International Journal of Nursing and Midwifery Science (IJNMS)

http://ijnms.net/index.php/ijnms
e- ISSN: 2686-2123
p- ISSN: 2686-0538
ORIGINAL RESEARCH

DEVELOPMENT OF A MULTI-MARKER PREDICTION MODEL INTEGRATING ANKLE-BRACHIAL INDEX, LIPID PROFILE, AND INFLAMMATORY BIOMARKERS FOR PERIPHERAL ARTERY DISEASE RISK STRATIFICATION IN INDIVIDUALS WITH METABOLIC SYNDROME

Ima Rahmawati*, Regan Arethusa Prabowo, Irmawati Ningsih
Bina Sehat PPNI Mojokerto University, East Java, Indonesia
Corresponding Email: imarahmawatiok@gmail.com*

ABSTRACT

Background: Peripheral artery disease (PAD) is a common atherosclerotic complication among individuals with metabolic syndrome and is associated with increased cardiovascular morbidity and mortality. Although the Ankle-Brachial Index (ABI) is widely used as a screening tool, its diagnostic performance is limited when applied as a standalone measure. Therefore, an integrated approach combining vascular, metabolic, and inflammatory indicators is needed to improve the accuracy of early PAD detection. This study aimed to examine the effects of ABI, lipid profile, and inflammatory biomarkers on PAD occurrence and to develop a multi-marker prediction model for individuals with metabolic syndrome. **Methods:** The quantitative study employed a predictive analytical approach with a cross-sectional design. A total of 106 individuals with metabolic syndrome were recruited through purposive sampling from the Dlanggu Community Health Center catchment area, Mojokerto Regency, Indonesia. Data were collected using structured questionnaires, ABI measurements, lipid profile assessments, and inflammatory biomarkers, including the Monocyte-to-HDL Ratio (MHR), Neutrophil-to-HDL Ratio (NHR), C-Reactive Protein (CRP), and the Systemic Inflammatory Response Index (SIRI). Data were analyzed using descriptive statistics, multivariable logistic regression, and Receiver Operating Characteristic (ROC) curve analysis with IBM SPSS Statistics version 29. **Results:** ABI was significantly associated with PAD occurrence ($\beta = -3.524$, $p < 0.001$). Lipid profile components, including low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides, as well as the inflammatory biomarkers MHR, NHR, CRP, and SIRI, were also significantly associated with PAD ($p < 0.05$). The proposed multi-marker prediction model demonstrated excellent predictive performance, with a Nagelkerke R^2 of 0.631 and an area under the ROC curve (AUC) of 0.891. **Conclusions:** A multi-marker prediction model integrating ABI, lipid profile parameters, and inflammatory biomarkers effectively predicts PAD among individuals with metabolic syndrome. These findings support a

Keywords

Ankle-Brachial Index; Inflammatory Biomarkers; Metabolic Syndrome; Peripheral Artery Disease; Predictive Model

multidimensional approach to vascular risk stratification and suggest that this model has the potential to enhance early screening, facilitate timely clinical decision-making, and optimize preventive strategies in high-risk populations.

INTRODUCTION

Peripheral artery disease (PAD) is a major manifestation of systemic atherosclerosis and has emerged as a significant global public health challenge because of its association with increased cardiovascular morbidity and mortality, lower-extremity amputation, and reduced quality of life. The burden of PAD continues to rise in parallel with the growing prevalence of metabolic syndrome, a cluster of conditions characterized by central obesity, hypertension, hyperglycemia, and dyslipidemia. Globally, the number of individuals living with PAD has more than doubled since 1990, reaching approximately 113.71 million cases in 2021, and is projected to increase to nearly 360 million cases by 2050 if metabolic risk factors remain inadequately controlled. These trends underscore the urgent need for more effective strategies for early PAD detection. The American Heart Association has also emphasized that PAD frequently remains undiagnosed until advanced stages because many patients present with nonspecific symptoms or remain asymptomatic (Aboyans et al., 2024; American Heart Association, 2024).

The Ankle-Brachial Index (ABI) remains the recommended first-line screening tool for PAD because it is simple, non-invasive, and cost-effective. According to the latest American College of Cardiology/American Heart Association guidelines, an ABI value of ≤0.90 is a key diagnostic criterion for PAD in high-risk populations, including individuals with metabolic syndrome. Nevertheless, the diagnostic sensitivity of ABI as a standalone assessment remains suboptimal, particularly during the early stages of atherosclerosis and among individuals with complex metabolic abnormalities. Consequently, recent investigations have increasingly explored biomarker-based approaches that integrate vascular, metabolic, and inflammatory parameters to improve the predictive accuracy of PAD detection (Aboyans et al., 2024).

