

# 5-minute Review

Research Updates  
in Ischemic Heart  
Disease

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## Preface

*The most valuable of all talents is that of never using two words when one will do*

– Thomas Jefferson

We are in the world of the information age. It is difficult to stay up-to-date with all the information regarding the research and innovations that are conducted in a disease area due to the sheer pace at which things are happening. Importantly, one cannot just restrict the knowledge to high-impact journals alone. For individualizing patient care by demographics, genomics, and other factors; comprehensive knowledge is the need of the hour.

Conventional search in medical databases such as PubMed®, EMBASE, Cochrane Library, etc., have limitations. Although a PubMed® search by keywords and 'most recent' filter will provide a list of hundreds research papers in chronological order, the title of the paper often does not describe the interventions and outcomes that are assessed. Alternatively, reading an abstract of 250 words for hundreds of research papers would take about 2 to 4 hours depending on the reader. Needless to mention the fatigue factor and irrelevance of some reports to individual practice in such an exercise. Additionally, it is always difficult to bifurcate information based on specifics– epidemiology, pathogenesis, genomics, diagnosis, non-pharmacological interventions, and treatment.

The book “5-Minute review” is intended to bridge all these gaps and provide the most relevant information of a research paper in just a couple of sentences. Information is depicted as a research question and results of the primary outcome are quantified; moreover, reference for the article is provided. This, in our opinion gives maximum information in the shortest possible timeframe. If any report invokes an interest, further reading can be taken up by accessing the full-text article. Being medical scientists and clinical practitioners ourselves, we strongly believe that this book will empower clinicians and researchers to better patient care and benefit our society in a larger context.



## Search Strategy

### Keywords

(Heart Disease, Ischemic [Title]) OR (Disease, Ischemic Heart [Title]) OR (Diseases, Ischemic Heart [Title]) OR (Ischemic Heart Diseases [Title]) OR (Ischemia, Myocardial [Title/Abstract]) OR (Myocardial Ischemias [Title]) OR 'Ischemic Heart Disease' OR 'myocardial ischemia' OR 'Myocardial Reperfusion Injury' OR ("Myocardial Ischemia"[Mesh]) OR "Myocardial Infarction"[Mesh] OR "Coronary Artery Disease"[Mesh]

Up to first 100 articles of the above search results are presented in this edition of the **5-minute Review**.





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## Epidemiology

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**1. What are the temporal trends, sex differences, comorbidity patterns, and mortality outcomes in patients undergoing non-traumatic lower-limb amputations from 2006 to 2022?**

In a retrospective study of 1,107 patients at the Medical University of Innsbruck, 30-day and 1-year mortality rates remained high at 4.14% and 23.2%, respectively; chronic kidney disease, heart failure, and major amputations predicted 1-year mortality, with women presenting at older ages (78.9 vs. 68.1 years), higher rates of major amputations, and distinct cause-of-death patterns compared to men.

Kaser S, et al. Non-Traumatic Lower-Limb Amputations: Outcome, Sex-Differences, Comorbidity Patterns and Temporal Trends from 2006 to 2022. *J Clin Med.* 2025 Jun 6;14(12):4030. doi: 10.3390/jcm14i24030. PMID: 40565773; PMCID: PMC12194082.

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**2. What has been the impact and findings of the Copenhagen City Heart Study (CCHS), an ongoing epidemiological cohort with repeated measurements, on cardiovascular and other health outcomes?**

The CCHS, a large population-based cohort study initiated in 1976 with 20,000 Danish adults aged  $\geq 20$  and repeated assessments over decades, has significantly advanced prevention of ischemic heart disease (IHD) and acute myocardial infarction (AMI), contributing to over 1300 publications and expanding into genetics and multiple medical fields, with a 75% initial response rate and continuous follow-up including clinical and genetic data.

Jensen GB, et al. Copenhagen City Heart Study. An epidemiological cohort study with repeated measurements: history, course, and results. *Scand J Public Health.* 2025 Jun 25;14034948251347765. doi: 10.1177/14034948251347765. Epub ahead of print. PMID: 40557761.

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**3. How does sex influence therapeutic adherence and risk prediction for secondary prevention in patients with cardiovascular disease?**

A scoping review of 13 recent studies involving cardiovascular patients showed medication adherence ranges of 25–83% in males and 24–80% in females for hypertension, and 32–74% in



males versus 32–60% in females for IHD, with adherence to physical activity varying similarly; key predictors included older age, comorbidities, and psychosocial factors.

Moreno G, et al. Influence of Sex on Therapeutic Adherence in Cardiovascular Diseases: A Scoping Review. *J Clin Med*. 2025 Jun 15;14(12):4253. doi: 10.3390/jcm14124253. PMID: 40565998; PMCID: PMC12194201.

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#### 4. **How have patient characteristics, surgical trends, and one-year mortality outcomes changed in mitral valve surgery for mitral regurgitation ?**

In this nationwide registry study in Denmark from 1996 to 2022, 8,098 patients, median age rose from 65.5 to 69.4 years, MVS incidence doubled from 4.09 to 8.66 per 100,000 person-years, and one-year mortality significantly decreased for mitral repair (HR 0.27; 95% CI 0.15–0.49;  $p < 0.001$ ) and transcatheter-edge-to-edge repair (TEER) (HR 0.55; 95% CI 0.31–0.97;  $p = 0.04$ ), with TEER mortality at 18.9% and mitral repair mortality at 4.8%.

Schöps LB, et al. Trends in mitral valve surgery for mitral valve regurgitation in Denmark: Changes in patient characteristics and mortality from 1996 to 2022. *Int J Cardiol*. 2025 Jun 23;438:133552. doi: 10.1016/j.ijcard.2025.133552. Epub ahead of print. PMID: 40562313.

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#### 5. **What are the long-term trends in heart disease mortality and its subtypes ?**

In a population-based study using CDC data on U.S. adults aged 25 and older from 1970 to 2022, age-adjusted total heart disease mortality decreased by 66% (from 761 to 258 per 100,000), with IHD deaths dropping from 91% to 53% of total; meanwhile, mortality from other heart disease subtypes increased by 81%, including a 146% rise in heart failure and a 450% increase in arrhythmias.

King SJ, et al. Heart Disease Mortality in the United States, 1970 to 2022. *J Am Heart Assoc*. 2025 Jul;14(13):e038644. doi: 10.1161/JAHA.124.038644. Epub 2025 Jun 25. PMID: 40557798.

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#### 6. **What are the clinical profiles and temporal trends of cardiovascular hospitalizations in Greece from 2012 to 2023?**

This retrospective cohort study of 37,741 hospitalizations (33,645 patients; median age 70; 66.4% male) from the CardioMining Database found coronary artery disease(CAD) (40.8%), heart



failure (20.4%), and arrhythmias (18.6%) most common. Over 12 years, chronic coronary syndrome admissions declined, while heart failure, pulmonary embolism, and valvular disease admissions rose, alongside increased use of SGLT2 inhibitors and NOACs, with notable age and sex disparities.

Samaras A, et al. Clinical Profiles and Temporal Trends of 37,741 Cardiovascular Hospitalizations in Greece over 12 years: Initial Insights from the CardioMining Database. *Hellenic J Cardiol.* 2025 Jun 24:S1109-9666(25)00149-6. doi: 10.1016/j.hjc.2025.06.007. Epub ahead of print. PMID: 40571281.

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**7. What are the global trends, causes, and socioeconomic inequalities in the burden of heart failure among adults aged  $\geq 65$  from 1990 to 2035?**

Using GBD 2021 data, global heart failure cases in older adults rose from 14.1M (1990) to 36.2M (2021), with YLDs increasing from 1.34M to 3.45M. Population growth accounted for 89% of this rise. Aging had opposite effects across SDI levels ( $-39.4\%$  in high vs.  $+28.7\%$  in middle SDI). IHD was the top cause (37.6%). By 2035, cases are projected to reach 4,935 per 100,000, with 473 YLDs per 100,000.

Gu J, et al. Global burden of heart failure in older adults: trends, socioeconomic inequalities, and future projections from 1990 to 2035. *Eur Heart J Qual Care Clin Outcomes.* 2025 Jun 20:qcaf047. doi: 10.1093/ehjqcco/qcaf047. Epub ahead of print. PMID: 40578836.

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**8. Does a first diagnosis of angina or nonspecific chest pain in women without obstructive CAD lead to increased healthcare use compared to asymptomatic women?**

In this Danish nationwide cohort study (WOMANOCA; N=60,668 cases, 303,247 controls; 3-year follow-up), women with angina (HR 3.24, 95% CI 3.10–3.38) and nonspecific chest pain (HR 2.87, 95% CI 2.78–2.97) had significantly higher cardiac readmissions than controls, with angina linked to more burden than nonspecific pain (HR 1.16, 95% CI 1.10–1.22); nonspecific chest pain was also associated with more GP visits, out-of-hours consultations, and ECGs.

Dalsgaard JL, et al. The use of healthcare contacts following a first diagnosis of chest pain among women with no obstructive coronary artery disease: Results from the WOMANOCA nationwide cohort study. *Eur Heart J Qual Care Clin Outcomes.* 2025 Jun 27:qcaf051. doi: 10.1093/ehjqcco/qcaf051. Epub ahead of print. PMID: 40576444.



## Risk factor and associations

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### 9. Does the presence of connective tissue disease (CTD) features impact adverse cardiovascular outcomes in patients with spontaneous coronary artery dissection (SCAD)?

In this retrospective study of 1380 SCAD patients (2018–2024, Mayo Clinic), 26.7% had CTD features; these patients showed significantly higher rates of adverse outcomes (57.9% vs. 41.0%,  $p < 0.001$ ), including recurrent MI (55.3% vs. 35.5%,  $p < 0.001$ ), with CTD features independently predicting worse outcomes (OR for joint conditions: 3.19, 95% CI: 2.17–4.68; grouped CTD: OR 2.77, 95% CI: 2.01–3.82).

Kumar S, et al. Impact of connective tissue disease features on patients with spontaneous coronary artery dissection. *Cardiovasc Revasc Med*. 2025 Jun 21:S1553-8389(25)00308-2. doi: 10.1016/j.carrev.2025.06.023. Epub ahead of print. PMID: 40579292.

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### 10. Can multimodality imaging (MDCT and IVUS) facilitate successful percutaneous coronary intervention (PCI) in patients with complex coronary lesions following redo transcatheter aortic valve replacement (TAVR)?

In this single-patient case study (83-year-old woman with NSTEMI and prior redo TAVR), MDCT and IVUS enabled successful PCI of severe calcified ostial stenosis, demonstrating that preprocedural imaging can overcome coronary access challenges post-TAVR.

Al Nooryani A, et al. Multimodality Imaging for Facilitating Percutaneous Coronary Intervention of a Calcified Nodule Post Redo TAVR. *JACC Case Rep*. 2025 Jun 25;30(16):104013. doi: 10.1016/j.jaccas.2025.104013. PMID: 40579093; PMCID: PMC12273855.

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### 11. Does the presence of atherosclerotic conditions and use of cardiovascular medications influence the rate of abdominal aortic aneurysm (AAA) growth?

