CHAPTER

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Risk Stratification and Management Algorithm of NSTEMI

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INTRODUCTION

A diagnosis of Non ST-segment elevation myocardial infarction (NSTEMI) can be made when the ischemia is sufficiently severe to cause myocardial damage that results in the release of a biomarker of myocardial necrosis into the circulation. In contrast, the patient is considered to have experienced Unstable Angina (UA) if no such biomarker can be detected in the bloodstream hours after the initial onset of ischemic chest pain. Unstable angina exhibits 1 or more of 3 principal presentations: (1) rest angina (usually lasting >20 minutes), (2) new-onset (<2 months previously) severe angina, and (3) a crescendo pattern of occurrence (increasing in intensity, duration, frequency, or any combination of these factors).[1] Roughly two-thirds of patients with MI have NSTEMI; the rest have STEMI (Figure 1).[2] Given the similarity in clinical presentation and the difficulty in distinguishing the 2 syndromes, the new guidelines favor the term non–ST-segment elevation acute coronary syndromes (NSTE-ACS) instead of UA or non–ST-segment elevation myocardial infarction.

Table 1: Risk Factors[4]

Major risk factors	Minor risk factors
High serum cholesterol level	Increasing age
Hypertension	Male gender
Diabetes mellitus	Family history
Cigarette smoking	Physical inactivity
	Obesity
	Excess alcohol consumption
	Excess carbohydrates intake
	Social deprivation
	Diets deficient in fresh vegetables, fruit and polyunsaturated fatty acids
	Competitive and stressful lifestyle with type A personality

PATHOPHYSIOLOGY[4] (TABLE 1)

NSTEMI usually occurs by developing a partial occlusion of a major coronary artery or a complete occlusion of a minor coronary artery previously affected by atherosclerosis. The deposited cholesterol ultimately forms a plaque called atherosclerotic plaque.The most common mechanism of NSTEMI is rupture or erosion of an atherosclerotic plaque that triggers platelet aggregation, which leads to formation of a thrombus (blood clot) in a coronary artery (Figure 2).

CLINICAL PRESENTATION

History and Physical Examination Findings

Often located in the substernal region (sometimes the epigastric area), the chest pain or pressure frequently radiates to the neck, jaw, left shoulder, and left arm. Some patients may present with "anginal equivalent" symptoms include dyspnea, nausea and vomiting, diaphoresis, and unexplained fatigue.[4] The 5 most important history-related factors that help identify ischemia due to CAD, ranked in order of importance, are the nature of the anginal symptoms (Table 2), a history of CAD, male sex, older age, and the number of traditional risk factors present.[8,9]

Electrocardiography

The ACC/AHA guidelines state that an experienced emergency physician should review the results of 12-lead ECG within no more than 10 minutes after the arrival in the ED of a patient with chest discomfort or other symptoms suggestive of ACS (Figure 3).[3]