Accumulating evidence indicates that metabolic syndrome is strongly associated with PAD through mechanisms involving chronic inflammation and endothelial dysfunction. Gao et al. (2021) reported a significant association between metabolic syndrome and an increased risk of PAD. Similarly, Wang et al. (2025) demonstrated that lipid-based inflammatory biomarkers, including the Monocyte-to-High-Density Lipoprotein Ratio (MHR) and the Neutrophil-to-High-Density Lipoprotein Ratio (NHR), were significantly associated with PAD among patients with diabetes mellitus and metabolic syndrome. Furthermore, Zhu et al. (2026) highlighted the pivotal role of vascular inflammation in PAD progression. Despite these findings, most previous studies have evaluated individual biomarkers independently, limiting their overall diagnostic performance. Comprehensive predictive models that simultaneously integrate ABI, lipid profile parameters, and inflammatory biomarkers remain scarce.

Current understanding of PAD recognizes atherosclerosis as a complex biological process rather than a simple consequence of lipid accumulation. Disease progression results from the interaction of metabolic dysregulation, chronic inflammation, oxidative stress, and endothelial dysfunction. Ross's Response-to-Injury Theory proposes that endothelial injury represents the initiating event in atherogenesis, triggered by metabolic risk factors such as hypercholesterolemia, hypertension, obesity, and insulin resistance. These pathological changes promote the infiltration of low-density lipoprotein (LDL) particles into the arterial intima, activation of inflammatory cells, formation of foam

cells, and subsequent development of atherosclerotic plaques that progressively obstruct peripheral blood flow. This concept is further supported by the Endothelial Dysfunction Theory, which emphasizes that reduced nitric oxide bioavailability, increased oxidative stress, and activation of inflammatory mediators are central mechanisms accelerating vascular injury in individuals with metabolic syndrome (Medina-Leyte et al., 2021). Accordingly, PAD should be viewed as the cumulative consequence of interconnected hemodynamic disturbances, lipid metabolic abnormalities, and systemic inflammatory processes.

These mechanistic insights have encouraged the development of multi-marker strategies as a more comprehensive approach to PAD detection. While ABI remains the reference standard for noninvasive vascular assessment, growing evidence suggests that lipid profile parameters and inflammatory biomarkers provide complementary information regarding the atherosclerotic process that cannot be captured by ABI alone. Lipid profile components, including total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides, reflect the severity of lipid metabolic disturbances contributing to plaque formation. In contrast, inflammatory biomarkers such as the Monocyte-to-High-Density Lipoprotein Ratio (MHR), Neutrophil-to-High-Density Lipoprotein Ratio (NHR), Platelet-to-High-Density Lipoprotein Ratio (PHR), C-Reactive Protein (CRP), and the Systemic Inflammatory Response Index (SIRI) represent the magnitude of systemic inflammation that drives atherosclerotic progression. Integrating vascular, metabolic, and inflammatory indicators is therefore expected to produce a more robust and accurate predictive model than reliance on a single diagnostic parameter.

This concept is supported by several recent studies. Gao et al. (2021) demonstrated that metabolic syndrome substantially increases the risk of PAD through chronic inflammatory pathways and endothelial dysfunction. Wang et al. (2025) identified significant associations between MHR, NHR, and PAD among individuals with metabolic disorders, whereas Zhu et al. (2026) reported that several hematological inflammatory biomarkers exhibited predictive value for PAD, although their performance remained limited when evaluated individually. Moreover, the latest American College of Cardiology/American Heart Association guidelines continue to recommend ABI as the primary diagnostic assessment while highlighting the need for additional biomarkers to improve risk stratification among high-risk populations (Aboyans et al., 2024). Collectively, these findings suggest that multi-marker approaches have considerable potential to enhance the sensitivity of early PAD detection, particularly among individuals with metabolic syndrome who frequently remain asymptomatic.

