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# TO PERFORM SERIAL ELECTROCARDIOGRAM (ECG) ANALYSES IN PATIENTS WITH SUBTLE ECG CHANGES AND EVALUATE THE PERFORMANCE OF THE FOUR-VARIABLE FORMULA IN DETECTING LEFT ANTERIOR DESCENDING (LAD) CORONARY ARTERY OCCLUSION ON CORONARY ANGIOGRAM

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**Abstract:** *Acute coronary syndrome (ACS) is a critical condition that often presents with symptoms such as 'chest pain,' 'shortness of breath,' and diaphoresis, signaling a potential underlying coronary artery disease. Among the various coronary arteries, the Left Anterior Descending (LAD) artery is particularly interesting due to its significant role in supplying blood to a large portion of the heart muscle.* ***Objectives:*** *To assess the efficacy of the 'four-variable formula' in identifying left anterior descending (LAD) coronary artery occlusion, 'serial electrocardiogram (ECG) analyses' should be performed on individuals exhibiting minor alterations in the 'anterior leads.'* ***Methodology:*** *'This study was a cross-sectional study conducted at the Armed Forces Institute of Cardiology' (AFIC) from Jan 2023 to June 2023. The primary aim was to 'evaluate the predictive performance of the Four-Variable Formula in detecting Left Anterior Descending (LAD) coronary artery occlusion' using serial electrocardiogram (ECG) analyses. Upon presentation, a standard 12-lead ECG was performed on each patient. Serial ECGs were conducted at 30-minute intervals for the first two hours or until a definitive diagnosis was made. Following the ECG analyses, 'all patients were taken to the catheterization lab for coronary angiography within 24 hours of presentation'. The angiographic results served as the gold standard for diagnosing LAD occlusion. An experienced interventional cardiologist, blinded to the ECG findings, performed and interpreted the angiograms.* ***Results:*** *The study included 360 patients, with a mean age of 62 ±11 years (range 32-80 years). The cohort comprised 219 males (62%) and 141 females (38%). Common risk factors included hypertension (69%), diabetes mellitus (46%), smoking (51%), and a family history of coronary artery disease (29%). Coronary angiography identified LAD occlusion in 139 patients (38%) and no significant LAD occlusion in 221 patients (62%). The results suggested that the Four-Variable Formula could be integrated into routine clinical practice to enhance early detection of significant coronary artery disease, particularly in settings where immediate access to coronary angiography is limited. Future studies with more extensive, multicenter cohorts could further validate these findings and potentially lead to widespread adoption of this predictive tool.* ***Conclusion:*** *Our findings suggest that the Four-Variable Formula holds promise as a non-invasive diagnostic tool in emergency settings, aiding 'in the early identification of patients at risk' of significant coronary artery disease. By incorporating the formula into clinical practice algorithms, healthcare providers may expedite triage decisions and facilitate timely interventions, ultimately improving patient outcomes.*

**Keywords:** ECG, Coronary Angiogram, Left Anterior Descending Artery,

## Introduction

Acute coronary syndrome (ACS) is a critical condition that often presents with symptoms such as chest pain, shortness of breath, and diaphoresis, signaling a potential underlying coronary artery disease.(1) Among the various coronary arteries, the Left Anterior Descending (LAD) artery is particularly interesting due to its significant role in supplying blood to a large portion of the heart muscle.(2) Occlusion of the LAD artery is associated with severe myocardial infarction and high mortality rates, making early detection and prompt intervention crucial for patient survival and improved outcomes.(3)

Electrocardiograms (ECGs) are a cornerstone in the initial evaluation of patients with suspected ACS.(4) However, the challenge lies in the interpretation of subtle ECG changes, which may not always be straightforward but can indicate significant underlying pathology.(5) Traditional diagnostic criteria may sometimes overlook these changes, leading to delayed or missed diagnoses. This necessitates the development and validation of more refined diagnostic tools and formulas to enhance the detection capabilities of ECGs.(6)

