Advances in Clinical Medicine 临床医学进展, 2026, 16(2), 1600-1605

https://doi.org/10.12677/acm.2026.162550

生物信息学分析联合孟德尔随机化分析在急性心肌梗死中的应用

赵永侠，单伟超*

承德医学院附属医院心脏内科，河北 承德

收稿日期：2026年1月5日；录用日期：2026年1月29日；发布日期：2026年2月9日

摘 要

心血管疾病是中国居民死亡的主要原因。为了制定有效和及时地应对心血管疾病流行挑战的策略，我们需要了解当前主要类型心血管疾病的流行病学特征以及这些特征对其预防和治疗的意义。急性心肌梗死更是心血管疾病最重要的临床表现。近些年来新的生物标志物不断被提出，为心肌梗死的诊断以及预后的评估提供了新的依据，国内外近些年来有许多基于生物信息学方法分析心肌梗死相关基因的研究，也报道了许多应用孟德尔随机化方法分析某暴露因素与心血管疾病之间的风险相关系数。在这篇文章中，我们概述了生物信息学的特点及应用，概述了孟德尔随机化分析的定义及应用，以及在心血管相关疾病的研究进展。

关键词

生物信息学分析，孟德尔随机化分析，急性心肌梗死

Application of Bioinformatics Analysis Combined with Mendelian Randomization Analysis in Acute Myocardial Infarction

Yongxia Zhao, Weichao Shan*

Department of Cardiology, Affiliated Hospital of Chengde Medical University, Chengde Hebei

Received: January 5, 2026; accepted: January 29, 2026; published: February 9, 2026

Abstract

Cardiovascular diseases are the leading cause of death among China's residents. To develop

---

*通讯作者。

文章引用: 赵永侠, 单伟超. 生物信息学分析联合孟德尔随机化分析在急性心肌梗死中的应用[J]. 临床医学进展, 2026, 16(2): 1600-1605. DOI: 10.12677/acm.2026.162550

effective and timely strategies to address the challenges posed by the prevalence of cardiovascular diseases, we need to understand the epidemiological characteristics of the major types of cardiovascular diseases currently and their significance for prevention and treatment. Acute myocardial infarction (AMI) is the most important clinical manifestation of cardiovascular diseases. In recent years, new biomarkers have been continuously proposed, providing new evidence for the diagnosis of myocardial infarction and the assessment of prognosis. Numerous studies have been conducted domestically and internationally in recent years, analyzing myocardial infarction-related genes using bioinformatics methods, and many have reported the application of Mendelian randomization to analyze the risk association coefficients between certain exposure factors and cardiovascular diseases. In this article, we outline the characteristics and applications of bioinformatics, provide an overview of the definition and application of Mendelian randomization, and summarize the research progress in cardiovascular-related diseases.

Keywords

Bioinformatics Analysis, Mendelian Randomization Analysis, Acute Myocardial Infarction (AMI)

1. 前言

2024 年《中国心血管健康与疾病报告》指出：随着社会经济的发展，国民生活方式的变化，心血管疾病(Cardiovascular Diseases, CVD)的发病率及其相关危险因素对公众健康的影响日益严重[1]，预计 2020~2030 年 CVD 预测发病率、死亡率和伤残调整生命年率将继续上升，“中国居民心血管和脑血管事件监测”项目结果也表明 18 岁及以上中国居民心血管和脑血管疾病的发病率随着年龄的增长而呈快速上升趋势[2]。CVD 中冠状动脉性心脏病(Coronary Heart Disease, CHD)占比最高[3]，也是影响人类的健康寿命损失的最重要原因，造成的很大一部分经济负担落在低收入和中等收入国家，同时也是一个巨大的全球经济负担[4]。急性心肌梗死(Acute Myocardial Infarction, AMI)是心源性猝死(Sudden Cardiac Death, SCD)危及生命的冠状动脉事件之一，也是 CHD 最严重的临床表现，它分为 ST 段抬高型心肌梗死和非 ST 段抬高型心肌梗死两类，每年有超过 300 万人患上 ST 段抬高型心肌梗死[5]。当肌钙蛋白值升高且至少有一个值高于 99%的上限参考值且在临床情况存在心肌缺血时，我们可定义为心肌梗死[6]。心电图作为最基本的辅助检查在诊断急性心肌梗死(AMI)方面的敏感性和特异性较低[7]，因为它具有一定时间相关性、非特异性和唯一性，而且在急性心包炎、左心室肥大、左束支传导阻滞、早期复极模式时也可能会观察到 ST 偏差。出现心肌损伤后血清学心肌坏死标志物也具有时间相关性[8]。而且 AMI 的常用的血清学炎性标志物不具有特异性，在不稳定型心绞痛中轻微的 cTnT 升高是常见的，这使得不稳定型心绞痛难以与非 ST 段抬高型心肌梗死区分[9]。时间就是心肌，早期诊断及治疗急性心肌梗死尤为重要[10]。

