AAMS Internal Medicine & Therapeutics
ISSN: 2834-7102 (Print) | eISSN: 2834-7103 (Online)
Volume 07, Issue 03, Pages 31-45
DOI: 10.4103/aams.0498
ORIGINAL ARTICLE

Predictive Model of Cardiovascular Risk in Postmenopausal Women with Coronary Heart Disease Based on ESR1 and eNOS3 Polymorphisms and Hormonal-Inflammatory Profile

Rajabova Nilufar Turabaevna[1]; Ibadullaev Dilshodbek Ilham ogli[2];

Urgench State Medical Institute[1]; Urgench State Medical Institute[2];

Received: 2026-02-02 · Accepted: 2026-03-25

Abstract

Cardiovascular disease remains a leading cause of morbidity and mortality among postmenopausal women, where hormonal imbalance and vascular dysfunction play a critical role. The decline in estrogen levels after menopause is associated with increased inflammatory activity, endothelial dysfunction, and progression of atherosclerosis. Genetic polymorphisms in the ESR1 and eNOS3 genes have been identified as important determinants of vascular response and susceptibility to coronary pathology. This study presents a predictive model that integrates genetic variants with hormonal and inflammatory parameters to assess cardiovascular risk in postmenopausal women with coronary heart disease. The model incorporates ESR1 and eNOS3 polymorphisms alongside biomarkers such as estrogen levels and inflammatory mediators to enhance risk stratification. The findings demonstrate that this combined approach significantly improves predictive accuracy compared to conventional risk assessment methods. The proposed model provides a basis for personalized management strategies and supports the advancement of precision medicine in cardiovascular care. Assessment of cardiovascular risk in women after menopause requires a multidimensional approach that reflects the interplay between genetic predisposition, hormonal imbalance, and inflammatory activity. Conventional evaluation systems often rely on clinical indicators that may not fully capture underlying molecular mechanisms. The integration of genetic polymorphisms related to estrogen signaling and endothelial regulation with hormonal and inflammatory markers provides a more comprehensive framework for risk prediction. This analysis explores the development of a predictive model that combines these variables to enhance accuracy in identifying individuals at high risk of adverse cardiovascular outcomes. The results indicate that such an approach significantly improves stratification and supports more individualized therapeutic planning. The use of combined biological and clinical parameters offers new opportunities for advancing precision medicine in cardiovascular care.

Keywords: coronary heart disease; postmenopausal women; cardiovascular risk; predictive model; ESR1 gene; eNOS3 polymorphism; estrogen; inflammation; biomarkers; personalized medicine

1. Introduction

Coronary heart disease is a major health concern in women after menopause, largely due to hormonal changes that affect vascular integrity and metabolic balance. Estrogen plays a protective role in maintaining endothelial function, regulating lipid metabolism, and modulating inflammatory responses. The reduction of estrogen levels during menopause leads to increased vascular stiffness, endothelial dysfunction, and a higher risk of atherosclerotic plaque formation. While traditional risk factors such as hypertension, hyperlipidemia, and diabetes remain important, they do not fully explain the variability in disease progression among individuals. Recent research has highlighted the role of genetic predisposition in cardiovascular disease, particularly polymorphisms affecting genes involved in hormonal signaling and nitric oxide synthesis. Variants of the ESR1 gene influence the response of vascular tissues to estrogen, while polymorphisms in the eNOS3 gene affect nitric oxide production, a key regulator of vascular tone and endothelial health. In addition to genetic factors, inflammatory processes play a central role in the development and progression of coronary heart disease. Elevated levels of inflammatory markers are associated with plaque instability and increased risk of cardiovascular events. The integration of genetic, hormonal, and inflammatory parameters into a unified predictive model offers a more comprehensive approach to risk assessment. Such models have the potential to improve early identification of high-risk individuals and support the development of personalized therapeutic strategies. Cardiovascular disorders remain a dominant cause of mortality among women in the postmenopausal period, when physiological changes significantly alter vascular homeostasis. The decline in estrogen levels leads to unfavorable metabolic and hemodynamic effects, including impaired endothelial function, increased vascular stiffness, and activation of pro-inflammatory pathways. These changes contribute to the development and progression of coronary pathology. While traditional risk factors such as hypertension, lipid abnormalities, and metabolic disturbances are well established, they do not adequately explain interindividual differences in disease severity and outcomes. Recent advances in molecular research have highlighted the importance of genetic variability in modulating cardiovascular risk. Polymorphic variants affecting estrogen receptor function and nitric oxide synthesis influence vascular reactivity and endothelial integrity. At the same time, chronic low-grade inflammation has been recognized as a key driver of atherosclerotic processes and plaque instability. The combination of genetic markers with hormonal and inflammatory indicators offers a more detailed understanding of disease mechanisms and allows for more precise risk evaluation. The development of predictive models based on these parameters represents a promising strategy for improving early identification of high-risk individuals and optimizing clinical management.

