



Risk Stratification and Clinical Eligibility of Invasive vs. Noninvasive Strategy in the Management of Non-ST Elevation Acute Coronary Syndrome Patients Admitted to Hawler Teaching Hospital

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ABSTRACT

Background and objectives: The term acute coronary syndrome (ACS) is a range of acute myocardial ischemic states including unstable angina (UA), non-ST segment (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). It is required to identify the cardiovascular events risk in those patients in order to select the beneficial therapeutic strategy during the first hours of presentation. The aim of the present study is to stratify the cardiac event risk and to determine the clinical eligibility of invasive vs. noninvasive therapeutic strategy in patients presented with UA and NSTEMI as defined as NSTEMI-ACS.

Methods: In the current observational cross-sectional study, 100 consecutive patients who visited the emergency department and admitted to coronary care unit diagnosed as NSTEMI-ACS were recruited. Their medical and clinical information were obtained from the patient and medical records. The cardiac event risk was estimated according to the GRACE risk score (Global Registry of Acute Coronary Events) and the TIMI risk score (Thrombolysis in Myocardial Infarction). The clinical eligibility of invasive vs. noninvasive (Ischemia-guided) therapeutic strategy was determined according to the latest AHA/ACC guideline for the management of patients with NSTEMI-ACS in 2014.

Results: Of patients presented with NSTEMI-ACS who underwent both therapeutic strategies most of them were males (71.0%). The mean \pm S.D. was 60-62 years for age. The mean \pm S.D. of body mass index (BMI), chest pain duration, systolic blood pressure and heart rate were comparable in two groups. In terms of clinical characteristics hypertension (72.0%), current smoking (56.0%), dyslipidemia (48.0%), and past history of coronary artery disease (CAD) (44.0%) were the most prevalent. Patients who underwent invasive strategy had significantly more ST-depression (75.6%) as compared to those who underwent non-invasive strategy (55.9%), $P=0.044$. However, non-invasive group had significantly more T-wave inversion, (59.3% vs. 34.1%; $P=0.013$). The studied groups showed no statistically significant difference in risk of mortality according to GRACE risk score ($P=0.505$), TIMI risk score ($P=0.057$), and Killip class ($P=0.252$). However, the majority of non-invasive group had low risk (67.8%) while, the invasive group more common to be at intermediate risk (29.3%) for 6-month mortality. There was no statistically significant predictor of two therapeutic strategies according to the patients characteristics and risk stratification ($p>0.05$).

Conclusions: The current study showed that invasive and non-invasive (Ischemia-guided) strategies could be applicable to NSTEMI-ACS patients with low, intermediate, or high risk of mortality with risk stratification. It is recommended to underscore on significant and prevalent electrocardiographic findings, demographic and clinical characteristics to consider eligibility for invasive and non-invasive therapeutic strategies to patients with NSTEMI-ACS.

1. INTRODUCTION

The term acute coronary syndrome (ACS) is a range of acute myocardial ischemic states. It includes unstable angina (UA), non-ST segment myocardial infarction (Non-STEMI), and ST-segment elevation infarction (STEMI). Unstable angina defined as a clinical syndrome between stable angina and acute myocardial infarction (Grech *et al.*, 2003, Chang *et al.*, 2012).

Disruption in the atheromatous plaque is an initial stage of an acute coronary syndrome. Continuous fissuring or rupture in these plaques and subsequent exposure to materials such as lipid, foam cells, and smooth muscle result in the local generation of thrombin and fibrin deposition. Consequently, it facilitates platelet aggregation, adhesion, and intracoronary thrombus formation (Chang *et al.*, 2012).

Non-STEMI-ACS cover a clinical spectrum ranging from UA to non-STEMI (Fitchett *et al.*, 2006). Unstable angina and Non-STEMI are responsible for 2.5 million of hospital admissions across the world. It has been considered to be the main risk factor for morbidity and mortality in Western countries. In-hospital mortality and re-infarction account for 5-10% one month following an acute episode with a higher long-term mortality risk compared to the patients with STEMI (Bertrand *et al.*, 2000).

