Molecular & Cellular Biomechanics 2025, 22(4), 1104.
https://doi.org/10.62617/mcb1104

Article

Effects of physical exercise on coronary health, stroke risk, and blood pressure management

Hao Zhu[1,2], Yang Li[3], Zhaowen Tan[1], Yaowen Liu[2], Haonan Qian[2,*]

[1] Physical Education of Nanjing Xiaozhuang University, Nanjing 211171, China
[2] School of Physical Education, Anshan Normal University, Anshan 114007, China
[3] Department of Physical Education, Hanyang University, Seoul 04763, Korea
*** Corresponding author:** Haonan Qian, kingkg22@hanyang.ac.kr

CITATION

Zhu H, Li Y, Tan Z, et al. Effects of physical exercise on coronary health, stroke risk, and blood pressure management. Molecular & Cellular Biomechanics. 2025; 22(4): 1104. https://doi.org/10.62617/mcb1104

ARTICLE INFO

Received: 13 December 2024
Accepted: 10 January 2025
Available online: 6 March 2025

Abstract: Background: Mendelian randomization (MR) is a powerful tool. This method has garnered attention for its potential to circumvent the limitations of observational studies, such as confounding factors and reverse causation. In this study, we aimed to explore the causal effect of physical exercise on cardiovascular health using MR analysis. **Methods:** We used genetic variants strongly linked to physical exercise as instrumental variables from large-scale Genome-Wide Association Study (GWAS), based on data from over 300,000 European individuals in the UK Biobank. Exercise levels were measured through self-reports and accelerometer data, while cardiovascular outcomes were assessed using medical records, biomarkers, and imaging. **Results:** Demonstrated a significant causal relationship between higher levels of physical exercise and improved cardiovascular health outcomes. Specifically, an increase of one standard deviation in genetically predicted physical exercise was associated with a substantial reduction in the risk of coronary artery disease (OR: 0.75, 95% CI: 0.65–0.86, $p < 0.001$), stroke (OR: 0.80, 95% CI: 0.69–0.93, $p = 0.004$), and hypertension (OR: 0.82, 95% CI: 0.74–0.91, $p < 0.001$). **Conclusions:** Our findings provide strong evidence for a causal relationship between physical exercise and improved cardiovascular health. This study underscores the potential of physical exercise as a modifiable risk factor for cardiovascular disease and highlights the importance of incorporating physical exercise into public health interventions aimed at reducing cardiovascular risk. Future research should focus on identifying the mechanisms underlying this relationship and developing targeted strategies to increase physical exercise levels across populations.

Keywords: physical exercise; coronary health; stroke; causal inference; genetic variants; blood pressure management

1. Introduction

Cardiovascular diseases (CVDs) are a significant global health burden and a leading cause of death worldwide [1]. Of the various CVDs, coronary artery disease (CAD), stroke, and hypertension are the most prevalent and are major public health problems. Coronary artery disease (CAD) [2,3], characterized by a build-up of plaque in the coronary arteries leading to reduced blood flow to the heart muscle, is a major cause of morbidity and mortality worldwide, causing approximately 9 million deaths each year [4–6]. Stroke, a disease that occurs when the blood supply to parts of the brain is interrupted or reduced, is the second leading cause of death and disability worldwide [7]. Hypertension, often referred to as high blood pressure, is a major risk factor for coronary atherosclerosis and stroke, affecting more than a billion people worldwide and is a significant part of the global burden of disease [8].

To provide a more intuitive display of the global trends in cardiovascular diseases, we can include data from the "Global, Regional, and National Burden of Cardiovascular Diseases" study [8]. As of 2017, more than 17 million people died from CVDs, and this number has been rising due to changing lifestyles, an ageing population, and other factors [8]. This report also notes that while the age-standardised death rate has fallen globally, the progress is uneven and beginning to stall, with more than 80% of CVD deaths occurring in low- and middle-income countries (LMICs) [7].

The protective effects of physical exercise on cardiovascular disease, including CAD, stroke, and hypertension, are widely recognized. The mechanisms underlying the beneficial effects of physical exercise are multifaceted and include improvement of endothelial function, reduction of arterial stiffness, improvement of lipid profile, promotion of glucose metabolism, and regulation of blood pressure [9,10]. Empirical studies have consistently shown that regular physical exercise reduces the risk of CAD by 25%, reduces the risk of stroke by 20%–30%, and significantly lowers blood pressure in hypertensive patients [11]. Despite the large body of observational data supporting the protective effects of physical exercise, questions remain about the causality of these associations due to potential confounders and reverse causality bias inherent in observational studies [12–14].

