

## 1. Title Page

# Electro-Mechanical Risk Score for Coronary Artery Disease Risk Estimation Using Seismocardiography

Short Title: EMR Score for CAD Likelihood Estimation

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### Financial Disclosure Statement:

Dr. Parastoo Dehkordi and Dr. Farzad Khosrow-khavar are employees of HeartForce Medical Inc., the company developing the EMR Score. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

### Clinical Trial Registration:

ClinicalTrials.gov Identifiers: NCT06880120, NCT06880133

### Tweet Summary:

The EMR Score leverages seismocardiography and clinical data to estimate CAD risk non-invasively—enhancing early triage of both symptomatic and asymptomatic patients. #CAD #DigitalHealth #SCG

**Total Word Count:** 4900

*(Includes text, references, and figure legends)*

## 2. Abstract

### **Background:**

Coronary artery disease (CAD) remains a leading cause of morbidity and mortality worldwide. Existing pretest probability (PTP) models often lack specificity, leading to overuse of diagnostic testing. A noninvasive, data-driven alternative may enhance risk stratification.

### **Objectives:**

To evaluate the performance of the Electro-Mechanical Risk (EMR) Score—a machine learning model integrating seismocardiographic (SCG) features and clinical data—for estimating the likelihood of obstructive CAD.

### **Methods:**

This diagnostic study included 2,110 adults enrolled from multiple cardiology centers. Participants underwent SCG recording at rest using an accelerometer placed on the sternum. Obstructive CAD was defined as  $\geq 50\%$  stenosis on coronary computed tomography angiography or invasive coronary angiography. A one-dimensional convolutional neural network was trained on SCG-derived features, age, sex, cardiovascular risk factors, and chest pain symptoms to compute the EMR Score. Performance was compared with the 2024 ESC Risk Factor–weighted Clinical Likelihood (RF-CL) model.

### **Results:**

Among 2,110 participants (mean [SD] age, 57.8 [10.3] years; 801 women [38%]), 760 had obstructive CAD. In symptomatic individuals, the EMR Score achieved an AUC of 0.88 (95% CI, 0.85–0.88), outperforming RF-CL (AUC, 0.85; 95% CI, 0.83–0.86;  $P = .023$ ), with higher specificity (53% vs 35%) and comparable sensitivity (94% vs 97%). In asymptomatic participants, the AUC was 0.89 (95% CI, 0.86–0.92). The EMR Score identified 23% of the cohort as having a very low likelihood, with a CAD prevalence of only 2%.

### **Conclusions:**

The EMR Score provides a noninvasive and accurate method for estimating CAD pretest probability, improving risk stratification in symptomatic and asymptomatic patients.

**Clinical Trial Registration:** ClinicalTrials.gov (NCT06880120, NCT06880133)

### **3. Key Words**

Seismocardiography, neural networks, noninvasive diagnostics, coronary artery disease, cardiovascular risk factors

## **4. Abbreviations**

**1D CNN** – One-Dimensional Convolutional Neural Network

**AUC** – Area Under the Receiver Operating Characteristic Curve

**CAC** – Coronary Artery Calcium

**CAC-CT** – Coronary Artery Calcium Scoring by Computed Tomography

**CCTA** – Coronary Computed Tomography Angiography

**CWT** – Continuous Wavelet Transform

**ECG** – Electrocardiography

**EMR Score** – Electro-Mechanical Risk Score

**ESC** – European Society of Cardiology

**ICA** – Invasive Coronary Angiography

**NPV** – Negative Predictive Value

**PPV** – Positive Predictive Value

**PTP** – Pretest Probability

**RF-CL** – Risk-Factor-weighted Clinical Likelihood

**SCG** – Seismocardiography

## 5. Introduction

Coronary artery disease (CAD) remains a leading global cause of morbidity and mortality, affecting both symptomatic and asymptomatic individuals.<sup>1</sup> This persistent burden underscores the need for accessible, noninvasive, and cost-effective diagnostic tools to identify individuals at risk. Current diagnostic pathways often begin with guideline-directed pretest probability (PTP) estimates, based on age, sex, symptoms, and conventional cardiovascular risk factors such as smoking and hypertension.<sup>2-4</sup> While PTP models provide an initial framework for clinical decision-making, their limited specificity contributes to high false-positive rates and unnecessary downstream testing.

The 2019 European Society of Cardiology (ESC) guidelines introduced the ESC2019 PTP model, which addressed overestimation inherent in earlier methods such as the Diamond-Forrester algorithm.<sup>2</sup> Despite improved calibration, its clinical utility is hindered by low specificity. In a cohort of 15,411 patients, the ESC2019 model achieved a sensitivity of 97.6% for detecting obstructive CAD but a specificity of only 12.1%, resulting in a substantial number of false-positive classifications.<sup>5</sup>

To improve discrimination, the 2024 ESC guidelines proposed the Risk-Factor–weighted Clinical Likelihood (RF-CL) model, which integrates clinical risk factors alongside demographic and symptom data.<sup>3,5</sup> This approach enhances calibration and increases the proportion of individuals reclassified into the very low-likelihood ( $\leq 5\%$ ) category, a group that may safely forgo further testing. However, the model still leaves diagnostic uncertainty in the low-likelihood range ( $>5\%$ – $15\%$ ), often requiring adjunctive assessments such as coronary artery calcium (CAC) scoring or stress testing.

