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Risk Factor–Weighted Clinical Probability for Predicting Obstructive Coronary Artery Disease in Patients Presenting with Unstable Angina

Gio Justisia Batubara [1*], Refli Hasan [1], Ali Nafiah Nasution [1], Harris Hasan [1], Anggia Chairuddin Lubis [1], Cut Aryfa Andra [1]

[1] *Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia*

***Corresponding Author**: Gio Justisia Batubara, E-mail: giojustisia@gmail.com

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ABSTRACT

Introduction: Determining the optimal invasive strategy for patients with unstable angina remains challenging, often resulting in unnecessary coronary angiography. Existing risk scores, including the GRACE and TIMI scores, were not designed to predict obstructive coronary artery disease. This study evaluated the predictive performance of a risk factor–weighted clinical likelihood model.

Methods: This retrospective analytical cohort study included 150 patients with low-to intermediate-risk unstable angina who underwent coronary angiography at a tertiary hospital. Predictive accuracy was assessed using receiver operating characteristic analysis and compared with the Diamond Forrester, Fladseth, guideline-based criteria, GRACE, and TIMI scores. Obstructive disease was defined as significant stenosis or physiologically relevant lesions.

Results: The prevalence of obstructive coronary disease was 60%. The model demonstrated superior discrimination, with an area under the curve of 0.885, which exceeded that of the comparator models. At a threshold score, 42.7% of angiographies were safely deferred, with a negative predictive value of 76.6%. Calibration improved after model adjustment.

Conclusion: The risk factor–weighted clinical likelihood model provides a robust prediction of obstructive coronary artery disease in patients with unstable angina. This may support objective decision-making and enable a more selective invasive strategy, thereby reducing unnecessary procedures while maintaining diagnostic safety.

Keywords

Coronary Angiography, Obstructive Coronary Artery Disease, Pre-Test Probability, Risk Factor-Weighted Clinical Likelihood, Unstable Angina, Diagnostic Accuracy

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INTRODUCTION

Unstable angina (UA), a clinical subset of non-ST-elevation acute coronary syndrome, has become increasingly challenging to define in the era of high-sensitivity cardiac troponin assays. Patients previously classified as having UA are now frequently reclassified as having non-ST-elevation myocardial infarction, resulting in a smaller yet more heterogeneous clinical population. Consequently, diagnostic uncertainty persists, particularly among patients without high-risk or very-high-risk features who nevertheless present with symptoms suggestive of ongoing myocardial ischemia [1-4]. Contemporary data from Indonesia further indicate that UA and non-ST-elevation acute coronary syndromes remain clinically relevant presentations in routine cardiovascular practice [5,6]. Importantly, the severity of symptoms does not consistently correlate with the anatomical burden of coronary artery disease (CAD). For instance, women may experience more pronounced anginal symptoms despite less extensive obstructive disease, and modern cohorts have demonstrated that a substantial proportion of patients undergoing coronary angiography for suspected UA do

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not exhibit significant obstructive CAD [7,8]. This discordance presents a critical clinical dilemma: clinicians must balance the need to promptly identify unstable ischemic disease against the imperative to minimize unnecessary invasive procedures, procedure-related risks, and healthcare resource utilization.

Current European Society of Cardiology and national PERKI guidelines endorse either an early invasive or selective invasive strategy in patients without high-risk features. However, robust and objective tools to estimate the likelihood of obstructive CAD in this subgroup remain limited. Additionally, real-world data have highlighted that UA presentations often coexist with acute comorbidities, such as severe hypertension, further complicating early decision-making [7,8]. Traditional prognostic scores, including TIMI and GRACE, were primarily developed to predict short-term ischemic events and mortality rather than the anatomical presence of obstructive CAD, thereby limiting their utility in guiding invasive diagnostic strategies [9,10]. The 2024 European Society of Cardiology guideline for chronic coronary syndromes introduced the risk factor–weighted clinical likelihood (RF-CL) model, which integrates demographic variables, symptom characteristics, and major cardiovascular risk factors to estimate the probability of obstructive CAD [11]. In stable chest pain populations, this model has demonstrated superior discriminative performance compared with traditional pretest probability tools. Emerging evidence also suggests that risk factor–based clinical likelihood assessment may retain predictive value in patients with unstable angina [12,13]. Therefore, this study aimed to evaluate the performance of the RF-CL model in predicting obstructive CAD among patients with UA and to compare its diagnostic accuracy with established models, including Diamond–Forrester, Fladseth, TIMI, GRACE, and guideline-based criteria.