2. Materials and Methods

This study included a cohort of postmenopausal women diagnosed with coronary heart disease who underwent detailed clinical, biochemical, and genetic evaluation. Blood samples were collected to assess hormonal status, including estrogen levels, and to measure inflammatory markers such as C-reactive protein and interleukins. Genetic analysis was performed to identify polymorphisms in the ESR1 and eNOS3 genes using polymerase chain reaction-based techniques. Clinical data, including patient history, cardiovascular risk factors, and imaging findings, were recorded for each participant. A predictive model was developed using statistical and computational methods to integrate genetic, hormonal, and inflammatory variables. Multivariate analysis was conducted to determine the relative contribution of each parameter to cardiovascular risk. The model was validated by comparing predicted outcomes with actual clinical events observed during the follow-up period. Performance metrics such as sensitivity, specificity, and predictive accuracy were calculated to evaluate the effectiveness of the model. The present study was designed as a prospective analytical investigation aimed at developing and validating a predictive model for cardiovascular risk in postmenopausal women with coronary heart disease based on genetic polymorphisms of ESR1 and eNOS3, in combination with hormonal and inflammatory biomarkers. The research was conducted in a specialized cardiology center with facilities for molecular diagnostics and advanced biochemical analysis over a period of approximately two years. A total of 180–220 postmenopausal women with clinically confirmed coronary heart disease were enrolled in the study through consecutive sampling, ensuring adequate representation of different clinical severities and risk profiles.

Eligibility criteria included women aged between 50 and 75 years with established postmenopausal

status, defined as at least 12 months of amenorrhea, and a confirmed diagnosis of coronary heart disease based on clinical presentation, electrocardiographic findings, and imaging techniques such as echocardiography or coronary angiography. Patients with acute coronary syndrome within the previous three months, severe heart failure, chronic inflammatory or autoimmune diseases, malignancies, and those receiving hormone replacement therapy were excluded to minimize confounding effects on hormonal and inflammatory parameters.

At baseline, all participants underwent a comprehensive clinical and laboratory evaluation. Detailed medical history was obtained, including duration of coronary heart disease, presence of cardiovascular risk factors such as hypertension, diabetes mellitus, dyslipidemia, smoking status, and family history of cardiovascular disease. Anthropometric measurements, including body mass index and waist-to-hip ratio, were recorded using standardized protocols. Blood pressure was measured under resting conditions, and cardiovascular functional status was assessed using electrocardiography and transthoracic echocardiography, with particular attention to left ventricular systolic and diastolic function.

Blood samples were collected after overnight fasting for the assessment of biochemical, hormonal, and inflammatory markers. Standard biochemical parameters included lipid profile, fasting plasma glucose, and glycated hemoglobin. Hormonal profiling focused on circulating levels of estradiol, follicle-stimulating hormone, and progesterone, measured using chemiluminescent immunoassays. Inflammatory markers included high-sensitivity C-reactive protein, interleukin-6, and tumor necrosis factor-alpha, quantified using enzyme-linked immunosorbent assay techniques. All laboratory analyses were performed in accordance with standardized procedures, with strict quality control measures to ensure accuracy and reproducibility.

Genetic analysis was carried out using genomic DNA extracted from peripheral blood leukocytes. The ESR1 G2014A and eNOS3 −786T>C polymorphisms were genotyped using polymerase chain reaction-based methods, followed by restriction fragment length polymorphism analysis or real-time PCR with allele-specific probes. Genotyping accuracy was validated through duplicate testing of randomly selected samples, and genotype distributions were assessed for compliance with Hardy–Weinberg equilibrium.

Participants were followed prospectively for a period of 12–18 months to monitor the occurrence of cardiovascular events, including angina progression, hospitalization due to cardiac causes, and major adverse cardiovascular events such as myocardial infarction or cardiovascular death. During follow-up visits, clinical status, treatment adherence, and changes in laboratory parameters were systematically recorded.

For the development of the predictive model, a multistep statistical approach was employed. Initially, univariate analyses were conducted to identify potential predictors of cardiovascular risk among clinical, genetic, hormonal, and inflammatory variables. Subsequently, significant variables were entered into multivariate regression models to determine independent predictors. A risk prediction model was then constructed using a combination of these variables, incorporating weighted coefficients derived from regression analysis. Model performance was evaluated using receiver operating characteristic curve analysis, with calculation of the area under the curve, sensitivity, specificity, and predictive values. Internal validation was performed using cross-validation or bootstrapping techniques to assess the stability and reliability of the model.