Unstable angina and Non-STEMI are closely associated medical conditions with similar clinical presentations making them indistinguishable. The distinction between them depends on severity sufficiency of ischemia to cause myocardial damage and release of detectable biomarkers quantities of myocyte necrosis. Cardiac troponin I and T are more specific and reliable biomarkers than creatinine kinase and its isoenzyme. The electrocardiogram (ECG) may show a normal or minor non-specific changes, ST segment depression, bundle branch block, T wave inversion, or transient ST-segment elevation and are resolved spontaneously or following giving nitrate (Braunwald *et al.*, 2002).

Preventing recurrent ACS and improving long-term outcomes are the management aims through selecting an appropriate treatment based on the risk estimation of an adverse outcome. Patients with NSTEMI-ACS do not adhere to the recommended treatments, and the risk stratification is not used by physicians to determine the appropriate treatment and access speed to coronary angiography (Fitchett *et al.*, 2006).

The risk stratification has its own importance as NSTEMI-ACS has a greater prevalence of early culprit coronary artery patency and a higher risk of recurrent ischemic events, and a wide range of therapeutic choices compared to STEMI.

Given to this wide range of therapeutic choices and the adverse events in NSTEMI-ACS, it is so important to choose management strategies with the greatest advantage to the patients. It is required to recognize those patients with the highest risk of cardiovascular events guiding the clinicians to select the patients who take benefit from invasive or noninvasive therapeutic interventions during the first hours of presentation.

Aim of the study

The aim of the present study is to stratify the cardiac event risk and to determine the clinical eligibility of invasive vs. noninvasive (Ischemia-guided) therapeutic strategy in patients presented with UA and NSTEMI as defined as NSTEMI-ACS.

2. METHODS

2.1. Study design and sampling

In the current observational cross-sectional study, the patients were visited the emergency department of Hawler Teaching Hospital for the cardiac-based issues and consecutively screened for the eligibility criteria between 20th June and 25th December 2017.

The patients met eligibility criteria including both gender, aged 18 years and older, diagnosed with NSTEMI-ACS through the medical history, clinical examination, ECG and cardiac biomarker indicators, and risk factors were identified and the whole evaluation was supervised by a specialist or consultant. Pregnant women and patients with STEMI were not included in the study. Of the total 336 patients screened for the eligibility criteria, 143 were diagnosed with STEMI, 56 had no suitable health status (octogenarians and nonagenarians, frail patients, chronic kidney disease patients on replacement therapy and

severely incapacitated patient with stroke), and 21 did not show their willingness to participate, 16 were pregnant, of those, 100 eligible patients were recruited in the present study.

All patients who diagnosed with NSTEMI-ACS at the corresponded department were managed with optimum medical therapy, including acetylsalicylic acid, P2Y12 inhibitors (mostly clopidogrel), statins, low molecular weight heparin and as appropriate with B-blockers, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, insulin, nitrate and other anti-hypertensive or anti-ischemic medication and diuretics. Some of them were already on medications e.g. oral hypoglycemic agents (30.0%) and diuretics (22.0%).

2.2. Diagnostic and measurement criteria

The demographic data and clinical characteristics of the patients was obtained from the patients and their medical records. The diagnosis of NSTEMI-ACS was established based on the historical descriptors of symptoms such as chest pain and recurrent angina or dyspnea. The ECG was checked carefully for ST-segment depression, T-wave inversion, dynamic ST-T wave changes, and transient ST-segment elevation. Repeated sampling of cardiac biomarkers including troponins and CK-MB were performed in all patients.

2.3. Risk stratification

The cardiac event risk was estimated according to the GRACE risk score (Global Registry of Acute Coronary Events) and the TIMI risk score (Thrombolysis in Myocardial Infarction). The GRACE risk score is based on the age, Killip class, systolic blood pressure, ST-segment deviation, serum creatinine level, cardiac arrest, heart rate, and cardiac

biomarkers. A series of points are given to each of the above mentioned clinical variables. In this score system, patients scoring <109 points are considered for noninvasive (Ischemia-guided) therapeutic strategy and ≥ 109 are considered for invasive therapeutic strategy (including immediate, early or delayed), (Appendix 1) according to the latest AHA/ACC guideline for the management of patients with NSTEMI-ACS in 2014.