2. 生物信息学分析与急性心肌梗死

冠状动脉疾病具有部分遗传性，AMI 作为其中一种类型也不例外，同样受遗传因素和环境因素影响[11]，但在基因及表达水平上的研究，尤其是从基因水平上研究候选基因与 AMI 的相关性处于初始阶段。随着基因测序技术的日益完善，高通量测序技术已进入医疗领域，在疾病的诊断与治疗中的应用日益广泛[12]。高通量测序技术又称为下一代测序技术(Next-generation Sequencing, NGS)，第一张人类基因组图

谱是用桑格测序技术绘制的，它花了 13 年的时间，集结多方努力以及超过 5 亿美元来完成。而使用 NGS，人类基因组测序可以在 48 小时内完成，成本少于 200 美元，而且精确度更高[13]。因此从基因水平上探求特异性血清学标志物对于早期诊断 AMI 以及治疗靶点具有重要意义，已经成为 AMI 诊断和治疗的新趋势和热点。代谢物被定义为细胞内由众多酶催化进行的代谢反应所产生的中间产物。由于基因变异和环境因素的影响，它们使我们能够探索基因与环境的相互作用，并更好地理解像心血管疾病这样的多因素疾病。发现生物标志物、改进心血管风险预测和早期疾病诊断，以及探索疾病发生和进展的详细机制。代谢组学已经发展成为研究动脉粥样硬化和心血管疾病复杂病理生理的有力工具[14]。冠状动脉疾病的全基因组关联研究(Genome-Wide Association Analysis, GWAS)已发现超过 300 个独立信号[15]，它的遗传性在多种细胞中显著增强[15]，包括血管壁中的内皮细胞、血管平滑肌细胞，以及影响胆固醇代谢的肝细胞[16]。生物信息学分析可用于鉴定和验证急性心肌梗死中的细胞凋亡相关基因[17]，可用于验证其他疾病(炎症性肠病)与急性心肌梗死的遗传联系[18]，可用于验证与 AMI 早期阶段有关的循环内皮细胞的早期诊断标志物[19]，可用于鉴定中性粒细胞外陷阱介导的 AMI 中枢基因，构建了 AMI 诊断模型，为 AMI 发生和治疗的分子机制提供了新的思路[20]。生物信息学分析不仅在识别新型生物标志物、调控网络和潜在的治疗靶点等方面具有研究价值，同样在疾病的预防、危险分层以及预后评估等方面发挥着不可小视的作用，并逐渐成为一种更准确、更敏感的方法[21]。