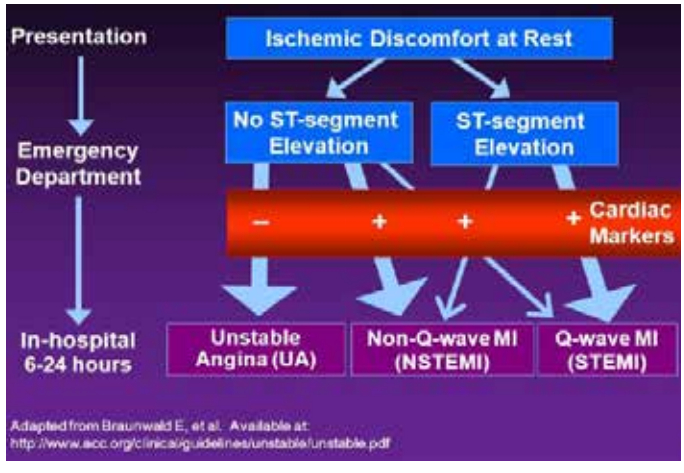


Fig. 1: Spectrum of Acute Coronary Syndromes

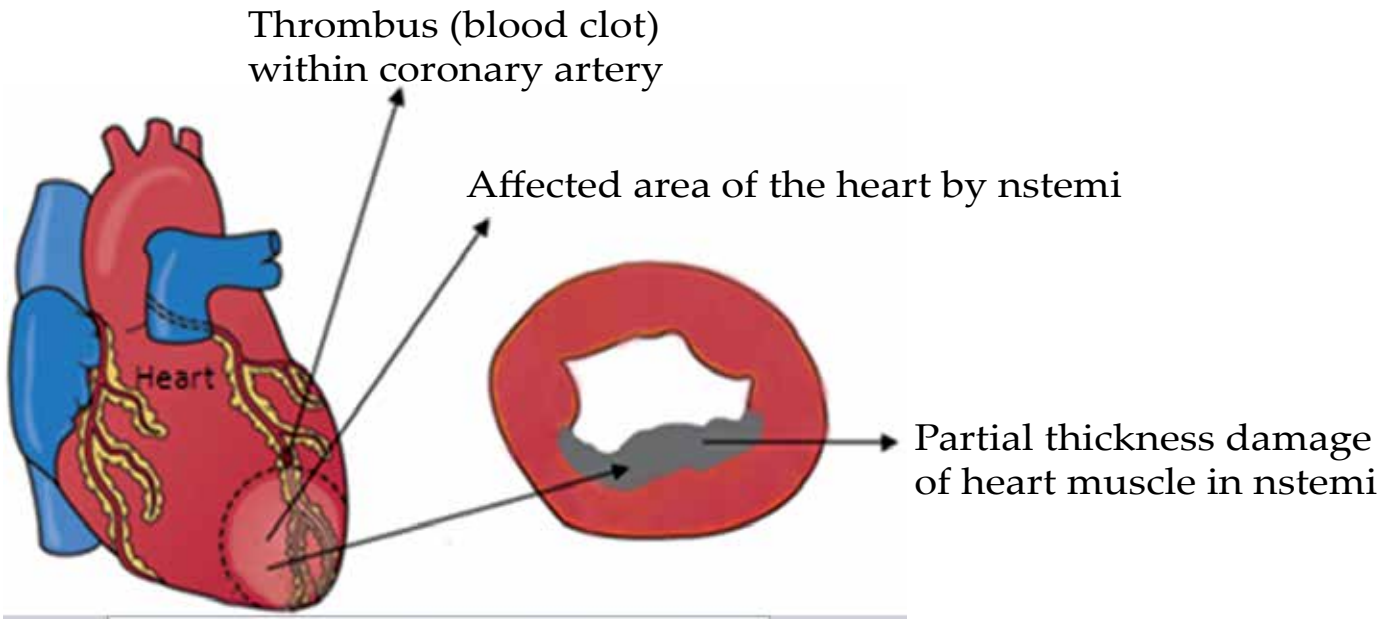
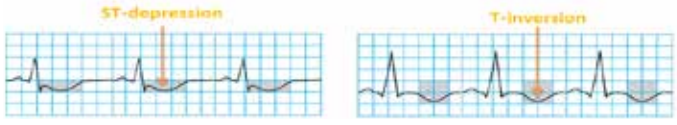


Fig. 2: Partial thickness damage of heart muscle in NSTEMI[7]



ST-segment depression in nstemi **T-wave inversion in nstemi**

Fig. 3

Findings on ECG associated with NSTEMI include ST-segment depression, transient ST-segment elevation, T-wave inversion, or some combination of these factors; depending on the severity of the clinical presentation, these findings are present in 30% to 50% of patients.[8,9] New ST-segment deviation, even of only 0.05 mV, is an important and specific measure of ischemia and prognosis.[11-13]

Cardiac Biomarkers of Necrosis

The advantages and disadvantages of the various biomarkers are shown in Table 3, and the timing of their release after acute MI is shown in Figure 3.

Early Risk Stratification

The management of patients with NSTE-ACS requires continuous risk stratification. Important prognostic information is derived from initial assessment, the patient's course during the early days of management, and the response to anti-ischemic and antithrombotic therapy. The choice of stress test is based on the patient's resting ECG and ability to exercise, local expertise, and available technologies. The exercise intensity of the treadmilltest (low level or symptom-limited) is used at the discretion of the attending clinician based on individual patient assessment. For invasively managed patients with residual nonculprit lesions, additional evaluation may be indicated to ascertain the significance of such lesions.

Noninvasive Test Selection

The goals of noninvasive testing in patients with a low or intermediate likelihood of CAD and high-risk patients who did not have an early invasive strategy are to detect ischemia and estimate prognosis. Because of its simplicity, lower cost, and widespread familiarity with its performance and interpretation, the standard low-level exercise electrocardiographic stress test remains the most reasonable test in patients who are able to exercise and who have a resting ECG that is interpretable for ST shifts. There is evidence that imaging studies are superior to exercise electrocardiographic evaluation in women for diagnosis of CAD. Patients with an electrocardiographic pattern that would interfere with interpretation of the ST segment (baseline ST abnormalities, bundle-branch block, LV hypertrophy with ST-T changes, intraventricular conduction defect, paced rhythm, pre-excitation, and digoxin) should have an exercise test with imaging. Patients who are unable to exercise should have a pharmacological stress test with imaging.