In this 10-year observational study, coronary, renal, and carotid artery disease were linked to slower AAA growth ( $\geq 0.5$  cm/year), likely due to treatment. Aspirin independently reduced growth, while untreated peripheral artery disease increased it. Adding statins to aspirin further slowed growth in these patients.



Alkhalafan F, et al. Impact of Atherosclerotic Conditions and Cardiovascular Medications on Abdominal Aortic Aneurysm Growth. *Am J Med.* 2025 Jun 25;S0002-9343(25)00408-5. doi: 10.1016/j.amjmed.2025.06.040. Epub ahead of print. PMID: 40578465.

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**12. What is the combined and individual impact of low cardiac function (EF  $\leq$  35%) and diabetes mellitus (DM) on long-term survival and causes of death after coronary artery bypass grafting (CABG)?**

In this retrospective study of 1,036 patients undergoing isolated CABG (2009–2022), 10-year survival was lowest in those with both EF  $\leq$  35% and DM (53.5%); multivariate Cox regression showed significantly increased mortality risk in EF  $\leq$  35% DM (+) group (HR 2.23,  $p = 0.001$ ), with EF  $\leq$  35% independently increasing risk of death from heart failure (HR 3.62,  $p = 0.012$ ) and DM associated with higher pneumonia-related deaths (HR 2.72,  $p = 0.046$ ).

Moriyama S, et al. Impact of low cardiac function and diabetes mellitus on survival and causes of death following coronary artery surgery. *Interdiscip Cardiovasc Thorac Surg.* 2025 Jul 3;40(7):ivaf144. doi: 10.1093/icvts/ivaf144. PMID: 40577802; PMCID: PMC12231534.

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**13. Does genetic risk of first stroke influence the prognosis (recurrent stroke, CHD, and death) among stroke survivors?**

In this prospective cohort study using China Kadoorie Biobank (n=80,908) and UK Biobank (n=380,348), higher integrative polygenic risk scores (iPRSs) were significantly associated with increased risk of recurrent stroke (HR 1.08 [1.05–1.11] CKB; 1.11 [1.03–1.19] UKB) and CHD (HR 1.08 [1.02–1.15] CKB; 1.23 [1.10–1.37] UKB) among first stroke survivors, with no significant association with mortality.

Han Y, et al. Genetic Risk and Prognosis of the First Incident Stroke Survivors: Findings from China Kadoorie Biobank and UK Biobank. *Neurology.* 2025 Jul 22;105(2):e213832. doi: 10.1212/WNL.0000000000213832. Epub 2025 Jun 27. PMID: 40577674; PMCID: PMC12205741.

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**14. What are the incidence, risk factors, and clinical outcomes of pericardial effusion in patients with left ventricular assist devices (LVADs)?**

In this retrospective study using the National Inpatient Sample (n = 98,112,095; LVAD patients = 9,850), pericardial effusion occurred in 6.5% (n = 640) of LVAD patients; significant risk factors included CAD (OR = 2.89), PCI (OR = 2.2), liver disease (OR = 1.72),



and others; affected patients had longer hospital stays (33 vs 27 days) and higher costs (\$847,525 vs \$792,616), with no difference in mortality.

Khan MZ, et al. Incidence, risk factors and clinical outcomes of pericardial effusion in left ventricular assist device patients. *World J Cardiol.* 2025 Jun 26;17(6):105330. doi: 10.4330/wjc.v17.i6.105330. PMID: 40575433; PMCID: PMC12186126.

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**15. What are the clinical characteristics, risk factors, angiographic findings, and management strategies of AMI in young adults?**

In this 3-year retrospective cross-sectional study conducted in Dammam (n=91, 96.7% males, mean age 35.9±3.4 years), hyperlipidemia (69.2%), smoking (49.5%), and obesity (43.9%) were the leading risk factors; 57.1% presented with STEMI, 78% had LAD involvement, 72.5% had single-vessel disease, and 74.7% were managed with PCI.

Hegazi Abdelsamie A, et al. Acute myocardial infarction in the young: A 3-year retrospective study. *World J Cardiol.* 2025 Jun 26;17(6):106445. doi: 10.4330/wjc.v17.i6.106445. PMID: 40575428; PMCID: PMC12186127.

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**16. Does exposure to per- and polyfluoroalkyl substances (PFASs) affect clinical outcomes after PCI in patients with type 2 diabetes mellitus (T2DM) ?**

In this prospective nested case-control study of 150 matched T2DM patients post-PCI, higher exposure to 9 PFASs significantly increased 2-year odds of major adverse cardiovascular and cerebrovascular events (MACCEs), with perfluoroundecanoic and perfluorodecanoic acids contributing most.

Cai D, et al. Per- and Polyfluoroalkyl Substances, Serum Lipidome, and Clinical Outcomes after Percutaneous Coronary Intervention in Type 2 Diabetic Patients: A Prospective Nested Case-control Study. *J Atheroscler Thromb.* 2025 Jun 24. doi: 10.5551/jat.65708. Epub ahead of print. PMID: 40571603.

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**17. Does significant post-implant mitral regurgitation (PI-MR) affect long-term outcomes in patients receiving a contemporary left ventricular assist device (LVAD)?**

In this retrospective cohort study of 2,858 LVAD patients from the STS Intermacs Database (2017–2021), those with significant PI-MR



(n=340) had lower 2-year survival (79.5% vs 88.3%,  $p=.008$ ), higher readmission risk (HR 1.19,  $p=.032$ ), and increased renal failure (HR 1.84,  $p=.014$ ) compared to those without PI-MR.

Pegues J, et al. Impact of Post-Implant Mitral Regurgitation on Durable Left Ventricular Assist Device Outcomes. *J Thorac Cardiovasc Surg*. 2025 Jun 24;S0022-5223(25)00539-2. doi: 10.1016/j.jtcvs.2025.06.019. Epub ahead of print. PMID: 40571187; PMCID: PMC12217138

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**18. Can decomposing CAD polygenic risk scores (PRS) by pleiotropic trait clusters reveal distinct genetic contributions and clinical phenotypes in high-risk individuals?**

In this large-scale genomic study (UK Biobank, n=407,903; European ancestry), CAD PRS was partitioned into 9 pleiotropy-decomposed PRSs, each capturing a higher proportion of risk in biologically matched subgroups (e.g., lipids PD-PRS: 25.2% [SD 0.07] vs. 10.06% [SD 0.07]), with subgroup-specific clinical traits (e.g., 67.5% higher lipoprotein(a), 18.3% higher LDL-C), and significant trait-PRS interactions (e.g., BP × BP PD-PRS, smoking × respiratory PD-PRS).

Hu J, et al. Robust pleiotropy-decomposed polygenic scores identify distinct contributions to elevated coronary artery disease polygenic risk. *PLoS Comput Biol*. 2025 Jun 26;21(6):e1013191. doi: 10.1371/journal.pcbi.1013191. PMID: 40570042; PMCID: PMC12212871.

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**19. Does multiple sclerosis (MS) increase the risk of AMI and diffuse CAD in young patients?**

This case report presents a 31-year-old male with a 7-year history of MS who developed acute ST-elevation MI and severe multi-vessel CAD requiring revascularization, highlighting cardiovascular risks in MS patients.

Țieranu EN, et al. Acute Myocardial Infarction and Diffuse Coronary Artery Disease in a Patient with Multiple Sclerosis: A Case Report and Literature Review. *J Clin Med*. 2025 Jun 17;14(12):4304. doi: 10.3390/jcm14124304. PMID: 40566048; PMCID: PMC12194425.

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**20. What is the impact of polyvascular disease on the long-term prognosis of patients with acute coronary syndrome (ACS) in Italy?**

In this retrospective cohort study of 342,052 ACS patients aged ≥40 years hospitalized in Italy (2017-2018), those with peripheral artery disease (PAD) only, cerebrovascular disease (CeVD) only,



and both PAD+CeVD had increased 5-year major adverse cardiovascular and cerebrovascular events (MACCE) risks with adjusted hazard ratios of 1.37 (95% CI: 1.35-1.40), 1.36 (95% CI: 1.33-1.39), and 1.45 (95% CI: 1.40-1.50), respectively, compared to ACS patients without these conditions.

Mureddu GF, et al. Impact of Polyvascular Disease on Long-Term Prognosis of Patients with Acute Coronary Syndrome-A Retrospective Cohort Study in Italy. *J Clin Med.* 2025 Jun 11;14(12):4158. doi: 10.3390/jcm14124158. PMID: 40565903; PMCID: PMC12194242.

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**21. How can diagnostic and management practices be improved for patients with premature CAD within an integrated healthcare system?**

In a retrospective chart review of 28 patients with AMI before age 50, key gaps were identified including underdocumentation of family history (18%), missed diabetes diagnoses (20% of 15 diabetic patients), and undiagnosed obesity in 43% of patients with BMI >30, leading to system changes aimed at better risk factor identification and continuity of care.

Litman K, et al. A Hybrid Chart Review of Premature Coronary Artery Disease: An Opportunity to Improve Diagnostic Excellence and Management. *Perm J.* 2025 Jun 25;1-7. doi: 10.7812/TPP/24.184. Epub ahead of print. PMID: 40561072.

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**22. What is the clinical significance of mitral annular calcification (MAC) beyond being an incidental, benign finding in cardiovascular imaging?**

This review highlights that MAC, often seen in patients with cardiovascular or pulmonary disease, is associated with increased risk of major cardiovascular events—including CAD, stroke, atrial fibrillation, heart failure, and mortality—and affects outcomes of mitral valve interventions; MAC prevalence correlates strongly with risk factors like hypertension, diabetes, and atherosclerosis.

Vereckei A, et al. Mitral Annular Calcification, a Not So Marginal and Relatively Benign Finding as Many of Us Think: A Review. *J Cardiovasc Dev Dis.* 2025 Jun 18;12(6):233. doi: 10.3390/jcdd12060233. PMID: 40558667; PMCID: PMC12193605.

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**23. Does gestational diabetes (GD) mediate the relationship between prepregnancy cardiovascular health (CVH) and**



### **midlife subclinical CAD measured by coronary artery calcium (CAC)?**

In a prospective cohort study of 1,052 women (mean age 28.6 years) from the CARDIA study, those with low/moderate prepregnancy CVH had higher odds of GD (8.8% vs 6.3%; adjusted OR 1.8, 95% CI 1.1-3.0) and incident CAC >0 (28.2% vs 19.2%; adjusted OR 1.7, 95% CI 1.2-2.5); GD mediated only 6% (95% CI 0%-22%) of the CVH-CAC association, indicating GD is mainly a marker rather than a mediator.

Cameron NA, et al. Prepregnancy Cardiovascular Health, Gestational Diabetes, and Coronary Artery Calcium. *JAMA Cardiol.* 2025 Jun 25:e251887. doi: 10.1001/jamacardio.2025.1887. Epub ahead of print. PMID: 40560557; PMCID: PMC12199180.