3. 孟德尔随机化分析与急性心肌梗死

孟德尔随机化(Mendelian Randomization, MR)是流行病学中广泛使用的一种重要方法，用于评估暴露因素与临床疾病之间的潜在因果关系。等位基因在受孕时的独立分离意味着它们不受潜在混杂因素的影响，形成类似于随机试验的自然实验，因此 MR 比传统的观察分析更可靠地了解暴露因素和疾病之间的潜在因果关系，是将疾病表型与一组基因或蛋白质相关联的强大工具[22]。随着大型遗传数据集的日益可用性，MR 已成为研究心血管疾病危险因素的强大且易于获取的工具[23]。MR 使用来自 GWAS 数据库的遗传变异作为工具变量，是评估暴露与结果之间潜在因果关系的有用方法[24]。通过孟德尔随机化分析，已经发现了 S100A8/A9 是急性心肌梗死后心力衰竭的预测因子和潜在的因果关系药物[25]，证实了白细胞介素-10 和白细胞介素-18 都是与 AMI 遗传相关的外周炎症因子[26]，验证了甘油三酯-葡萄糖指数可以作为心血管疾病更灵敏的早期诊断指标，而血糖和甘油三酯的联合指标则能为心脏代谢结果提供定量风险评估[27]，探讨了胆石症对 AMI 存在负面的因果影响，并且提示 rs4245791 是这种影响的致病位点，为胆石症患者 AMI 的预防和病因研究提供了新的思路和证据[28]，揭示了偏头痛相关特征具有预测和弯曲 AMI 的意义，为 AMI 的未来诊断和治疗策略提供信息[29]，鉴定出与 AMI 相关的基因座，强调了吸烟、脂质代谢和炎症与 AMI 相关的生物学机制的相关性等[30]。总而言之，MR 在确立因果关系、验证危险因素、发掘新的致病因素方面卓有成效。但 MR 亦有它的局限性，首先，孟德尔随机化分析的核心假设是工具变量仅通过暴露因素影响结局，而无多效性。多效性效应是指基因变异对多个生物途径产生的影响。通过另一个特征或途径对所研究的方面产生影响，被称为水平多效性。通过所关注的风险因素对其他特征产生影响，这种现象被称为垂直多效性[31]。水平多效性会干扰孟德尔随机化检验，导致因果效应估计失真、统计功效降低，并可能产生虚假的因果关系结论[32]。我们需要用 MR-Egger 回归、加权中位数法、MR-PRESSO 等敏感性分析来检测水平多效性。由于心血管风险因素与疾病之间共享复杂的遗传网络，广泛存在的多效性仍是孟德尔随机化应用中的潜在局限[33]。其次，连锁不平衡会导致工具变量之间不独立，违反 MR 核心假设，会导致工具变量的强度将被高估，因果效应估计值产生偏倚[34]。

4. 生物信息学分析联合孟德尔随机化分析

传统的生物信息学分析方法，如差异表达分析、基因集富集分析、蛋白质相互作用网络构建等，在

识别与特定疾病或表型相关的关键分子(如基因、蛋白质、代谢物)和功能通路方面，发挥了不可或缺的作用[35]。但生物信息学分析通常只能揭示分子与表型之间的统计关联，无法区分是因果关系、伴随关系还是反向因果关系。当我们引入孟德尔随机化，利用遗传工具变量，为生物信息学筛选出的关键分子与疾病结局之间提供因果证据。这极大地增强了研究结论的说服力和科学价值[36]。我们可以利用生物信息学筛选候选基因，再通过孟德尔随机化(MR)和共定位分析推断因果关系。通过分析 GEO 数据库中的 AMI 基因表达数据集，利用差异表达基因分析和加权基因共表达网络分析找出关键基因和共表达模块[37]。再根据公开的全基因组关联研究数据，利用 cis-eQTL/pQTL 作为工具变量，通过两样本 MR 分析其与暴露因素与疾病的因果关系[38]。近年来，生物信息学联合 MR 对 AMI 作出了一定的贡献[25] (表 1)，发现 TNF 可抑制 AMI 中的炎症和氧化应激反应，对心脏起到保护作用。相信在未来，将生物信息学分析与孟德尔随机化分析联合应用，能够使我们对疾病的了解更加透彻，也能使患者拥有更精准的个体化治疗。

Table 1. Key molecules identified in the field of acute myocardial infarction (AMI) through bioinformatics combined with mendelian randomization analysis

表 1. 生物信息学联合孟德尔随机化分析在 AMI 领域发现的关键分子

关键分子	类型	暴露与结局	MR 因果效应	主要生物学功能
S100A8/A9	蛋白质	暴露：血浆蛋白水平 结局：AMI 后心力衰竭	AMI 后 HF 风险：OR ≈ 1.04 (每增加 1 个 SD)。	在中性粒细胞中储存，促进心肌损伤和炎症。
TNF	蛋白质	暴露：单核苷酸多态性(SNPs) 结局：AMI	OR = 0.946	由活化的单核或巨噬细胞产生，激活 NF-κB 等信号通路，诱导炎症因子释放，放大炎症反应。

参考文献

[1] Liu, M., He, X., Yang, X. and Wang, Z. (2025) 2024 Annual Report on Cardiovascular Health and Diseases in China: Data and Trend. *Chinese Medical Journal*, **138**, 3037-3049. https://doi.org/10.1097/cm9.0000000000003902

[2] Liu, M.B., He, X.Y., Yang, X.H., *et al.* (2025) Interpretation of Annual Report on Cardiovascular Health and Diseases in China 2024. *Biomedical and Environmental Sciences*, **38**, 893-917.

