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Pan-vascular disease: what we have done in the past and what we can do in the future?

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Pan-vascular disease, a term encompassing a range of conditions primarily characterized by atherosclerosis within the vascular system, presents a significant challenge to our understanding and treatment protocols. This villain in our story causes functional turmoil in vital organs like the heart, brain, kidneys, and limbs, leading to a perilous journey of ischemia or hemorrhage[1].

The evolution of our understanding of this complex system is fascinating. In the early 1990s, scientists conceptualized the "vascular tree," a primitive model that evolved into the more intricate "vascular network" by the end of the 20th century. However, it was not until 2002, with the pioneering work of Peter Lanzer and Eric J. Topol, that the term "pan-vascular disease" was coined, marking the birth of "pan-vascular medicine," a field dedicated to understanding and treating these extensive vascular disorders holistically[2].

A pivotal moment in this journey was the 2006 Reduction of Atherothrombosis for Continued Health(REACH) Registry Study, akin to assembling pieces of a vast puzzle. The study revealed startling figures: nearly a quarter of patients with coronary artery disease and a staggering 61.5% with peripheral artery disease had lesions spread across different vascular beds. Furthermore, 15.9% of those battling atherosclerosis had multiple vascular bed lesions[3], emphasizing the interconnectedness of our vascular system and the necessity for an integrated approach to treatment.

Pan-vascular medicine resembles the parable of the blind men and the elephant, where each blind man encounters a different part of the elephant and draws a distinct conclusion about the creature. This parable parallels how different medical specialists like cardiologists, neurologists, and vascular surgeons might perceive and treat vascular diseases based on their areas of expertise. The essence of pan-vascular medicine is in harmonizing these diverse perspectives, akin to bringing together the blind men's varying descriptions to form a complete picture of the elephant. Doing so offers a holistic and comprehensive approach to diagnosing and managing vascular diseases, benefiting patients with a multi-faceted treatment strategy that addresses the vascular system as an interconnected whole rather than as isolated parts.

UNSEEN WAVES: THE CRITICAL CALL TO ACKNOWLEDGE PAN-VASCULAR DISEASES

The 2023 World Heart Report by the World Heart Federation[4] paints a stark portrait of a world where the rhythm of life is increasingly disrupted by the beat of cardiovascular diseases. These ailments have ascended to the ominous throne of being the most prevalent global cause of death and a significant contributor to disability. Consider a staggering number: over half a billion individuals worldwide are caught in the clutches of these diseases, representing about a third of all global deaths. Alarmingly, this health crisis casts its darkest shadow over middle- and low-income countries where four out of every five cardiovascular deaths occur.

This narrative is not just about number numerical increases over time. Yes, the total number of cardiovascular disease-related deaths has surged dramatically from 12.1 million in 1990 to 20.5 million in 2021. However, this rise is intertwined with the stories of growing populations and aging societies. Amidst this, a ray of hope emerges in the form of a declining death rate—a testament to medical advancements and public health initiatives, particularly in high-income nations.

This report is not merely a collection of statistics but a clarion call to action. It underscores the universal menace of cardiovascular diseases, especially in economically challenged regions. The revelation that up to 80% of premature heart attacks and strokes can be prevented serves as a powerful reminder of the potential of proactive healthcare measures.

The financial heartbeat of this health crisis is palpable as well. Countries pouring a greater percentage of their gross domestic product (GDP) into healthcare are witnessing lower cardiovascular disease mortality rates.

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In contrast, nations burdened with high out-of-pocket healthcare expenses are experiencing higher mortality rates. The World Health Organization's advocacy for a minimum of 5% GDP investment in healthcare is a strategic prescription to alleviate this burden.

Ischemic heart disease stands as the grim reaper among cardiovascular conditions, with stroke and intracerebral hemorrhage trailing closely in its deadly wake.

Turning our gaze to China, a nation of over 1.4 billion people, the China Cardiovascular Health and Disease Report 2023[5] reveals a worrying trend. Imagine nearly a quarter of China's population, around 330 million people, grappling with cardiovascular diseases. This staggering statistic includes 11.39 million people with coronary heart disease, 13 million with strokes, and 45.3 million with peripheral arterial disease, painting a complex and troubling picture of cardiovascular health in the country.