METHODS

This retrospective cohort study utilized medical record data from H. Adam Malik General Hospital, Medan, Indonesia. Adult patients diagnosed with unstable angina who underwent index-hospitalization coronary angiography were included. Unstable angina was defined according to contemporary acute coronary syndrome criteria. Exclusion criteria included patients with elevated or dynamically rising high-sensitivity troponin, high-risk or very-high-risk presentations, alternative structural causes of chest pain, recent coronary revascularization within 30 days, incomplete data required for RF-CL calculation, or non-evaluable angiographic findings. The primary outcome was obstructive coronary artery disease confirmed by invasive coronary angiography, defined as $\geqslant$70% stenosis in a major epicardial coronary artery, $\geqslant$50% stenosis in the left main or proximal left anterior descending artery, or intermediate stenosis with functionally significant ischemia based on fractional flow reserve or instantaneous wave-free ratio. The risk factor–weighted clinical likelihood (RF-CL) score was calculated for each patient. Comparator models included Diamond–Forrester, the Fladseth pre-test probability model, TIMI, GRACE, and guideline-derived intermediate-risk criteria.

Consecutive sampling was performed until the minimum sample size required for the receiver operating characteristic analysis was achieved. Missing data were handled using complete-case analysis. The collected variables included demographic characteristics, symptom profile, cardiovascular risk factors, admission electrocardiographic findings, hemodynamic parameters, left ventricular ejection fraction, and angiographic results. Categorical variables were analyzed using the chi-square or Fisher 'sexact test, whereas continuous variables were assessed using the independent t-test or Mann–Whitney U test, as appropriate. Discriminative performance was evaluated using receiver operating characteristic analysis with the area under the curve. Comparisons between models were performed using pairwise area under the curve analysis. Diagnostic performance metrics, including sensitivity, specificity, positive predictive value, and negative predictive value, were calculated to determine the optimal cutoff thresholds. Model calibration in the unstable angina population was assessed using logistic recalibration and the Hosmer–Lemeshow goodness-of-fit test. Statistical analyses were performed using standard statistical software. A two-sided p-value <0.05 was considered statistically significant.

Ethical approval was obtained from the Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara (no. 720/KEPK/USU/2025). Given the retrospective design and the use of de-identified data, the requirement for informed consent was waived.

RESULTS

During the study period, 289 patients with an unstable angina working diagnosis were screened. After applying the predefined eligibility criteria, 150 patients were included in the final analysis. The main reasons for exclusion were the use of coronary computed tomography angiography as the primary diagnostic modality (n=42), reclassification to non-ST-elevation myocardial infarction following serial troponin assessment (n=35), and the absence of coronary angiography during index hospitalization (n=36). Overall, obstructive coronary artery disease (CAD) was identified in 90 patients, corresponding to a prevalence of 60.0%. The mean age of the cohort was 58.81 ± 9.74 years, and 51.3% were men. Typical angina was present in two-thirds of the patients, while traditional cardiovascular risk factors, including hypertension, dyslipidemia, diabetes mellitus, and smoking, were highly prevalent. Patients with obstructive CAD were more frequently men and exhibited a higher prevalence of typical angina, smoking, and dyslipidemia. In addition, they demonstrated significantly higher RF-CL, Diamond–Forrester, and Fladseth scores, as well as lower left ventricular ejection fraction, compared to those without obstructive disease (Table 1).