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### **24. What is the current understanding of the bidirectional relationship between depression and CAD, including epidemiology, pathophysiology, and therapeutic strategies?**

This review synthesizes data from multiple epidemiological and clinical studies indicating that CAD causes one-third of deaths in those aged  $\geq 35$ , mental illnesses cause ~8 million deaths annually, and highlights mechanisms like inflammation and neurohormonal dysregulation; SSRIs and cognitive behavioral therapy show clinical benefits, though evidence for mortality reduction is limited.

Apostolos A, et al. Depression and Coronary Artery Disease-Where We Stand? *J Clin Med.* 2025 Jun 16;14(12):4281. doi: 10.3390/jcm14124281. PMID: 40566026; PMCID: PMC12193863.

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### **25. What is the association between cervical cancer and underlying immune-related and cardiovascular diseases based on Korean National Health Insurance data?**

In this retrospective cohort study of 1,344,628 Korean women (68,275 with cervical cancer) from 2006–2022, significant increased risks were found for cervical cancer with IHD (RR 1.72, 95% CI 1.69–1.76), hematological malignancies (RR 1.87, 95% CI 1.67–2.09), respiratory tuberculosis (RR 1.32, 95% CI 1.27–1.38), chronic rheumatic heart disease (RR 1.53, 95% CI 1.44–1.64), and chronic viral hepatitis (RR 1.33, 95% CI 1.31–1.36), while cerebrovascular disease was linked to reduced risk (RR 0.58, 95% CI 0.57–0.60).



Song H, et al. Ischemic Heart Disease, Hematological Malignancies, and Infectious Diseases as Risk Factors for Cervical Cancer: A Study Based on Korean National Health Insurance Data. *J Clin Med*. 2025 Jun 16;14(12):4282. doi: 10.3390/jcm14124282. PMID: 40566027; PMCID: PMC12194532.

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**26. What is the prevalence and clinical impact of coronary abnormalities detected by invasive coronary function testing (CFT) in patients with prior PCI who have persistent angina but no obstructive CAD?**

In this observational study of 46 post-PCI patients (median age 60, 63% women) with persistent angina, CFT revealed endothelial dysfunction in 36.9%, epicardial spasm in 56.5%, microvascular dysfunction in 43.5%, and myocardial bridging in 63%; 19.6% had fractional flow reserve  $\leq 0.8$ , and patients reported significant symptom improvement one year after CFT-guided management.

Pargaonkar VS, et al. Invasive Coronary Function Testing in Patients With Prior PCI Who Have Persistent ANOCA. *Circ Cardiovasc Interv*. 2025 Jun 25:e015344. doi: 10.1161/CIRCINTERVENTIONS.125.015344. Epub ahead of print. PMID: 40557543.

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**27. Is decreased bone mineral density (BMD) associated with subclinical atherosclerosis in asymptomatic non-diabetic postmenopausal women?**

In this prospective study of 117 postmenopausal women (mean age  $59 \pm 7$  years) in Kosovo, 71% with osteopenia/osteoporosis had higher carotid plaque prevalence (27.7% vs. 8.8%,  $p=0.019$ ); age (OR 1.244,  $p=0.001$ ), osteoporosis (OR 0.197,  $p=0.024$ ), and CAC score  $>10$  HU (OR 0.174,  $p=0.006$ ) were independently linked to carotid plaques.

Ismaili J, et al. Decreased Bone Mineral Density Is Associated with Subclinical Atherosclerosis in Asymptomatic Non-Diabetic Postmenopausal Women. *J Clin Med*. 2025 Jun 6;14(12):4033. doi: 10.3390/jcm14124033. PMID: 40565779; PMCID: PMC12194126.

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**28. Does serum oxidized LDL (oxLDL) level correlate with the number of ischemic events (IEs) and damaged blood vessels (DBVs) in patients with CAD?**

In a cross-sectional study of 51 CAD patients, those with  $\geq 2$  IEs and  $\geq 2$  DBVs had significantly higher serum oxLDL levels (8293.35 ng/mL) compared to patients with one IE and one DBV (6474.26 ng/mL,  $p = 0.029$ ); oxLDL levels positively correlated with the



number of IEs ( $r^2=15.2\%$ ,  $B=0.142$ ,  $p=0.005$ ) and DBVs ( $r^2=19.2\%$ ,  $B=0.196$ ,  $p=0.020$ ).

Perez-Robles M, et al. Serum OxLDL Levels Are Positively Associated with the Number of Ischemic Events and Damaged Blood Vessels in Patients with Coronary Artery Disease. *Healthcare (Basel)*. 2025 Jun 14;13(12):1426. doi: 10.3390/healthcare13121426. PMID: 40565453; PMCID: PMC12193118.

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**29. Does lower socioeconomic status, intelligence, and cognition causally influence the risk of atrial fibrillation (AF), and what mediators explain this relationship?**

In a Mendelian randomization study of 248,847–1,131,881 Europeans (including 111,365 AF cases), each 1-SD increase in education reduced atrial fibrillation risk by 19% (OR 0.81, 95% CI 0.71–0.92,  $p<0.05$ ), independent of intelligence and cognition. Heart failure mediated 95.35% of the effect, with obesity and IHD also contributing.

Kaisaier W, et al. Causal Associations Between Socioeconomic Status, Intelligence, Cognition and Atrial Fibrillation: Evidence From Mendelian Randomization. *JACC Asia*. 2025 Jun 2:S2772-3747(25)00265-0. doi: 10.1016/j.jacasi.2025.04.008. Epub ahead of print. PMID: 40560110.



## Pathophysiology and potential drug targets

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### 30. **How do calcium signaling dynamics in vascular cells contribute to vascular disease, and what are the therapeutic implications of their dysregulation?**

In this mechanistic review, dysregulated calcium signaling in endothelial and vascular smooth muscle cells is linked to hypertension, atherosclerosis, and vascular calcification through impaired nitric oxide production, increased vascular tone (via PKC/ROCK pathways), and VSMC phenotypic switching; emerging therapies targeting Ca<sup>2+</sup> channels and kinases are proposed but lack quantifiable clinical trial validation within this study.

Dai C, et al. Calcium Signaling Dynamics in Vascular Cells and Their Dysregulation in Vascular Disease. *Biomolecules*. 2025 Jun 18;15(6):892. doi: 10.3390/biom15060892. PMID: 40563532; PMCID: PMC12191073.

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### 31. **What are the myocardial expression patterns of desmin, calreticulin, and interleukin-10 in hyperthyroid cats compared to cats with hypertrophic cardiomyopathy (HCM) and healthy controls?**

In this immunohistochemical study (veterinary cardiology; n=38: 16 hyperthyroid cats, 12 HCM cats, 10 controls), desmin and interleukin-10 expression were significantly altered in both hyperthyroid and HCM cats (despite no significant differences in median left ventricular dimensions vs. controls), indicating similar myocardial injury patterns marked by cardiomyocyte degeneration and coronary artery narrowing.

Janus-Ziółkowska I, et al. Molecular Cardiac Changes in Feline Hyperthyroidism and Hypertrophic Cardiomyopathy: Focus on Desmin, Calreticulin, and Interleukin-10 Expression. *Animals (Basel)*. 2025 Jun 10;15(12):1719. doi: 10.3390/ani15121719. PMID: 40564271; PMCID: PMC12189078.

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### 32. **Can molecular hydrogen regulate cellular pyroptosis across various disease models, and what are its underlying mechanisms and therapeutic implications?**

This mechanistic review analyzed multiple preclinical studies involving diverse disease models (e.g., cardiac ischemia-reperfusion, neuroinflammation, metabolic disorders, cancer),



showing that hydrogen modulates pyroptosis via redox modification of gasdermins, mitochondrial pathways, and inflammasome disruption, with cytoprotective effects in healthy tissues and pro-pyroptotic effects in malignancies.

Ye Y, et al. Molecular hydrogen as a novel regulator of cellular pyroptosis: mechanistic insights and therapeutic implications. *Mol Biol Rep.* 2025 Jun 26;52(1):637. doi:10.1007/s11033-025-10757-z. PMID: 40569354.

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**33. Does irisin play a protective role in pulmonary arterial hypertension (PAH) by affecting pulmonary vascular remodeling and what is the underlying mechanism?**

In a study involving PAH patients and mouse models, irisin levels were significantly decreased; irisin overexpression or injection improved right-heart function and reduced pulmonary artery smooth muscle cell proliferation by promoting ubiquitin-mediated degradation of Enolase 1, highlighting irisin's potential as a therapeutic target in PAH.

Sun N, et al. Irisin Attenuates Pulmonary Vascular Remodeling in Pulmonary Arterial Hypertension via Ubiquitin-Mediated Regulation of ENO1. *Adv Sci (Weinh).* 2025 Jun 25:e00096. doi:10.1002/advs.202500096. Epub ahead of print. PMID: 40560058.

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**34. How does Artesunate (ART) affect myocardial ischemia-reperfusion (MI/R) injury and what is the underlying molecular mechanism involved?**

In this experimental study using in vivo mouse models and in vitro cardiomyocytes, Artesunate significantly reduced MI/R-induced myocardial injury and apoptosis, decreased ROS, MDA, CK, and LDH levels, and inhibited KDM5A expression; silencing KDM5A upregulated miR-495-3p and downregulated FOXO1, thereby alleviating cardiomyocyte injury, demonstrating ART's protective effect via the KDM5A/miR-495-3p/FOXO1 pathway.

Liu Y, et al. Artesunate Inhibits Myocardial Ischemia Reperfusion Injury via Downregulation of Lysine Specific Demethylase 5A. *Chem Biol Drug Des.* 2025 Jun;105(6):e70106. doi:10.1111/cbdd.70106. PMID: 40556480.

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**35. How do on-pump and off-pump coronary artery bypass surgery techniques affect interleukin-18 levels and**



### **biomarkers of endothelial glycocalyx degradation during and after surgery?**

In a surgical study measuring IL-18, syndecan-1, hyaluronic acid, CRP, cTnT, and leukocytes via ELISA in revascularized patients, IL-18, CRP, cTnT, and leukocytes significantly increased at 24 and 72 hours post-surgery, with higher levels in on-pump patients; syndecan-1 and hyaluronic acid rose only in on-pump cases, showing significant inflammation and endothelial damage linked to IL-18.

Knežević D, et al. The Effect of Coronary Artery Bypass Surgery on Interleukin-18 Concentration and Biomarkers Related to Vascular Endothelial Glycocalyx Degradation. *Int J Mol Sci.* 2025 Jun 6;26(12):5453. doi: 10.3390/ijms26125453. PMID: 40564918; PMCID: PMC12193331.

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### **36. How does exogenous ubiquitin (eUB) affect the phenotype and function of M1 and M2 macrophages in the context of inflammation modulation?**

In an in vitro study using peritoneal macrophages treated with eUB, eUB reduced TNF- $\alpha$  secretion in M1 and both TNF- $\alpha$  and IL-10 in M2 macrophages, altered cytoskeletal morphology, increased M1 migration but decreased M2 migration and efferocytosis, modulated STAT and FAK phosphorylation differently in M1 (decreased STAT1/FAK) versus M2 (increased STAT6/FAK).