[3] Wong, N.D. (2014) Epidemiological Studies of CHD and the Evolution of Preventive Cardiology. *Nature Reviews Cardiology*, **11**, 276-289. https://doi.org/10.1038/nrcardio.2014.26

[4] Ralapanawa, U. and Sivakanesan, R. (2021) Epidemiology and the Magnitude of Coronary Artery Disease and Acute Coronary Syndrome: A Narrative Review. *Journal of Epidemiology and Global Health*, **11**, 169-177. https://doi.org/10.2991/jegh.k.201217.001

[5] Salari, N., Morddarvanjoghi, F., Abdolmaleki, A., Rasoulpoor, S., Khaleghi, A.A., Hezarkhani, L.A., *et al.* (2023) The Global Prevalence of Myocardial Infarction: A Systematic Review and Meta-Analysis. *BMC Cardiovascular Disorders*, **23**, Article No. 206. https://doi.org/10.1186/s12872-023-03231-w

[6] Ibanez, B., James, S., Agewall, S., Antunes, M.J., Bucciarelli-Ducci, C., Bueno, H., *et al.* (2017) 2017 ESC Guidelines for the Management of Acute Myocardial Infarction in Patients Presenting with ST-Segment Elevation: The Task Force for the Management of Acute Myocardial Infarction in Patients Presenting with ST-Segment Elevation of the European Society of Cardiology (ESC). *European Heart Journal*, **39**, 119-177. https://doi.org/10.1093/eurheartj/ehx393

[7] Aydin, S., Ugur, K., Aydin, S., Sahin, İ. and Yardim, M. (2019) biomarkers in Acute Myocardial Infarction: Current Perspectives. *Vascular Health and Risk Management*, **15**, 1-10. https://doi.org/10.2147/vhrm.s166157

[8] Thygesen, K., Alpert, J.S., Jaffe, A.S., Chaitman, B.R., Bax, J.J., Morrow, D.A., *et al.* (2018) Fourth Universal Definition of Myocardial Infarction (2018). *Journal of the American College of Cardiology*, **72**, 2231-2264. https://doi.org/10.1016/j.jacc.2018.08.1038

[9] Eggers, K.M., Jernberg, T. and Lindahl, B. (2017) Unstable Angina in the Era of Cardiac Troponin Assays with Improved Sensitivity—A Clinical Dilemma. *The American Journal of Medicine*, **130**, 1423-1430.e5. https://doi.org/10.1016/j.amjmed.2017.05.037

[10] Scott, I.A. (2010) “Time Is Muscle” in Reperfusing Occluded Coronary Arteries in Acute Myocardial Infarction. *Medical*

Journal of Australia, **193**, 493-495. https://doi.org/10.5694/j.1326-5377.2010.tb04030.x

[11] Musunuru, K. and Kathiresan, S. (2019) Genetics of Common, Complex Coronary Artery Disease. *Cell*, **177**, 132-145. https://doi.org/10.1016/j.cell.2019.02.015

[12] McCombie, W.R., McPherson, J.D. and Mardis, E.R. (2018) Next-Generation Sequencing Technologies. *Cold Spring Harbor Perspectives in Medicine*, **9**, a036798. https://doi.org/10.1101/cshperspect.a036798

[13] Rodriguez, R. and Krishnan, Y. (2023) The Chemistry of Next-Generation Sequencing. *Nature Biotechnology*, **41**, 1709-1715. https://doi.org/10.1038/s41587-023-01986-3

[14] Iida, M., Harada, S. and Takebayashi, T. (2019) Application of Metabolomics to Epidemiological Studies of Atherosclerosis and Cardiovascular Disease. *Journal of Atherosclerosis and Thrombosis*, **26**, 747-757. https://doi.org/10.5551/jat.rv17036