Addressing these challenges, seismocardiography (SCG) offers a novel, non-invasive approach to assessing cardiac function. SCG records subtle vibrations on the chest wall generated by cardiac motion during the cardiac cycle, providing detailed insights into cardiac mechanical activity. These vibrations, typically captured using a highly sensitive accelerometer, reflect the dorsoventral, head-to-foot, and lateral movements of the heart (Supplemental Figure 1 in the Supplemental Appendix).<sup>6</sup> Its portability and low cost make it especially suitable for diverse clinical environments.

SCG has been studied since the 1960s, initially to examine cardiac timing and variability.<sup>6,7</sup> Later research linked SCG waveforms to myocardial ischemia and coronary stenosis, including during balloon angioplasty and exercise stress testing.<sup>8,10</sup> Despite early promise, adoption was limited by inadequate signal processing capabilities and lack of integration into diagnostic workflows.

Recent advances in sensor design and machine learning have revived interest in SCG. Our prior studies demonstrated that applying machine learning to SCG signals yielded high diagnostic accuracy for detecting CAD, including models trained on rest and exercise recordings.<sup>11,12</sup> These findings support SCG's potential to enable noninvasive, data-driven CAD assessment.

To further expand its clinical utility, we developed the Electro-Mechanical Risk (EMR) Score, a predictive model that integrates SCG-derived features with clinical variables.<sup>13</sup> The EMR Score is designed to improve initial risk stratification by identifying patients who may safely avoid unnecessary diagnostic testing while still capturing those at high risk for obstructive CAD. Our preliminary study showed that the EMR Score outperformed the ESC2019 PTP model in specificity. In the present work, we validate the EMR Score in a larger, prospectively enrolled cohort and compare its diagnostic performance with the updated RF-CL model. We also refine SCG feature extraction, optimize the model architecture, and assess the EMR Score's utility in

asymptomatic individuals. Together, these advances aim to improve specificity and enhance CAD risk stratification through a scalable, noninvasive solution.

## **6. Methods**

### **Study Design and Participants**

This multicenter diagnostic study included 2,600 participants prospectively enrolled between 2019 and 2023 at regional hospitals in Qarshi and Tashkent, Uzbekistan. The study population comprised patients with suspected CAD and asymptomatic healthy volunteers. Ethical approval was obtained from the hospital ethics board (record no. 1-16-02-388-19), and all participants provided written informed consent. The trial protocol is shown in Supplement 1. The study adhered to the Declaration of Helsinki and Good Clinical Practice guidelines. This study followed the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) reporting guideline.

Patients with suspected CAD were referred for coronary computed tomography angiography (CCTA) or invasive coronary angiography (ICA). Coronary anatomy was documented using a standardized 15-segment model. Healthy controls underwent a structured screening protocol, including laboratory testing, electrocardiography (ECG), echocardiography, and coronary artery calcium (CAC) scoring.

For all participants, SCG and ECG signals were recorded simultaneously for 5 minutes in the supine position using a triaxial accelerometer–based device with a single-lead ECG configuration, placed on the sternum near the xiphoid process (CardioClin, HeartForce Medical Inc, Canada). SCG signals were captured in three orthogonal directions: dorsoventral,

head-to-foot, and lateral (x, y, z). Signals were sampled at 250 Hz with 16-bit resolution. Standardized acquisition protocols were applied across all study sites. Details of inclusion and exclusion criteria are provided in Supplemental Figure 2 in the Supplemental Appendix.

### **Electro-Mechanical Risk (EMR) Score Development and Validation**

The Electro-Mechanical Risk (EMR) Score was developed through a multi-step process involving signal preprocessing, feature extraction, and model training as illustrated in the Central Illustration. Seismocardiographic (SCG) signals were bandpass filtered (0.5 - 40 Hz), normalized, and transformed into time-frequency representations using a continuous wavelet transform. Cardiac cycles were segmented using Q-wave detection from simultaneously recorded ECG signals. Features were extracted from all three SCG axes (x, y, z), then averaged and flattened into fixed-length vectors. Additional preprocessing and segmentation details are provided in the Supplement.

These SCG-derived features, combined with clinical variables (age, sex, chest pain symptoms, and cardiovascular risk factors including smoking, hypertension, hyperlipidemia, diabetes, and family history), were used to train a one-dimensional convolutional neural network (1D CNN). Model development employed five-fold cross-validation. Network architecture and training parameters are detailed in Figure 1.

### **Comparator Models**

The EMR Score was benchmarked against the 2019 ESC Pretest Probability (PTP) model<sup>2</sup> and the 2024 Risk-Factor–weighted Clinical Likelihood (RF-CL) model. The ESC2019 PTP model uses age, sex, and symptom type, while the RF-CL model incorporates additional cardiovascular risk factors via logistic regression. Model scores were computed using tables published in the original guideline manuscripts.<sup>2,3</sup>

## **Assessment of CAD and CAD Severity**

In this study, *obstructive CAD* refers specifically to  $\geq 50\%$  epicardial diameter stenosis on either CCTA or ICA. Individuals without such lesions are defined as having *non-CAD*, meaning no coronary stenosis  $\geq 50\%$ . To avoid implying the absence of any atherosclerosis, we use the term *non-CAD* only to denote the absence of obstructive disease.