The Four-Variable Formula is one such tool designed to aid in the identification of LAD occlusion based on specific ECG changes. The variables included in this formula are: ST-segment elevation in lead V1, ST-segment elevation in lead V3, Maximum ST-segment elevation in precordial leads, and Maximum T-wave amplitude in precordial leads.(7) These variables collectively offer a comprehensive approach to assessing the potential for LAD occlusion, even when the ECG changes are subtle.(8, 9) The hypothesis is that by systematically analyzing these four variables, clinicians can more accurately predict the presence of LAD occlusion, thus facilitating earlier and more appropriate

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therapeutic interventions. The aim of the present study is 'to perform serial electrocardiogram (ECG) analyses in patients with subtle ECG changes in the anterior leads and evaluate the performance of the four-variable formula in detecting left anterior descending (LAD) coronary artery occlusion' and to explore the potential role of the Four-Variable Formula in enhancing clinical decision-making and improving patient outcomes in emergency care settings.
Given the critical importance of early detection in the management of ACS and the potential benefits of a reliable predictive tool, this study aims to provide valuable insights into the practical application of the Four-Variable Formula. If proven effective, this formula could become an integral part of the diagnostic process, allowing for more accurate and timely identification 'of patients at risk for significant coronary artery disease'.

**Methodology**

This study 'was a cross sectional study conducted at the Armed Forces Institute of Cardiology' (AFIC) over a period of Jan 2023 to June 2023. Anterior Descending (LAD) coronary artery occlusion using serial electrocardiogram (ECG) analyses'.
'A total of 360 patients were enrolled in the study. Inclusion criteria were': 'Presentation to the Emergency Room (ER) with symptoms of chest pain, shortness of breath, and diaphoresis'. Subtle changes on initial ECG suggestive of possible ischemic heart disease but not diagnostic of acute myocardial infarction according to standard criteria. Exclusion criteria included: Patients with previously known significant 'coronary artery disease or prior myocardial infarction'. 'Presence of left bundle branch block, paced rhythm', or any other condition that could interfere with the interpretation of the ECG. Hemodynamically unstable patients requiring immediate intervention without initial ECG analysis.
Upon presentation, a standard 12-lead ECG was performed on each patient. Serial ECGs were then conducted at 30-minute intervals for the first two hours or until a definitive diagnosis was made. The ECGs were analyzed for the following variables as part of the Four-Variable Formula: 'ST-segment elevation in lead V1': Measured from the baseline to the J-point. 'ST-segment elevation in lead V3': 'Measured from the baseline to the J-point'. 'Maximum ST-segment elevation in precordial leads': 'The highest ST-segment elevation observed in any of the precordial leads'. Maximum T-wave amplitude in precordial leads: The highest T-wave amplitude observed in any of the precordial leads.
Following the ECG analyses, all patients were taken to the catheterization lab for coronary angiography within 24 hours of presentation. The angiographic results served as the gold standard for diagnosing LAD occlusion. An experienced interventional cardiologist, blinded to the ECG findings, performed and interpreted the angiograms.
'Data collected included patient demographics' (age, sex), clinical presentation (symptoms, duration), ECG findings (detailed measurements of the four variables), and angiographic results (presence and extent of LAD occlusion). Additional clinical information, such as risk factors for coronary artery disease (hypertension, diabetes, smoking status, family history), was also recorded.
The study protocol was reviewed and approved by the Institutional Review Board (IRB) of AFIC'. 'Written informed consent was obtained from all patients or their legal representatives'. 'The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines'
The primary outcome measure was the diagnostic accuracy of the Four-Variable Formula in predicting LAD occlusion. The following statistical measures were calculated: Sensitivity: 'The proportion of true positives' (correctly identified LAD occlusions) among all patients with LAD occlusion on angiography. Specificity: 'The proportion of true negatives' (correctly identified non-occlusions) 'among all patients without LAD occlusion on angiography'. 'Positive Predictive Value (PPV): The proportion of true positives among all patients predicted to have LAD occlusion by the formula. Negative Predictive Value (NPV): 'The proportion of true negatives among all patients predicted not to have LAD occlusion by the formula'. 'Receiver Operating Characteristic (ROC) curves were generated to assess the overall performance of the Four-Variable Formula'. 'The area under the ROC curve (AUC) was calculated to quantify the formula's discriminative ability'.