The TIMI risk score (Thrombolysis in Myocardial Infarction) is determined by the sum of the presence of 7 variables at admission; 1 point is given for each of the following variables: ≥ 65 y of age; ≥ 3 risk factors for CAD; prior coronary stenosis $\geq 50\%$; ST deviation on ECG; ≥ 2 angina events in prior 24 h; use of aspirin in prior 7 days and elevated cardiac biomarkers. In this score system, patients scoring 0-1 point are considered for noninvasive (Ischemia-guided) therapeutic strategy and ≥ 2 points are considered for invasive therapeutic strategy, (Appendix 2, 3) according to the latest AHA/ACC guideline for the management of patients with NSTEMI-ACS in 2014.

2.4. Statistical Methods

The descriptive purposes of the study were examined through the frequency distribution. A *p*-value of < 0.05 was considered as the statistically significant difference. The SPSS version 24 was used for statistical calculations. The Univariate analysis of variance was performed to determine the predictors of invasive and non-invasive strategies and chi-squared test for statistical difference between risk stratification according to GRACE and TIMI score systems.

2.5. Ethical considerations

The ethical clearance of the present study was obtained from the local corresponded department in Erbil Teaching Hospital in 2017. The patients have not undergone any medical intervention or invasive procedures unless consented and the written consent form was taken from all patients prior study implementation

3. RESULTS

Of the total patients recruited in this study, more than two third of them were males (71.0%). The mean age \pm S.D. of the patients who underwent invasive strategy was 60.88 and non-invasive strategy was 62.36 years with no statistically significant difference ($P=0.490$). In addition, the patients mean \pm S.D. in two groups were comparable in regard to body mass index (BMI) ($P=0.053$), chest pain duration ($P=0.186$), systolic blood pressure ($P=0.302$), and heart rate ($P=0.621$). In terms of clinical-based information of NSTEMI-ACS patients, the study revealed that hypertension (72.0%), current smoking (56.0%), dyslipidemia (48.0%), and past history of coronary artery disease (CAD) (44.0%) were the most prevalent characteristics followed by diabetes mellitus (31.0%), and renal failure (12.0%). The prevalence of family history of CAD was 22.0%. On the other hand this study showed no statistical significant difference between the patients in two groups in regard to demographic and parameters of clinical presentations ($P>0.05$) as shown in Table 1.

Table 1: Demographic and clinical characteristics according to eligibility of invasive vs. non-invasive therapeutic strategy in NSTEMI-ACS patients

Demographic and clinical characteristics	NSTEMI-ACS patients (no. 100)			P-Value
	Invasive Strategy (Mean ± S.D.)	non-invasive Strategy (Mean ± S.D.)		
Age (year)	60.88 ± 10.51	62.36 ± 10.46		0.490*
Body Mass Index (BMI)	26.93 ± 4.29	25.44 ± 2.68		0.053*
Chest Pain Duration (hour)	10.98 ± 12.67	14.91 ± 16.91		0.186*
Systolic Blood Pressure	151.13 ± 32.90	144.83 ± 23.82		0.302*
Heart Rate	80.15 ± 19.60	78.36 ± 14.62		0.621*
	Invasive Strategy no. 41 (%)	non-invasive Strategy no. 59 (%)	NSTEMI-ACS no. (%)	P-Value
Gender				0.195**
Male	32 (78.0)	39 (66.1)	71 (71)	
Female	9 (22.0)	20 (33.9)	29 (29)	
Smoking				0.984**
Current smoker	24 (56.1)	32 (56.1)	56 (56)	
Ex-smoker	7 (14.6)	9 (15.8)	16 (16)	
Never smoker	12 (29.3)	16 (28.1)	28 (28)	
Refractory Angina				0.351**
Yes	6 (14.6)	5 (8.5)	11 (11)	
No	35 (85.4)	54 (91.5)	89 (89)	
Shortness of Breath				0.456**
Yes	13 (31.7)	23 (39.0)	36 (36)	
No	28 (68.3)	36 (61.0)	64 (64)	
Diabetes Mellitus				0.899**
Yes	13 (31.7)	18 (30.5)	31 (31)	
No	28 (68.3)	41 (69.5)	69 (69)	