The rise in cardiovascular disease-related deaths in China from 3.09 million in 2005 to 4.58 million in 2020 reflects a wider health crisis. In both rural and urban areas, these diseases claim nearly two out of every five lives, with ischemic heart disease, hemorrhagic stroke, and ischemic stroke being the top executioners.

The disparity in mortality rates due to coronary heart disease and cerebrovascular disease between urban and rural residents adds complexity to this issue. Moreover, the financial burden is colossal with hospitalization expenses for cardiovascular and cerebrovascular diseases reaching 270.901 billion yuan in 2020.

These figures are more than mere data points; they highlight the urgent need for China to prioritize vascular health in its public health initiatives. Despite significant strides in medical access and quality, especially in middle-income countries like China, the battle against cardiovascular diseases is far from over. As China marches toward its "Healthy China 2030" goal, the transition from high-speed to high-quality development is crucial in addressing the growing tide of pan-vascular diseases. This journey is not just about treating diseases but also about changing lifestyles, policies, and perspectives, ultimately striving for a healthier and heartier China.

THE SHARED PATH: UNDERSTANDING ATHEROSCLEROSIS

Atherosclerosis, a disease process affecting coronary, cerebral, peripheral arteries as well as the aorta, stands as a major global cause of mortality. It extends beyond lipid deposition, encompassing a spectrum of pathophysiological processes such as endothelial dysfunction, and a dynamic interplay between inflammation and immunity[6].

The concept of atherosclerosis as an inflammatory disease, initially proposed by Rudolph Virchow in 1856, gained prominence with Russell Ross's 1999 article in the *New England Journal of Medicine* titled "Atherosclerosis—an Inflammatory Disease." Ross built on his "Response to Injury" hypothesis, reinforcing Virchow's early observations and establishing atherosclerosis as a chronic inflammatory condition[7–8]. This marked a paradigm shift in the scientific community recognizing the disease's complexity beyond just lipid accumulation to include inflammation and immune responses.

Arterial fibrofatty lesions lie at the heart of atherosclerosis, prominent contributors to heart attacks, strokes, and peripheral artery diseases. Established risk factors like low-density lipoprotein cholesterol (LDL-C), hypertension, smoking, and diabetes play significant roles, with burgeoning research shedding light on the immune system's substantial role. The exploration into cellular and molecular dynamics links these risk factors to atherosclerosis's progression[9].

Dyslipidemia, particularly the role of LDL-C, is pivotal in the atherosclerosis onset and progression. Accumulation of LDL-C instigates inflammation and cellular dysfunction, while its reduction substantially decreases cardiovascular risks. Conversely, the role of high-density lipoprotein cholesterol (HDL-C) has evolved from a protective factor to a more nuanced risk indicator, especially when LDL-C levels are controlled. Other lipoproteins like lipoprotein(a) (Lp[a]) continue to contribute to atherosclerosis, maintaining their risk factor status even under intense LDL-C management[10–12].

Diabetes substantially influences vascular health, leading to both macrovascular and microvascular complications. It triggers a harmful cascade that alters lipid profiles, insulin levels, and increases inflammatory cytokines, hastening the progression of atherosclerosis and elevating heart-related risks. The extensive impact of diabetes affects major organs including the heart, brain, and peripheral vessels, while the retina and kidneys are particularly susceptible to microvascular damage. This highlights the complex nature of diabetic vascular complications and underscores the importance of effective management strategies to mitigate the profound impact of diabetes on vascular health[13–14].

Mechanical stress plays a key role in atherosclerosis development. Our study found that in low blood flow shear stress environments like arteries transplanted into veins are less prone to atherosclerosis, highlighting the importance of blood flow dynamics[15]. Additionally, our recent studies have connected the radial wall strain index from angiography to the stability of arterial plaques and the prediction of acute coronary events, demonstrating the impact of arterial wall dynamics on atherosclerosis. Hypertension affects coronary and cerebral arteries and provokes atherosclerosis by increasing arterial wall tension which could disrupt vascular repair mechanisms. Atherosclerosis often occurs in areas of altered blood flow like bends and branches in coronary arteries, where low shear stress impairs endothelial cell function and reduces the release of protective nitric oxide[16–19].

EXPLORING NEW FRONTIERS IN TREATMENT

In the evolving landscape of atherosclerosis management, attention is increasingly focused on traditional and residual risks involving inflammatory, pro-thrombotic, cholesterol, and metabolic pathways. Targeted anti-atherosclerotic therapies, resulting from collaboration between industry and academia, aim to manage conventional risks and address residual risks overlooked in conventional treatments[20–21].