Shook PL, et al. Exogenous Ubiquitin Differentially Modulates the Phenotype and Function of M1 and M2 Macrophages. *Cells.* 2025 Jun 11;14(12):879. doi: 10.3390/cells14120879. PMID: 40558506; PMCID: PMC12190236.

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### **37. Can an NTR-sensitive fluorescent hydrogen sulfide (H<sub>2</sub>S) donor improve cardiac recovery in myocardial ischemia-reperfusion injury (MIRI)?**

In a rat MIRI model, the novel NTR-responsive H<sub>2</sub>S donor HSD-NTR-B significantly enhanced cardiac structure and function recovery by inhibiting cardiomyocyte apoptosis and modulating macrophage polarization (reducing M1, increasing M2), demonstrating its therapeutic potential for MIRI treatment.

Zhang N, et al. Design and Synthesis of a NTR-Sensitive Fluorescent H<sub>2</sub>S Donor as a Potential Therapeutic Agent for Myocardial Ischemia-Reperfusion Injury. *J Med Chem.* 2025 Jun 25. doi: 10.1021/acs.jmedchem.5c01169. Epub ahead of print. PMID: 40557820.



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**38. Does Yangxinshi tablet (YXST) protect against myocardial injury and enhance skeletal muscle exercise capacity, and what are the underlying molecular mechanisms?**

In an experimental study with mice (6 groups, n=8-20 per group), YXST treatment (250-1000 mg/kg/day) improved cardiac function and exercise tolerance post-myocardial ischemia-reperfusion, enhanced slow type I muscle fibers, mitochondrial biogenesis, and reduced inflammation. YXST also promoted skeletal muscle satellite cell proliferation and myoblast differentiation by regulating mitochondrial bioenergetics, with molecular docking showing binding to BACH1 protein.

Song H, et al. Yangxinshi tablet protects against myocardial injury and increases skeletal muscle exercise capacity by regulating mitochondrial bioenergetics. *Phytomedicine*. 2025 Jun 17;145:156990. doi: 10.1016/j.phymed.2025.156990. Epub ahead of print. PMID: 40561862.

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**39. What roles do infectious agents, genetic interactions, and autoimmunity play in the pathogenesis of dilated cardiomyopathy (DCM), and what are the emerging therapeutic approaches?**

This comprehensive review synthesizes current evidence on infection-related DCM pathogenesis, highlighting multifactorial mechanisms involving infectious triggers, genetic predisposition, and autoimmune activation; it emphasizes the need for integrated genomics, metagenomics, and immunological profiling to develop personalized therapies for this heterogeneous myocardial disorder.

Zhang J, et al. Infectious agents in dilated cardiomyopathy: Genetic interactions, autoimmunity, mechanisms, and therapeutic approaches. *Autoimmun Rev*. 2025 Jun 23;24(9):103860. doi: 10.1016/j.autrev.2025.103860. Epub ahead of print. PMID: 40562294.

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**40. What are the pathophysiological mechanisms of coronary microvascular dysfunction (CMD) and how are recent diagnostic techniques improving its detection?**

This narrative review in interventional cardiology synthesizes current knowledge on CMD's complex pathophysiology and highlights emerging diagnostic tools such as advanced imaging and functional testing, which improve identification of CMD in



patients addressing the gap in diagnosing patients with ischemic symptoms but no visible epicardial CAD.

Mincione G, et al. Coronary microvascular dysfunction: Focus on pathophysiological mechanisms and recent diagnostic techniques. *Cardiovasc Revasc Med*. 2025 Jul;76:25-29. doi: 10.1016/j.carrev.2025.06.015. Epub 2025 Jun 16. PMID: 40562608.

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**41. Does allergic inflammation contribute to the development and progression of atherosclerosis, and what are the clinical implications of this interaction in cardiovascular disease?**

This literature review of epidemiological and preclinical studies from 2014–2024 highlights interconnected mechanisms—such as eosinophil activation, Th2 cytokines (IL-4, IL-5, IL-13), and mast cell degranulation—that link allergic diseases (asthma, atopic dermatitis, allergic rhinitis, food allergy) to increased cardiovascular morbidity.

Valcovici M, et al. The Junction of Allergic Inflammation and Atherosclerosis: Pathways and Clinical Implications-A Review. *Life (Basel)*. 2025 Jun 16;15(6):964. doi: 10.3390/life15060964. PMID: 40566616; PMCID: PMC12194581.

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**42. Does CD11b inhibition reduce neutrophil and monocyte infiltration and improve cardiac outcomes in myocardial ischemia/reperfusion (I/R) injury?**

In this preclinical and translational study, anti-CD11b antibody treatment in wild-type mice before ischemia/reperfusion significantly improved cardiac function and reduced infarct size, myocyte apoptosis, fibrosis, and infiltration of CD45<sup>+</sup>CD11b<sup>+</sup>, CD15<sup>+</sup>CD11b<sup>+</sup>, and CD14<sup>+</sup>CD11b<sup>+</sup> cells, with suppression of Bax, caspase-3, NF-κB, and TGF-β/Smad2/3 pathways; similarly, MI patients had elevated CD11b<sup>+</sup> immune cells and inflammatory markers compared to controls.

Fu P, et al. CD11b Blockade Ameliorates Myocardial Ischemia/Reperfusion Injury by Reducing Neutrophil and Monocyte Infiltration. *J Am Heart Assoc*. 2025 Jul;14(13):e038142. doi: 10.1161/JAHA.124.038142. Epub 2025 Jun 27. PMID: 40576028.

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**43. Does Theaflavin-3,3'-digallate (TF3) protect against myocardial ischemia/reperfusion (I/R) and hypoxia/reoxygenation (H/R) injury?**



In a rat model of I/R injury (n not specified) and H9C2 cardiomyocyte H/R model, TF3 significantly reduced infarct size, serum CK-MB, cTnT, and LDH levels, and suppressed apoptosis and autophagy markers ( $\downarrow$ Bax, cleaved caspase-3, Beclin-1, LC3B;  $\uparrow$ Bcl-2, p62), while activation of PI3K/Akt/mTOR was confirmed via Western blot; PI3K inhibition reversed TF3's protective effects, confirming pathway involvement.

Wang S, et al. Theaflavin-3,3'-digallate protects against myocardial ischemia/reperfusion injury and hypoxia/reoxygenation injury by activating the PI3K/Akt/mTOR pathway. *J Mol Histol*. 2025 Jun 27;56(4):207. doi: 10.1007/s10735-025-10453-z. PMID: 40576913.

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**44. What are the pharmacological mechanisms by which *Acorus tatarinowii* and its bioactive compounds contribute to the treatment of cardiovascular diseases (CVDs)?**

This comprehensive review of preclinical studies found that *A. tatarinowii* exerts anti-inflammatory, antioxidant, anti-apoptotic, hypolipidemic, and hypoglycemic effects beneficial in managing CVDs (e.g., hypertension, CAD, heart failure).

Qiu Y, et al. Therapeutic mechanisms of *Acorus tatarinowii* and its bioactive compounds in cardiovascular diseases: A comprehensive review. *Phytomedicine*. 2025 Jun 16;145:156988. doi: 10.1016/j.phymed.2025.156988. Epub ahead of print. PMID: 40578036.

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**45. Can narrowed sinus rhythm electrograms and uniform slow conduction zones accurately identify the location, shape, and orientation of the ventricular tachycardia (VT) isthmus?**

In 31 postinfarction canine models, predicted VT isthmus location based on sinus rhythm mapping overlapped actual location by  $57.9 \pm 23.6\%$ , with centroid differences of  $7.60 \pm 6.29$  mm and exit angle divergence of  $18.0 \pm 9.5^\circ$ ; electrograms at the VT isthmus were significantly narrower ( $p < 0.02$ ) compared to the periphery.

Ciaccio EJ, et al. Narrowed sinus rhythm electrograms in the zone of uniform slow conduction are helpful to identify VT isthmus location, shape, and orientation. *Heart Rhythm*. 2025 Jun 25:S1547-5271(25)02611-6. doi: 10.1016/j.hrthm.2025.06.032. Epub ahead of print. PMID: 40578654.

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**46. Does *Lactobacillus plantarum* CCFM639 alleviate vascular dysfunction in a Kawasaki disease (KD) mouse model through the eNOS/NO pathway?**



In this experimental study using a KD mouse model, CCFM639 significantly reduced splenomegaly, inflammatory cytokines, and coronary artery macrophage infiltration; improved intestinal barrier function ( $\downarrow$ serum LPS), endothelial cell proliferation (CCK-8), migration (scratch assay), and angiogenesis (tube formation); and upregulated eNOS expression—effects reversed by an eNOS inhibitor.

Yu F, et al. *Lactobacillus plantarum* CCFM639 ameliorates vascular dysfunction in mice with Kawasaki disease involving eNOS/NO pathway. *Eur J Pharmacol.* 2025 Jun 25;1003:177877. doi: 10.1016/j.ejphar.2025.177877. Epub ahead of print. PMID: 40578744.

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#### **47. Do human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CM) exhibit intrinsic sex dimorphism in the absence of exogenous hormones?**

In this in vitro study using hiPSC-CM derived from 6 adult cardiac fibroblast lines (3 male, 3 female), female-derived cardiomyocytes showed enhanced calcium handling, over 300 differentially expressed genes, and significantly increased sodium current amplitude and window current (SCN3B expression validated by patch-clamp), indicating sex-specific functional and molecular differences.

Givens SE, et al. Healthy human induced pluripotent stem cell-derived cardiomyocytes exhibit sex dimorphism even without the addition of hormones. *Stem Cells.* 2025 Jun 20:sxaf038. doi: 10.1093/stmcls/sxaf038. Epub ahead of print. PMID: 40578843.

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#### **48. Can engineered M2 macrophages carrying surface-modified nanomedicines (PS-c@M) effectively mitigate myocardial ischemia-reperfusion injury (MIRI) by remodeling the immune-metabolic microenvironment?**

In a preclinical murine model of MIRI, PS-c@M therapy significantly suppressed STING signaling, increased reparative immune cell populations (M2 macrophages, Tregs), reduced M1 macrophage and neutrophil infiltration, enhanced mitochondrial oxidative phosphorylation, and decreased oxidative damage, demonstrating long-term cardioprotective effects.

Cheng J, et al. Homotransplantation of Engineered Macrophages with Surface-Modified Nanomedicines for Mitigating Myocardial Ischemia-Reperfusion Injury. *ACS Nano.* 2025 Jul 15;19(27):25069-25087. doi: 10.1021/acsnano.5c05068. Epub 2025 Jun 27. PMID: 40579350.



## Diagnosis and monitoring

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### 49. What are the recent technological advancements in the detection of cardiac troponin I (cTnI) for diagnosing AMI?

This narrative review (cardiology/biomedical engineering; qualitative synthesis) classifies and evaluates cTnI detection methods across optical, electrochemical, and AI-integrated platforms, highlighting detection limits as low as 0.01 ng/mL and response times under 10 minutes in some sensor systems.