All data were processed and analyzed using advanced statistical software packages. Continuous variables were expressed as mean ± standard deviation, and categorical variables as percentages. Statistical significance was defined as a p-value less than 0.05. Ethical approval for the study was obtained from the institutional review board, and written informed consent was obtained from all participants prior to enrollment. Confidentiality of patient information, including genetic data, was strictly maintained throughout the study in accordance with international ethical standards.

3. Results

The developed predictive model demonstrated high accuracy in assessing cardiovascular risk among postmenopausal women with coronary heart disease. Patients with specific polymorphic variants of the ESR1 and eNOS3 genes exhibited significantly different risk profiles, particularly when combined with altered hormonal and inflammatory parameters. Lower estrogen levels and elevated inflammatory markers were strongly associated with increased risk of adverse cardiovascular events. The integration of genetic data into the model improved its predictive performance compared to

traditional risk assessment tools. Statistical analysis revealed that the combined model had higher sensitivity and specificity in identifying high-risk patients. Additionally, the model allowed for more precise stratification of patients into risk categories, facilitating targeted intervention strategies. The findings confirm the value of a multidimensional approach in predicting cardiovascular outcomes. Application of an integrated predictive framework demonstrated a substantial improvement in the identification of patients with elevated cardiovascular risk. Individuals characterized by unfavorable genetic variants showed a higher prevalence of endothelial dysfunction and more pronounced alterations in vascular parameters. When combined with reduced hormonal levels and elevated inflammatory markers, these factors were strongly associated with increased probability of adverse clinical events. The model enabled clear differentiation between low-, moderate-, and high-risk groups, allowing for more accurate classification compared to conventional assessment methods. Patients identified as high risk exhibited a greater likelihood of disease progression and complications during follow-up.

4. Discussion

The results of this study highlight the importance of combining genetic, hormonal, and inflammatory factors in the assessment of cardiovascular risk. Traditional models often rely on clinical and biochemical parameters alone, which may not fully capture individual variability in disease progression. The inclusion of ESR1 and eNOS3 polymorphisms provides additional insight into the molecular mechanisms underlying vascular dysfunction and atherosclerosis. Hormonal imbalance, particularly reduced estrogen levels, further contributes to endothelial impairment and inflammatory activation. The integration of these factors into a predictive model enhances its ability to identify patients at increased risk and supports the development of personalized management strategies. This approach aligns with the principles of precision medicine, which emphasize individualized care based on biological characteristics. However, the implementation of such models in clinical practice requires consideration of factors such as cost, accessibility of genetic testing, and the need for standardized protocols. Future research should focus on validating these findings in larger populations and refining the model to improve its clinical applicability. The integration of genetic, hormonal, and inflammatory factors into a unified predictive approach represents an important advancement in cardiovascular medicine. Traditional assessment tools, while useful, often fail to capture the complexity of disease mechanisms, particularly in populations with unique physiological characteristics such as postmenopausal women. Genetic polymorphisms affecting vascular regulation contribute to variability in disease susceptibility and therapeutic response, while hormonal deficiency and inflammatory activation further exacerbate vascular damage. By combining these elements, the predictive model offers a more comprehensive evaluation of patient status. This approach supports the transition toward personalized medicine, where treatment strategies are tailored according to individual biological profiles. Despite its advantages, several challenges must be considered, including the need for standardized testing methods, cost-effectiveness, and integration into routine clinical workflows. Continued research and technological development are essential for refining these models and ensuring their practical application in diverse healthcare settings.

5. Conclusion

The development of a predictive model incorporating genetic polymorphisms, hormonal status, and inflammatory markers represents a significant advancement in cardiovascular risk assessment for postmenopausal women with coronary heart disease. This integrated approach provides more accurate risk stratification and supports personalized therapeutic decision-making. The findings underscore the potential of combining molecular and clinical data to improve patient outcomes and reduce the burden of cardiovascular disease. Continued research and technological advancements will further enhance the effectiveness and accessibility of such predictive models in clinical practice. A predictive strategy that incorporates genetic variability, hormonal status, and inflammatory activity provides a more accurate assessment of cardiovascular risk in postmenopausal women. This comprehensive approach enhances early detection of high-risk individuals and facilitates the development of targeted therapeutic interventions. The findings highlight the potential of combining molecular and clinical data to improve outcomes and support the evolution of individualized cardiovascular care.

Indexed & Abstracted In

This journal is indexed and abstracted in the following international scientific databases.

Google Scholar

ISSN

ORCID

CiteFactor

ResearchBib

DOI

Zenodo

Crossref

Grammarly

Article Verification

Scan the QR code to verify the authenticity of this article

DOI: 10.4103/aams.0498