The Gensini Score was used to quantify angiographic CAD burden by assigning weighted values to coronary lesions based on the degree of luminal narrowing and lesion location.<sup>13</sup>

## **Statistical Analysis**

Continuous variables were summarized as mean (SD) or median (IQR) and compared using the Mann–Whitney U test. Categorical variables were compared using  $\chi^2$  or Fisher exact test. Effect sizes were reported using Cramér’s V and rank-biserial correlation, with thresholds of 0.1 (small), 0.3 (moderate), and 0.5 (large).

Model discrimination was assessed by the area under the receiver operating characteristic curve (AUC), and model comparisons were tested using DeLong’s test. Calibration was evaluated graphically and with calibration slope and intercept estimates. Net reclassification improvement (NRI) was calculated to assess reclassification accuracy, and decision curve analysis was used to estimate net clinical benefit.

A prespecified subgroup analysis was conducted in asymptomatic individuals using the EMR Score only, as guideline-based tools (ESC2019 and RF-CL) are not validated for this population. Metrics included AUC, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), with 95% confidence intervals obtained via bootstrapping.

All statistical analyses were conducted using Python version 3.10.13 (Python Software Foundation). A two-sided P value  $<.05$  was considered statistically significant.

## 7. Results

The final dataset included 2,110 participants: 1,350 without obstructive CAD and 760 with CAD confirmed by ICA or CCTA. Of these, 467 participants were asymptomatic at enrollment, and CAC-CT data were available for 1,097 individuals ( Supplemental Figure 2 in the Supplemental Appendix). Baseline characteristics of participants were summarized in Table 1.

### Group Differences by CAD Status

Significant clinical and imaging differences were observed between patients with and without CAD (Table 1). Typical chest pain and CAC = 0 were the most discriminative features (Cramér's  $V = 0.59$  and  $0.54$ , respectively; both  $p < 0.001$ ). Moderate associations were found for smoking ( $V = 0.35$ ), hypertension ( $V = 0.27$ ), and male sex ( $V = 0.28$ ). In contrast, dyslipidemia showed no significant group differences.

Age, which was included in the model, and ejection fraction, which was not, also differed significantly between groups, with rank-biserial correlation values of  $0.368$  and  $-0.42$ , respectively, indicating moderate associations in opposite directions—age tended to be higher in CAD patients, while ejection fraction was lower.

The EMR Score was significantly higher among CAD patients, with a mean of  $55.2$  ( $SD = 25.0$ ) compared to  $23.0$  ( $SD = 20.9$ ) in non-CAD participants ( $p < 0.01$ ), further supporting its ability to differentiate between disease states ( Supplemental Table 1 in the Supplement Appendix).

### Model Performance

Across the entire dataset, the EMR Score achieved an AUC of 0.90 (95% CI: 0.88–0.91) (Table 2). In symptomatic patients, the EMR Score outperformed the RF-CL model (AUC 0.88 vs. 0.85;  $p = 0.023$ ) and the ESC2019 PTP model (AUC 0.83;  $p < 0.001$ ) (Supplemental Figure 3.A in the Supplemental Appendix). Among asymptomatic patients, where RF-CL and ESC2019 are not applicable, the EMR Score maintained strong performance (AUC = 0.89; 95% CI: 0.86–0.92).

In symptomatic individuals, the EMR Score achieved a specificity of 53% with a sensitivity of 94%, compared to RF-CL's 35% specificity and 97% sensitivity.

In the asymptomatic group, the EMR Score correctly identified 15 of 19 CAD cases, yielding a sensitivity of 80%, specificity of 80%, and an NPV of 99% (Supplemental Table 2 in the Supplemental Appendix and Table 2).

A cutoff of 15% was used for the EMR Score, while 5% was used for the RF-CL and ESC2019 PTP models.

### **Risk Stratification by Likelihood Category**

Table 3 details the distribution of patients and CAD prevalence across clinical likelihood categories. The RF-CL model assigned most symptomatic patients to the low (35%) and moderate (44%) categories, with no classifications in the high or very high categories—both of which require additional testing under the 2024 ESC guidelines. Similarly, the ESC2019 PTP model concentrated patients in the moderate (55%) and low (27%) groups, with smaller proportions in the very low (12%) and high (6%) categories.

In contrast, the EMR Score demonstrated a more balanced distribution across risk categories. It classified 11% of patients into the very low-risk group (EMR Score  $\leq 5\%$ ), with a CAD

prevalence of only 4%, aligning with ESC criteria for deferring further testing. An additional 17% were categorized as low-risk, with an observed CAD prevalence of 11%. These distributions support the EMR Score's ability to streamline diagnostic pathways and reduce unnecessary testing (Figure 2, Supplemental Figure 5). Notably, none of the patients classified in the very low-risk group had severe CAD (Gensini  $\geq 40$ ), reinforcing the model's safety in ruling out clinically significant disease ( Supplemental Table 3 in Supplement 2). In contrast, the RF-CL model assigned 3 patients with severe CAD to the very low-risk category ( Supplemental Table 4 in Supplement 2).