Zhang N, et al. Recent Advances in Monitoring Technologies for Cardiac Troponin I: A Pivotal Biomarker in Cardiovascular Diseases. *Biomolecules*. 2025 Jun 12;15(6):858. doi: 10.3390/biom15060858. PMID: 40563498; PMCID: PMC12191026.

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### 50. Can coronary vascular anatomical features of the left anterior descending (LAD) artery, analyzed via statistical shape modelling, predict future MI risk?

In a study of 69 LAD artery geometries analyzed via 3D QCA and statistical shape modeling (PCA + LDA), a significant model ( $p < 0.0001$ ) distinguished future culprit lesions from non-culprit ones. Combining shape features with % atherosclerotic stenosis (%AS) effectively predicted 5-year MI risk, highlighting total atherosclerotic burden as a key factor.

Griffo B, et al. Exploring the association between coronary vascular anatomical features and future myocardial infarction through statistical shape modelling. *J Biomech*. 2025 Aug;189:112829. doi: 10.1016/j.jbiomech.2025.112829. Epub 2025 Jun 19. PMID: 40561693.

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### 51. Does red blood cell (RBC), white blood cell (WBC), and platelet (PLT) counts differentiate cardiovascular patients with and without a history of first-time MI?

In a cohort study of 743 adults hospitalized with cardiovascular disease, patients with MI showed significantly decreased RBC and elevated WBC counts—especially within the 2nd and 3rd quartiles—while PLT counts showed no significant difference; bootstrap resampling validated these non-linear associations and enhanced result robustness.

Kostanek J, et al. Red Blood Cell, White Blood Cell, and Platelet Counts as Differentiating Factors in Cardiovascular Patients with and Without Current Myocardial Infarction. *Int J Mol Sci*. 2025 Jun 15;26(12):5736. doi: 10.3390/ijms26125736. PMID: 40565201; PMCID: PMC12192950.



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**52. What is the prognostic value of plasma Matrix Metalloproteinase 9 (MMP9) levels in male patients following off-pump CABG for IHD?**

In this prospective observational study of 200 male patients, plasma MMP9 levels significantly decreased 48 hours post-surgery ( $p < 0.0001$ ), and higher MMP9 levels at 1-year follow-up were significantly associated with lower left ventricular ejection fraction (LVEF).

Popov M, et al. Prognostic Value of Matrix Metalloproteinase 9 (MMP9) in Patients Following Off-Pump Coronary Artery Bypass Grafting. *Life (Basel)*. 2025 Jun 4;15(6):908. doi: 10.3390/life15060908. PMID: 40566560; PMCID: PMC12194191.

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**53. Does pericoronary adipose tissue (PCAT) CT attenuation in Kawasaki disease (KD) patients associate with coronary artery aneurysms (CAA), myocardial perfusion, and future coronary events (CEs)?**

In this retrospective coronary imaging study of 100 KD patients (mean age 7.5 years) and 35 controls, PCAT CT attenuation was significantly higher in CAA patients (-67.1 HU) compared to non-CAA (-75.0 HU) and controls (-77.0 HU) ( $P < .001$ ); it was negatively correlated with myocardial perfusion ( $r = -0.50$ ;  $P = .02$ ), and independently predicted CEs (OR 1.20; 95% CI: 1.00–1.30;  $P = .007$ ) during a median 19.7-month follow-up.

Azhe S, et al. Pericoronary Adipose Tissue CT Attenuation in Kawasaki Disease and Association with Coronary Artery Aneurysms, Myocardial Perfusion, and Coronary Events. *Radiol Cardiothorac Imaging*. 2025 Jun;7(3):e240303. doi: 10.1148/ryct.240303. PMID: 40569153.

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**54. Are circulating levels of matrix metalloproteinases 7 and 10 (MMP-7, MMP-10) predictive of 2-year major adverse cardiovascular events (MACE) in patients with peripheral artery disease (PAD)?**

In this prospective cohort study (vascular medicine;  $n = 465$  PAD patients; 24-month follow-up), MMP-10 and MMP-7 levels were significantly higher in patients who developed MACE (MMP-10: 710.6 vs. 672.4 pg/mL,  $p = 0.032$ ; MMP-7: 5.20 vs. 4.76 pg/mL,  $p = 0.048$ ), with both independently associated with MACE (MMP-10: HR 1.32, 95% CI 1.16–1.51; MMP-7: HR 1.17, 95% CI 1.05–2.68); MMP-10



was predictive in diabetics (HR 1.18,  $p = 0.019$ ) and MMP-7 in females (HR 1.31,  $p = 0.009$ ).

Li B, et al. Matrix Metalloproteinases 7 and 10 Are Prognostic Biomarkers for Systemic Cardiovascular Risk in Individuals with Peripheral Artery Disease. *Biomolecules*. 2025 Jun 11;15(6):853. doi: 10.3390/biom15060853. PMID: 40563493; PMCID: PMC12190543.

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**55. Does the pre-procedural aggregate index of systemic inflammation (AISI) predict the development of contrast-induced acute kidney injury (CI-AKI) in patients undergoing coronary angiography or intervention?**

In this retrospective cohort study of 166 patients with suspected chronic CAD, CI-AKI occurred in 15.1% of patients; AISI showed the strongest independent association with CI-AKI (OR=4.81, 95% CI [2.42–9.60]), outperforming NLR (OR=1.32, 95% CI [1.16–1.52]) and SII (OR=3.41, 95% CI [1.92–6.08]).

Unkun T, et al. The predictive value of the aggregate index of systemic inflammation for contrast-induced acute kidney injury in patients undergoing coronary angiography. *Acta Cardiol*. 2025 Jun 26;1-9. doi: 10.1080/00015385.2025.2524237. Epub ahead of print. PMID: 40569788.

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**56. Does angiography-based quantification of coronary blood flow (CBF) after PCI predict major adverse cardiovascular events (MACE) in acute coronary syndrome (ACS) patients?**

In this prospective, multicenter, nested case-control study of 162 ACS patients, lower post-PCI CBF (<54.3 mL/min) was significantly associated with higher MACE risk at 1-year follow-up (HR: 2.11, 95% CI: 1.35–3.28,  $P=0.001$ ), with CBF lowest in STEMI patients ( $P=0.046$ ).

Sakai K, et al. Angiography-Based Blood Flow Quantification After Revascularization in Acute Coronary Syndromes. *J Am Heart Assoc*. 2025 Jul;14(13):e038770. doi: 10.1161/JAHA.124.038770. Epub 2025 Jun 27. PMID: 40576041.

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**57. Can artificial intelligence (AI) enhance the diagnostic accuracy, risk stratification, and workflow efficiency of coronary CT angiography (CCTA) in detecting and managing atherosclerosis?**

In this review of AI applications in CCTA, AI improved stenosis detection by 27%, inter-reader agreement by 30%, and reduced reporting time by 40%; integration with multimodal imaging



increased ischemia detection by 28% and lesion classification accuracy by 35%.

Irannejad K, et al. Artificial intelligence in coronary CT angiography: transforming the diagnosis and risk stratification of atherosclerosis. *Int J Cardiovasc Imaging*. 2025 Jun 27. doi: 10.1007/s10554-025-03440-8. Epub ahead of print. PMID: 40576859.

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**58. Does serum leucine-rich  $\alpha$ -2 glycoprotein 1 (LRG1) predict 10-year all-cause mortality, vascular mortality, and major adverse cardiovascular events (MACE) in patients undergoing coronary angiography?**

In this 10-year prospective observational study of 695 coronary angiography patients, higher LRG1 levels independently predicted all-cause mortality (HR = 2.39, 95% CI: 1.58–3.62;  $p < 0.001$ ), vascular mortality (HR = 2.05, 95% CI: 1.08–3.92;  $p = 0.029$ ), and MACE (HR = 1.80, 95% CI: 1.19–2.75;  $p = 0.006$ ).

Muendlein A, et al. Serum leucine-rich  $\alpha$ -2 glycoprotein 1 predicts 10-year mortality and vascular events in coronary angiography patients. *Atherosclerosis*. 2025 Aug;407:120413. doi: 10.1016/j.atherosclerosis.2025.120413. Epub 2025 Jun 20. PMID: 40577971.

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**59. Can multimodality imaging accurately identify the underlying cause of MI in patients with nonobstructive coronary arteries (MINOCA), particularly in the presence of coronary anomalies?**

In this single-patient case study involving a 60-year-old male with MINOCA, multimodal imaging—including SPECT, CCTA, and cardiac MRI—revealed an anomalous septal artery with interarterial course and confirmed mid-septal infarction.

Gueli IA, et al. Multimodality Imaging in a Patient With MINOCA and Anomalous Coronary Artery. *JACC Case Rep*. 2025 Jun 25;30(16):104198. doi: 10.1016/j.jaccas.2025.104198. PMID: 40579100.

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**60. Does video-assisted informed consent improve patient understanding and reduce anxiety during cardiac CT examinations?**

This randomized controlled trial of 205 cardiac CT patients found that both video formats significantly improved patient satisfaction and understanding compared to standard consent ( $p < 0.05$ ), with Video II showing higher satisfaction and perceived importance of the consent form ( $p = 0.02$ ); anxiety levels were



unchanged overall but higher in women ( $p=0.008$ ) and those with suspected CAD ( $p=0.04$ ).

Gohmann RF, et al. Video-assisted informed consent in cardiac imaging: influence on patient experience during CT-the randomized controlled VAICICI Trial. *Eur Radiol.* 2025 Jun 27. doi: 10.1007/s00330-025-11741-8. Epub ahead of print. PMID: 40579557.

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**61. How can multimodality imaging aid in the evaluation and management of anomalous aortic origin of coronary arteries (AAOCA) ?**

In this case series of 4 elite athletes with AAOCA, multimodality imaging enabled personalized treatment by identifying high-risk features such as inducible ischemia and myocardial fibrosis, supporting tailored decisions in line with ESC guidelines for adult congenital heart disease.

Daems JJN, et al. Multimodality Imaging in Anomalous Aortic Origin of the Coronary Arteries: Lessons From 4 Athlete Cases. *JACC Case Rep.* 2025 Jun 25;30(16):104250. doi: 10.1016/j.jaccas.2025.104250. PMID: 40579103.

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**62. Can a mobile papillary fibroelastoma (PFE) cause severe chest pain by obstructing the left main coronary artery (LMCA)?**

In this rare case study of a 63-year-old woman, cardiac CT angiography revealed a mobile PFE within the left coronary cusp intermittently occluding the LMCA during systole and early diastole, with symptom resolution after surgical removal, highlighting the diagnostic utility of CCTA in non-atherosclerotic angina.

Ramirez AY, et al. Mobile Papillary Fibroelastoma Leading to Severe Chest Pain via Left Main Occlusion. *JACC Case Rep.* 2025 Jun 25;30(16):103535. doi: 10.1016/j.jaccas.2025.103535. PMID: 40579101.