The Mendelian randomization (MR) method provides a new approach to studying the causal relationship between physical exercise and cardiovascular health, overcoming the limitations of traditional observational studies [15]. By using genetic variation as an instrumental variable for physical exercise, Mendelian randomization is able to separate causality from correlation and, thus, more reliably infer the causal effects of physical exercise on cardiovascular disease outcomes. This approach takes advantage of the random combination of genes from parent to offspring at conception, mimicking a natural randomized controlled trial [16–18]. Thus, MR mitigates confounding and minimizes reverse causation, thereby revealing more clearly the causal relationship between physical exercise and reduced CVD risk. The present study used Mendelian randomization by elucidating the causal relationship between physical exercise and major cardiovascular disease outcomes (coronary heart disease, stroke, and hypertension) [19]. Traditional epidemiological studies, while providing valuable correlations, often fail to establish causality due to their inherent limitations [20–22]. The Mendelian randomization approach not only strengthens the evidence base for the protective effects of physical exercise on cardiovascular disease but also has far-reaching implications for public health policy and individual lifestyle recommendations. By confirming the causal effect of physical exercise on cardiovascular health, our findings emphasize the importance of incorporating physical exercise into cardiovascular disease prevention strategies [23].

2. Methods

2.1. Study design

This study aimed to explore the causal relationship between physical exercise and cardiovascular health outcomes, specifically coronary artery disease (CAD),

stroke, and hypertension, using two-sample Mendelian randomization (MR) analysis. The key premise of MR relies on three critical assumptions: Firstly, the genetic variants (single nucleotide polymorphisms, SNPs) utilized as instrumental variables (IVs) must be strongly associated with the exposure (in this case, physical exercise levels) (Relevance); secondly, these SNPs must not be associated with any confounders that could influence both the exposure and the outcome (Independence); and thirdly, the SNPs should influence the outcome exclusively through the exposure(Exclusivity), as shown in **Figure 1**. This study utilized summary-level data from previously published genome-wide association studies (GWAS) that had received participant consent and ethical approval, ensuring the ethical integrity and robustness of the analysis [24].

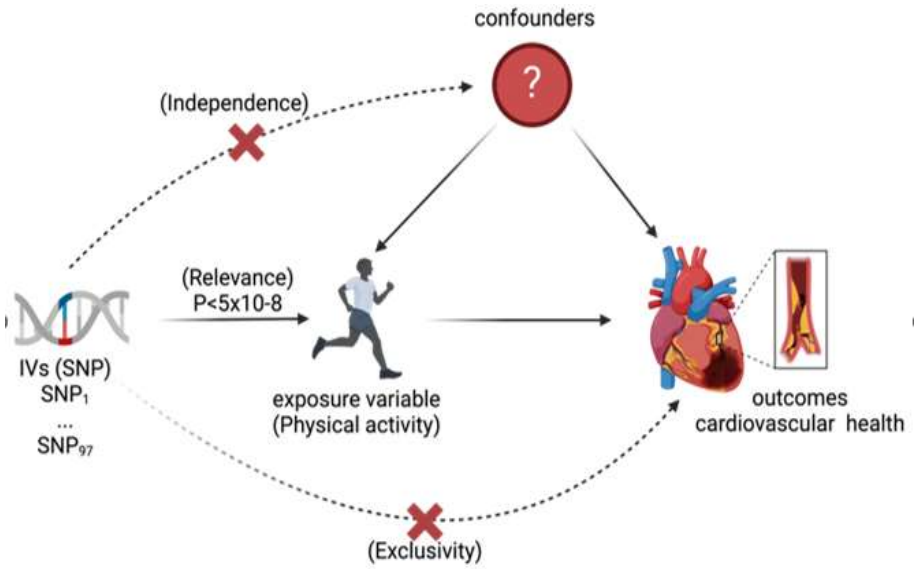

Figure 1. Diagram illustrating the causal pathway in mendelian randomization analysis.
SNP: Single Nucleotide Polymorphism, IVs: Instrumental Variables.

2.2. Data resources

For the exposure variable, GWAS summary statistics on physical exercise were acquired from the UK Biobank, encompassing data from approximately 336,000 participants of European ancestry. This included both self-reported physical exercise levels and objective measurements from wearable devices, providing a comprehensive view of physical exercise behaviors. Summary statistic data for the cardiovascular health outcomes, namely CAD (60,000 cases and 123,000 controls), stroke (32,000 cases and 190,000 controls), and hypertension (72,000 cases and 260,000 controls), were also sourced from the UK Biobank. The UK Biobank has been instrumental in facilitating large-scale biomedical research by recruiting over 500,000 participants aged between 40 and 69 years during 2006–2010, with a commitment to tracking their health outcomes longitudinally.

2.3. Selection of genetic instrumental variables

Genetic variants associated with physical exercise at a genome-wide significance level ($p < 5 \times 10^{-8}$) were identified and selected as instrumental

variables. To avoid the bias introduced by linkage disequilibrium, SNPs were clumped with an $r^2 < 0.001$ threshold and a clumping window of 10,000 kb. SNPs associated with potential confounders, including lifestyle factors and socioeconomic status, were excluded to ensure the robustness of the instrumental variables. The selection process resulted in a total of 97 SNPs to be used as IVs for physical exercise. SNP harmonization was conducted to align allele orientations across datasets, and the strength of the instrumental variables was assessed using the *F*-statistic, with all selected SNPs showing *F*-statistics ranging from 30 to 60, indicating a strong association with physical exercise and minimal risk of weak instrument bias.