### **Reclassification Performance**

Compared to the RF-CL model, the EMR Score improved reclassification performance, with a Net Reclassification Index (NRI) of +0.098. This improvement was driven by down-classification of non-CAD patients ( $\text{NRI}_{\text{non-CAD}} = +0.129$ ), while a modest net loss in reclassification occurred among CAD patients ( $\text{NRI}_{\text{CAD}} = -0.031$ ) ( Supplemental Figure 3.B in the Supplemental Appendix)

### **Association with CAD Severity and Coronary Calcification**

The EMR Score showed a strong positive correlation with the Gensini Score (Spearman  $\rho = 0.677$ ,  $p < 0.001$ ), indicating its ability to reflect both CAD presence and burden. Median EMR scores increased progressively with higher Gensini categories ( Supplemental Figure 5-6 in the Supplemental Appendix).

Similarly, EMR scores rose across increasing CAC score categories ( Supplemental Figure 7 in the Supplemental Appendix). A moderate correlation was observed between EMR and CAC

scores (Spearman  $\rho = 0.393$ ,  $p < 0.001$ ). A significant difference in EMR values was observed between those with CAC = 0 and those with higher scores ( $p = 0.001$ ), supporting its relevance as a non-invasive indicator of subclinical atherosclerosis.

## **8. Discussion**

The EMR Score offers a noninvasive, scalable method for estimating the likelihood of obstructive CAD by integrating seismocardiographic (SCG) features with conventional clinical risk factors. In this large, prospectively enrolled cohort, the model demonstrated strong discriminative performance in both symptomatic and asymptomatic individuals. Its ability to generate individualized likelihood estimates directly from cardiac mechanical activity represents an important step toward expanding pre-test probability assessment beyond traditional symptom-based frameworks.

A key strength of the EMR Score is its ability to distribute patients across the full spectrum of clinical likelihood categories. This balanced stratification enabled clear differentiation between very low-, low-, moderate-, high-, and very high-likelihood groups, with each showing consistent alignment with observed disease prevalence. Individuals classified as very low likelihood exhibited a CAD prevalence of only 2%, and none had severe disease, supporting the potential safety of avoiding additional imaging in this group. Conversely, patients assigned to high and very-high likelihood categories demonstrated high observed disease burden, indicating that EMR effectively concentrates risk at the upper end of the spectrum.

Compared with contemporary clinical models, EMR provides complementary insights derived from physiologic cardiac motion. The RF-CL model remains effective at identifying patients with very low clinical likelihood based on demographic and risk-factor information, whereas the

EMR Score incorporates mechanical signatures from SCG that reflect underlying disease burden and enhance separation across intermediate and higher likelihood categories. These differences highlight the distinct foundations of clinical and physiologic prediction approaches and underscore the value of integrating mechanical cardiac information into pre-test probability estimation.

Beyond likelihood estimation, the EMR Score correlated strongly with angiographic disease severity and showed a moderate association with coronary calcium burden. These findings indicate that SCG-derived mechanical features capture physiologic signals related to both obstructive disease and underlying atherosclerotic burden, even when measured at rest. The strong performance in asymptomatic individuals further supports this interpretation and suggests that physiologic deviations in cardiac motion may precede or complement symptom-based risk assessment.

Seismocardiography itself offers practical advantages: it is rapid, portable, radiation-free, and does not require contrast agents or specialized imaging systems. These characteristics make it particularly suited for settings where access to advanced cardiac imaging is limited or where efficient triage is needed. Incorporating SCG-derived information into a pre-test probability model provides clinicians with an additional, noninvasive tool to refine risk assessment and potentially reduce unnecessary diagnostic testing.

Several methodological considerations warrant acknowledgment. The study cohort included a substantial proportion of patients referred for invasive angiography, resulting in a higher prevalence of obstructive CAD than would be expected in typical CCTA-based populations and potentially introducing selection bias. In addition, CCTA interpretation and Gensini scoring were performed locally rather than by a centralized core laboratory, which may introduce

interobserver variability. Finally, patients with arrhythmias were excluded due to the need for stable cardiac cycles, and future work should investigate strategies for incorporating irregular rhythms.

Overall, these findings support the EMR Score as a physiologically grounded, noninvasive method for estimating pre-test probability of obstructive CAD. By leveraging mechanical cardiac information together with clinical risk factors, the EMR Score provides individualized risk estimates that may support more efficient decision-making, broaden accessibility to early risk evaluation, and optimize resource utilization. Future studies should evaluate its integration into clinical workflows across diverse healthcare environments and assess its impact on patient management and downstream testing.

## **Conclusion**

The EMR Score improves CAD risk stratification by combining SCG features with clinical risk factors, offering improved specificity and more balanced classification across risk categories compared with established models. It performs well in both symptomatic and asymptomatic populations and supports more personalized, efficient diagnostic pathways. Future research should explore its integration into routine workflows and evaluate its effects on clinical outcomes, resource utilization, and patient care.