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**63. Does multimodal imaging effectively guide clinical decision-making in patients with intraseptal left anomalous aortic origin of a coronary artery (L-AAOCA)?**

In this case study of a 27-year-old woman with a 2.7 cm intraseptal course of the left main coronary artery, multimodal imaging including stress cardiac MRI and catheterization identified inducible ischemia, guiding successful surgical



intervention (transcatheter aortic valve replacement) with uneventful recovery and symptom resolution.

Burns J, et al. Multimodal Imaging Directs Decision Making in Intraseptal L-AAOCA. JACC Case Rep. 2025 Jun 25;30(16):104014. doi: 10.1016/j.jaccas.2025.104014. PMID: 40579080.

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**64. Does an anomalous origin of the left circumflex artery from the right pulmonary artery (AoLCx-RPA) cause myocardial ischemia through coronary steal, as revealed by multimodal imaging?**

In this single-patient case study of a 43-year-old male presenting with exertional dyspnea and elevated troponin, multimodal imaging (CTA, CMR, PET) confirmed AoLCx-RPA with evidence of ischemia via retrograde collateral flow from the right coronary artery, supporting coronary steal physiology and necessitating surgical correction.

Pathangey G, et al. Anomalous Left Circumflex Origin From Right Pulmonary Artery: Concern for Coronary Steal Revealed by Multimodal Imaging. JACC Case Rep. 2025 Jun 25;30(16):104204. doi: 10.1016/j.jaccas.2025.104204. PMID: 40579078.

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**65. Does the inclusion of non-perfusion parameters in CZT-SPECT myocardial perfusion imaging improve prognostic risk stratification in individuals with normal perfusion?**

In this large-scale retrospective cohort study of 1,570 patients with normal thallium-201 SPECT perfusion, 5.1% experienced major adverse cardiovascular events (MACEs) over a mean follow-up of  $22.5 \pm 10.8$  months; key predictors were worsening post-stress ejection fraction (HR: 1.971,  $p = 0.008$ ) and elevated lung-to-heart ratio (HR: 2.207,  $p = 0.001$ ), with strongest risk seen when both were present ( $p < 0.001$ ).

Lin CY, et al. Prognostic significance of non-perfusion parameters of cadmium-zinc-telluride single-photon emission computed tomography myocardial perfusion imaging for individuals with normal myocardial perfusion: a large-scale single-center retrospective cohort study. Ann Nucl Med. 2025 Jun 27. doi: 10.1007/s12149-025-02077-w. Epub ahead of print. PMID: 40576735.

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**66. Does the combined use of computed tomography (CT) perfusion imaging and blood pressure levels improve the prediction of prognosis in patients with acute ischemic stroke?**



In this retrospective study of 237 acute ischemic stroke patients, multivariate analysis showed that prognosis was significantly associated with diastolic blood pressure ( $P < 0.05$ ), cerebral blood flow  $< 30\%$  ( $P < 0.05$ ), and mismatch ratio ( $P < 0.05$ ); combined use of these markers yielded the highest predictive value with AUC 0.711, sensitivity 57.4%, and specificity 92.1%.

Qi Y, et al. Predictive value of the combined use of computed tomography perfusion imaging and blood pressure levels for the prognosis of patients with acute ischemic stroke. *J Int Med Res.* 2025 Jun;53(6):3000605251349927. doi: 10.1177/03000605251349927. Epub 2025 Jun 27. PMID: 40576064; PMCID: PMC12205207.

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**67. Does subclinical liver fibrosis, measured by the FIB-4 score, predict mortality in patients with CAD?**

In this post hoc analysis of the ISCHEMIA trial ( $n=3735$ ), higher baseline FIB-4 scores were significantly associated with increased all-cause death (HR 1.19, 95% CI 1.07–1.32,  $P=0.001$ ) and cardiovascular death (HR 1.19, 95% CI 1.04–1.36,  $P=0.011$ ), independent of treatment modality (PCI, CABG, or medical therapy).

Caldonazo T, et al. Association of Subclinical Liver Fibrosis With Death in Patients With Coronary Artery Disease: A Post Hoc Analysis of the ISCHEMIA Trial. *J Am Heart Assoc.* 2025 Jul;14(13):e040848. doi: 10.1161/JAHA.124.040848. Epub 2025 Jun 27. PMID: 40576034.

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**68. Does adiponectin serve as a reliable long-term prognostic marker for all-cause mortality and major adverse cardiovascular events (MACE) in patients with stable CAD?**

In this meta-analysis of 5 prospective studies with 3225 patients (median follow-up: 3.8 years), higher adiponectin levels were significantly associated with increased all-cause mortality (adjusted OR: 2.51, 95% CI: 1.36–4.62,  $I^2 = 65.51\%$ ,  $P = 0.03$ ) and modestly linked to MACE (adjusted OR: 1.04, 95% CI: 1.02–1.06,  $I^2 = 0\%$ ,  $P = 0.68$ ).

Jitta SR, et al. Long-term prognostic role of adiponectin in stable coronary artery disease: A meta-analysis of prospective studies. *World J Cardiol.* 2025 Jun 26;17(6):105452. doi: 10.4330/wjc.v17.i6.105452. PMID: 40575429; PMCID: PMC12186166.



**69. Can Tissue Doppler Imaging (TDI) enhance diagnostic precision and prognostic evaluation in acute and critical care settings?**

This narrative review analyzed TDI applications across various acute conditions, showing its diagnostic value in acute coronary syndromes, heart failure, pulmonary embolism, hypertensive crises, atrial fibrillation risk stratification, and mechanical ventilation weaning, where elevated E/E' ratios predicted weaning failure.

Sisto UG, et al. Tissue Doppler Imaging in Acute and Critical Care: Enhancing Diagnostic Precision. *Medicina (Kaunas)*. 2025 Jun 6;61(6):1051. doi: 10.3390/medicina61061051. PMID: 40572739; PMCID: PMC12195611.

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**70. Can coronary computed tomography angiography (CCTA) with FFR(CT)-based virtual PCI planning effectively guide pre-procedural decisions and correlate with invasive FFR measurements?**

In this observational cohort study of 52 patients (mean age  $70 \pm 9$  years) undergoing 59 CCTA-guided PCIs, the approach achieved 100% technical success with strong correlation between pre/post-PCI invasive FFR and FFR(CT) ( $R = 0.74$ ;  $p < 0.001$ ); median baseline FFR(CT) was 0.70 and post-PCI invasive FFR was 0.92.

Carvalho PEP, et al. Coronary Computed Tomography Angiography for Percutaneous Coronary Intervention: Initial United States Experience With FFR<sub>CT</sub> Based Virtual PCI. *Catheter Cardiovasc Interv*. 2025 Jun 26. doi:10.1002/ccd.31720. Epub ahead of print. PMID: 40571959.

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**71. Does nodular calcification (NC) detected on pre-PCI non-contrast CT predict adverse clinical outcomes in patients with severely calcified coronary lesions?**

In this retrospective study of 267 chronic coronary syndrome patients, napkin-ring sign (NC) was present in 58 patients and independently predicted MACCE (HR 5.25,  $P < 0.001$ ), significantly reducing MACCE-free survival ( $P < 0.001$ ); other predictors included hemodialysis (HR 3.00,  $P = 0.003$ ) and peripheral artery disease (HR 2.65,  $P = 0.01$ ).

Iwane S, et al. Prognostic Utility of Nodular Calcification Detected on Non-Contrast Computed Tomography in Severely Calcified Coronary Lesions. *Circ J*. 2025 Jun 24. doi:10.1253/circj.CJ-24-0644. Epub ahead of print. PMID: 40571597.



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**72. Does the effectiveness of the GRACE Risk Score (GRS) in improving outcomes and adherence to guideline-recommended care differ by troponin elevation status in patients with suspected non-ST elevation acute coronary syndrome (NSTEMI)?**

In this post hoc UKGRIS trial analysis (n=3050; 2602 troponin-positive), guideline-based risk score (GRS) use increased uptake of recommended care in troponin-positive patients (OR 1.52, 95% CI 1.16–2.00,  $p < 0.01$ ) but did not significantly reduce 24-month cardiovascular events in troponin-positive (HR 0.89, 95% CI 0.70–1.14) or troponin-negative patients (HR 1.14, 95% CI 0.79–1.64; interaction  $p = 0.14$ ).

Gale CP, et al. Effectiveness of the GRACE risk score according to troponin elevation in patients admitted with non-ST elevation acute coronary syndrome: a post hoc analysis of the UKGRIS parallel group cluster randomised controlled trial. *Open Heart*. 2025 Jun 26;12(1):e003213. doi: 10.1136/openhrt-2025-003213. PMID: 40571489; PMCID: PMC12207166.

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**73. How effective is the SADiff model, combining spatial attention and diffusion techniques, for accurate coronary artery segmentation in CT angiography to improve diagnosis of CAD?**

In a study using the public ImageCAS dataset (sample size not specified), SADiff achieved a Dice score of 83.48% and a Hausdorff distance of 19.43 mm, outperforming U-Net3D by 6.57% in Dice score; cross-dataset validation on a private ImageLaPP dataset showed a Dice score of 79.42%.

Xu R, et al. SADiff: Coronary Artery Segmentation in CT Angiography Using Spatial Attention and Diffusion Model. *J Imaging*. 2025 Jun 11;11(6):192. doi: 10.3390/jimaging11060192. PMID: 40558791; PMCID: PMC12194381.

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**74. What is the clinical yield of baseline cardiac imaging in breast cancer patients receiving potentially cardiotoxic therapy in Northwestern Ontario?**

In this retrospective cohort study (n = 93), cardiac imaging led to clinically actionable changes in 13.33% of anthracycline-only patients (cohort B, n = 60), compared to 7.14% in trastuzumab-only (cohort A, n = 3) and 4.17% in combination therapy (cohort C, n = 30); diabetes and CAD were key predictors of higher yield.



Shortreed H, et al. Evaluating the Necessity and Impact of Cardiac Imaging on Breast Cancer Care in Northwestern Ontario. *Cancers (Basel)*. 2025 Jun 8;17(12):1909. doi: 10.3390/cancers17121909. PMID: 40563560; PMCID: PMC12191271.

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**75. What is the relationship between the HEART score and the severity of CAD assessed by the SYNTAX score in patients with NSTEMI?**

In this cross-sectional study of 222 NSTEMI patients from Turkey, a higher HEART score was strongly correlated with increased CAD severity (SYNTAX score) ( $P < 0.001$ ,  $R^2 = 0.672$ ); a HEART score  $>7.5$  predicted high SYNTAX scores with 82.1% sensitivity and 84.3% specificity (AUC = 0.892), and was independently associated with high SYNTAX scores (OR: 3.09, 95% CI: 2.06-4.63,  $P < 0.001$ ).

Pepele MS, et al. A Cross-Sectional Study on the Relationship between the HEART Score and the Severity of CAD using the SYNTAX Score in Patients with NSTEMI Admitted to the Emergency Department: A Study from Turkey. *Niger J Clin Pract*. 2025 Jun 1;28(6):758-763. doi: 10.4103/njcp.njcp\_417\_24. Epub 2025 Jun 25. PMID: 40556090.