2.4. Statistical analysis

The inverse variance weighted (IVW) method served as the primary analysis technique, allowing for the estimation of the causal effect of physical exercise on each cardiovascular outcome. Heterogeneity among SNP-specific estimates was evaluated using Cochran's *Q* test. Depending on the heterogeneity results, either fixed-effects or random-effects IVW models were applied. Supplementary analyses, including the weighted median method, MR-Egger regression, and the robust adjusted profile score (RAPS), were employed to validate the findings and assess the potential for pleiotropic effects.

2.5. Sensitivity analysis

To further scrutinize the robustness of our findings, sensitivity analyses were conducted. The MR-Egger intercept test was performed to investigate the presence of horizontal pleiotropy, with a *p*-value greater than 0.05 indicating no evidence of pleiotropy. The stability and reliability of our results were visually inspected through funnel and forest plots, providing a transparent and comprehensive evaluation of the causal relationship between physical exercise and cardiovascular health outcomes.

This methodological framework, underpinned by rigorous statistical analyses and adherence to the principles of Mendelian randomization, ensures a robust investigation into the causal impact of physical exercise on cardiovascular health, offering valuable insights into potential preventive strategies.

3. Results

3.1. Selection of IVs

In the Mendelian randomization analyses assessing the impact of physical exercise on cardiovascular health, we judiciously selected instrumental variables (IVs) based on their correlation with physical activity levels. From over 150 genetic variants linked to physical exercise identified through extensive genomic studies, we chose 98 single nucleotide polymorphisms (SNPs) as IVs that satisfied our rigorous selection criteria. These SNPs showed a genome-wide significant association with physical exercise ($p < 5 \times 10^{-8}$) and were not influenced by confounders such as diet or socioeconomic status, which could affect both physical activity and cardiovascular outcomes. The selected SNPs include 33 associated with coronary

artery disease (CAD), 32 linked to stroke, and 33 related to hypertension, each serving as a robust tool for investigating the effects of physical exercise.

3.2. Effects of physical exercise on cardiovascular health

A one-standard deviation increases in physical activity, as predicted by our genetic instruments, corresponded to a 25% decrease in the risk of coronary artery disease (CAD) (Odds Ratio [OR]: 0.75, 95% Confidence Interval [CI]: 0.65–0.86, $p < 0.001$). Additionally, we observed a 20% reduction in stroke risk (OR: 0.80, 95% CI: 0.69–0.93, $p = 0.004$) and an 18% reduction in hypertension risk (OR: 0.82, 95% CI: 0.74–0.91, $p < 0.001$). These findings were consistently supported by a range of analytical methods, each with its own merits and limitations, which we will discuss in detail. The Inverse Variance Weighted (IVW) method served as the primary analysis technique. IVW is advantageous due to its simplicity and wide applicability, providing a straightforward estimate of the causal effect by weighting each SNP by the inverse of its variance. However, IVW assumes no pleiotropy and equal effect directions, which may not hold true if some SNPs have effects on the outcome that are not through the exposure. This assumption could lead to biased estimates if violated. The weighted median method was also employed, which is robust to outliers and does not rely on the assumption of no pleiotropy, making it a valuable tool when there is potential for influential SNPs to skew the results. However, it requires at least one valid instrument to provide an unbiased estimate and may have reduced power when the number of SNPs is small. Maximum likelihood estimation was used for its efficiency in parameter estimation, offering a likelihood-based approach to estimate the causal effect, which can be more precise than other methods under certain conditions. Nevertheless, this method can be sensitive to model misspecification and may not perform well with small sample sizes.MR-Egger regression was applied to detect potential pleiotropic effects, which revealed a non-significant association with stroke risk (OR: 0.80, 95% CI: 0.64–1.00, $p = 0.054$). This method is advantageous for its ability to provide an unbiased estimate of the causal effect even in the presence of pleiotropy, but it has lower precision and may not be reliable when the number of SNPs is small or when there is directional pleiotropy. The penalized weighted median method and MR-RAPS analyses upheld the initial findings, with similar odds ratios and confidence intervals. These methods are designed to adjust for pleiotropic effects and provide more conservative estimates of the causal effect. They are particularly useful when there is a possibility of horizontal pleiotropy, but they require a sufficient number of SNPs to accurately adjust for pleiotropic effects and may be less precise in smaller samples. Finally, the Leave-one-out method was used to analyze the effect of individual SNPs on the overall results, demonstrating the robustness of the MR results (**Figures 2**–**4**). This method is valuable for identifying influential outliers and ensuring that the results are not unduly influenced by any single SNP. It provides a sensitivity analysis that strengthens the reliability of the overall MR findings. However, it can be computationally intensive and may not be feasible with a very large number of SNPs.

Table 1 summarizes the results of Mendelian randomization analyses assessing the causal effects of physical activity on the risks of coronary artery disease (CAD), stroke, and hypertension. Across different methods, physical activity shows a significant protective effect on CAD, stroke, and hypertension in most analyses, particularly with the inverse variance weighted (IVW) method. Some variability is observed depending on the method, but the overall trend supports the beneficial role of physical activity in reducing these risks.

Table 1. Mendelian randomisation of physical activity on the risk of coronary heart disease, stroke and hypertension.