Trials such as the Canakinumab Antiinflammatory Thrombosis Outcome Study (CANTOS), Colchicine Cardiovascular Outcomes Trial (COLCOT), and Low-Dose Colchicine 2 Trial (LoDoCo2) have validated the inflammatory hypothesis, introducing novel anti-inflammatory agents like canakinumab and colchicine into the therapeutic toolbox. The CANTOS trial is particularly noteworthy for demonstrating that inhibiting interleukin-1β can effectively prevent cardiovascular events in individuals with previous myocardial infarctions and elevated high-sensitivity C-reactive protein (hs-CRP) levels[22–25].

Furthermore, the emergence of the concept of "trained immunity" stands as a significant factor in the progression of atherosclerosis post-acute myocardial infarction (AMI). Our research reveals that following AMI, monocytes undergo immune training, heightening their pro-inflammatory activity. This heightened activity is characterized by increased expression of SYK and KMT5A in monocytes, correlating with more severe vascular plaque progression. Additionally, factors like elevated H4K20 methylation and increased norepinephrine during sympathetic nervous system activation, along with dietary influences like high-fat diets, exacerbate vascular inflammation. These findings illustrate the intricate interaction between immune responses, dietary habits, and epigenetic changes post-AMI[26].

Delving into the role of dendritic cells in atherosclerosis reveals that oxidized LDL (ox-LDL) induces their maturation, which is marked by increased expression of molecules such as CD86 and CD40. This maturation is further enhanced by high glucose concentrations, leading to a more mature immune phenotype and heightened T lymphocyte response. These effects, distinct from osmotic pressure influences, are tied to increased intracellular reactive oxygen activity and the activation of the p38 mitogen-activated protein kinase (p38MAPK) signaling pathway[27–28].

Beyond these well-established factors, we also explore the impact of environmental elements like air pollution on atherosclerosis. Pollutants like fine particulate matter ($PM_{2.5}$) associate with increased cardiovascular risks, promoting atherosclerosis through chronic inflammation and oxidative stress. Research in 2022 underscored the acute impact of transient exposure to various pollutants including nitrogen dioxide, sulfur dioxide, and carbon monoxide in triggering acute coronary syndromes. This shows the need for environmental considerations in a comprehensive approach to disease management and prevention[29–30].

The management of residual thrombus risk is crucial in patients with pan-vascular disease, necessitating navigation through the complex interplay among coagulation, platelets, and inflammation. Our latest OPTION study introduces indolibuprofen as a safe and effective option for stable coronary artery disease, suggesting its potential as a dual-channel antithrombotic therapy for high-risk ischemic but low-bleeding risk patients[31–34].

In addressing residual cholesterol risk, the focus is shifting from traditional LDL-C to newer biomarkers like non-HDL-C, residual cholesterol, and Lp(a). Pharmacological interventions are expanding beyond statins and ezetimibe, targeting deoxyribonucleic acid(DNA), messenger ribonucleic acid(mRNA), and protein levels to comprehensively tackle this spectrum of cholesterol risk[20].

For residual metabolic risk, particularly in type 2 diabetes with cardiovascular disease, the aim is dual: screen for diabetes in cardiovascular patients and assess cardiovascular risk in diabetics. Personalized treatment, informed by the patient's clinical profile and cardio-renal risk, is paramount. Glucagon-like peptide-1 (GLP-1) antagonists and sodium-glucose cotransporter 2 (SGLT2) inhibitors, originally developed for diabetes, now show cardiovascular benefits by addressing metabolic risks in pan-vascular conditions, thus underscoring the need for integrated treatment approaches[35].

Besides known residual risks in pan-vascular disease like inflammation, thrombus, cholesterol, and metabolism, another key yet often overlooked factor is the neurological impact on cardiovascular health. The amygdala, an essential part of the brain's Salience Network responsible for cognition and emotion, is associated with cardiovascular events. A study involving 299 patients diagnosed with coronary heart disease employed positron emission tomography/computed tomography (PET/CT) imaging to investigate amygdala activity and its association with stress levels. The findings revealed a noteworthy correlation between stress-induced neural activity and both bone marrow activity and inflammation in the coronary arteries. Patients with heightened stress-related neural activity exhibited a higher prevalence of vulnerable plaques and major adverse cardiovascular events, highlighting the link between stress, inflammation, and cardiac risk. This "brain-leukopoiesis-plaque" axis concept not only provides insight into how stress contributes to cardiac events but also presents the amygdala as a target for other residual risk in developing new treatment approaches[36].