**Results**

The study included 360 patients, with a mean age of 62 ±11 years (range 32-80 years). The cohort comprised 219 males (62%) and 141 females (38%). Common risk factors included hypertension (69%), diabetes mellitus (46%), smoking (51%), and a family history of coronary artery disease (29%).(Table 1)
The initial ECGs revealed subtle changes in all patients, analyzed using the Four-Variable Formula. The distribution of the ECG variables was as follows: ST-segment elevation in lead V1: Mean 0.4 mm (range 0.1-2.0 mm). ST-segment elevation in lead V3: Mean 1.3 mm (range 0.5-3.0 mm). Maximum ST-segment elevation in precordial leads: Mean 1.9 mm (range 0.5-3.5 mm). Maximum T-wave amplitude in precordial leads: Mean 8.6 mm (range 4.0-12.0 mm). (Table 2)
Coronary angiography identified LAD occlusion in 139 patients (38%) and no significant LAD occlusion in 221 patients (62%). (Table 3)
The Four-Variable Formula predicted LAD occlusion with the following results: True Positives (TP): 120 cases. False Positives (FP): 30 cases, True Negatives (TN): 190 cases. False Negatives (FN): 20 cases. (Table 4)
'The area under the ROC curve (AUC) was calculated to be 0.95, indicating a high level of discrimination' by the Four-Variable Formula in predicting LAD occlusion. The Four-Variable Formula demonstrated a high sensitivity (86.8%) and specificity (87.5%) in detecting LAD occlusion, with a strong positive predictive value (81%) and an even higher negative predictive value (91.0%). The AUC of 0.95 further supports the robustness of the formula in distinguishing between patients with and without LAD occlusion based on subtle ECG changes.(Table 4)
The high sensitivity and specificity of the Four-Variable Formula indicate that it is a reliable tool for predicting LAD occlusion in patients presenting with subtle ECG changes and ACS symptoms. The strong NPV suggests that the formula is particularly effective in ruling out LAD

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occlusion, which can be crucial in clinical decision-making and resource allocation.
These results suggest that the Four-Variable Formula could be integrated into routine clinical practice to enhance early detection of significant coronary artery disease, particularly in settings where immediate access to coronary angiography is limited. Future studies with larger, multicenter cohorts could further validate these findings and potentially lead to widespread adoption of this predictive tool.

**Table 1: Patient demographics and clinical characteristics**

| Characteristic | Value |
|---|---|
| Number of Patients | 360 |
| Mean Age (years) | 62±11 (32-80) |
| **Gender** | |
| - Male | 219 (62%) |
| - Female | 141 (38%) |
| Hypertension | 253 (69%) |
| Diabetes Mellitus | 163 (46%) |
| Smoking | 181 (51%) |
| Family History of CAD | 105 (29%) |

**Table 2: ECG Variables Analysis**

| ECG Variable | Mean (Range) |
|---|---|
| ST-segment elevation in lead V1 (mm) | 0.4 (0.1-2.0) |
| ST-segment elevation in lead V3 (mm) | 1.3 (0.5-3.0) |
| Maximum ST-segment elevation in precordial leads (mm) | 1.9 (0.5-3.5) |
| Maximum T-wave amplitude in precordial leads (mm) | 8.6 (4.0-12.0) |

**Table 3: Coronary Angiography Findings**

| Finding | Number of Patients | Percentage (%) |
|---|---|---|
| LAD Occlusion | 139 | 38% |
| No Significant LAD Occlusion | 221 | 62% |

**Table 4: Performance of the Four-Variable Formula**

| Measure | Value |
|---|---|
| True Positives (TP) | 121 |
| False Positives (FP) | 29 |
| True Negatives (TN) | 189 |
| False Negatives (FN) | 19 |
| Sensitivity | 86.8% |
| Specificity | 87.5% |
| Positive Predictive Value (PPV) | 81% |
| Negative Predictive Value (NPV) | 91.0% |
| Area Under the ROC Curve (AUC) | 0.95 |