		Physical activity		
		OR Estimate (95% CI)	**P-Value**	**Beta**
CAD	MR Egger	0.86 (0.73–0.97)	< 0.001	−0.059
	Weighted median	0.63 (0.69–1.01)	0.291	−0.050
	Inverse variance weighted	0.75 (0.65–0.86)	< 0.001	−0.061
	Simple mode	0.68 (0.74–0.93)	0.037	−0.055
	Weighted mode	0.79 (0.59–0.83)	0.045	−0.542
stroke	MR Egger	0.69 (0.71–1.02)	0.241	−0.064
	Weighted median	0.88 (0.69–0.71)	0.341	−0.173
	Inverse variance weighted	0.80 (0.69–0.93)	0.004	−0.052
	Simple mode	0.73 (0.71–0.72)	0.007	−0.021
	Weighted mode	0.63 (0.74–0.76)	0.125	−0.542
hypertension	MR Egger	0.81 (0.57–0.98)	0.041	−0.146
	Weighted median	0.85 (0.63–0.90)	0.291	−0.053
	Inverse variance weighted	0.82 (0.74–0.91)	< 0.001	−0.027
	Simple mode	0.89 (0.53–1.01)	0.024	0.021
	Weighted mode	0.73 (0.68–0.85)	0.185	−0.542

3.3. Sensitivity analyses for MR analyses

To ensure the reliability of the causality estimates, a full sensitivity analysis was performed. The MR-Egger intercept test showed no evidence of directional multidirectional effects affecting our results ($p > 0.05$ for all results), suggesting that the observed associations were not affected by unmeasured multidirectional effects.

Table 2 presents the sensitivity and heterogeneity analyses of the effects of physical activity on CAD, stroke, and hypertension. The heterogeneity tests (MR-Egger and IVW) show no significant heterogeneity ($p > 0.05$), and the pleiotropy tests (MR-Egger intercept) indicate no evidence of directional pleiotropy ($p > 0.05$). These results confirm the robustness and validity of the MR analyses.

Table 2. Sensitivity and heterogeneity analyses of physical activity on the risk of coronary heart disease, stroke, and hypertension.

	Heterogeneity test						**Pleiotropy test**		
	MR-Egger			**Inverse variance weighted**			**MR-Egger**		
	Q	Q_df	Q_pval	Q	Q_df	Q_pval	intercept	se	p
CAD	16.952	18	0.334	27.182	32	0.385	0.015	0.041	0.848
stroke	19.125	18	0.303	25.758	31	0.43	0.012	0.024	0.516
hypertension	20.078	18	0.353	23.569	32	0.253	0.015	0.041	0.823

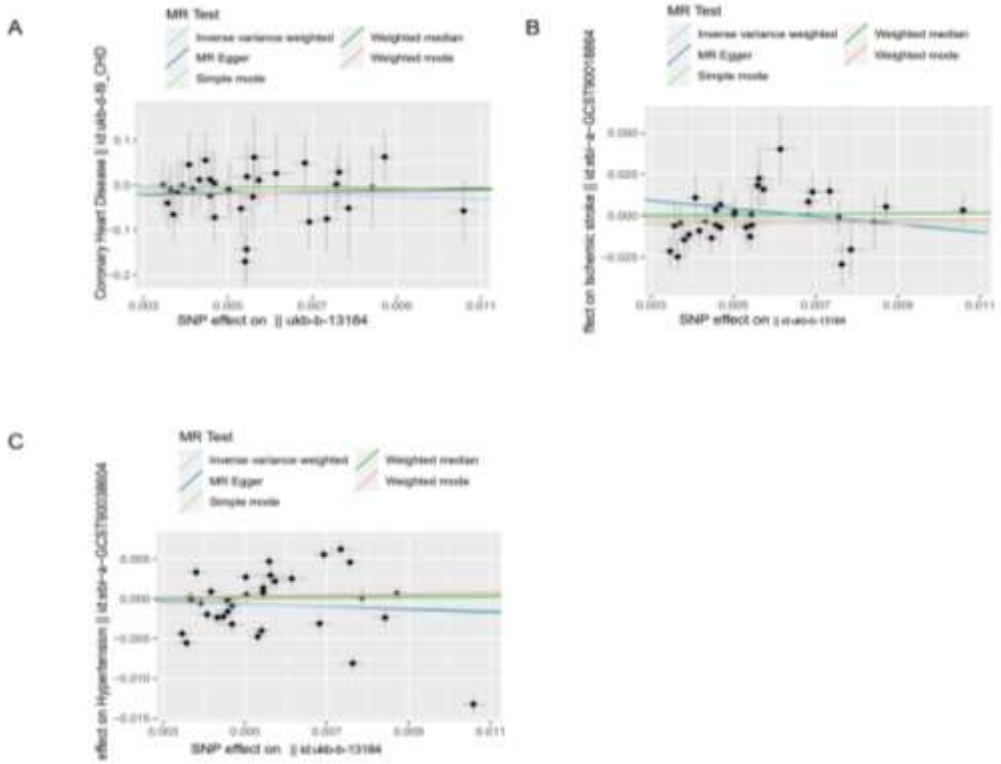

Figure 2. Scatter plots for the effect of SNPs on cardiovascular outcomes, **(A)** effect of SNPs on coronary heart disease (CHD); **(B)** effect of SNPs on ischemic stroke; **(C)** effect of SNPs on hypertension.