Hypertension				0.261**
Yes	32 (78.0)	40 (67.8)	72 (72)	
No	9 (22.0)	19 (32.2)	28 (28)	
Family History of CAD				0.051**
Yes	13 (31.7)	9 (15.3)	22 (22)	
No	28 (68.3)	50 (84.7)	78 (78)	
Dyslipidemia				0.896**
Yes	20 (48.8)	28 (47.5)	48 (48)	
No	21 (51.2)	31 (52.5)	52 (52)	
Renal failure				0.222**
Yes	7 (17.1)	5 (8.5)	12 (12)	
No	34 (82.9)	54 (91.5)	88 (91)	
Past History of CAD				0.422**
Yes	20 (48.8)	24 (40.7)	44 (44)	
No	21 (51.2)	35 (59.3)	56 (56)	
(PCI)				0.302**
Yes	3 (7.3)	1 (1.7)	4 (4)	
No	38 (92.7)	58 (98.3)	96 (96)	
Previous (CABG)				
Yes	0 (0.0)	0 (0.0)	0 (0.0)	-
No	41 (100)	59 (100)	100 (100)	-
<p>*Independent t-test, ** Chi-squared, and Fishers' exact tests were performed for statistical analyses.</p> <p>The bold numbers show the higher prevalence. NSTE-ACS = Non ST Elevation-Acute Coronary Syndrome; CAD =</p> <p>Coronary Artery Disease; CABG = Coronary Artery Bypass Graft Surgery; PCI = Percutaneous Coronary Intervention.</p>				

The patients who underwent invasive strategy had significantly more ST-depression (75.6%) as compared to those who underwent non-invasive strategy (55.9%), $P=0.044$. on the other hand, the non-invasive group of the study

had significantly more T-wave inversion, (59.3% vs. 34.1%; $P=0.013$). The other Electrocardiographic and Echocardiographic features were not statistically significant between both groups of the study, as shown in Table 2.

Table 2: Electrocardiographic and Echocardiographic findings according to eligibility of invasive vs. non-invasive therapeutic strategy in NSTEMI-ACS patients

Electrocardiographic and Echocardiographic findings	NSTEMI-ACS patients (no. 100)		P-Value
	Invasive Strategy no. 41 (%)	non-invasive Strategy no. 59 (%)	
ST depression			0.044*
Yes	31 (75.6)	33 (55.9)	
No	10 (24.4)	26 (44.1)	
T-wave inversion			0.013*
Yes	14 (34.1)	35 (59.3)	
No	27 (65.9)	24 (40.7)	
Dynamic ST-T changes			1.000**
Yes	2 (4.9)	2 (3.4)	
No	39 (95.1)	57 (96.6)	
Ventricular fibrillation (VF)			0.066**
Yes	3 (7.3)	0 (0.0)	
No	38 (92.7)	59 (100.0)	
Ventricular tachycardia (VT)			0.166**
Yes	2 (4.9)	0 (0.0)	
No	39 (95.1)	59 (100)	
Cardiac Arrest			0.142**
Yes	0 (0.0)	4 (6.8)	
No	41 (100)	55 (93.2)	
LVEF (%) – Mean \pm S.D.	50.73 \pm 11.350	52.44 \pm 10.927	0.456***

The numbers are in frequency (percentage) except where mentioned.

*Chi-squared, ** Fishers' exact, and *** independent t-tests were performed for statistical analyses. The bold numbers show the significant difference. NSTEMI-ACS = Non ST Elevation-Acute Coronary Syndrome;

The differences of lab investigations were examined in Table 3. The study showed that the patients in both invasive and non-invasive groups had comparable values of serum

creatinine (P=0.827), troponin (P=0.085), and estimated glomerular filtration rate (eGFR) (P=0.168) and revealed no statistical significance.