Selection for Coronary Angiography

In contrast to noninvasive tests, coronary angiography provides detailed structural information for assessment of prognosis and appropriate management. When combined with LV angiography, it also provides an assessment of global and regional LV function. Coronary angiography is usually indicated in patients with NSTE-ACS who have recurrent symptoms or ischemia despite adequate medical therapy or who are at high risk as categorized by clinical findings (HF, serious ventricular arrhythmias), noninvasive test findings (significant LV dysfunction with EF<40, large anterior or multiple perfusion defects or wall motion abnormalities on echocardiography, high-risk Duke treadmill score ≤−11), high-risk TIMI or GRACE scores, or markedly elevated troponin levels. Patients with NSTE-ACS who have had previous PCI or CABG also should be considered for early coronary angiography, unless prior coronary angiography data indicate that no further revascularization is feasible.

Before giving revascularization treatment, risk analysis

Table 2: Likelihood that Signs and Symptoms Indicate an ACS Secondary to CAD

Feature	High likelihood Any of the following	Intermediate likelihood *Absence of high-likelihood features and presence of any of the following*	Low likelihood *Absence of high or intermediate-likelihood features but may have*
History	Chest or left arm pain or discomfort as chief symptom reproducing previously documented angina Known history of CAD. including MI	Chest or left arm pain or discomfort as chief symptom Age ≥70 y Male sex Diabetes mellitus	Probable ischemic symptoms in absence of any of the intermediate-likelihood characteristics Recent cocaine use
Examination	Transient MR murmur, hypotension. diaphoresis, pulmonary edema, or rales	Extracardiac vascular disease	Chest discomfort reproduced by palpation
ECG	New, or presumably new, transient ST-segment deviation (≥1 mm) or T-wave inversion in multiple precordial leads	Fixed Q waves ST depression of 0.5-1.0 mm or T-wave inversion >1.0 mm	T-wave flattening or inversion <1 mm in leads with dominant R waves Normal ECG tracing
Cardiac markers	Elevated cardiac **Tnl,** TnT, or CK-MB levels	Normal	Normal

ACS = acute coronary syndrome: CAD = coronary artery disease; CK-MB = muscle and brain fraction of creatine kinase; ECG= electrocardiography: MI = myocardial infarction: MR = mitral regurgitation: Tnl = troponin 1: TnT = troponin T. Adapted from Agency for Health Care Policy and Research Clinical Practice Guidelines No. 10.[45]

in patients with NSTEMI should be done immediately after hospital admission. Several systems are available for risk stratification, but TIMI score and GRACE score are the best. These systems categorized the patients into low, medium and high risk groups.

Medium to high risk patients should be considered for early coronary angiography and revascularization, either by PCI (percutaneous coronary intervention) or by CABG (coronary artery bypass grafting). Early medical treatment is appropriate in low risk patients, and coronary angiography and revascularization are reserved for those who fail to settle with medical treatment.

Timi Score (Table 5)

The Thrombolysis in Myocardial Infarction (TIMI) Score is used to determine the likelihood of ischemic events or mortality in patients with unstable angina or non–ST-segment elevation myocardial infarction (NSTEMI)

Grace Score (Table 6)

GRACE (Global Registry of Acute Coronary Events) score is used for risk assessment in ACS (acute coronary syndrome) which includes NSTEMI, STEMI and UA. This score is more accurate because it is derived from a multinational registry of unselected patients and includes hospitals in Europe, Asia, North America, South America, Australia and New Zealand. Risk assessment should be performed at the time of hospital admission and is important because it gives an idea about probability of in-hospital death and also guides the appropriate treatment plan in nstemi and unstable angina.

Management of NSTEMI

Once the patient is diagnosed with NSTE-ACS, a combination of common therapies, including oxygen as needed, antianginal, antiplatelets and anticoagulants are initiated.

Oxygen

The role for routine O2 is much less clear than it was. O2 is a vasoconstrictor and as such may have detrimental effects Supplemental oxygen is indicated for patients who are hypoxic or at risk of hypoxia. For other patients a short period of O2 supplementation is reasonable during stabilisation. Unless the patient is in respiratory distress, has O2 saturation < 90% or high risk features of hypoxemia, oxygen is not indicated.[2]

Anti-anginals

Patients with ischemic chest pain and without contraindications to nitroglycerin should continue to get nitroglycerin for up to 3 doses. After 3 doses, IV Nitroglycerinis indicated, especially in the presence of 1) persistent chest pain, 2) hypertension and 3) heart failure.[2] Relief of chest pain with nitroglycerin was seen in 35% of patients with NSTE-ACS compared with 41% without NSTE-ACS.[10]Therefore, resolution of pain with nitroglycerine is neither sensitive nor specific in the diagnosis ACS.