Table 1. Baseline Characteristics by Angiographic Outcome

Variable	Total (n=150)	Non-obstructive (n=60)	Obstructive (n=90)	p value
Age, years	58.81 ± 9.74	57.68 ± 10.15	59.57 ± 9.45	0.247
Male, n (%)	77 (51.3)	24 (40.0)	53 (58.9)	0.023
Typical angina, n (%)	100 (66.7)	16 (26.7)	84 (93.3)	<0.001
Smoking, n (%)	74 (49.3)	21 (35.0)	53 (58.9)	0.004
Dyslipidemia, n (%)	85 (56.7)	20 (33.3)	65 (72.2)	<0.001
RF-CL, %	17.47 ± 12.22	8.33 ± 7.02	23.56 ± 11.17	<0.001
D–F, %	22.00 ± 19.00	13.62 ± 9.27	28.41 ± 12.88	<0.001
Fladseth	12.88 ± 3.56	11.02 ± 3.50	14.12 ± 3.04	<0.001
LVEF, %	56.11 ± 11.16	60.73 ± 8.01	53.02 ± 11.92	<0.001

In the univariable analysis, several clinical and model-based variables were significantly associated with obstructive CAD, including male sex, smoking, dyslipidemia, typical angina, RF-CL, Diamond–Forrester, TIMI, and Fladseth scores, as well as reduced left ventricular ejection fraction and ischemic electrocardiographic abnormalities. Among these, typical angina was the strongest predictor, demonstrating a markedly elevated odds ratio relative to other variables (Table 2).

Table 2. Univariable Logistic Regression for Predictors of Obstructive CAD

Variable	OR (95% CI)	p value
Age (per 10 years)	1.02 (0.25–1.22)	0.246
Male	2.15 (1.10–4.18)	0.024
No angina	Reference	—
Non-cardiac angina	0.37 (0.02–6.72)	0.500
Atypical angina	1.56 (0.15–16.46)	0.714
Typical angina	36.75 (4.23–319.44)	0.001
Smoking	2.66 (1.35–5.23)	0.005
Dyslipidemia	5.20 (2.56–10.55)	<0.001
Hypertension	1.03 (0.48–2.20)	0.938

Calibration analysis revealed that the RF-CL model systematically underestimated the absolute probability of obstructive CAD when applied to patients with acute unstable angina. Logistic recalibration yielded the equation $\text{logit}(p) = -2.509 + 0.205 \times \text{RF-CL}$, indicating a substantial upward shift in the observed risk. For instance, an RF-CL value of 15% corresponded to an observed probability of approximately 63.8%, underscoring the divergence between the stable and acute coronary populations (Table 3).

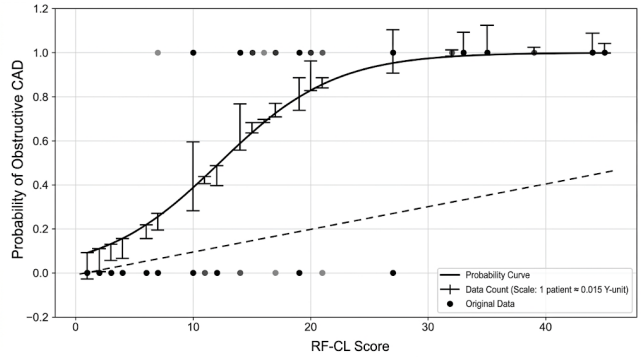

Figure 1. Calibration Curve Comparing RF-CL Probability between CCS and UA Populations

Table 3. RF-CL Calibration

RF-CL (CCS), %	Observed (UA), %
0	7.5
5	18.5
10	38.7
12	43.6
13	53.9
14	59.0
15	63.8
20	83.1
25	93.2
30	97.4
35	99.1
40	99.7
45	99.9

Note: RF-CL, risk factor-weighted clinical likelihood; CCS, chronic coronary syndrome; UA, unstable angina.