Table 3: Laboratory findings according to eligibility of invasive vs. non-invasive therapeutic strategy in NSTEMI-ACS patients

Laboratory Findings	NSTEMI-ACS patients (no. 100)		P-Value
	Invasive Strategy no. 41 (%)	non-invasive Strategy no. 59 (%)	
Serum Creatinine (mg/dL)	1.06 ± 0.46	1.09 ± 0.54	0.827
Troponin (ng/mL)	1.60 ± 3.10	0.69 ± 1.27	0.085
eGFR (ml/min)	87.60 ± 48.44	75.35 ± 33.31	0.168

NSTEMI-ACS = Non ST Elevation-Acute Coronary Syndrome; eGFR = estimated Glomerular Filtration Rate.

Furthermore, the study did not show the patients who underwent invasive and non-invasive therapeutic strategies were more at

risk of mortality according to GRACE risk score (P=0.505), TIMI risk score (P=0.057), and Killip class (P=0.252), as shown in Table 4.

Table 4: Risk stratification by GRACE, TIMI risk scores and Killip Class according to eligibility of invasive vs. non-invasive therapeutic strategy in NSTEMI-ACS patients

Risk stratification	NSTEMI-ACS patients (no. 100)		P-Value
	Invasive Strategy no. 41 (%)	non-invasive Strategy no. 59 (%)	
GRACE Risk Score	105.40 ± 31.71	100.97 ± 33.43	0.505*
TIMI Risk Score	4.43 ± 1.68	3.75 ± 1.76	0.057*
Killip Class			0.252**
1	27 (65.9)	43 (72.9)	
2	11 (26.8)	12 (20.3)	
3	1 (2.4)	4 (6.8)	
4	2 (4.9)	0 (0.0)	

*Independent t-test and ** Fishers' Exact test were performed for statistical analyses.
NSTEMI-ACS = Non ST Elevation-Acute Coronary Syndrome; GRACE = Global Registry of Acute Coronary Events; TIMI = Thrombolysis in Myocardial Infarction.

Moreover, the mortality risk in patients who underwent invasive or non-invasive strategies was examined according to GRACE risk

categories in Table 5. The study did not show the one group is more at risk of mortality compared to other one (P=0.358).

Table 5: Risk stratification by 3-class of severity (low to very high) according to eligibility of invasive vs. non-invasive therapeutic strategy in NSTEMI-ACS patients

GRACE Categories	NSTEMI-ACS patients (no. 100)			P-Value
	Invasive Strategy no. 41 (%)	non-invasive Strategy no. 59 (%)	NSTEMI-ACS no. (%)	
Low Risk (GRACE <109)			62 (62)	0.358*
Moderate Risk (GRACE 109-140)	22 (53.7)	40 (67.8)	24 (24)	
High Risk (GRACE >140)	12 (29.3)	12 (20.3)	14 (14)	
	7 (17.1)	7 (11.9)		

*Independent t-test was performed for statistical analysis.
NSTEMI-ACS = Non ST Elevation-Acute Coronary Syndrome; GRACE = Global Registry of Acute Coronary Events.

Upon univariate logistic regression application on NSTEMI-ACS patients, the invasive or non-invasive strategy was considered as a dependent variable and its association with gender, diabetes, hypertension, dyslipidemia,

age and left ventricular ejection fraction (LVEF) as predictors were examined in Table 6. The study did not show that the mentioned characteristics are the predictors of strategic types.