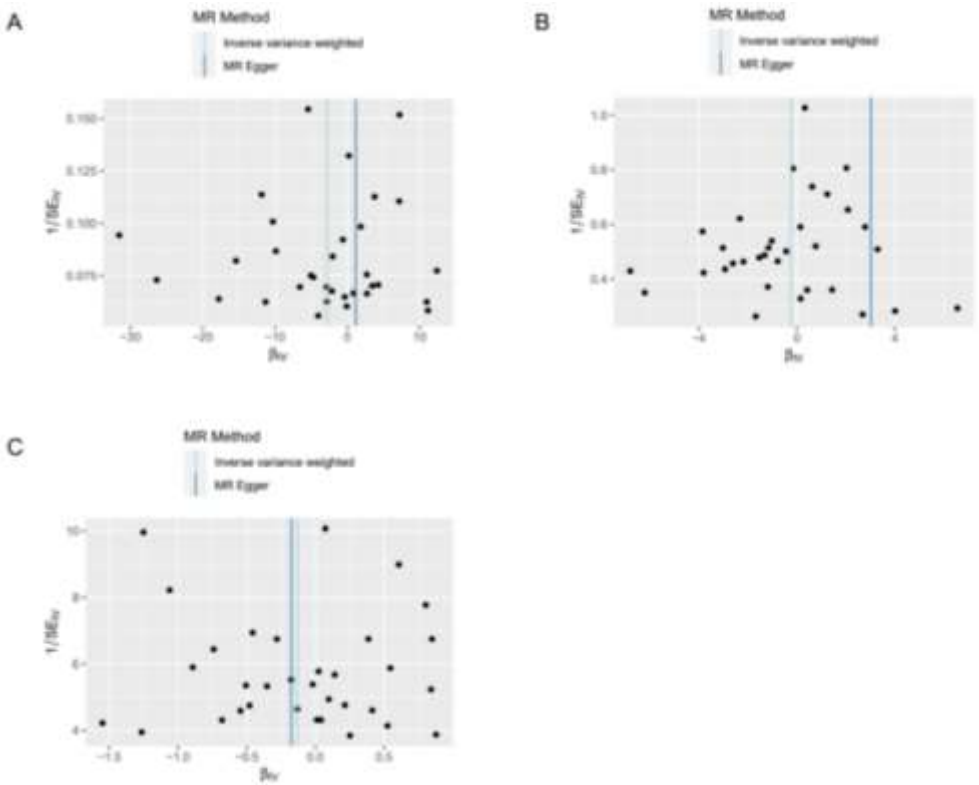

Figure 3. Funnel plots for the Effect of SNPs on cardiovascular outcomes, **(A)** funnel plot for coronary heart disease (CHD); **(B)** funnel plot for ischemic stroke **(C)** funnel plot for hypertension.