The RF-CL model demonstrated the highest discriminative performance, with an area under the curve (AUC) of 0.885. It significantly outperformed all comparator models, including Diamond–Forrester (AUC 0.820) and Fladseth (AUC 0.752). The TIMI score showed limited discrimination, whereas the GRACE and AHA/ESC criteria performed poorly and were not meaningfully different from chance.

Table 4. Model Discrimination

Model	AUC	Cut-off	Sens	Spec	p
RF-CL	0.885	12	83.3	81.7	<0.001
D–F	0.820	15	84.4	60.0	<0.001
Fladseth	0.752	12.5	68.9	66.7	<0.001
TIMI	0.611	1.5	66.7	48.3	0.021
AHA/ESC	0.581	TIMI >1 / GRACE >109	67.8	48.3	0.095
GRACE	0.551	80.5	52.2	51.7	0.292

Note: AUC, area under the curve; Sens, sensitivity; Spec, specificity; D–F, DiamondForrester; RF-CL, risk factor-weighted clinical likelihood.

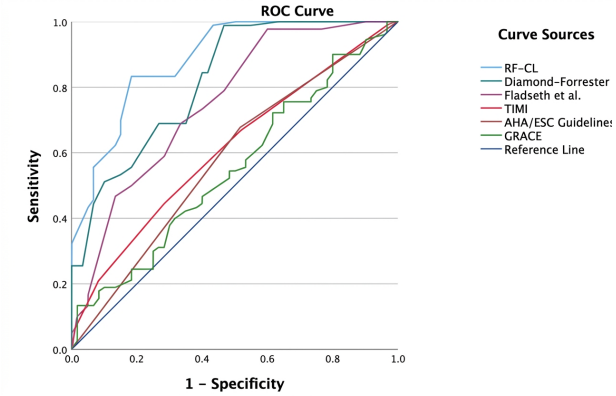

Figure 2. Receiver operating characteristic curves of prediction models

From a clinical decision-making perspective, the RF-CL model showed meaningful utility in guiding selective invasive strategies. At a cutoff value of ≤12, the model would have deferred immediate coronary angiography in 42.7% of patients, while maintaining a negative predictive value of 76.6%. This corresponded to a miss rate of 23.4%. Lower thresholds improved diagnostic safety at the expense of reduced deferral, whereas higher thresholds increased deferral but compromised sensitivity and negative predictive value (Table 5).

Table 5. RF-CL for Selective Invasive Triage

Cut-off	Rule-out, %	NPV	Sens	Spec	PPV	Miss
≤10	37.3	73.2	83.3	68.3	79.8	26.8
≤11	38.7	74.1	83.3	71.7	81.5	25.9
≤12	42.7	76.6	83.3	81.7	87.2	23.4
≤13	42.7	76.6	83.3	81.7	87.2	23.4
≤14	52.0	65.4	70.0	85.0	87.5	34.6
≤15	54.0	63.0	66.7	85.0	87.0	37.0

Note: NPV, negative predictive value; PPV, positive predictive value; Sens, sensitivity; Spec, specificity.

DISCUSSION

The present study demonstrates that the risk factor–weighted clinical likelihood (RF-CL) model provides superior discriminative performance for predicting obstructive coronary artery disease (CAD) in patients with unstable angina. With an area under the curve of 0.885, RF-CL consistently outperformed traditional pretest probability models and widely used prognostic scores. This finding reinforces the concept that integrating classical cardiovascular risk factors into symptom-based assessment substantially enhances diagnostic accuracy. Importantly, our results extend the original observations from stable chest pain populations to an acute, lower-to-intermediate-risk unstable angina cohort, thereby supporting the broader applicability of risk factor–based likelihood estimation in contemporary clinical practice [14]. The prevalence of obstructive CAD in this study (60.0%) was higher than that reported in other contemporary cohorts, where rates ranged from approximately 45% to 53%. This discrepancy likely reflects differences in baseline cardiovascular risk burden, particularly the high prevalence of smoking, dyslipidemia, and diabetes mellitus observed in our population, as well as referral patterns inherent to tertiary care centers. Consistent with prior studies, male sex, typical angina, smoking, dyslipidemia, reduced left ventricular ejection fraction, and ischemic electrocardiographic abnormalities were strongly associated with obstructive CAD [15]. Among these, typical angina was the most powerful predictor, underscoring the continued importance of careful clinical phenotyping despite advances in diagnostic technologies.