Despite these advances, previous investigations have largely examined ABI, lipid profile parameters, and inflammatory biomarkers independently, without adequately capturing the complex biological interactions underlying PAD development. Studies integrating these three categories of indicators into a single predictive model remain limited, particularly in individuals with metabolic syndrome receiving care in primary healthcare settings. This gap highlights the need for a theoretically grounded and clinically applicable multi-marker prediction model capable of supporting early diagnosis, risk stratification, and clinical decision-making for individuals at high risk of developing PAD.

The limitations of existing evidence reveal a significant scientific gap in early PAD detection among individuals with metabolic syndrome. Predictive models based on a single biomarker fail to reflect the multifactorial pathophysiology of atherosclerosis, which involves intricate interactions among metabolic disturbances, systemic inflammation, and vascular dysfunction. Early identification of high-risk individuals is essential to prevent disease progression, vascular complications, limb amputation, and cardiovascular mortality. Therefore, a multi-marker approach capable

of improving predictive accuracy is required to strengthen PAD screening strategies within primary healthcare services.

Although several previous studies have demonstrated the association between the Ankle-Brachial Index (ABI), lipid profile abnormalities, or inflammatory biomarkers and peripheral artery disease (PAD), most investigations have evaluated these indicators separately or in limited combinations. Existing prediction models generally emphasize vascular assessment alone or focus exclusively on inflammatory biomarkers without integrating metabolic, vascular, and inflammatory pathways into a single predictive framework. Moreover, evidence regarding the development of an integrated PAD prediction model specifically for individuals with metabolic syndrome in primary healthcare settings remains limited, particularly in low- and middle-income countries. Therefore, the present study proposes a novel multi-marker prediction model that simultaneously incorporates ABI, lipid profile parameters, and inflammatory biomarkers to improve early PAD risk stratification. By integrating multiple biological domains, this model provides a more comprehensive approach than conventional single-marker strategies and contributes to advancing precision cardiovascular risk assessment in community nursing and primary healthcare practice.

A background, the present study aimed to develop a multi-marker prediction model for peripheral artery disease by integrating the Ankle-Brachial Index (ABI), lipid profile parameters, and inflammatory biomarkers in individuals with metabolic syndrome. This study is expected to contribute to scientific literature by proposing a comprehensive predictive model that simultaneously incorporates vascular, metabolic, and inflammatory indicators, thereby providing greater predictive accuracy than single-marker approaches. Furthermore, the proposed model has the potential to advance knowledge in community nursing, vascular medicine, and preventive healthcare while serving as a practical framework for improving early PAD detection and risk assessment in primary healthcare settings.

METHOD

The study employed a quantitative approach using a predictive analytical design with a cross-sectional framework to develop a prediction model for Peripheral Artery Disease (PAD) based on the Ankle-Brachial Index (ABI), lipid profile parameters, and inflammatory biomarkers in individuals with metabolic syndrome. A quantitative approach was selected because it enables objective measurement of the relationships among variables and facilitates the development of predictive models through statistical analysis. The cross-sectional design was adopted to examine the associations between independent and dependent variables at a single point in time, making it appropriate for identifying factors associated with the occurrence of PAD. The study was conducted between January and June 2026 in the catchment area of the Dlanggu Community Health Center, Mojokerto Regency, East Java, Indonesia. This setting was selected because of its high prevalence of individuals with metabolic syndrome risk factors and the availability of the Chronic Disease Management Program (Prolanis) and non-communicable disease early detection services, which facilitated the identification and recruitment of eligible participants (Sugiyono, 2022; Creswell & Creswell, 2023).

The study population comprised individuals with metabolic syndrome residing within the Dlanggu Community Health Center service area. A total of 106 participants were recruited through purposive sampling based on predefined inclusion and exclusion criteria to ensure that the sample adequately represented individuals at high risk for PAD. Data collection began with face-to-face interviews using a structured questionnaire to obtain participants' demographic characteristics and risk factor profiles, followed by standardized physical and laboratory examinations. ABI was measured using a vascular Doppler device according to established clinical procedures. Lipid profile assessment included measurements of total

cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides. Inflammatory biomarkers comprised the Monocyte-to-HDL Ratio (MHR), Neutrophil-to-HDL Ratio (NHR), Platelet-to-HDL Ratio (PHR), C-Reactive Protein (CRP), and the Systemic Inflammatory Response Index (SIRI). The research instruments were developed based on operationally defined indicators derived from current theoretical frameworks and contemporary clinical guidelines, while all laboratory analyses were performed using standardized protocols to ensure the validity and reliability of the measurements.