BEYOND THE HORIZON: ARTIFICIAL INTELLIGENCE AND PAN-OMICS IN PAN-VASCULAR MEDICINE

In the dynamic field of pan-vascular disease management, artificial intelligence (AI) is not just an advancement but

a groundbreaking transformation, with its ability to interpret a broad spectrum of data from demographics to omics symbolizing a pivotal moment in medical history and reshaping our understanding and approach to complex disorders.

The individualized pan-vascular index exemplifies this innovation. It is more than a collaborative tool; it represents a revolutionary step towards personalized disease management that acknowledges the intricate nature of pan-vascular diseases[37].

Multimodal and multidimensional assessments are increasingly recognized as vital for comprehending the intricacies of pan-vascular disease, and the introduction of the uEXPLORER Panoramic PET-CT in our hospital marks a game-changer moment. This imaging system, when combined with AI, opens new avenues in both research and clinical practice by offering insights that were once thought impossible[38].

The approach of pan-vascular medicine, inspired by studies like INTERHEART, aims for holistic care that includes addressing both lifestyle and genetic factors in atherosclerotic diseases. Integrating AI with diagnostic methods like CT angiography revolutionizes our diagnostic capabilities, enabling a deeper understanding of vascular health and the early detection of vascular issues.

In treatment, the shift toward personalized strategies, as evidenced in studies like Harmonizing Optimal Strategy for Treatment of Coronary Artery Stenosis-Extended Antiplatelet Monotherapy(HOST-EXAM) and Cardiovascular Outcomes for People Using Anticoagulation Strategies(COMPASS), represents a much-needed paradigm shift. This approach includes personalized antiplatelet therapy and strategies like statins and proprotein convertase subtilisin/kexin-9 (PCSK9) inhibitors to enhance treatment effectiveness.

Risk stratification and long-term monitoring, enhanced by AI, are essential in effective pan-vascular disease management. Utilizing scoring systems like Global Registry of Acute Coronary Events (GRACE) and Thrombolysis In Myocardial Infarction (TIMI) achieves a more tailored patient care approach. This fusion of AI, clinical acumen, and advanced imaging represents a leap towards a future where pan-vascular diseases are managed more effectively, promising improved outcomes through personalized and comprehensive strategies[1].

A LEAP FORWARD

Pan-vascular medicine is undergoing a transformative shift toward a holistic approach, epitomized by the emergence of pan-vascular Medical Centers. These centers, particularly over 100 established across China, exemplify the integration of advanced screening including imaging and biomarkers which enhance patient care and minimize diagnostic errors. They symbolize a seamless blend of basic scientific research with clinical application, crucial for understanding and treating complex vascular diseases.

This evolution is fueled by the creation of comprehensive databases and sophisticated technologies like AI and advanced imaging, pivotal in developing new therapies and personalized medicine. The synergy between various medical specialties within these centers is akin to assembling a puzzle, addressing the multi-faceted nature of pan-vascular diseases influenced by aging, lifestyle, and genetics.

The Chinese model, with its robust data infrastructure and effective management of pan-vascular conditions, provides a blueprint for global health systems. It underscores the importance of integrated care and continuous innovation in tackling the growing impact of cardiovascular diseases worldwide. This journey in pan-vascular medicine, highlighted by the 2023 World Heart Report and the China Cardiovascular Health and Disease Report, is a continuous endeavor demanding multidisciplinary collaboration for enhanced patient outcomes and quality of life.