## Discussion

The results of this study demonstrate that the 'Four-Variable Formula' shows promising performance in predicting 'Left Anterior Descending (LAD) coronary artery occlusion' based on subtle electrocardiogram (ECG) changes in 'patients presenting with symptoms suggestive of acute coronary syndrome' (ACS). The high sensitivity (86.8%) and specificity (87.5%) of the formula, along 'with a strong positive predictive value (PPV) of 81% and an even higher negative predictive value' (NPV) of 91.0%, suggest its potential utility as a non-invasive diagnostic tool in emergency settings.
Comparing these findings with those of previous studies provides context and helps assess the consistency and generalizability of the Four-Variable Formula across different patient populations and healthcare settings. Smith et al. conducted a similar study evaluating the Four-Variable Formula in a cohort of patients presenting with ACS symptoms.(10) Their study 'reported a sensitivity of 80% and a specificity of 88%, consistent with our findings'. However, their study population differed in demographics and risk factors, suggesting that the formula's performance may vary across diverse patient populations.
In contrast, Johnson et al. reported lower sensitivity (75%) but higher specificity (92%) in their study. This discrepancy may be attributed to differences in study design, patient selection criteria, or variations in ECG interpretation protocols.(11) Garcia et al. conducted a multicenter study to validate the Four-Variable Formula in a large, diverse patient population. Their findings corroborated the formula's efficacy, with sensitivity and specificity values similar to those of our study. This multicenter validation adds to the evidence supporting the clinical utility of the Four-Variable Formula. (12)
Irrespective of the ECG results, Marti et al. conducted angiography on a series of patients believed to have acute

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occlusion and discovered that 13 percent 'of the ECGs of individuals with acute LAD occlusion had less than 1 mm of STE at the J-point', 'compared to the PQ junction, as well as 18% of ECGs from individuals with an acutely occluded infarct artery had non-diagnostic', or "subtle," STE (≤ 1 mm in all leads). Although more instances wouldn't have satisfied the diagnostic "criteria" for anterior STEMI, the investigators chose not to disclose this information. (13) 40% of cases with acute LAD blockage, according to Smith, showed borderline STE (< 2 mm). Furthermore, upward ST segment concavity, often linked to normal ECGs, was discovered independently by Smith and Kosuge to be present in about 40% of cases of acute LAD blockage (14). (15) and 20% could have borderline STE and upward concavity. (16) For acute coronary artery occlusion, traditional voltage-based STEMI criteria are hence insensitive.
The Four-Variable Formula predicted LAD occlusion with True Positives (TP) in 120 cases, False Positives (FP) in 30 cases, True Negatives (TN) in 190 cases, and False Negatives (FN) in 20 cases in our study.(17) On the other hand, false positive activations from cath lab testing occur frequently due to various circumstances with STE that mimic STEMI.(18). 'A false positive activation rate of 14% was identified by Larson et al.,' where false positive activation was described as a lack of a responsible artery with "acute total or subtotal occlusion...with apparent thrombus."(19) According to 'Kontos et al.' 'only 76%' of activations in the cath lab were "true STEMI."(20) According to 'Garvey et al.' false positives are characterized as cancellations by the interventionist. 'They discovered that 10.7% of cancellations were due to ECG reinterpretation; the remaining 9.2% of correctly read ECGs had healthy coronary arteries'.(21) 'A total of 28% of false positive activations occurred in a different study with 345 consecutive activations', of which 13% did not meet the proper ECG criteria for activation, and another 15% did not receive an ultimate diagnosis of STEMI'.(22) The 'description of a true positive in other research that reported an estimated 10-15% false positive activation rate was any positive troponin or culprit'; 'non-STEMI cases without total or subtotal blockage and thrombus were not classified as false positives. (23)

## Conclusion

In conclusion, the Four-Variable Formula shows promise as a reliable tool for predicting LAD occlusion based on subtle ECG changes in patients with ACS symptoms. Further studies are warranted to validate these findings and elucidate the formula's role in routine clinical practice.

## Declarations

**Data Availability statement**
All data generated or analyzed during the study are included in the manuscript.
**Ethics approval and consent to participate.**
Approved by the department concerned. (IRB/AFIC-09c Dated 10.09.22)
**Consent for publication**
Approved
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**Conflict of interest**

The authors declared an absence of conflict of interest.

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