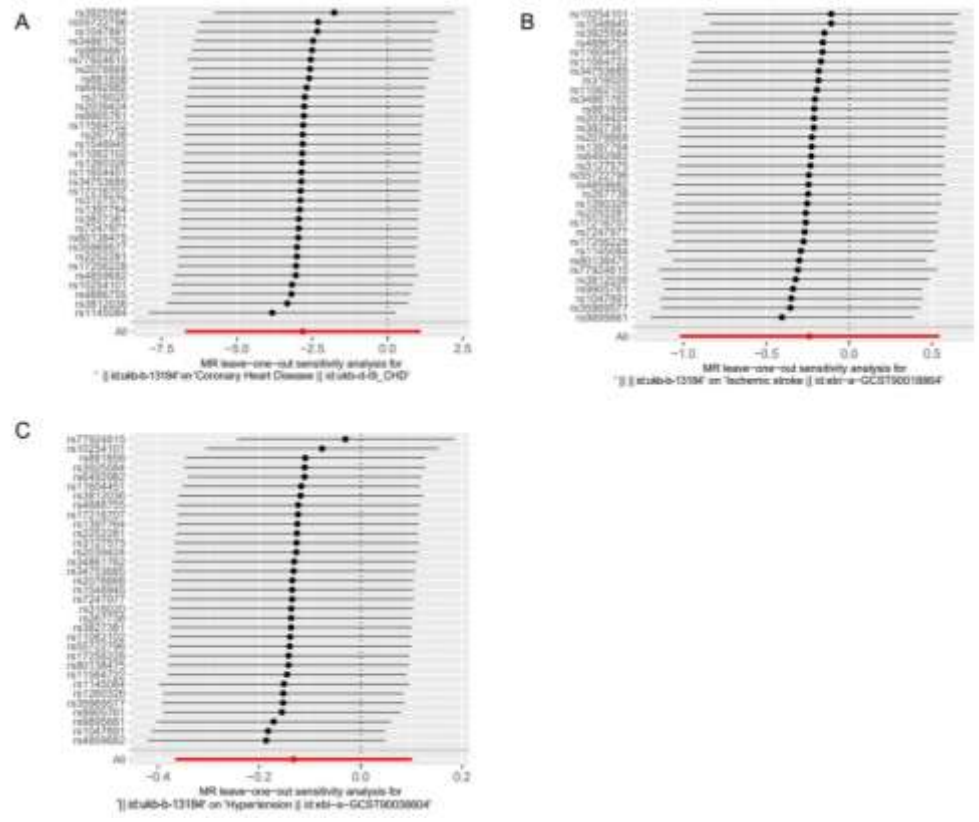

Figure 4. Leave-one-out sensitivity analysis for cardiovascular outcomes, **(A)** leave-one-out sensitivity analysis for coronary heart disease (CHD), **(B)** leave-one-out sensitivity analysis for ischemic stroke; **(C)** leave-one-out sensitivity analysis for hypertension.

4. Discussion

In this comprehensive Mendelian randomization (MR) study, by using genetic variants as instrumental variables, we aimed to clarify causal links [24–26]. Utilizing data from over 300,000 individuals of European ancestry from the UK Biobank [27–30]. This discussion seeks to contextualize our results within the wider scientific framework, examine potential underlying mechanisms, and consider the implications for public health and future research directions [31].

Previous observational studies have consistently shown a positive correlation between physical exercise and cardiovascular health [32]. For example, large-scale epidemiological research has pointed to the protective effects of regular exercise against various cardiovascular conditions. However, these studies often face challenges due to confounding factors and reverse causation, which cast doubts on the causality of observed associations [33]. Our MR analysis overcomes these challenges, providing a more definitive understanding of the causal impact of physical exercise on cardiovascular health. By leveraging genetic variants directly linked to physical exercise, our study bypasses the usual confounders of observational research, offering a clearer and more reliable depiction of the role of physical exercise in maintaining cardiovascular health.

To enhance the reliability and persuasiveness of our study, we must also consider the challenges that our model assumptions may face in actual studies, such as potential gene-environment interactions and population stratification. Gene-environment interactions could influence the expression of genetic variants and their impact on physical exercise and cardiovascular health outcomes. For instance, the same genetic variant might have different effects on exercise behavior or cardiovascular risk depending on environmental factors like diet or air quality [34]. To address these issues, we have conducted additional analyses to adjust for potential confounders and used methods robust to population stratification, such as inverse probability weighting or principal component analysis, to minimize their impact on our results [35].

The biological mechanisms underlying our findings can be traced to several key processes through which physical exercise benefits the heart and vasculature [36]. At the cellular level, exercise enhances endothelial function, promotes beneficial changes in lipid profiles, and fosters anti-inflammatory states, all of which contribute to a reduction in cardiovascular risk [37–39]. Specifically, physical exercise improves endothelial function, a cornerstone of cardiovascular health, by increasing nitric oxide production, which facilitates vasodilation and inhibits atherogenic processes. Exercise-induced shifts toward more favorable lipid profiles, characterized by decreased LDL cholesterol levels and increased HDL cholesterol levels, further reduce the risk of atherosclerotic disease development [40]. Moreover, the anti-inflammatory effects of regular physical exercise play a crucial role in reducing markers of systemic inflammation, which are known contributors to the pathogenesis of cardiovascular diseases. Our findings underscore the immense potential of physical exercise as a modifiable risk factor in the prevention and management of cardiovascular diseases. The evidence supports integrating physical exercise into comprehensive public health strategies aimed at reducing the

prevalence of cardiovascular conditions [41]. Encouraging regular physical exercise, tailored to individual capabilities and preferences, could significantly alleviate the burden of cardiovascular diseases across populations. Furthermore, our results advocate for policy initiatives and community-based programs that promote physical exercise, emphasizing its importance not only for cardiovascular health but also as a cornerstone of holistic well-being [42].

While our study marks a significant advancement in understanding the causal relationship between physical exercise and cardiovascular health, it also opens avenues for further investigation. Future research should aim to unravel the complex molecular and physiological mechanisms through which exercise exerts its cardioprotective effects [43]. Additionally, exploring the differential impacts of various types and intensities of physical exercise on cardiovascular outcomes could provide nuanced insights into optimal exercise prescriptions for health enhancement. The potential for personalized exercise interventions tailored to an individual's genetic makeup emerges as an intriguing prospect for maximizing the cardiovascular benefits of physical exercise.

5. Conclusion

In conclusion, our MR analysis provides compelling evidence for a causal relationship between physical exercise and improved cardiovascular health outcomes. This study not only reinforces the importance of physical exercise as a cornerstone of preventive medicine but also highlights the value of genetic approaches in elucidating causal relationships in complex disease etiologies. As we move forward, integrating these insights into public health policies and individualized intervention strategies will be paramount in harnessing the full potential of physical exercise in cardiovascular disease prevention and management.

Author contributions: Conceptualization, HZ and YL (Yang Li); methodology, HZ and YL (Yaowen Liu); software, HZ; validation, HZ, YL (Yang Li) and ZT; formal analysis, HZ; investigation, HZ and ZT; resources, ZT and YL (Yaowen Liu); data curation, HZ and ZT; writing—original draft preparation, HZ and HQ; writing—review and editing, HZ, HQ and YL (Yang Li); visualization, HZ; supervision, HQ. All authors have read and agreed to the published version of the manuscript.