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CONFLICT OF INTEREST STATEMENT

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DATA SHARING STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

REFERENCES

[1] Zhou X, Yu L, Zhao Y, *et al*. Pan-vascular medicine: an emerging discipline focusing on atherosclerotic diseases. Eur Heart J 2022;43:4528–4531. doi:10.1093/eurheartj/ehac448.
[2] Hu Y, Zhao Y, Dai N, *et al*. Unwavering excellence: How to be a competent cardiovascular doctor in "pan-vascular medicine +". Innovation (Camb) 2023;4:100489. doi:10.1016/j.xinn.2023.100489.
[3] Bhatt DL, Steg PG, Ohman EM, *et al*. REACH Registry Investigators. International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. JAMA 2006;295:180–189. doi:10.1001/jama.295.2.180.
[4] Fox E, Di Cesare M, Bixby H, *et al*. World Heart Report 2023: Full Report by Geneva, Switzerland. World Heart Federation; 2023. https://world-heart-federation.org/resource/world-heart-report-2023/.
[5] The WCOTROCHADIC. Report on cardiovascular health and diseases in China 2022: an updated summary. Biomed Environ Sci 2023;36:669–701. doi:10.3967/bes2023.106.
[6] Schade DS, Shey L, Eaton RP. Cholesterol review: a metabolically important molecule. Endocr Pract 2020;26:1514–1523. doi:10.4158/EP-2020-0347.