A key observation of this study is the limited performance of traditional prognostic scores when applied to an anatomical diagnostic question. TIMI and GRACE were originally developed to estimate short-term ischemic risk and mortality rather than the probability of obstructive epicardial disease [16-18]. Their modest to poor discrimination in the present analysis highlights a fundamental mismatch between prognostic risk stratification and anatomical disease prediction. This finding is further supported by regional data, in which GRACE has been predominantly utilized as a prognostic rather than diagnostic tool in acute coronary syndromes [19]. Clinically, this distinction is critical, as decisions regarding invasive coronary angiography should be guided by the likelihood of obstructive disease rather than solely by future event risk. Moreover, randomized evidence suggests that routine invasive strategies do not uniformly confer mortality benefits across all lower-risk non-ST-elevation acute coronary syndrome subgroups, further emphasizing the need for more precise patient selection [20,21]. Despite its strong discriminative ability, RF-CL demonstrated systematic miscalibration when applied to the unstable angina population, consistently underestimating absolute risk. This is expected, given that the model was originally derived from chronic coronary syndrome cohorts with a lower baseline prevalence of obstructive disease. In practical terms, RF-CL probabilities should therefore be interpreted cautiously in acute settings without recalibration. Nevertheless, the model retained meaningful clinical utility. A threshold value of ⩽12 identified a substantial subgroup of patients in whom a selective invasive strategy, complemented by further non-invasive evaluation, could reasonably be considered. From a

broader perspective, this supports the role of RF-CL as a pragmatic triage tool that may contribute to more efficient resource utilization and a more individualized, risk-based approach to invasive decision-making.

Several limitations should be acknowledged. First, the retrospective design introduces potential bias related to data completeness and accuracy. Second, the study was conducted at a single tertiary center, which may limit generalizability. Third, verification bias cannot be excluded, as only patients who underwent coronary angiography were included. Finally, external validation in prospective, multicenter cohorts is required before RF-CL can be adopted as a standalone decision-making tool in unstable angina.

CONCLUSION

The risk factor–weighted clinical likelihood (RF-CL) model demonstrated superior performance in predicting obstructive coronary artery disease among patients with unstable angina, markedly outperforming traditional prognostic scores, such as TIMI and GRACE, for this diagnostic purpose. An RF-CL threshold of $\leqslant 12$ identified a clinically relevant subgroup in whom a selective invasive strategy may be safely considered, supporting a more targeted and efficient approach to coronary angiography. However, the model systematically underestimated absolute risk in the acute setting, indicating the need for recalibration prior to routine clinical implementation. Overall, RF-CL represents a promising tool for improving diagnostic precision and optimizing invasive decision-making in unstable angina.

DECLARATIONS

Ethical approval was obtained from the Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara (no. 720/KEPK/USU/2025). Given the retrospective design and use of de-identified data, the requirement for informed consent was waived.

CONSENT FOR PUBLICATION

The Authors agree to the publication in the Journal of Society Medicine.

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COMPETING INTERESTS

All authors have reviewed and approved the final version of the manuscript and agreed to its publication in the Journal of Society Medicine.

AUTHORS' CONTRIBUTIONS

GJB conceptualized and designed the study, performed data collection and analysis, and drafted the manuscript. RH supervised the study and critically revised the manuscript. ANN contributed to methodological refinement, data validation, and critical revision. HH, ACL, and CAA contributed to data interpretation and manuscript review. All authors approved the final version and take responsibility for the content.

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