Morphine

One study has suggested an increased mortality associated with morphine use in NSTEMI patients. There were significant problems with this trial and further study needed; in the meantime the use of morphine has been downgraded from a class 1 to a class 2a recommendation. ie. may be useful.

Table 3: Biochemical Cardiac Markers for the Evaluation and Management of Patients with Suspected ACS but without ST Segment Elevation on 12-Lead ECG

Marker	Advantages	Disadvantages	POC test	Comment	Clinical recommendations
Cardiac troponins	1. Powerful tool for risk stratification 2. Greater sensitivity and specificity than CK-MB 3. Detection of recent Ml up to 2 wk after onset 4. Useful for selection of therapy 5. Detection of reperfusion	1. Low sensitivity in very early phase of MI (<6 h after symptom onset) and requires repeated measurement at 8 to 1 2 h, if results are negative 2. Limited ability to detect late minor reinfarction	Yes	Data on diagnostic performance and potential therapeutic implications increasingly available from clinical trials	Useful as a single test for efficiently diagnosing NSTEMI (including minor myocardial damage), with serial measurements Clinicians should familiarize themselves with diagnostic "cutoffs" used in their local hospital laboratory
CK-MB	1. Rapid, cost-efficient, accurate assays 2. Ability to detect early reinfarction	1. Loss of specificity in setting of skeletal muscle disease or injury, including surgery 2. Low sensitivity during very early Ml (<6 h after symptom onset) or later after symptom onset (>36 h> and for minor myocardial damage (detectable with troponins)	Yes	Familiar to most clinicians	Previous standard and still acceptable diagnostic test in most clinical circumstances
Myoglobin	1. High sensitivity 2. Useful in early detection of Ml 3. Detection of reperfusion 4. Most useful in ruling out Ml	1. Very- low specificity in setting of skeletal muscle injury or disease 2. Rapid return to normal range limits sensitivity for later presentations	Yes	More convenient early marker than CK-MB isoforms because of greater availability of *assays* for myoglobin; rapid-release kinetics make myoglobin useful for noninvasive monitoring of reperfusion in patients with established Ml	

ACS= acute coronary syndrome: CK-MB = muscle and brain fraction of creatine kinase; ECG = electrocardiography; Ml = myocardial infarction: NSTEMI = non-ST-segment elevation Ml: POC = point-of-care. From *J.Am Coll Cardiol.*[42] with permission from Elsevier.

Nitrates

Nitrates are routinely used to control Pain, CHF and Hypertension. Initially sublingually and then topically, orally or intravenously.needed. IV nitrates should be started at 10 mcg / min (= 6ml/hr of 25mg GTN in 250ml dextrose and titrated every 5 minutes according to symptoms and BP. Using ceiling dose is 600mcg/min (=120ml per hour). SBP should not be allowed to fall rapidly or below 100mmHg It is advisable to change to an interrupted regime (oral/ topical) within 24 to 48 hrs if possible, in order to avoid tachyphylaxis.

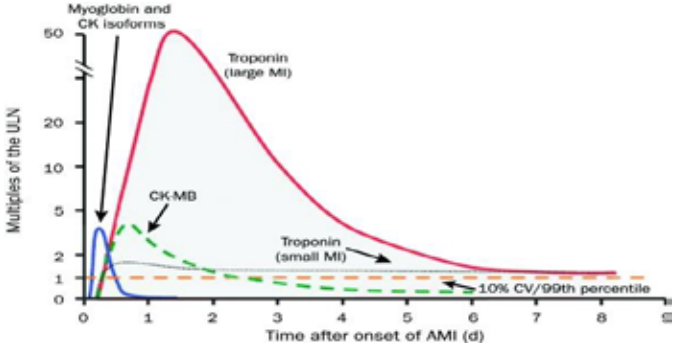


Fig. 4: Timing of release of biomarkers after MI

Beta Blockers

Aggressive beta blockade is now less favoured than it was in the management of UA/NSTEMI patients. CHF/Poor LV function is probably now a stronger indication for the use of beta blockers. It may be harmful toadminister IV beta blockers toUA/NSTEMI patients who have contraindications to beta blockade, signs of HF or low-output state, or other risk factors for cardiogenic shock. The usual starting dose is short acting Metoprolol 25 mg tds, though 12.5mg tds may be more appropriate if there are concerns about tolerance.