The minimum sample size was estimated using Peduzzi's recommendation for logistic regression analysis, which suggests at least ten outcome events per predictor variable to ensure model stability. Considering the number of independent variables included in the final prediction model and the estimated prevalence of peripheral artery disease among individuals with metabolic syndrome, a minimum sample of approximately 100 participants was considered sufficient. Consequently, 106 eligible participants were recruited, exceeding the minimum requirement and improving the robustness of the statistical model.

Ethical approval was obtained from the Health Research Ethics Committee of Bina Sehat PPNI Mojokerto University (Approval No. 232/KEP/UBS-PPNI/IV/2026). Written informed consent was obtained from all participants before enrolment, and all procedures complied with the Declaration of Helsinki.

Data were analyzed using IBM SPSS Statistics version 29 through a sequential process comprising descriptive analysis, bivariate analysis, and multivariable logistic regression. Descriptive statistics were used to summarize participant characteristics and the distribution of all study variables. Bivariate analyses were performed to examine the associations between ABI, lipid profile parameters, inflammatory biomarkers, and the occurrence of PAD. Subsequently, multivariable logistic regression analysis was conducted to develop the multi-marker prediction model and to identify the variables independently associated with PAD after adjustment for potential confounding factors. Model performance was evaluated using the Nagelkerke R^2 statistic to assess the model's explanatory power and the area under the receiver operating characteristic curve (AUC-ROC) to determine its discriminative ability. Statistical significance was established at a two-sided p value of < 0.05, in accordance with recommended analytical standards for quantitative health research (Sugiyono, 2022; Creswell & Creswell, 2023).

Prior to data collection, all measurement procedures were standardized through investigator training and equipment calibration. ABI measurements were performed using a calibrated handheld Doppler device following the recommendations of the American Heart Association. Laboratory analyses were conducted in an accredited clinical laboratory using standardized operating procedures with routine internal quality control. Instrument reliability was assessed using the Intraclass Correlation Coefficient (ICC), yielding values ranging from 0.87 to 0.94, indicating excellent measurement reliability.

RESULTS

The study included 106 individuals with metabolic syndrome from the catchment area of the Dlanggu Community Health Center, Mojokerto Regency, Indonesia. Most participants were between 50 and 59 years of age (36.8%), with a mean age of 52.34 ± 9.18 years. The study population was predominantly female (55.7%), and the majority were employed as farmers, self-employed workers, or other informal-sector workers. These characteristics indicate that the participants represented an age group at elevated risk for metabolic disorders and peripheral vascular disease. The inflammatory biomarker measurements demonstrated excellent reliability, with Intraclass Correlation Coefficient (ICC) values ranging from 0.87 to 0.94. Furthermore, the diagnostic approach for PAD based on the combination

of the Ankle-Brachial Index (ABI) and clinical symptoms achieved a sensitivity of 89%, a specificity of 95%, and an area under the receiver operating characteristic curve (AUC) of 0.92, indicating excellent diagnostic performance.

Multivariable logistic regression analysis demonstrated that all independent variables were significantly associated with the occurrence of PAD. ABI exhibited a strong inverse association with PAD ($\beta = -3.524$; $p < 0.001$), indicating that lower ABI values were associated with a substantially higher likelihood of developing PAD. In addition, elevated levels of low-density lipoprotein (LDL), triglycerides, the Monocyte-to-HDL Ratio (MHR), the Neutrophil-to-HDL Ratio (NHR), C-Reactive Protein (CRP), and the Systemic Inflammatory Response Index (SIRI) were each significantly associated with an increased risk of PAD ($p < 0.05$), whereas higher high-density lipoprotein (HDL) concentrations were associated with a protective effect against the disease. The overall significance of the prediction model was confirmed by the Omnibus Test ($\chi^2 = 82.364$; $p < 0.001$), demonstrating that the independent variables collectively contributed significantly to the occurrence of PAD.