## **Acknowledgment**

Parastoo Dehkordi and Farzad Khosrow-Khavar are employees of HeartForce Medical Inc., which develops the CardioClin device used in this study. No other disclosures were reported.

The authors used ChatGPT (OpenAI) to assist in revising and editing the manuscript for clarity and grammar. All content was reviewed and verified by the authors to ensure accuracy and integrity.

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## Figure Titles and Legends

### **Figure 1. Architecture of the EMR Model Combining SCG Features and Clinical Data**

Diagram of the 1D convolutional neural network (CNN) integrating SCG-derived time-frequency features with clinical risk factors to estimate the EMR Score.

**Abbreviations:** EMR, electro-mechanical risk; SCG, seismocardiography; CNN, convolutional neural network.

### **Figure 2. Distribution of Patients and Observed CAD Prevalence by Risk Category**

Bar plots show the number of patients classified into each predicted risk category by the ESC2019 PTP model, the RF-CL model, and the EMR Score. Risk categories are color-coded based on ESC guidelines: very low (blue), low (green), moderate (yellow), high (orange), and very high (red). Dashed lines represent observed CAD prevalence in each group, indicating the alignment (or mismatch) between estimated risk and actual disease burden.

**Abbreviations:** CAD, coronary artery disease; EMR, electro-mechanical risk; ESC, European Society of Cardiology; PTP, pretest probability; RF-CL, risk factor-weighted clinical likelihood.

### **Central Illustration. Overview of the Electro-Mechanical Risk (EMR) Score**

The Electro-Mechanical Risk (EMR) Score integrates seismocardiographic (SCG) features and clinical risk factors into a one-dimensional convolutional neural network (1D CNN) to estimate the likelihood of obstructive coronary artery disease (CAD). The EMR Score outperformed pretest probability models from the 2019 and 2024 European Society of Cardiology guidelines (ESC2019 PTP and RF-CL), demonstrating higher specificity and extending applicability to asymptomatic individuals. Metrics reflect the prediction of obstructive CAD ( $\geq 50\%$  stenosis).

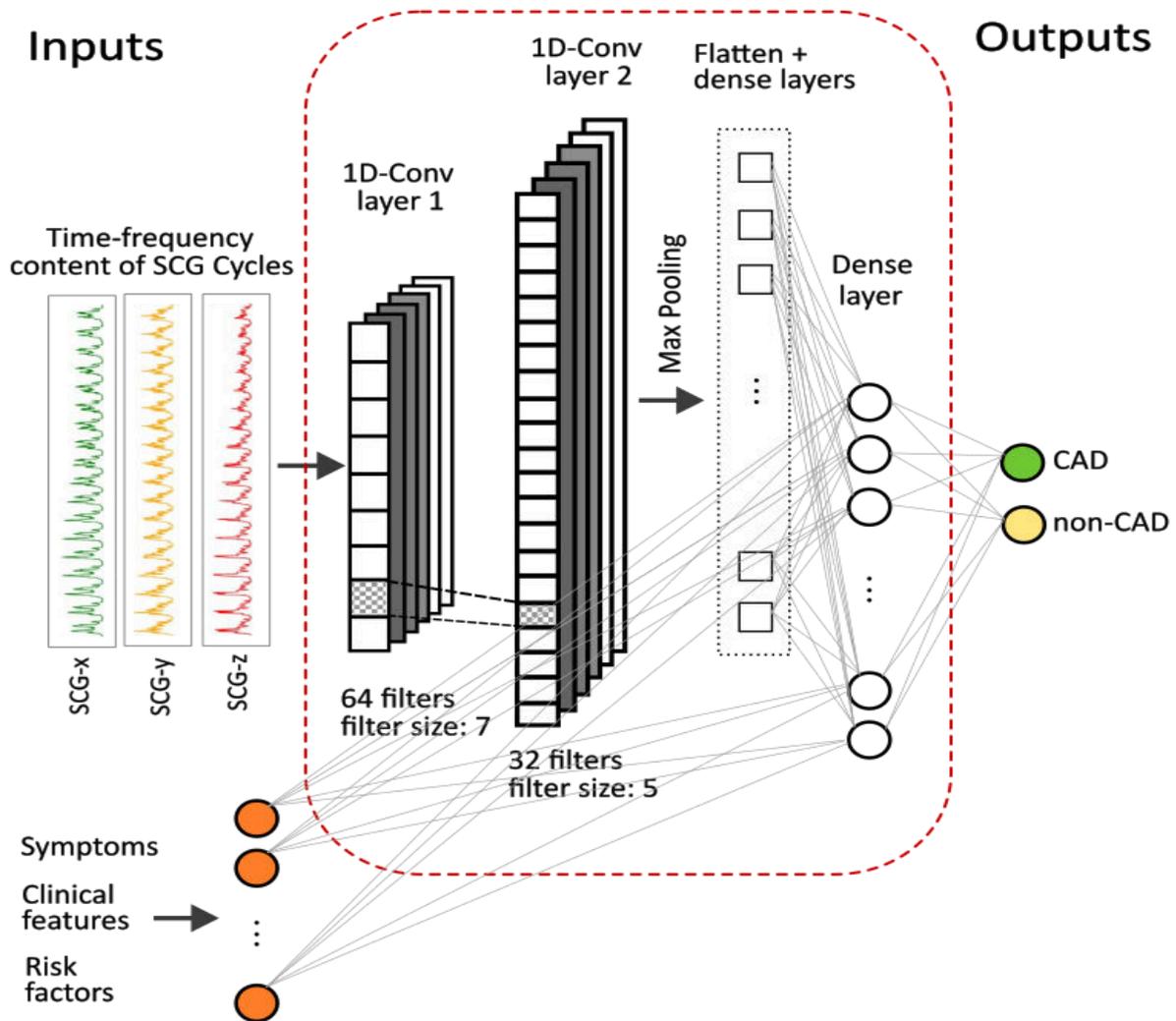
**Abbreviations:** AUC, area under the curve; CAD, coronary artery disease; CNN, convolutional neural network; EMR, electro-mechanical risk; ESC, European Society of Cardiology; NPV, negative predictive value; PPV, positive predictive value; PTP, pretest probability; RF-CL, risk factor-weighted clinical likelihood; SCG, seismocardiography.