Aim for Metoprolol CR 95 mg daily by discharge but titrate slowly if there are concerns about haemodynamic stability or poor LV function. IV Metoprolol may be

Table 4: Clinical Assessment and Initial Evaluation

High-risk ACS	Intermediate-risk ACS	Lower-risk ACS
Prolonged chest pain cither > 20 min or ongoing, with one or more high-risk features: • ECG- Transient ST-segment elevation or depression > 0.5 mm Sustained ST-scgmcnt depression > 0.5 mm T-wave inversion > 1 mm in > 5 leads Deep (e.g., > 5 mm) T-wave inversion • *Positive biochemical markers:* Troponin level / CK-MB fraction clearly abnormal with compatible history • *Recurrent myocardial ischemia* with ECG ST-segment shift with or without pain • *Acute myocardial infarction in past 4 weeks;* pain with ECG ST abnormalities • *Hemodynamic compromise with ongoing chest pin* heart failure / hypotension 30-day rate of death or myocardial infarction: 12%-30%	No high-risk features, but one or more of: • *Ongoing chest pain,* yet no high-risk features • *Crescendo angina* preceding rest pain • *Borderline positive troponin:* e.g., troponin 1 level 0.4-2.0 ng4 • *Previous **intervention:*** percutaneous transluminal coronary angioplasty / coronary artery bypass surgery • *Increased baseline risk:* e.g., diabetes, elderly 30-day rate of death or myocardial infarction: 4V8%	No high- or intermediate-risk features • Chest *pain:* single episode at rest, crescendo exertional angina • FCG: normal or nonspecific abnormalities or unchanged from previous May include patients with history of known coronary artery disease or with risk factors for coronary artery disease 30-day rate of death or myocardial infarction: < 2%
ASA + heparin Glycoprotein lib/Ilia inhibitor Early cardiac catheterization	**ASA** + clopidogrel Heparin or low-molecular-weight heparin Decision for cardiac catheterization after stress testing	ASA monotherapy No heparin Observation for higher-risk indications

reasonable for initially persistent pain that fails to settle with nitrates.

Calcium Channel Blockers

These are not usual first line therapy. They should be considered in patients who cannot tolerate beta blockers or in whom a combination of nitrates and beta blockers does notcontrol symptoms.

Diltiazem is the preferred agent. Initially 30mg tds then slow release preparations. Amlodipine or Felodipine may be considered especially if the patient has poor LV function. They are safer if used in combination with beta blockers (less likely to induce tachycardia).

Anti-platelets

If there are no contraindications, every patient presenting with NSTE-ACS should be given an initial dose of aspirin 162mg to 325mg, keeping in mind that higher doses are not more effective.[2,11,12] Giving aspirin as soon as possible produces up to 46% reduction in composite events of non-fatal MI, non-fatal stroke and vascular deaths in patients with NSTE-ACS.[18] The first dose should be chewed or crushed to establish high blood levels quickly. Patients with contraindications to aspirin can be given 75 mg Clopidogrel as a substitute (Figure 5).[11,12]

Table 5: TIMI score

	Yes 1 point	No 0 points
Age ≥65		
≥3 risk factors for ACS; hypertension, hyperlipidemia, smoking, diabetes, family history		
Use of aspirin in last 7 days		
Prior coronary stenosis >50%		
>2 angina events in 24 hours or persisting discomfort		
ST-segment deviation of >0.05 mV on initial ECG		
Elevated cardiac biomarkers		
Total score		
Low risk	0-2	
Intermediate risk	3-4	
High risk	5-7	

Dual-Antiplatelet Therapy

In addition to aspirin, clopidogrel is part of the dual-antiplatelet therapy and should be initiated regardless of definitive treatment of NSTE-ACS.[11] Having both aspirin and clopidogrel on board prevents platelet adhesion and aggregation, which are the earliest steps in coronary artery thrombus formation. The loading dose of clopidogrel is 300mg.

NOVEL ANTICOAGULANTS

Novel OACs, including dabigatran, apixaban, rivaroxaban and darexaban, have been studied for secondary prevention of ACS. The only one of these novel OACs to show a positive benefit–risk profile was a low-dose regimen of rivaroxaban. The results of the ATLAS ACS 2 TIMI 51 trial showed that in patients treated with standard antiplatelet therapy (thienopyridine plus ASA or ASA alone), treatment with rivaroxaban 2.5 mg twice daily led to a significant reduction in the composite of cardiovascular death, MI and stroke over 24 months compared with placebo (9.1% vs 10.7%; hazard ratio 0.84; p=0.02). As expected, the rate of major bleeding was significantly increased with rivaroxaban versus placebo (1.8% vs 0.6%; hazard ratio 3.46; p<0.001).However, in selected patients with elevated biomarkers and no history of stroke or transient ischaemic attack, the rate of fatal bleeding with rivaroxaban 2.5 mg twice daily was similar to placebo (0.1% vs 0.3%). Moreover, in this patient subgroup, treatment with rivaroxaban 2.5 mg twice daily significantly reduced cardiovascular mortality and all-cause mortality (by 45% and 42%, respectively) compared with placebo. Based on this, rivaroxaban 2.5 mg twice daily has been approved in Europe (but not in the US) as an adjunct to standard antiplatelet therapy with thienopyridine plus ASA or ASA alone, for prevention of atherothrombotic events in patients who have experienced a recent ACS event and have elevated cardiac biomarkers and no history of stroke or transient ischaemic attack.[25]