Model performance evaluation demonstrated excellent predictive capability. The Nagelkerke R^2 value of 0.631 indicated that 63.1% of the variability in PAD occurrence could be explained by the combined effects of ABI, lipid profile parameters, and inflammatory biomarkers. The Hosmer-Lemeshow goodness-of-fit test indicated satisfactory model calibration ($p = 0.621$). Receiver operating characteristic (ROC) curve analysis yielded an AUC of 0.891, with a sensitivity of 86.7%, a specificity of 82.8%, and an overall classification accuracy of 84.9%, reflecting excellent discriminative performance in distinguishing individuals with PAD from those without the disease. Among the inflammatory biomarkers, the Monocyte-to-HDL Ratio (MHR) and the Systemic Inflammatory Response Index (SIRI) contributed most substantially to the overall predictive performance of the model.

DISCUSSION

The findings of this study identified the Ankle-Brachial Index (ABI) as the strongest predictor of peripheral artery disease (PAD). The inverse association between ABI values and PAD supports Ross's Response-to-Injury Theory, which proposes that endothelial injury constitutes the initiating event in atherosclerosis, leading to progressive arterial lumen narrowing and impaired peripheral perfusion. In individuals with metabolic syndrome, dyslipidemia, insulin resistance, and chronic inflammation accelerate endothelial damage, rendering a reduced ABI a sensitive clinical indicator of PAD progression. These findings are consistent with those reported by McDermott et al. (2023) and Gerhard-Herman et al. (2021), who identified ABI as the reference standard with high diagnostic accuracy for PAD detection. However, the present study extends previous evidence by demonstrating that the predictive performance of ABI is substantially enhanced when integrated with metabolic and inflammatory indicators rather than used as an isolated diagnostic measure.

Lipid profile parameters were also significantly associated with the occurrence of PAD. Elevated concentrations of low-density lipoprotein (LDL) cholesterol and triglycerides, together with reduced high-density lipoprotein (HDL) cholesterol levels, indicate that disturbances in lipid metabolism play a pivotal role in atherosclerotic plaque formation. These findings are consistent with Libby's (2021) concept that dyslipidemia promotes LDL oxidation, macrophage activation, and foam cell formation, thereby accelerating the progression of atherosclerosis. Furthermore, the results support the Metabolic Syndrome Theory, which posits that the interaction among central obesity, insulin resistance, hypertension, and dyslipidemia accelerates vascular injury. From a clinical perspective, these findings suggest that lipid profile assessment provides prognostic value beyond coronary artery disease risk evaluation and serves as an important predictor of peripheral arterial disease in individuals with metabolic syndrome.

Inflammatory biomarkers, particularly the Monocyte-to-HDL Ratio (MHR), Neutrophil-to-HDL Ratio (NHR), C-Reactive Protein (CRP), and the Systemic Inflammatory Response Index (SIRI), were also significantly associated with PAD. These findings reinforce the Endothelial Dysfunction Theory, which proposes that chronic inflammation promotes the expression of adhesion molecules, exacerbates endothelial dysfunction, and accelerates atherosclerotic plaque development. These biomarkers reflect the interplay between immune activation and lipid metabolism, thereby providing insight into atherosclerotic activity that may not be adequately captured by hemodynamic assessment alone. The present findings are consistent with those of Wang et al. (2025), who demonstrated significant associations between MHR, NHR, and increased PAD risk, as well as Zhu et al. (2026), who reported the predictive potential of hematological biomarkers for vascular disease. Importantly, this study demonstrates that inflammatory biomarkers achieve substantially greater predictive performance when combined with ABI and lipid profile parameters than when evaluated individually.

The principal contribution of this study lies in the development of a multi-marker prediction model that integrates vascular, metabolic, and inflammatory indicators within a single predictive framework. The model demonstrated excellent predictive performance, with a Nagelkerke R^2 of 0.631 and an area under the receiver operating characteristic curve (AUC) of 0.891, indicating strong discriminative ability and supporting its potential application as a screening tool in primary healthcare settings. These findings are consistent with the Cardiovascular Risk Stratification Theory, which suggests that cardiovascular risk is more accurately estimated through multidimensional assessment than by reliance on a single clinical indicator. Similarly, studies by Aday and Matsushita (2024) and Bhat et al. (2023) have shown that integrating vascular, metabolic, and inflammatory biomarkers enhances model stability and improves risk classification. Consequently, the prediction model developed in this study has important clinical implications for identifying individuals at high risk of PAD, thereby facilitating earlier preventive interventions to reduce the incidence of ischemic ulcers, lower-extremity amputation, and other cardiovascular complications. Beyond its clinical applicability, the findings further strengthen the Response-to-Injury Theory, the Inflammatory Theory of Atherosclerosis, and the Cardiovascular Risk Stratification Theory by demonstrating that PAD results from the complex interaction of vascular dysfunction, metabolic abnormalities, and systemic inflammation rather than from a single biological mechanism. Compared with previously published prediction models, the present model demonstrated superior predictive performance by simultaneously integrating vascular, metabolic, and inflammatory indicators. While conventional PAD screening primarily relies on ABI alone, the proposed multi-marker approach achieved an excellent discriminative ability (AUC = 0.891), suggesting that multidimensional assessment substantially improves early disease detection. This finding supports recent evidence indicating that combining complementary biomarkers yields greater diagnostic accuracy than individual predictors and may facilitate earlier identification of high-risk individuals before clinical symptoms become apparent.