# Figures

**Figure 1. Architecture of the EMR Model Combining SCG Features and Clinical Data**

Diagram of the 1D convolutional neural network (CNN) integrating SCG-derived time-frequency features with clinical risk factors to estimate the EMR Score.

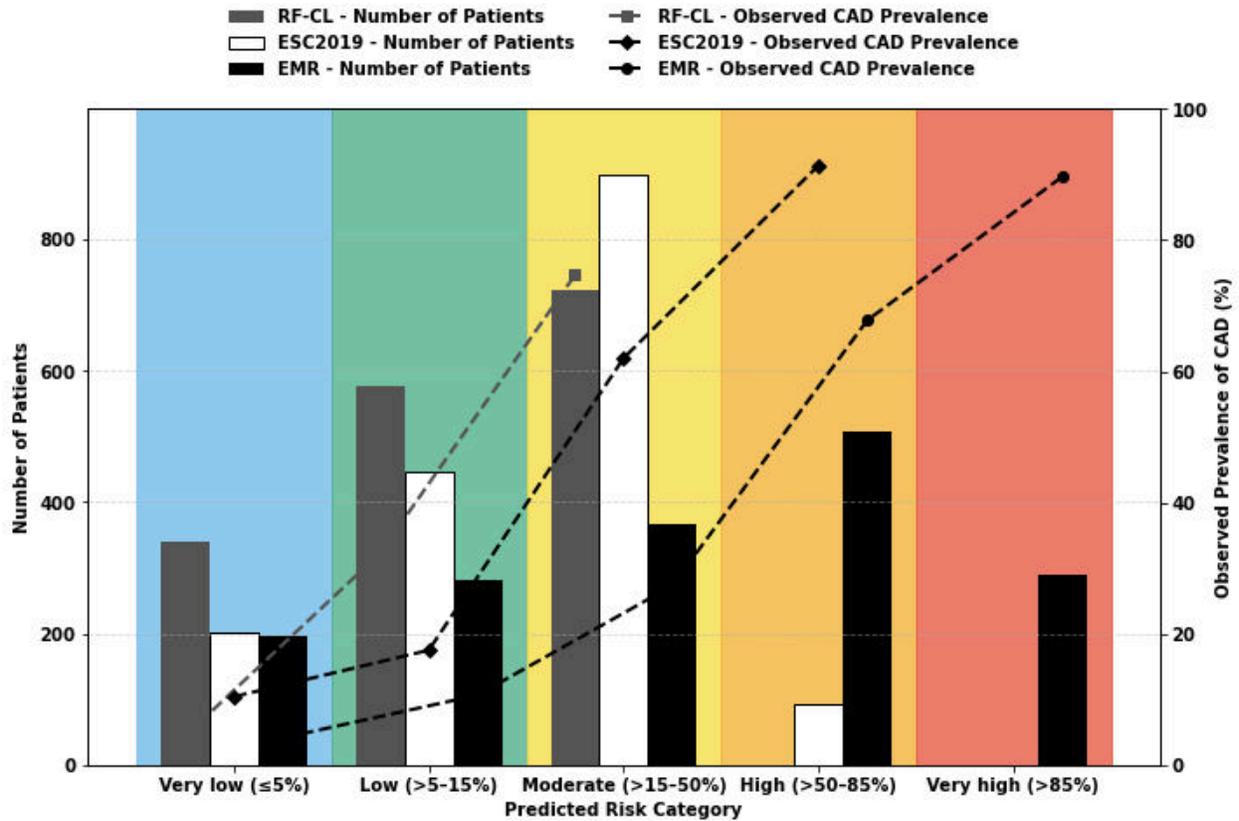
Abbreviations: EMR, electro-mechanical risk; SCG, seismocardiography; CNN, convolutional neural network.