After an acute coronary syndrome, dual antiplatelet therapy with clopidogrel plus aspirin is still considered

Table 6: Grace Score

Age	Points	HR	Points	SBP	Points	Cr	Points	Killip class	Points
<39	0	<70	0	<80	40	0.0-0.39	1	I	0
40-49	18	70-89	5	80-99	37	0.4-0.79	4	II	15
50-59	36	90-109	10	100-119	30	0.8-1.19	7	III	29
60-69	55	110-149	17	120-139	23	1.2-159	10	IV	44
70-79	73	150-199	26	140-159	17	1.6-1.99	13	Cardiac arrest	30
80-89	91	>200	34	160-199	7	2.0-3.99	21	Elevated cardiac markers	13
>90	100	-	-	>200	0	>4	28	ST-segment deviation	17
Low risk								1-88	
Intermediate risk								89-118	
High risk								>119	

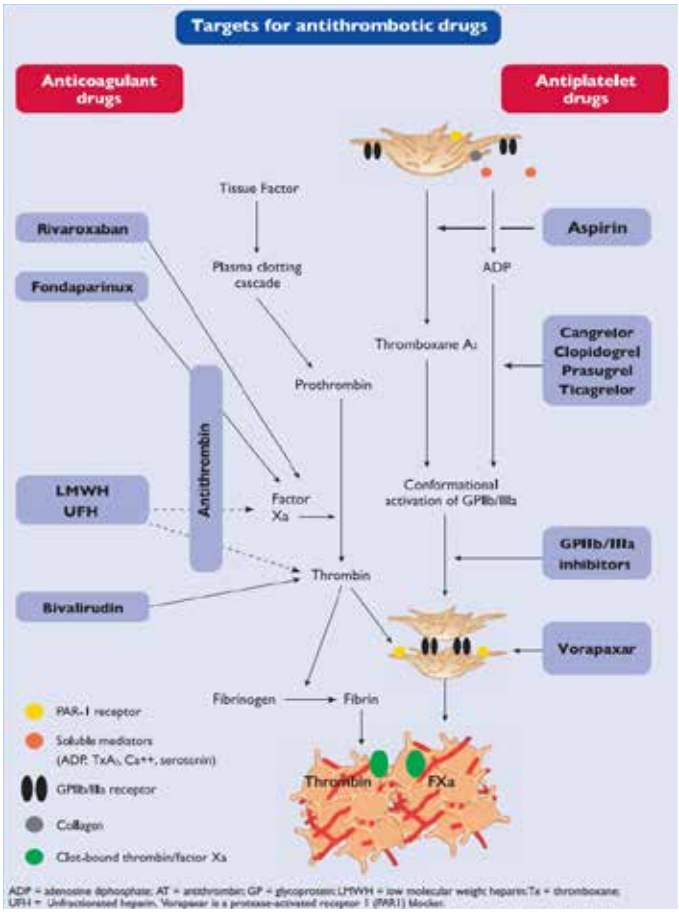


Fig. 5: Targets of available antithrombotic drugs

a standard of care. However, new therapeutic approaches are increasingly being explored[22,23] and, in particular, addition of a new oral anticoagulant (NOAC) to dual therapy ("triple therapy") has been studied quite extensively.

Even if one considers the most effective NOAC in combination with clopidogrel + ticagrelor, this triple therapy is not more effective than ticagrelor + aspirin. On the other hand, the increased risk of bleeding with triple regimens is well demonstrated. We therefore conclude that these triple regimens did not play any important roles in the patients experiencing an acute coronary syndrome.[24]

Anti-coagulation

Once antiplatelet treatment has been initiated, it is recommended that all patients should be started on anticoagulation, irrespective of treatment strategy.[2] Although, multiple anti-coagulants can be used, enoxaparin has the best evidence for use in decreasing recurrent cardiac events.[14,15,16]. The ESSENCE trial found Enoxaparin to be more effective than unfractionated heparin in preventing death at 30 days.[14] The rates of recurrent ischemic events and invasive diagnostic and therapeutic procedures were also greatly reduced when enoxaparin was used over unfractionated heparin.[15]

Fibrinolytics

There is a higher incidence of intracranial hemorrhage and myocardial infarctions in NSTE-ACS patients treated with fibrinolytics[17] and they are therefore are not indicated.[2]

Disposition

Optimal treatment for patients with NSTE-ACS is not as clear-cut as those with STEMI. After diagnosing NSTE-ACS and initiating treatment with anti-platelet, anti-anginal and anticoagulant medications, there are three pathways to definitively treat NSTE-ACS:

1. Immediate invasive strategy, (angiography and revascularization) within 2 hours.
2. Early-invasive treatment, (angiography followed by revascularization) within 24 hours.
3. Ischemia-guided treatment involves maximal medical therapy with antiplatelet and anticoagulant agents.