Table 6: Univariate logistic regression analysis between invasive therapeutic strategy eligibility

Dependent Variable: Invasive Strategy Eligibility				
Predictors	Mean Square	F	Significance	Partial Eta Squared*
Gender	0.887	3.786	0.056	0.059
Diabetes Mellitus	0.004	0.017	0.898	0.000
Hypertension	0.031	0.130	0.719	0.002

Dyslipidemia	0.037	0.159	0.691	0.003
Age	0.274	1.169	0.295	0.391
\Left ventricular ejection fraction (LVEF)	0.012	0.051	0.822	0.001
* Partial eta-squared: is a measure of effect size that express the amount of variance accounted for by one or more independent variables				

4. Discussion

The present study conducted on NSTEMI-ACS patients showed that those who underwent invasive and non-invasive treatments were comparable in demographic, clinical characteristics and lab investigations. In addition, they were comparable in echocardiographic findings. The electrocardiographic changes revealed more prevalence of ST depression in invasive group and more T-wave inversion in non-invasive arm of the study. Despite these parameters, patients in both groups did not disclose a significant more risk of mortality according to the GRACE, TIMI risk scores, and Killip's class systems of stratification. The study did not show that gender, diabetes, hypertension, dyslipidemia, age and LVEF are the predictors of strategic types.

The majority of NSTEMI-ACS patients in this study were managed by both the internists and cardiologists that may reflect the importance of the establishment and implementation of the treatment guidelines in the form of clinical plans or algorithms to guide the clinicians for

optimal therapeutic interventions. Risk assessment has been shown to be a dynamic and continuous process aiming to identify new higher risk features within the early presentation hours assisting the clinicians to implement different management strategies for NSTEMI-ACS patients.

According to the earlier Europe and North American registries, the treatment of patients with NSTEMI-ACS is not based on the current guidelines (Eagle *et al.*, 2002, Fox *et al.*, 2002, Steg *et al.*, 2002). For instance, patients with lower risk are undergoing cardiac catheterization more often at an earlier time than higher-risk patients (Bhatt *et al.*, 2004).

Clinical conditions of the patients with NSTEMI-ACS are quite complicated and have a high mortality risk and recurrent myocardial infarction. Therefore, it is important to manage the patients according to evidence-based strategies.

The current study identified the majority of the patients with a low risk according to the GRACE risk stratification system underwent

noninvasive management. The stratification risk is highly important to determine the patients with a severe ischemic episode, left ventricular dysfunction, and severe and/or extensive proximal coronary stenosis. In addition, simultaneous and multiple plaque rupture within several coronary arteries has been shown to be common in ACS patients (Goldstein *et al.*, 2000, Roffi *et al.*, 2016).

The study showed that 53.7% and 67.8% of the patients in invasive and non-invasive treatments, respectively had a low risk of mortality according to the GRACE system. These patients require careful and ongoing observation and further medical testing to determine that they are not at higher risk features. These patients must be considered to be low risks until confirmation by serial ECG and troponin level over a time scheduled period. Importantly, the patients with negative serial biomarkers and no ECG ST-segment change may still be located as higher risk (Sanchez *et al.*, 2004) because the sensitivity of both troponin I and T is 60% at this time and it is increased over 14 to 18 hours of presentation (Zimmerman *et al.*, 1999).

The patients with a high mortality risk were 17.1% and 11.9% in invasive and non-invasive treatment groups, respectively in the present study. These patients must be under continuous medical care to avoid the worse conditions with features of higher risk. Ongoing medical care must be continued until stabilization of

higher risk features with conservative therapy as the mean age of the patients in the study is relatively high. These patients take a great benefit from a more aggressive antiplatelet and antithrombotic regimen and an early invasive strategy than the patients with a lower risk (Hoedemaker *et al.*, 2017, Tubaro *et al.*, 2017). Although we could not find any predictor in this regard, this finding could back to the patient clinical heterogeneity rather than other characteristics. Hypotension, tachycardia, elevated troponin, dynamic ST-segment changes, frequent episode of ischemia, and refractory have been documented to be high-risk predictors by clinical trials (Eagle *et al.*, 2004, Boersma *et al.*, 2000). Therefore, the decision must be taken according to the signs and symptoms of the ACS likelihood if these medical tests are not available at this period of time.

The patients with “background risk” such as known CAD, diabetes mellitus, or renal failure or having very typical ischemic cardiac symptoms, even with no high-risk changes in ECG abnormalities and lower levels of troponin must be considered for admission for further observations (Fitchett *et al.*, 2006).

5. Limitations of the study

The findings reported in the present study must be analyzed with caution owing to its design and sample size. The patients recruited in the present study have been selected from one geographic location precluding the study to generalize to other regions or across the country.