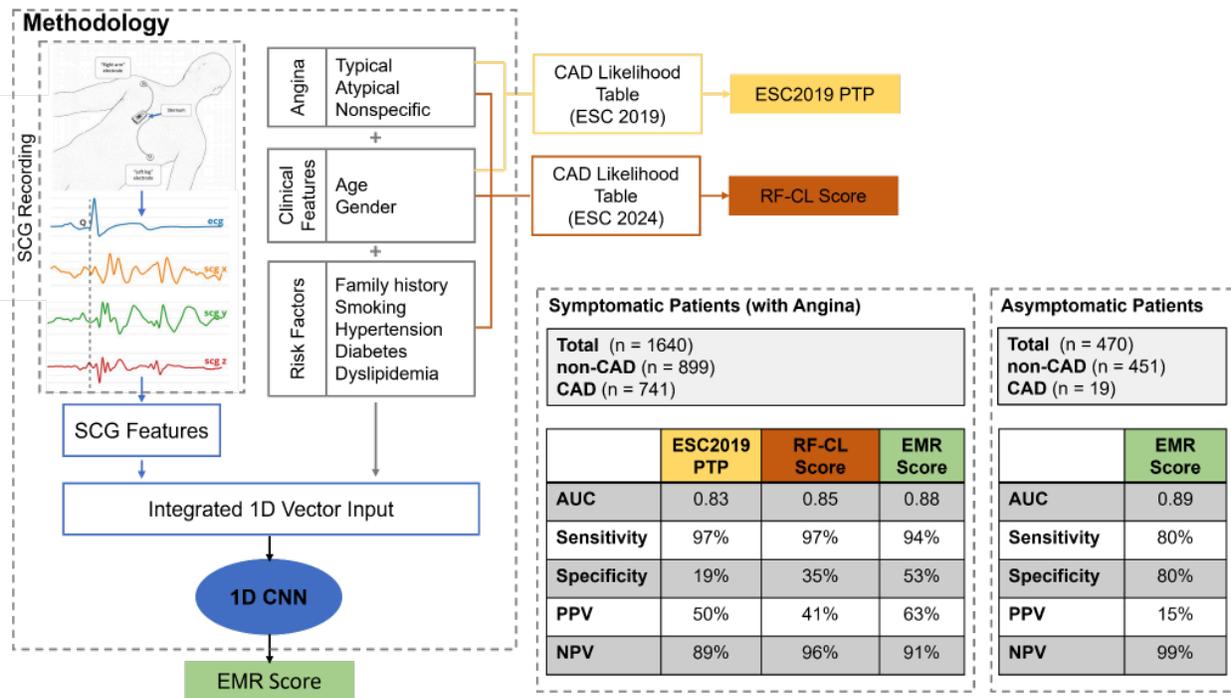
**Figure 2. Distribution of Patients and Observed CAD Prevalence Across Predicted Risk Categories**

Bar plots showing patient counts across ESC2019, RF-CL, and EMR-predicted risk categories. Dashed lines indicate observed CAD prevalence. Risk categories correspond to ESC-defined thresholds: very low (blue), low (green), moderate (yellow), high (orange), and very high (red).

Abbreviations: CAD, coronary artery disease; EMR, electro-mechanical risk; ESC, European Society of Cardiology; RF-CL, risk factor-weighted clinical likelihood.



# Central Illustrations



**Overview:** The Electro-Mechanical Risk (EMR) Score integrates seismocardiographic (SCG) features and clinical risk factor data into a one-dimensional convolutional neural network (1D CNN) to estimate the likelihood of obstructive coronary artery disease (CAD). The EMR Score outperformed pretest probability models from the 2019 and 2024 European Society of Cardiology guidelines (ESC2019 PTP, RF-CL Score), demonstrating improved specificity and extending applicability to asymptomatic patients.

AUC indicates area under the receiver operating characteristic curve; CAD, coronary artery disease; PPV, positive predictive value; NPV, negative predictive value. Metrics reflect the prediction of obstructive CAD ( $\geq 50\%$  stenosis).

## Tables

**Table 1. Clinical and Demographic Characteristics by CAD Status**

Comparison of clinical variables, cardiac function, symptoms, and coronary artery calcium (CAC) categories between participants with and without obstructive CAD  
 Abbreviations: CAD, coronary artery disease; CAC, coronary artery calcium. Tests include  $\chi^2$  for categorical and Mann–Whitney U for continuous variables. Effect sizes are shown as Cramér’s V or rank-biserial r.

	non-CAD	CAD	p-value	Effective size
Coronary artery disease				
Number of patients, No. (%)	1350 (64%)	760 (36%)	NA	NA
Characteristics				
Sex, No. (%)				
-Male	592 (52%)	551 (48%)	< 0.001	0.275
-Female	758 (78%)	209 (22%)		
Age, mean (SD), year	55.17(11.09)	61.78(44)	< 0.001	0.368
Risk factors and symptoms				
Family History of early CAD, No. (%)				
-Yes	370 (56%)	285 (44%)	< 0.001	0.103
-No	980 (67%)	475 (33%)		
Smoking, No. (%)				
-Yes	166 (34%)	326 (66%)	< 0.001	0.346
-No	1184 (73%)	434 (27%)		
Dyslipidemia, No. (%)				
-Yes	669 (66%)	347 (34%)	0.0909	0.037
-No	681 (62%)	413 (35%)		
Hypertension, No. (%)				
-Yes	944 (57%)	706 (43%)	< 0.001	0.265
-No	406 (88%)	54 (12%)		