Immediate-Invasive Treatment

Immediate-invasive treatment is indicated for the patient with NSTE-ACS that continues to have refractory angina despite intensive medical therapy, hemodynamic instability due to cardiogenic shock or overt heart failure, or sustained VT or VF, despite maximal medical therapy.[2] Within 2 hours, these patients should be taken to the catheterization lab or transfer to a facility with interventional capabilities.

Early-Invasive Treatment

When a patient with NSTE-ACS has any of the below features, they benefit more from early-invasive management:[2,17]

1. GRACE Score >140, TIMI Score > 3
2. Temporal change in Troponin or
3. New or presumably new ST-depressions

Although these are the current recommendations, the decision for invasive management should be coordinated with the cardiologist.

Ischemia-guided Treatment

Formerly known as early-conservative treatment, ischemia-guided treatment involves maximum medical therapy withdual-antiplatelet therapy and anti-coagulants and is the preferred treatment for[2,17]

1. TIMI score 0-2 (low risk) or GRACE Score < 109
2. Low risk, Troponin-Negative Women
3. Absence of high-risk features

Multiple studies have shown equivocal outcomes between early-invasive and ischemia-guided treatment in low-risk patients.[17,20,21] However, if the low-risk patient is in the emergency department and starts having recurrent chest pain or becomes hemodynamically unstable, then invasive management should be pursued (Figure 6).

CORONARY REVASCULARIZATION (FIGURE 7)[1]

Coronary revascularization (PCI or CABG) is carried out to improve prognosis, relieve symptoms, prevent

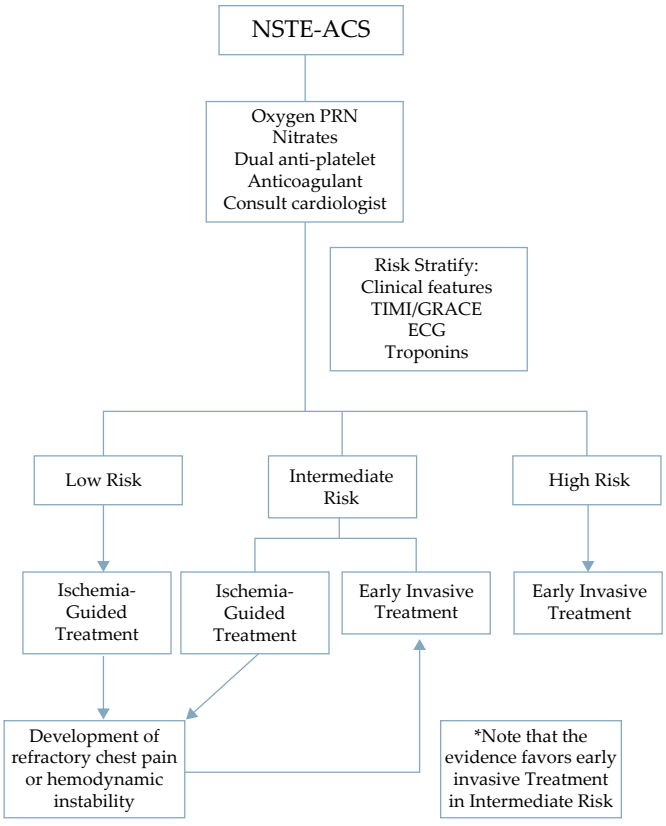


Fig. 6: Algorithm for Patients with UA/NSTEMI Managed by an Initial Conservative Strategy

ischemic complications, and improve functional capacity. The decision to proceed from diagnostic angiography to revascularization is influenced not only by the coronary anatomy but also by a number of additional factors, including anticipated life expectancy, ventricular function, comorbidity, functional capacity, severity of symptoms, and quantity of viable myocardium at risk. These are all important variables that must be considered before revascularization is recommended. For example, patients with distal obstructive coronary lesions or those who have large quantities of irreversibly damaged myocardium are unlikely to benefit from revascularization, particularly if they can be stabilized on medical therapy. Patients with high-risk coronary anatomy are likely to benefit from revascularization in terms of both symptom improvement and long-term survival. The indications for coronary revascularization in patients with UA/NSTEMI are similar to those for patients with chronic stable angina.