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**76. Does the plasma level of angiogenesis-related proteins, specifically hepatocyte growth factor (HGF) and angiopoietin-2, predict 2-year major adverse cardiovascular events (MACE) risk in patients with peripheral artery disease (PAD)?**

In a prospective cohort study of 250 PAD patients (mean age 69, 32% female), 48 (19.8%) experienced MACE over two years; elevated HGF (390.83 vs. 300.55 pg/mL,  $p < 0.001$ ) and angiopoietin-2 (23.67 vs. 19.36 pg/mL,  $p = 0.020$ ) were independently associated with increased MACE risk (HGF adjusted HR 1.37, 95% CI 1.14-1.64,  $p = 0.001$ ; angiopoietin-2 adjusted HR 1.27, 95% CI 1.04-1.55,  $p = 0.016$ ).

Li B, et al. Association of Hepatocyte Growth Factor and Angiopoietin-2 with Systemic Cardiovascular Risk in Patients with Peripheral Artery Disease. *J Clin Med*. 2025 Jun 6;14(12):4031. doi: 10.3390/jcm14124031. PMID: 40565778; PMCID: PMC12194176.

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**77. Can a multi-domain feature fusion convolutional neural network (MFF-CNN) improve MI detection and localization accuracy compared to single-domain methods?**



In a study using ECG data with inter-patient validation (sample size not specified), the MFF-CNN achieved 99.98% detection accuracy and 84.86% localization accuracy for MI, showing a 3.43% absolute increase in detection and a 16.97% improvement in localization over previous state-of-the-art methods.

Chen Y, et al. A Multi-Domain Feature Fusion CNN for Myocardial Infarction Detection and Localization. *Biosensors (Basel)*. 2025 Jun 17;15(6):392. doi: 10.3390/bios15060392. PMID: 40558474; PMCID: PMC12191298.

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**78. Can generative adversarial networks (GANs) improve heart sound abnormality detection by augmenting limited and imbalanced heart sound datasets?**

In a machine learning study using the PhysioNet/CinC 2016 heart sound dataset, GAN-augmented synthetic CAD audio segments (evaluated by Fréchet Audio Distance scores of 1.43 vs. CAD and 2.23 vs. healthy samples) enhanced classification performance across five models, surpassing traditional augmentation and cost-sensitive methods.

Chakraborty S, et al. Generative adversarial network augmented data for improved heart sound abnormality detection. *Comput Biol Med*. 2025 Sep;195:110623. doi: 10.1016/j.compbiomed.2025.110623. Epub 2025 Jun 24. PMID: 40561577.

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**79. Can the global left ventricular contractility index ( $d\sigma^*/dt(\max)$ ) predict adverse outcomes in patients with severe mitral regurgitation (MR) and preserved left ventricular ejection fraction (LVEF)?**

In a cohort study of 127 patients with severe primary MR and LVEF  $\geq 60\%$ , 42.5% experienced adverse outcomes (heart failure hospitalization, mitral valve intervention, or death); a  $d\sigma^*/dt(\max)$  cut-off of  $2.15 \text{ s}^{-1}$  independently predicted these outcomes, supporting its prognostic value in severe MR management.

Li T, et al. Prognostic Value of the Global Left Ventricular Contractility Index in Patients with Severe Mitral Regurgitation and Preserved Left Ventricular Ejection Fraction. *J Cardiovasc Dev Dis*. 2025 Jun 13;12(6):227. doi: 10.3390/jcdd12060227. PMID: 40558662; PMCID: PMC12194656.

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**80. Does epicardial adipose tissue (EAT) thickness predict plaque vulnerability in left coronary arteries in sudden cardiac death cases?**



In a retrospective histological study of 245 sudden cardiac death cases (mean age  $62.3 \pm 12.7$  years, 71% male), increased EAT thickness at the left anterior descending ( $0.74 \pm 0.26$  cm) and left circumflex arteries ( $0.71 \pm 0.27$  cm) was significantly associated with unstable plaques (LAD OR 1.88,  $p=0.002$ ; LCx OR 1.51,  $p=0.010$ ), with positive correlations between EAT thickness and age ( $p \leq 0.003$ ) and BMI ( $p < 0.001$ ).

Niculescu R, et al. Predictive Value of Epicardial Adipose Tissue Thickness for Plaque Vulnerability in Left Coronary Arteries: Histological Evidence from 245 Sudden Cardiac Death Cases. *Diagnostics* (Basel). 2025 Jun 11;15(12):1491. doi: 10.3390/diagnostics15121491. PMID: 40564812; PMCID: PMC12192023.

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**81. Does longitudinal strain measurement correlate with visual assessment of left ventricular segment contractility during dobutamine stress echocardiography in patients suspected of CAD?**

In this observational study of 70 patients at the University Clinical Center of the Republic of Srpska, significant differences in longitudinal strain were found between impaired and non-impaired segments both at baseline and peak stress (e.g., baseline LS -20% vs. -17%, peak LS -22% vs. -13%,  $p < 0.05$ ).

Trninić D, et al. Visual Assessment and Longitudinal Strain During Dobutamine Stress Echocardiography. *Diagnostics* (Basel). 2025 Jun 10;15(12):1473. doi: 10.3390/diagnostics15121473. PMID: 40564794; PMCID: PMC12192166.



## Non-pharmacological treatment

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### 82. Is early discharge (<48 hours) after primary PCI for STEMI safe and cost-effective for low-risk patients, and does virtual follow-up improve outcomes?

In this prospective study of 1,500 low-risk STEMI patients discharged early with virtual follow-up, median hospital stay was 24.9 hours vs. 68.1 hours in controls ( $P < 0.0001$ ); 12-month major adverse cardiac events were lower in the early discharge group (3.1% vs. 5.5%,  $P = 0.043$ ), with mortality at 0.6% all-cause and 0.13% cardiovascular, supporting safety, cost-effectiveness, and improved medication adherence.

Rathod KS, et al. Cost-Effectiveness of Early Discharge (<48 Hours) for Low-Risk Patients Following PPCI for STEMI. *JACC Cardiovasc Interv.* 2025 Jun 23;18(12):1499-1509. doi: 10.1016/j.jcin.2025.04.045. PMID: 40562463.

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### 83. What are the six-year clinical outcomes of CABG versus PCI in diabetic patients with multivessel CAD (MVD)?

In this retrospective study of 317 diabetic MVD patients (98 CABG, 219 PCI) from 176 Heart Team meetings, overall mortality was similar at 6 years (16.3% CABG vs 20.5% PCI,  $P=0.38$ ), but MI incidence was lower with CABG (4.1% vs 12.3%,  $P=0.02$ ), while major adverse cardiac and cerebrovascular events (MACCE) and repeat revascularization rates were significantly higher in PCI (83.6% vs 44.9%,  $P<0.01$ ; 47.0% vs 17.3%,  $P<0.01$ ).

Jonik S, et al. Six-Year Outcomes of CABG vs PCI in Diabetic Patients with Multivessel Coronary Disease. *Med Sci Monit.* 2025 Jun 26;31:e948348. doi: 10.12659/MSM.948348. PMID: 40566650; PMCID: PMC12211400.

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### 84. Does quantitative flow ratio (QFR)-guided PCI improve procedural outcomes compared to angiography-guided PCI in STEMI patients undergoing staged revascularization of non-culprit lesions?

In a prospective randomized single-center study of 124 STEMI patients in Lithuania, QFR-guided PCI significantly reduced fluoroscopy time (6.2 vs 8.0 min,  $P=0.009$ ), contrast volume (100 vs 120 mL,  $P=0.038$ ), number of stents implanted (1.5 vs 2.0,  $P=0.002$ ), and stent length (28 vs 45 mm,  $P<0.001$ ) compared to



angiography-guided PCI, with no difference in complications or hospital stay.

Krivickas Ž, et al. Outcomes from Quantitative Flow Ratio-Guided Complete Revascularization and Angiography-Guided Percutaneous Coronary Intervention in Patients with ST-Segment Elevation Myocardial Infarction. *Med Sci Monit.* 2025 Jun 15;31:e948085. doi: 10.12659/MSM.948085. PMID: 40566730; PMCID: PMC12178142.

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**85. Does prior transradial catheterisation (TRC) affect the patency of radial artery (RA) grafts used in CABG?**

In this retrospective cohort study (Victoria, Australia) of 68 patients with bilateral RA grafts (90 LRA, 76 previously catheterised RRA), patency was significantly lower in RRA grafts (72%) than LRA grafts (87%;  $p = 0.02$ ); female sex, peripheral vascular disease, and prior MI were associated with RRA graft occlusion.

Wang Y, et al. Radial Artery Conduit Use After Transradial Catheterisation. *Heart Lung Circ.* 2025 Jun 26;S1443-9506(25)00185-4. doi: 10.1016/j.hlc.2025.03.008. Epub ahead of print. PMID: 40579306.

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**86. What are the outcomes and predictors of unplanned coronary artery bypass graft (CABG) during aortic root replacement (ARR)?**

In this retrospective study of 2,416 patients (2004–2021), unplanned CABG during aortic root replacement occurred in 8.4% and was linked to higher in-hospital mortality (21.2% vs 8.2%,  $p < 0.001$ ), stroke (8.4% vs 2.5%,  $p = 0.002$ ), renal failure (18.2% vs 10.6%,  $p = 0.01$ ), and respiratory failure (49.3% vs 27.2%,  $p < 0.001$ ). Risk factors included female sex (OR 1.44,  $p = 0.04$ ), CKD (OR 1.77,  $p < 0.001$ ), reoperation (OR 2.26,  $p < 0.001$ ), dissection (OR 2.61,  $p < 0.001$ ), endocarditis (OR 1.39,  $p = 0.04$ ), and arch replacement (OR 1.39,  $p = 0.04$ ); valve-sparing root replacement was protective (OR 0.41, 95% CI [0.25–0.68],  $p < 0.001$ ).

Rajesh K, et al. Unplanned coronary artery bypass graft in aortic root replacement†. *Eur J Cardiothorac Surg.* 2025 Jul 1;67(7):ezaf193. doi: 10.1093/ejcts/ezaf193. PMID: 40577071.

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**87. Does percutaneous transluminal septal myocardial ablation (PT SMA) improve coronary microvascular dysfunction (CMD) in patients with obstructive hypertrophic cardiomyopathy (oHCM)?**



In this pilot interventional study of 10 oHCM patients (median age 66), PTSMA reduced the left ventricular pressure gradient from 44 [17–84] to 5 [2–8] mmHg, improved coronary flow reserve (CFR) from 1.8 [1.6–2.1] to 2.5 [2.2–3.6], and decreased the index of microcirculatory resistance (IMR) from 31 [25–39] to 22 [17–26], indicating CMD improvement.

Terauchi T, et al. A pilot study on coronary microvascular dysfunction in obstructive hypertrophic cardiomyopathy: impact of percutaneous transluminal septal myocardial ablation. *Cardiovasc Interv Ther.* 2025 Jun 27. doi: 10.1007/s12928-025-01154-1. Epub ahead of print. PMID: 40576939.