**Table 1. Clinical and Demographic Characteristics by CAD Status- Continued**

	<b>non-CAD</b>	<b>CAD</b>	<b>p-value</b>	<b>Effective size</b>
Diabetes, No. (%)				
-Yes	109 (45%)	135 (55%)	< 0.001	0.144
-No	1241 (66%)	625 (32%)		
Ejection Fraction, mean (SD), %	59.51 ± 5.79	53.78 ± 9.48	< 0.001	-0.420
<b>Cardiac symptoms at referral</b>				
- Typical chest pain, No. (%)	350 (35%)	662 (65%)	< 0.001	0.587
- Atypical chest pain, No. (%)	225 (84%)	42 (16%)	< 0.001	0.16
- Non-angina chest pain, No. (%)	323 (90%)	37 (10%)	< 0.001	0.247
- Asymptomatic, No. (%)	452 (96%)	19 (4%)	< 0.001	0.356
<b>Coronary Artery Calcium Score (CACs) (n = 1096)</b>				
0 (n = 868), No. (%)	826 (95%)	42 (5%)	< 0.001	0.542
1-10 (n = 41), No. (%)	34 (83%)	7 (17%)	0.0169	0.052
11-100 (n = 90), No. (%)	62 (69%)	28 (31%)	0.3776	0.019
101-400 (n = 62), No. (%)	27 (44%)	35 (56%)	0.0011	0.071
> 400 (n = 35), No. (%)	13 (37%)	22 (63%)	0.0016	0.069

**Table 2. Diagnostic Performance of ESC2019, RF-CL, and EMR Score Models**

Performance metrics for each model including AUC, sensitivity, specificity, PPV, and NPV for detecting obstructive CAD. The cutoff values used were 5% for the ESC2019 PTP and RF-CL models and 15% for the EMR score.

Abbreviations: AUC, area under the curve; CAD, coronary artery disease; EMR, electro-mechanical risk; ESC2019 PTP, European Society of Cardiology 2019 pretest probability; RF-CL, risk factor–weighted clinical likelihood; PPV, positive predictive value; NPV, negative predictive value.

	No.	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
<b>ESC2019 PTP (symptomatic patients)</b>	1640	0.83 (0.81-0.85)	97% (96%-98%)	19% (17%-22%)	50% (49%-51%)	89% (84%-93%)
<b>RF-CL (symptomatic patients)</b>	1640	0.85 (0.83-0.86)	97% (96%-98%)	35% (32%-39%)	41% (55%-57%)	96% (93%-97%)
<b>EMR Score (symptomatic patients)</b>	1640	0.88 (0.85-0.89)	94% (92%-95%)	53% (50%-57%)	63% (61%-64%)	91% (89%-93%)
<b>EMR Score (symptomatic + asymptomatic patients)</b>	2110	0.90 (0.88- 0.91)	94% (90%-95%)	66% (64%-69%)	58% (57%-60%)	95% (93%-96%)
<b>EMR Score (asymptomatic patients)</b>	470	0.89 (0.86-0.92)	80% (65%-94%)	80% (77%-84%)	15% (12%-19%)	99% (97%-100%)

**Table 3. Distribution of Risk Categories and CAD Prevalence Across Prediction Models**

Risk category assignments and corresponding CAD prevalence for ESC2019 PTP, RF-CL, and EMR models in symptomatic and asymptomatic participants. Values are the number of patients in each likelihood category (percentage of total), followed by CAD prevalence in that group.

Abbreviations: CAD, coronary artery disease; EMR, electro-mechanical risk; ESC2019 PTP, 2019 ESC pretest probability model; RF-CL, risk factor–weighted clinical likelihood.

	<b>Very low (≤5%)</b>	<b>low (&gt;5%-15%)</b>	<b>moderate (&gt;15%-50%)</b>	<b>high (&gt;50%-85%)</b>	<b>very high (&gt; 85%)</b>
<b>ESC2019 PTP (symptomatic patients)</b>	198 (12%) 10% CAD	450 (27%) 17% CAD	898 (55%) 62% CAD	94 (6%) 91% CAD	0 (0%) 0% CAD
<b>RF-CL (symptomatic patients)</b>	337 (20%) 4% CAD	579 (35%) 32% CAD	724 (44%) 75% CAD	0 (0%) 0% CAD	0 (0%) 0% CAD
<b>EMR Score (symptomatic patients)</b>	193 (11%) 4% CAD	283 (17%) 11% CAD	367 (22%) 27% CAD	505 (31%) 68% CAD	292 (18%) 90% CAD
<b>EMR Score (symptomatic + asymptomatic patients)</b>	492 (23%) 2% CAD	391 (18%) 38 CAD	426 (20%) 26% CAD	509 (24%) 67% CAD	292 (14%) 90% CAD
<b>EMR Score (asymptomatic patients)</b>	299 (64%) 0% CAD	108 (23%) 8 CAD	59 (12%) 17% CAD	4 (1%) 25% CAD	0 (0%) 0% CAD