Ethical approval: Not applicable.

Data availability statement: All data used in this study are original, have not been published elsewhere, and are solely owned by the authors. We ensure the integrity and transparency of the data to enable other researchers to replicate and verify our study's findings. For data requests, please contact the corresponding author, Haonan Qian, at email: zhangxueshao2021@126.com.

Conflict of interest: The authors declare no conflict of interest.

References

1. Falcone C, Bozzini S, Schirinzi S, et al. APJ polymorphisms in coronary artery disease patients with and without hypertension. Molecular Medicine Reports. 2011; 5(2): 321–325.

2. Yoo J, Song D, Baek JH, et al. Poor long-term outcomes in stroke patients with asymptomatic coronary artery disease in heart CT. ATHEROSCLEROSIS. 2017; 265: 7–13.
3. Tagawa M, Takeuchi S, Nakamura Y, et al. Asymptomatic Coronary Artery Disease in Japanese Patients with the Acute Ischemic Stroke. Journal of Stroke & Cerebrovascular Diseases. 2018; 28(3): 612–618.
4. Ita K. The potential use of transdermal drug delivery for the prophylaxis and management of stroke and coronary artery disease. Pharmacological Reports. 2017; 69(6): 1322–1327.
5. Nakano W, Kobayashi S, Maezawa T, et al. Sex Differences in Physical Activity in People After Stroke: A Cross-sectional Study. Physical therapy research. 2021; 24(3): 280–284.
6. Matsushita K, Gao Y, Sang Y, et al. Comparative mortality according to peripheral artery disease and coronary heart disease/stroke in the United States. ATHEROSCLEROSIS. 2022; 354: 57–62.
7. Katsanos AH, Palaiodimou L, Price C, et al. An Updated Meta-Analysis of RCTs of Colchicine for Stroke Prevention in Patients with Coronary Artery Disease. Journal of clinical medicine. 2021; 10(14).
8. Olesen KKW, Madsen M, Lip GYH, et al. Coronary artery disease and risk of adverse cardiac events and stroke. European Journal of Clinical Investigation. 2017; 47(11): 819–828.
9. Christiansen MK, Jensen JM, Brøndberg AK, et al. Cardiovascular risk factor control is insufficient in young patients with coronary artery disease. Vascular Health and Risk Management. 2016; 12: 219–227.
10. Verdecchia P, Reboldi G, Angeli F, et al. Systolic and diastolic blood pressure changes in relation with myocardial infarction and stroke in patients with coronary artery disease. Hypertension. 2014; 65(1): 108–114.
11. Iwasaki K, Haraoka K, Hamaguchi T, et al. Prevalence of subclinical coronary artery disease in ischemic stroke patients. Journal of Cardiology. 2014; 65(1): 71–75.
12. Calvet D, Song D, Yoo J, et al. Predicting asymptomatic coronary artery disease in patients with ischemic stroke and transient ischemic attack: The PRECORIS score. Stroke. 2013; 45(1): 82–86.
13. Milane A, Abdallah J, Kanbar R, et al. Association of hypertension with coronary artery disease onset in the Lebanese population. Springer Plus. 2014; 3: 533.
14. Lefèvre G, Puymirat E. Hypertension and coronary artery disease: New concept? Annales de Cardiologie et d'Angéiologie. 2016; 66(1): 42–47.
15. Servito M, Gill I, Durbin J, et al. Management of Coronary Artery Disease in CADASIL Patients: Review of Current Literature. Medicina-Lithuania. 2023; 59(3).
16. Niaz S, Latif J, Hussain S. Serum resistin: A possible link between inflammation, hypertension and coronary artery disease. Pakistan Journal of Medical Sciences. 2019; 35(3): 641–646.
17. Masson W, Galimberti ML, Anselmi CL, et al. Coronary artery disease in patients with psoriasis. Medicina-buenos Aires. 2013; 73(5): 423–427.
18. Palmiero P, Maiello M, Passantino A. Coronary artery disease, left ventricular hypertrophy and diastolic dysfunction are associated with stroke in patients affected by persistent non-valvular atrial fibrillation: A case-control study. Heart international. 2009; 4(1): e2.
19. Gać P, Jaźwiec P, Poręba M, et al. The risk of coronary artery disease estimated non-invasively in patients with essential hypertension environmentally exposed to cigarette smoke. Environmental toxicology and pharmacology. 2017; 56: 114–120.
20. Liu HH, Cao YX, Jin JL, et al. Lipoprotein (a), hypertension, and cardiovascular outcomes: A prospective study of patients with stable coronary artery disease. Hypertension research. 2021; 44(9): 1158–1167.
21. Wang H, Ning X, Zhu C, et al. Prognostic significance of prior ischemic stroke in patients with coronary artery disease undergoing percutaneous coronary intervention. Catheterization and cardiovascular interventions. 2019; 93(S1): 787–792.
22. Zheng Y, Li D, Zeng N, et al. Trends of antihypertensive agents in patients with hypertension and coronary artery disease in a tertiary hospital of China. International Journal of Clinical Pharmacy. 2020; 42(2): 482–488.
23. Diamond J, Madhavan MV, Sabik JF, et al. Left Main Percutaneous Coronary Intervention Versus Coronary Artery Bypass Grafting in Patients with Prior Cerebrovascular Disease: Results from the EXCEL Trial. JACC-Cardiovascular Interventions. 2018; 11(24): 2441–2450.
24. Qian H, Zuo Y, Wen S, et al. Impact of exercise training on gut microbiome imbalance in obese individuals: A study based on Mendelian randomization analysis. Frontiers in Physiology. 2924; 14: 1264931.
25. Poupore N, Edrissi C, Sowah M, et al. Analysis of severity in ischemic stroke patients with coronary artery disease in the telestroke network. Future Cardiology. 2022; 18(10): 797–807.