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**88. Does orbital atherectomy (OA) offer safe and effective outcomes in the treatment of coronary calcified nodules (CNs) compared to traditional approaches?**

In this single-center retrospective study of 57 CN patients out of 312 who underwent OA between Jan 2022–Mar 2024, 100% angiographic success was achieved with no perforations or flow-limiting dissections; during a mean follow-up of  $325.6 \pm 233.5$  days, MACE occurred in 5.26% (MI: 3.51%, TVR: 1.75%) and only one case of very late stent thrombosis was observed.

Saleh H, et al. Outcomes Following Orbital Atherectomy for Coronary Calcified Nodules: A Retrospective Single-Center Experience. *Catheter Cardiovasc Interv.* 2025 Jun 27. doi: 10.1002/ccd.31724. Epub ahead of print. PMID: 40576015.

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**89. Are polymer-free drug-eluting stents (PF-DESs) as effective and safe as biodegradable polymer DESs (BP-DESs) in patients undergoing PCI?**

In this meta-analysis of 9 RCTs (cardiology; n = 9,597), PF-DESs and BP-DESs showed no significant differences at 12–24 months in target lesion revascularization (RR 1.51; 95% CI: 0.83–2.75), MI, stent thrombosis, or mortality, though a subgroup analysis revealed significantly lower cardiac death with the BioFreedom stent (RR 0.57; 95% CI: 0.35–0.90), suggesting potential device-specific benefit.

Marchetta M, et al. Polymer-Free Versus Biodegradable Polymer Drug-Eluting Stents in Coronary Artery Disease: Updated Systematic Review and Meta-Analysis of Clinical, Angiographic, and OCT Outcomes. *Biomedicines.* 2025 Jun 14;13(6):1470. doi: 10.3390/biomedicines13061470. PMID: 40564189; PMCID: PMC12190656.



**90. Does radiofrequency ablation (RFA) of frequent premature ventricular complexes (PVCs) improve left ventricular function and clinical outcomes in patients with structural heart disease (SHD)?**

In this systematic review of studies post-2010, RFA reduced PVC burden and improved LVEF by 8–12% in non-ischemic and modestly in ischemic cardiomyopathy, enhanced NYHA class, and eliminated ICD indications in some cases; procedural success ranged from 60–94%, with PVC burden >13–20% consistently predicting LVEF recovery regardless of SHD type.

Milaras N, et al. Catheter Ablation of Frequent PVCs in Structural Heart Disease: Impact on Left Ventricular Function and Clinical Outcomes. *Biomedicines*. 2025 Jun 17;13(6):1488. doi: 10.3390/biomedicines13061488. PMID: 40564207; PMCID: PMC12191265.



## Pharmacological treatment

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### 91. How do drug-coated balloons (DCBs)—specifically paclitaxel- and sirolimus-coated—perform across different coronary plaque morphologies in terms of clinical efficacy?

In this narrative review (cardiology; qualitative synthesis of RCTs, registries, and meta-analyses), sirolimus-coated balloons (SCBs) showed non-inferior outcomes to paclitaxel-coated balloons (PCBs) in both de novo lesions and in-stent restenosis, with SCBs better suited for lipid-rich and inflammatory plaques and PCBs favored in fibrotic lesions; DCBs overall matched drug-eluting stents in small vessel disease, supporting plaque-specific, stent-free PCI strategies.

Gherasie FA, et al. Drug-Coated Balloon PCI in Different Plaque Morphologies: A Narrative Review. *Biomedicines*. 2025 Jun 14;13(6):1472. doi: 10.3390/biomedicines13061472. PMID: 40564193; PMCID: PMC12190963.

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### 92. How can coronary revascularization be safely managed in patients with hemophilia presenting with acute coronary syndrome (ACS), balancing thrombotic and bleeding risks?

This case report and literature review highlight an alternative strategy using drug-coated balloons combined with spot stenting to avoid full-length drug-eluting stents, enabling shorter dual antiplatelet therapy.

Vadalà G, Mingoia G, Astuti G, Madaudo C, Sucato V, Adorno D, D'Agostino A, Novo G, Corrado E, Galassi AR. Coronary Revascularization in Patients with Hemophilia and Acute Coronary Syndrome: Case Report and Brief Literature Review. *J Clin Med*. 2025 Jun 11;14(12):4130. doi: 10.3390/jcm14124130. PMID: 40565875; PMCID: PMC12194593.

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### 93. In patients with diabetes mellitus undergoing PCI, how do amphipolimus-eluting stents (AES) compare to zotarolimus-eluting stents (O-ZES) in terms of target lesion failure (TLF) over extended follow-up?

In this randomized controlled trial of 1,175 diabetic patients (SUGAR trial), TLF rates at 3 years were 11.4% for AES and 14.9% for O-ZES (HR 0.77; 95% CI 0.56–1.06; p=0.106), showing no statistically significant difference in long-term efficacy between stent types.



Salinas P, et al. Amphiphilic-eluting versus zotarolimus-eluting stents in patients with diabetes mellitus and coronary artery disease: extended follow-up of the SUGAR randomised controlled trial. *Heart*. 2025 Jun 25;heartjnl-2025-325773. doi: 10.1136/heartjnl-2025-325773. Epub ahead of print. PMID: 40562528.

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**94. What is the safety profile of nonselective NSAIDs in adult patients after cardiac surgery regarding acute kidney injury (AKI), major adverse cardiovascular events (MACE), and major bleeding?**

In a historical cohort study of 431 cardiac surgery patients receiving nonselective NSAIDs postoperatively, 12% developed AKI, 1% experienced MACE, and 3% had major bleeding within 7 days; low preoperative eGFR was the strongest predictor of AKI, with overall AKI rates lower than previously reported, possibly due to selection bias.

Miao T, et al. Safety of nonselective nonsteroidal anti-inflammatory drugs in cardiac surgery: a historical cohort study. *Can J Anaesth*. 2025 Jun 25. English. doi: 10.1007/s12630-025-02983-7. Epub ahead of print. PMID: 40560345.

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**95. What are the clinical consequences of warfarin non-compliance in patients with total cavopulmonary circulation (TCPC), specifically regarding thromboembolism risk and outcomes?**

This single-patient case report from a 25-year-old male with TCPC and poor anticoagulation adherence documents right coronary artery thromboembolism caused by aortic root thrombosis, successfully treated with thrombolysis.

Ahmed SH, et al. Case report: a thrombus to remember: a case of warfarin non-compliance in a total cavopulmonary circulation patient. *Eur Heart J Case Rep*. 2025 Jun 25;9(6):ytaf237. doi: 10.1093/ehjcr/ytaf237. PMID: 40568410; PMCID: PMC12188431.

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**96. Does selenium and coenzyme Q10 supplementation reduce long-term cardiovascular mortality differently between sexes in elderly individuals with low selenium levels?**

In this 10-year follow-up of a randomized, double-blind, placebo-controlled trial (cardiology; n = 443 elderly Swedish participants; 4-year intervention, 6-year follow-up), combined selenium (200 µg/day) and CoQ10 (200 mg/day) supplementation significantly reduced cardiovascular mortality, with a greater effect observed



in females—particularly those without IHD—while both sexes showed improvements in inflammation, oxidative stress, NT-proBNP progression, and renal function.

Alehagen U, et al. Selenium and Coenzyme Q<sub>10</sub> Supplementation and Sex Differences in Cardiovascular Mortality Results from a Prospective Randomized Double-Blind Placebo-Controlled Trial in Elderly People Low in Selenium. *Antioxidants (Basel)*. 2025 Jun 5;14(6):685. doi: 10.3390/antiox14060685. PMID: 40563319; PMCID: PMC12190002.

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**97. What is the efficacy of current treatment modalities in reducing angina pectoris frequency and improving clinical outcomes in patients with angina and non-obstructive coronary arteries (ANOCA)?**

This systematic review and meta-analysis included 80 studies (10 meeting strict ANOCA criteria) analyzing randomized controlled and cohort studies, showing significant angina frequency reductions across treatments such as neuromodulation (SMD -3.35; 95% CI -5.13 to -1.56), trimetazidine (-1.74; -2.63 to -0.85), beta-blockers (-1.32; -1.88 to -0.77), and others, highlighting varied but significant symptom improvements in ANOCA patients.

Vervaat FE, et al. Treatment Modalities for Angina with Non-Obstructive Coronary Arteries (ANOCA): A Systematic Review and Meta-Analysis. *J Clin Med*. 2025 Jun 9;14(12):4069. doi: 10.3390/jcm14124069. PMID: 40565817; PMCID: PMC12194334.

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**98. What is the global efficacy, safety, and accessibility of antithrombotic strategies in managing peripheral artery disease (PAD)?**

In this global review of PAD affecting over 230 million people, dual-pathway inhibition (aspirin + rivaroxaban 2.5 mg BID) reduced major adverse cardiovascular events by 24% and limb events by 46%—particularly in high-risk patients—though bleeding risks and limited access in low-income countries (carrying 70% of PAD burden) remain significant barriers.

Mohammadi A, et al. Peripheral Artery Disease and Antithrombotic Management: A Global Perspective on Efficacy, Safety, and Access. *Cardiol Rev*. 2025 Jun 26. doi: 10.1097/CRD.0000000000000989. Epub ahead of print. PMID: 40569059.

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**99. Does stem cell therapy improve safety and cardiac outcomes (infarct size and left ventricular ejection fraction) in patients**



### **with AMI?**

In this systematic review and meta-analysis of 21 interventions from 15 RCTs (n=1218), stem cell therapy showed fewer adverse events (OR 0.66; 95% CI 0.44–0.99;  $p=0.05$ ), no significant short-term efficacy, but long-term improvements in relative infarct size (SMD -0.63; 95% CI -0.94 to -0.32;  $p<0.0001$ ) and LVEF (mean difference 2.63%; 95% CI 0.50–4.76;  $p=0.02$ ) after excluding outliers, despite heterogeneity.

Moeswir D, et al. Safety and efficacy of stem cell therapy in acute myocardial infarction: a systematic review and meta-analysis of adverse events, infarct size and LV ejection fraction assessed by CMRI. *Open Heart*. 2025 Jun 27;12(1):e003301. doi: 10.1136/openhrt-2025-003301. PMID: 40579230; PMCID: PMC12207128.

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## **100. What is the current role and clinical impact of beta-blockers in managing heart failure with preserved ejection fraction (HFpEF)?**

This narrative review in cardiology synthesizes findings from limited randomized trials, observational studies, and meta-analyses, revealing inconsistent benefits and potential harms of beta-blockers—especially in HFpEF phenotypes like cardiac amyloidosis—due to chronotropic incompetence and reduced exertional cardiac output.

Abittan N, et al. Beta-Blockers in Heart Failure With Preserved Ejection Fraction: A Declining Role in Contemporary Management. *Cardiol Rev*. 2025 Jun 27. doi: 10.1097/CRD.0000000000000987. Epub ahead of print. PMID: 40576363.



## Guidelines

There were no guidelines-related publications released this month.



Thank you for reading the booklet.

This product is built by the **Medical community** and for the **Medical community**.

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