-00538-3

[58] Pan, X. (2022) The Roles of Fatty Acids and Apolipoproteins in the Kidneys. *Metabolites*, **12**, Article 462. https://doi.org/10.3390/metabo12050462

[59] Sniderman, A.D. and Kiss, R.S. (2007) The Strengths and Limitations of the ApoB/ApoA-I Ratio to Predict the Risk of Vascular Disease: A Hegelian Analysis. *Current Atherosclerosis Reports*, **9**, 261-265. https://doi.org/10.1007/s11883-007-0031-6

[60] Nurtazina, A., Kozhakhmetova, D., Dautov, D., Shakhanova, A. and Chattu, V.K. (2020) Apolipoprotein B/A1 Ratio as a Diagnostic Alternative to Triglycerides and HDL-Cholesterol for the Prediction of Metabolic Syndrome among Hypertensives in Kazakhstan. *Diagnostics*, **10**, Article 510. https://doi.org/10.3390/diagnostics10080510