6. Conclusions

The present study showed that hypertension, current smoking, dyslipidemia, and past history of CAD were the most prevalent features among patients with NSTEMI-ACS. Those who underwent invasive strategy had significantly more ST-depression. However, those eligible for non-invasive strategy had significantly more T-wave inversion. There was no statistically significant difference between invasive and non-invasive strategies applied according to risk stratification with GRACE, TIMI risk scores and Killip class. The studied groups show no statistically significant difference in the risk of mortality. However, the majority of non-invasive group was at low risk as compared to invasive group who was common to be at intermediate risk for 6-month mortality. There was no statistically significant predictor of the two therapeutic strategies according to patient characteristics and risk stratification as well.

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Appendix 1: GRACE risk score.

([AHA/ACC guideline for the management of patients with NSTEMI-ACS](#) 2014).

1. Find Points for Each Predictive Factor:

Killip Class	Points	SBP, mm Hg	Points	Heart Rate, Beats/min	Points	Age, y	Points	Creatinine Level, mg/dL	Points
I	0	≤80	58	≤50	0	≤30	0	0-0.39	1
II	20	80-99	53	50-69	3	30-39	8	0.40-0.79	4
III	39	100-119	43	70-89	9	40-49	25	0.80-1.19	7
IV	59	120-139	34	90-109	15	50-59	41	1.20-1.59	10
		140-159	24	110-149	24	60-69	58	1.60-1.99	13
		160-199	10	150-199	38	70-79	75	2.00-3.99	21
		≥200	0	≥200	46	80-89	91	>4.0	28
						≥90	100		

Other Risk Factors	Points
Cardiac Arrest at Admission	39
ST-Segment Deviation	28
Elevated Cardiac Enzyme Levels	14

2. Sum Points for All Predictive Factors:



3. Look Up Risk Corresponding to Total Points:

Total Points	≤60	70	80	90	100	110	120	130	140	150	160	170	180	190	200	210	220	230	240	≥250
Probability of In-Hospital Death, %	≤0.2	0.3	0.4	0.6	0.8	1.1	1.6	2.1	2.9	3.9	5.4	7.3	9.8	13	18	23	29	36	44	≥52

Appendix 2: TIMI Risk Score* for NSTEMI-ACS

TIMI Risk Score	All-Cause Mortality, New or Recurrent MI, or Severe Recurrent Ischemia Requiring Urgent Revascularization Through 14 d After Randomization, %
0-1	4.7
2	8.3
3	13.2
4	19.9
5	26.2
6-7	40.9

*The TIMI risk score is determined by the sum of the presence of 7 variables at admission; 1 point is given for each of the following variables: ≥65 y of age; ≥3 risk factors for CAD; prior coronary stenosis ≥50%; ST deviation on ECG; ≥2 angina events in prior 24 h; use of aspirin in prior 7 d; and elevated cardiac biomarkers.

Appendix 3: Factors Associated With Appropriate Selection of Early Invasive Strategy or Ischemia-Guided Strategy in Patients with NSTEMI-ACS.

(2014 AHA/ACC Guideline for the management of patients with NSTEMI-ACS)

Ischemia-guided strategy	Low-risk score (e.g., TIMI [0 or 1], GRACE [<109])
	Low-risk Tn-negative female patients
	Patient or clinician preference in the absence of high-risk features
Immediate invasive (within 2 h)	Refractory angina
	Signs or symptoms of HF or new or worsening mitral regurgitation
	Hemodynamic instability
	Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy
	Sustained VT or VF
Early invasive (within 24 h)	None of the above, but GRACE risk score >140
	Temporal change in Tn (Section 3.4)
	New or presumably new ST depression
Delayed invasive (within 25–72 h)	None of the above but diabetes mellitus
	Renal insufficiency (GFR <60 mL/min/1.73 m ²)
	Reduced LV systolic function (EF <0.40)
	Early post-infarction angina
	PCI within 6 month
	Prior CABG
	GRACE risk score 109–140; TIMI score ≥ 2