[15] Schnitzler, G.R., Kang, H., Fang, S., Angom, R.S., Lee-Kim, V.S., Ma, X.R., *et al*. (2024) Convergence of Coronary Artery Disease Genes onto Endothelial Cell Programs. *Nature*, **626**, 799-807. https://doi.org/10.1038/s41586-024-07022-x

[16] Turner, A.W., Wong, D., Dreisbach, C.N. and Miller, C.L. (2018) GWAS Reveal Targets in Vessel Wall Pathways to Treat Coronary Artery Disease. *Frontiers in Cardiovascular Medicine*, **5**, Article ID: 72. https://doi.org/10.3389/fcvm.2018.00072

[17] Zhu, H., Li, M., Wu, J., Yan, L., Xiong, W., Hu, X., *et al*. (2024) Identification and Validation of Apoptosis-Related Genes in Acute Myocardial Infarction Based on Integrated Bioinformatics Methods. *PeerJ*, **12**, e18591. https://doi.org/10.7717/peerj.18591

[18] Fu, Q., Shen, T., Qiu, W., Liao, Y., Yu, M. and Zhou, Y. (2025) FOSB Is a Key Factor in the Genetic Link between Inflammatory Bowel Disease and Acute Myocardial Infarction: Multiple Bioinformatics Analyses and Validation. *BMC Medical Genomics*, **18**, Article No. 63. https://doi.org/10.1186/s12920-025-02129-0

[19] Huang, K., Wen, F., Li, J., Niu, W., Chen, H., Wan, S., *et al*. (2025) Early Diagnosis of Acute Myocardial Infarction via Hub Genes Identified by Integrated Weighted Gene Co-Expression Network Analysis. *American Heart Journal Plus: Cardiology Research and Practice*, **56**, Article 100554. https://doi.org/10.1016/j.ahjo.2025.100554

[20] Yuan, H., Yu, Y., Liu, W., Liu, X., Han, Q., Shi, J., *et al*. (2025) Identification of Neutrophil Extracellular Traps-Related Genes for the Diagnosis of Acute Myocardial Infarction Based on Bioinformatics and Experimental Verification. *Journal of Inflammation*, **22**, Article No. 35. https://doi.org/10.1186/s12950-025-00462-w

[21] Benincasa, G., Suades, R., Padró, T., Badimon, L. and Napoli, C. (2023) Bioinformatic Platforms for Clinical Stratification of Natural History of Atherosclerotic Cardiovascular Diseases. *European Heart Journal-Cardiovascular Pharmacotherapy*, **9**, 758-769. https://doi.org/10.1093/ehjcvp/pvad059

[22] Larsson, S.C., Butterworth, A.S. and Burgess, S. (2023) Mendelian Randomization for Cardiovascular Diseases: Principles and Applications. *European Heart Journal*, **44**, 4913-4924. https://doi.org/10.1093/eurheartj/ehad736

[23] Levin, M.G. and Burgess, S. (2024) Mendelian Randomization as a Tool for Cardiovascular Research. *JAMA Cardiology*, **9**, 79. https://doi.org/10.1001/jamacardio.2023.4115

[24] Shen, R., Pan, C., Yu, J., Dong, C., Li, Z., Zhang, J., *et al*. (2024) Primary Aldosteronism Influences Cardiac Structure, Function, and Disease Risk: Evidence from Mendelian Randomization Analysis. *The Journal of Clinical Hypertension*, **26**, 1301-1309. https://doi.org/10.1111/jch.14912

[25] Ma, J., Li, Y., Li, P., Yang, X., Zhu, S., Ma, K., *et al*. (2024) S100A8/A9 as a Prognostic Biomarker with Causal Effects for Post-Acute Myocardial Infarction Heart Failure. *Nature Communications*, **15**, Article No. 2701. https://doi.org/10.1038/s41467-024-46973-7

[26] Chen, Y. and Zeng, L. (2023) Peripheral Inflammatory Factors and Acute Myocardial Infarction Risk: A Mendelian Randomization Study. *Global Heart*, **18**, Article 55. https://doi.org/10.5334/gh.1269