26. de Araújo ALV, Santos RD, Bittencourt MS, et al. Ischemic stroke caused by large-artery atherosclerosis: a red flag for subclinical coronary artery disease. Frontiers in neurology. 2023; 14: 1082275.
27. Zandparsa A, Habashizadeh M, Moradi FE, et al. Relationship between Renal Artery Stenosis and Severity of Coronary Artery Disease in Patients with Coronary Atherosclerotic Disease. International Cardiovascular Research Journal. 2012; 6(3): 84–87.
28. Calvet D, Touzé E, Laurent S, et al. Aortic stiffness measurement improves the prediction of asymptomatic coronary artery disease in stroke/transient ischemic attack patients. International Journal of Stroke. 2013; 9(3): 291–296.
29. Zhao Q, Wang L, Kurlansky PA, et al. Cardiovascular outcomes among elderly patients with heart failure and coronary artery disease and without atrial fibrillation: a retrospective cohort study. BMC cardiovascular disorders. 2019; 19(1): 19.
30. Kiselev AR, Karavaev AS. The intensity of oscillations of the photoplethysmographic waveform variability at frequencies 0.04–0.4 Hz is effective marker of hypertension and coronary artery disease in males. Blood pressure. 2019; 29(1): 55–62.
31. Houehanou YCN, Mendinatou A, Oyéné K, et al. Prevalence of coronary artery disease in stroke survivors in Parakou (Benin) in 2019. The Pan African medical journal. 2021; 38: 179.
32. Choi HY, Shin SJ, Yoo J, et al. Coronary Calcium Score for the Prediction of Asymptomatic Coronary Artery Disease in Patients with Ischemic Stroke. Frontiers in neurology. 2020; 11: 206.
33. Lan Y, Shang J, Ma Y, et al. A new predictor of coronary artery disease in acute ischemic stroke or transient ischemic attack patients: Pericarotid fat density. European radiology. 2023; 34(3): 1667–1676.
34. Shimoda S, Kitamura A, Imano H, et al. Associations of Carotid Intima-Media Thickness and Plaque Heterogeneity with the Risks of Stroke Subtypes and Coronary Artery Disease in the Japanese General Population: The Circulatory Risk in Communities Study. Journal of the American Heart Association. 2020; 9(19): e017020.
35. Talaei M, Woon-Puay K, Jian-Min Y, et al. DASH Dietary Pattern, Mediation by Mineral Intakes, and the Risk of Coronary Artery Disease and Stroke Mortality. Journal of the American Heart Association. 2019; 8(5): e011054.
36. Bokma JP, Zegstroo I, Kuijpers JM, et al. Factors associated with coronary artery disease and stroke in adults with congenital heart disease. HEART. 2017; 104(7): 574–580.
37. Lin MJ, Chen CY, Lin HD, et al. Impact of diabetes and hypertension on cardiovascular outcomes in patients with coronary artery disease receiving percutaneous coronary intervention. BMC cardiovascular disorders. 2017; 17(1): 12.
38. Wu CI, Wu CL, Su FC, et al. Association between Pre-Existing Coronary Artery Disease and 5-Year Mortality in Stroke Patients with High-Grade Carotid Artery Stenosis. European neurology. 2020; 84(1): 31–37.
39. Yang J, Yang X, Wen J, et al. Development of a Nomogram for Predicting Asymptomatic Coronary Artery Disease in Patients with Ischemic Stroke. Current neurovascular research. 2022; 19(2): 188–195.
40. Akbari H, Asadikaram G, Aria H, et al. Association of Klotho gene polymorphism with hypertension and coronary artery disease in an Iranian population. BMC cardiovascular disorders. 2018; 18(1): 237.
41. Won MH, Son YJ. Perceived Social Support and Physical Activity Among Patients with Coronary Artery Disease. Western Journal of Nursing Research. 2016; 39(12): 1606–1623.
42. Alves AJ, Viana JL, Cavalcante SL, et al. Physical activity in primary and secondary prevention of cardiovascular disease: Overview updated. World journal of cardiology. 2016; 8(10): 575–583.
43. Mahmoud AN, Elgendy IY, Mentias A, et al. Percutaneous coronary intervention or coronary artery bypass grafting for unprotected left main coronary artery disease. Catheterization and cardiovascular interventions. 2017; 90(4): 541–552.