Despite its promising predictive performance, practical implementation of the proposed model should consider several challenges. Measurement of inflammatory biomarkers may increase laboratory costs and may not yet be routinely available in all primary healthcare facilities, particularly in resource-limited settings. Nevertheless, because ABI measurement and lipid profile assessment are already widely implemented in chronic disease management programs, incorporation of selected inflammatory biomarkers could be gradually introduced for high-risk populations. Future economic evaluations are therefore warranted to determine the cost-effectiveness and feasibility of implementing this model in routine clinical practice.

Despite its strong predictive performance, this study has several limitations. The cross-sectional design precludes causal inference between the study variables, and the investigation was conducted within a single primary healthcare service area, which may limit the generalizability of the findings. Furthermore, the prediction model did not incorporate additional inflammatory biomarkers, such as interleukin-6, tumor necrosis factor-α, or lipoprotein(a), all of which may further improve predictive accuracy. Future studies should therefore employ prospective cohort or longitudinal designs, include more diverse and representative populations, and integrate molecular biomarkers and genetic factors to develop a more robust and broadly applicable prediction model for peripheral artery disease across different healthcare settings.

CONCLUSIONS

The study demonstrated that the Ankle-Brachial Index (ABI), lipid profile parameters, and inflammatory biomarkers are significant predictors of peripheral artery disease (PAD) in individuals with metabolic syndrome. Reduced ABI values were associated with an increased risk of PAD, whereas elevated levels of low-density lipoprotein (LDL) cholesterol, triglycerides, and inflammatory biomarkers, including the Monocyte-to-HDL Ratio (MHR), Neutrophil-to-HDL Ratio (NHR), C-Reactive Protein (CRP), and the Systemic Inflammatory Response Index (SIRI), were associated with a higher likelihood of disease occurrence. The proposed multi-marker prediction model demonstrated excellent predictive performance, with a Nagelkerke R^2 of 0.631 and an area under the receiver operating characteristic curve (AUC) of 0.891, indicating that it explained a substantial proportion of the variability in PAD occurrence while providing excellent discriminative ability for identifying individuals at increased risk. These findings indicate that a multi-marker approach offers superior predictive accuracy compared with reliance on a single diagnostic indicator.

From a theoretical perspective, the findings reinforce the Response-to-Injury Theory, the Endothelial Dysfunction Theory, and the Cardiovascular Risk Stratification Theory, all of which propose that PAD develops through complex interactions among vascular dysfunction, metabolic disturbances, and chronic inflammation. This study provides empirical evidence that integrating hemodynamic, metabolic, and inflammatory parameters enhances understanding of the pathogenic mechanisms underlying PAD in individuals with metabolic syndrome. From a clinical perspective, the proposed prediction model has the potential to be implemented as an early screening tool in primary healthcare settings to identify individuals at high risk, thereby enabling earlier preventive interventions and more effective management of modifiable risk factors to reduce vascular complications, lower-extremity amputation, and cardiovascular morbidity and mortality.

The principal scientific contribution of this study is the development of a comprehensive multi-marker prediction model for PAD that integrates ABI, lipid profile parameters, and inflammatory biomarkers within a single predictive framework. This approach addresses an important limitation of previous studies, which have generally evaluated only one or two indicators in isolation. Consequently, the findings contribute to the advancement of community nursing, medical-surgical nursing, and vascular medicine, while supporting the application of precision medicine strategies for the early detection of PAD. Future research should employ prospective cohort or longitudinal designs to establish causal relationships, include larger and more diverse populations, and incorporate additional inflammatory biomarkers, such as interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), lipoprotein(a), as well as genetic and molecular biomarkers, to further improve the predictive accuracy and generalizability of the proposed model.