[27] Si, S., Li, J., Li, Y., Li, W., Chen, X., Yuan, T., *et al*. (2021) Causal Effect of the Triglyceride-Glucose Index and the Joint Exposure of Higher Glucose and Triglyceride with Extensive Cardio-Cerebrovascular Metabolic Outcomes in the UK Biobank: A Mendelian Randomization Study. *Frontiers in Cardiovascular Medicine*, **7**, Article ID: 583473. https://doi.org/10.3389/fcvm.2020.583473

[28] Fu, Q., Shen, T., Yu, Q., Jiang, L. and Yang, R. (2023) Causal Effect of Gallstone Disease on the Risk of Coronary Heart Disease or Acute Myocardial Infarction: A Mendelian Randomization Study. *Scientific Reports*, **13**, Article No. 18807. https://doi.org/10.1038/s41598-023-46117-9

[29] Zhu, Y., Chen, Y., Xu, J. and Zu, Y. (2024) Unveiling the Potential of Migrasomes: A Machine-Learning-Driven Signature for Diagnosing Acute Myocardial Infarction. *Biomedicines*, **12**, Article 1626. https://doi.org/10.3390/biomedicines12071626

[30] Fernández-Sanlés, A., Sayols-Baixeras, S., Subirana, I., Sentí, M., Pérez-Fernández, S., de Castro Moura, M., *et al*. (2021)

DNA Methylation Biomarkers of Myocardial Infarction and Cardiovascular Disease. *Clinical Epigenetics*, **13**, Article No. 86. https://doi.org/10.1186/s13148-021-01078-6

[31] Davies, N.M., Holmes, M.V. and Davey Smith, G. (2018) Reading Mendelian Randomisation Studies: A Guide, Glossary, and Checklist for Clinicians. *BMJ*, **362**, k601. https://doi.org/10.1136/bmj.k601

[32] Verbanck, M., Chen, C., Neale, B. and Do, R. (2018) Detection of Widespread Horizontal Pleiotropy in Causal Relationships Inferred from Mendelian Randomization between Complex Traits and Diseases. *Nature Genetics*, **50**, 693-698. https://doi.org/10.1038/s41588-018-0099-7

[33] Wang, K., Shi, X., Zhu, Z., Hao, X., Chen, L., Cheng, S., *et al*. (2022) Mendelian Randomization Analysis of 37 Clinical Factors and Coronary Artery Disease in East Asian and European Populations. *Genome Medicine*, **14**, Article No. 63. https://doi.org/10.1186/s13073-022-01067-1

[34] Burgess, S., Davey Smith, G., Davies, N.M., Dudbridge, F., Gill, D., Glymour, M.M., *et al*. (2019) Guidelines for Performing Mendelian Randomization Investigations: Update for Summer 2023. *Wellcome Open Research*, **4**, Article 186. https://doi.org/10.12688/wellcomeopenres.15555.1

[35] Zhang, B., Wang, J., Wang, X., Zhu, J., Liu, Q., Shi, Z., *et al*. (2014) Proteogenomic Characterization of Human Colon and Rectal Cancer. *Nature*, **513**, 382-387. https://doi.org/10.1038/nature13438

[36] Xu, S., Li, X., Zhang, S., Qi, C., Zhang, Z., Ma, R., *et al*. (2023) Oxidative Stress Gene Expression, DNA Methylation, and Gut Microbiota Interaction Trigger Crohn’s Disease: A Multi-Omics Mendelian Randomization Study. *BMC Medicine*, **21**, Article No. 179. https://doi.org/10.1186/s12916-023-02878-8

[37] Zhu, D., Zhang, X., Fang, Y., Xu, Z., Yu, Y., Zhang, L., *et al*. (2024) Identification of a Lactylation-Related Gene Signature as the Novel Biomarkers for Early Diagnosis of Acute Myocardial Infarction. *International Journal of Biological Macromolecules*, **282**, Article 137431. https://doi.org/10.1016/j.ijbiomac.2024.137431

[38] Feng, Y., Li, C., Cheng, B., Chen, Y., Chen, P., Wang, Z., *et al*. (2024) Identifying Genetically-Supported Drug Repurposing Targets for Non-Small Cell Lung Cancer through Mendelian Randomization of the Druggable Genome. *Translational Lung Cancer Research*, **13**, 1780-1793. https://doi.org/10.21037/tlcr-24-65