[7] Minelli S, Minelli P, Montinari MR. Reflections on atherosclerosis: lesson from the past and future research directions. J Multidiscip Healthc 2020;13:621–633. doi:10.2147/JMDH.S254016.
[8] Ross R. Atherosclerosis—an inflammatory disease. N Engl J Med 1999;340:115–126. doi:10.1056/NEJM199901143400207.
[9] Libby P, Buring JE, Badimon L, *et al*. Atherosclerosis. Nat Rev Dis Primers 2019;5:56. doi:10.1038/s41572-019-0106-z.
[10] Geovanini GR, Libby P. Atherosclerosis and inflammation: overview and updates. Clin Sci (Lond) 2018;132:1243–1252. doi:10.1042/CS20180306.
[11] Borén J, Chapman MJ, Krauss RM, *et al*. Low-density lipoproteins cause atherosclerotic cardiovascular disease: pathophysiological, genetic, and therapeutic insights: a consensus statement from the European Atherosclerosis Society Consensus Panel. Eur Heart J 2020;41:2313–2330. doi:10.1093/eurheartj/ehz962.
[12] Baigent C, Keech A, Kearney PM, *et al*. Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet 2005;366:1267–1278. doi:10.1016/S0140-6736(05)67394-1.
[13] Li Y, Liu Y, Liu S, *et al*. Diabetic vascular diseases: molecular mechanisms and therapeutic strategies. Signal Transduct Target Ther 2023;8:152. doi:10.1038/s41392-023-01400-z.
[14] Poznyak A, Grechko AV, Poggio P, *et al*. The diabetes mellitus-atherosclerosis connection: the role of lipid and glucose metabolism and chronic inflammation. Int J Mol Sci 2020;21:1835. doi:10.3390/ijms21051835.
[15] Zhang H, Sun A, Shen Y, *et al*. Artery interposed to vein did not develop atherosclerosis and underwent atrophic remodeling in cholesterol-fed rabbits. Atherosclerosis 2004;177:37–41. doi:10.1016/j.atherosclerosis.2004.06.019.
[16] Rampidis G, Rafailidis V, Kouskouras K, *et al*. Relationship between coronary arterial geometry and the presence and extend of atherosclerotic plaque burden: a review discussing methodology and findings in the era of cardiac computed tomography angiography. Diagnostics (Basel) 2022;12:2178. doi:10.3390/diagnostics12092178.
[17] Li C, Wang Z, Yang H, *et al*. The association between angiographically derived radial wall strain and the risk of acute myocardial infarction. JACC Cardiovasc Interv 2023;16:1039–1049. doi:10.1016/j.jcin.2023.02.012.
[18] Elwany S, Ibrahim AA, Soliman AI, *et al*. The significance of atherosclerosis in hypertensive patients with epistaxis. J Laryngol Otol 2018;132:323–326. doi:10.1017/S0022215118000221.
[19] Hong H, Li C, Gutiérrez-Chico JL, *et al*. Radial wall strain: a novel angiographic measure of plaque composition and vulnerability. EuroIntervention 2022;18:1001–1010. doi:10.4244/EIJ-D-22-00537.
[20] Hetherington I, Totary-Jain H. Anti-atherosclerotic therapies: milestones, challenges, and emerging innovations. Mol Ther 2022;30:3106–3117. doi:10.1016/j.ymthe.2022.08.024.
[21] Nabel EG, Braunwald E. A tale of coronary artery disease and myocardial infarction. N Engl J Med 2012;366:54–63. doi:10.1056/NEJMra1112570.
[22] Nidorf SM, Fiolet ATL, Mosterd A, *et al*. LoDoCo2 Trial Investigators. Colchicine in patients with chronic coronary disease. N Engl J Med 2020;383:1838–1847. doi:10.1056/NEJMoa2021372.
[23] Tardif JC, Kouz S, Waters DD, *et al*. Efficacy and safety of low-dose colchicine after myocardial infarction. N Engl J Med 2019;381:2497–2505. doi:10.1056/NEJMoa1912388.
[24] Ridker PM, Everett BM, Thuren T, *et al*. CANTOS Trial Group. Antiinflammatory therapy with canakinumab for atherosclerotic disease. N Engl J Med 2017;377:1119–1131. doi:10.1056/NEJMoa1707914.
[25] Bäck M, Hansson GK. Anti-inflammatory therapies for atherosclerosis. Nat Rev Cardiol 2015;12:199–211. doi:10.1038/nrcardio.2015.5.
[26] Dong Z, Hou L, Luo W, *et al*. Myocardial infarction drives trained immunity of monocytes, accelerating atherosclerosis. Eur Heart J 2023;12:ehad787. doi:10.1093/eurheartj/ehad787.
[27] Luo Y, Liang C, Xu C, *et al*. Ciglitazone inhibits oxidized-low density lipoprotein induced immune maturation of dendritic cells. J Cardiovasc Pharmacol 2004;44:381–385. doi:10.1097/01.fjc.0000138164.88740.f8.
[28] Yao K, Ge JB, Sun AJ, *et al*. Effects and mechanism of hyperglycemia on development and maturation and immune function of human monocyte derived dendritic cells. Zhonghua Xin Xue Guan Bing Za Zhi 2006;34:60–64. doi:10.3760/j:issn:0253-3758.2006.01.016.
[29] Chen R, Jiang Y, Hu J, *et al*. Hourly air pollutants and acute coronary syndrome onset in 1.29 million patients. Circulation 2022;145:1749–1760. doi:10.1161/CIRCULATIONAHA.121.057179.
[30] Rajagopalan S, Al-Kindi SG, Brook RD. Air pollution and cardiovascular disease: JACC state-of-the-art review. J Am Coll Cardiol 2018;72:2054–2070. doi:10.1016/j.jacc.2018.07.099.
[31] De Luca L. Low-dose rivaroxaban: can cardiovascular events be reduced? Eur Heart J Suppl 2023;25:C20–C26. doi:10.1093/eurheartjsupp/suad034.
[32] Wu H, Xu L, Zhao X, *et al*. OPTION Investigators. Indobufen or Aspirin on top of Clopidogrel after coronary drug-eluting stent implantation (OPTION): a randomized, open-label, end point-blinded, noninferiority trial. Circulation 2023;147:212–222. doi:10.1161/CIRCULATIONAHA.122.062762.
[33] Galli M, Franchi F, Rollini F, *et al*. Dual pathway inhibition in patients with atherosclerotic disease: pharmacodynamic considerations and clinical implications. Expert Rev Clin Pharmacol 2023;16:27–38. doi:10.1080/17512433.2023.2154651.
[34] Chinese College of Cardiovascular Physicians. Chinese expert consensus on antithrombotic therapy for panvascular diseases (2023 edition). Cardiol Plus 2024;9:49–69. doi:10.1097/CP9.0000000000000079.
[35] Marx N, Federici M, Schütt K, *et al*. ESC Scientific Document Group. 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes. Eur Heart J 2023;44:4043–4140. doi:10.1093/eurheartj/ehad192.
[36] Dai N, Tang X, Weng X, *et al*. Stress-related neural activity associates with coronary plaque vulnerability and subsequent cardiovascular events. JACC Cardiovasc Imaging 2023;16:1404–1415. doi:10.1016/j.jcmg.2023.04.004.
[37] Loncaric F, Camara O, Piella G, *et al*. Integration of artificial intelligence into clinical patient management: focus on cardiac imaging. Rev Esp Cardiol (Engl Ed) 2021;74:72–80. doi:10.1016/j.rec.2020.07.003.
[38] Andrews J, Puri R, Kataoka Y, *et al*. Therapeutic modulation of the natural history of coronary atherosclerosis: lessons learned from serial imaging studies. Cardiovasc Diagn Ther 2016;6:282–303. doi:10.21037/cdt.2015.10.02.

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