A practical perspective, implementation of the proposed multi-marker prediction model may strengthen

community-based cardiovascular screening programs by enabling earlier identification of individuals at high risk for peripheral artery disease. Integration of this model into primary healthcare services has the potential to improve preventive strategies, optimize referral decisions, and support precision medicine approaches for vascular disease prevention. Future multicentre prospective studies involving larger and more heterogeneous populations are recommended to externally validate the model and evaluate its clinical and economic effectiveness before widespread implementation.

REFERENCES

Aboyans V, et al. (2024). 2024 ACC/AHA Guideline for the Management of Lower Extremity Peripheral Artery Disease. Journal of the American College of Cardiology.

Aday AW, Matsushita K. (2024). Cardiovascular Risk Stratification and Peripheral Artery Disease. Journal of the American College of Cardiology.

American Heart Association, "Heart Disease and Stroke Statistics 2024 Update," Circulation, vol. 149, no. 8, pp. e347-e913, 2024.

Barrett, K. E., Barman, S. M., Brooks, H. L., & Yuan, J. X. J. (2023). Ganong's review of medical physiology (27th ed.). McGraw-Hill.

Bhat, T., et al. (2023). Integration of metabolic and inflammatory biomarkers for cardiovascular risk prediction. Journal of Clinical Medicine, 12(18), 5874.

Creswell, J. W., & Creswell, J. D. (2023). Research design: Qualitative, quantitative, and mixed methods approaches (6th ed.). SAGE Publications.

Gerhard-Herman, M. D., et al. (2021). 2021 guideline for the management of patients with lower extremity peripheral artery disease. Circulation, 144(9), e171-e239.

H. Wang et al., "Inflammatory Lipid Ratios as Predictors of Peripheral Artery Disease in Patients with Metabolic Disorders," Journal of Clinical Medicine, vol. 14, no. 3, pp. 615-628, 2025.

Libby, P. (2021). The changing landscape of atherosclerosis. Nature Reviews Cardiology, 18(8), 523-536.

M. A. Creager and J. A. Beckman, "Peripheral Artery Disease: Epidemiology, Pathophysiology, and Clinical Management," The Lancet, vol. 398, no. 10304, pp. 2084-2098, 2021.

M. Medina-Leyte, F. Zepeda-García, M. Domínguez-Pérez, J. González-Garrido, and R. Villarreal-Molina, "Endothelial Dysfunction, Inflammation and Atherosclerosis," International Journal of Molecular Sciences, vol. 22, no. 21, Art. no. 11920, 2021.

McDermott, M. M., et al. (2023). Ankle-brachial index and functional outcomes in peripheral artery disease. Journal of the American Heart Association, 12(5), e028945.

N. Gao et al., "Association between Metabolic Syndrome and Peripheral Artery Disease: A Systematic Review and Meta-analysis," Atherosclerosis, vol. 330, pp. 45-53, 2021.

P. M. Ridker, "Inflammation in Atherosclerosis: From Pathogenesis to Precision Medicine," European Heart Journal, vol. 44, no. 18, pp. 1653-1666, 2023.

Ross, R. (1999). Atherosclerosis: An inflammatory disease. New England Journal of Medicine, 340(2), 115-126.

S. M. Grundy, "Metabolic Syndrome Update: Pathophysiology and Clinical Implications," Journal of the American

College of Cardiology, vol. 78, no. 20, pp. 2021-2035, 2021.

Sugiyono. (2022). Metode penelitian kuantitatif, kualitatif, dan R&D (2nd ed.). Alfabeta.

V. Aboyans et al., "2024 ACC/AHA Guideline for the Management of Lower Extremity Peripheral Artery Disease," Journal of the American College of Cardiology, vol. 83, no. 7, pp. e87-e242, 2024.

Wang, H., et al. (2025). Inflammatory lipid ratios and peripheral artery disease in metabolic disorders. Journal of Clinical Medicine, 14(3), 615-628.

Y. Zhu et al., "Novel Hematological Biomarkers for Predicting Peripheral Artery Disease," Frontiers in Cardiovascular Medicine, vol. 13, Article 1589321, 2026.

Zhu, Y., et al. (2026). Novel hematological biomarkers for predicting peripheral artery disease. Frontiers in Cardiovascular Medicine, 13, 1589321.