CONCLUSIONS[1]

In general, the indications for PCI and CABG in UA/NSTEMI are similar to those in stable angina. High-risk patients with LV systolic dysfunction, 2-vessel disease with severe proximal LAD involvement, severe 3-vessel disease, or left main disease should be considered for CABG. Many other patients will have less severe CAD that does not put them at high risk for cardiac death. However, even less severe disease can have a substantial negative affect on the quality of life. Compared with high-risk patients, low-risk patients receive negligible or very modestly increased chances of long-term survival with

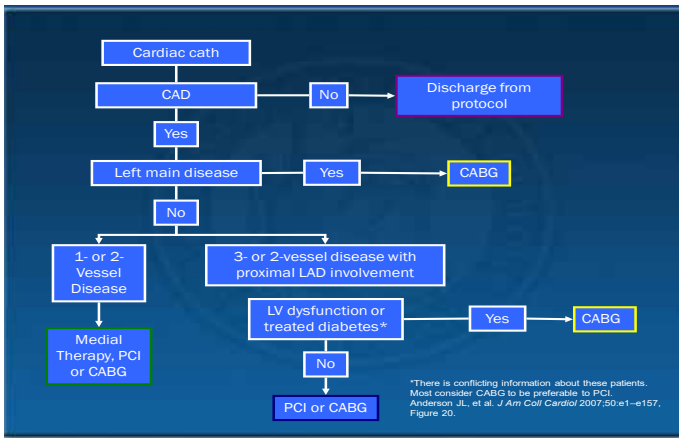


Fig. 7: Revascularization Strategy in UA/NSTEMI

CABG. Therefore, in low-risk patients, quality of life and patient preferences are given more weight than are strict clinical outcomes in the selection of a treatment strategy. Low-risk patients whose symptoms do not respond well to maximal medical therapy and who experience a significant negative affect on their quality of life and functional status should be considered for revascularization.

V. Hospital Discharge and Post–Hospital Discharge Care[(1)]

The acute phase of UA/NSTEMI is usually over within 2 months. The risk of progression to MI or the development of recurrent MI or death is highest during that period. At 1 to 3 months after the acute phase, most patients resume a clinical course similar to that of patients with chronic stable coronary disease.

Return to normal activities

1. Appropriate advice will vary from patient to patient.
2. Revascularised patients can return to activities sooner.
3. Work – normally 2 weeks
4. Sexual activity – normally 7-10/7
5. Air Travel – normally 2 weeks
6. Driving - normally 2 weeks post uncomplicated MI

Lifestyle Modification / Discharge considerations

1. Encourage smoking cessation.
2. Aim for regular daily exercise of 30-60 min
3. Yearly influenza vaccination
4. Screen and treat for depression
5. Referral to cardiac CNS for cardiac rehabilitation

REFERENCES

1. ACC/AHA Guidelines for the Management of Patients With Unstable Angina and Non–ST-Segment Elevation Myocardial Infarction: Executive Summary and Recommendations.A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina) Eugene Braunwald, Elliott

M. Antman, John W. Beasley, Robert M. Califf, Melvin D. Cheitlin, Judith S. Hochman, Robert H. Jones et al

2. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014; 130:2354-2394. http://www.ncbi.nlm.nih.gov/pubmed/25249586
3. Platelet Receptor Inhibition for Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-PLUS) Trial Investigators Inhibition of the platelet glycoprotein IIb/IIIa receptor with tirofiban in unstable angina and non-Q-wave myocardial infarction [published correction appears in *N Engl J Med* 1998; 339:415] *N Engl J Med* 1998; 338:1488-1497.
4. Anderson JL, Adams CD, Antman EM, et al. Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction. *J Am Coll Cardiol* 2007; 50:e1-e157
5. Abidov A, Rozanski A, Hachamovitch R, et al. Prognostic significance of dyspnea in patients referred for cardiac stress testing. *N Engl J Med* 2005; 353:1889-1898.
6. Pryor DB, Shaw L, McCants CB, et al. Value of the history and physical in identifying patients at increased risk for coronary artery disease. *Ann Intern Med* 1993; 118:81-90.
7. Morise AP, Haddad WJ, Beckner D. Development and validation of a clinical score to estimate the probability of coronary artery disease in men and women presenting with suspected coronary disease. *Am J Med* 1997; 102:350-356.
8. Jayes RL, Jr, Beshansky JR, D'Agostino RB, Selker HP. Do patients' coronary risk factor reports predict acute cardiac ischemia in the emergency department? A multicenter study. *J Clin Epidemiol* 1992; 45:621-626.
9. Cannon CP, McCabe CH, Stone PH, et al. The electrocardiogram predicts one-year outcome of patients with unstable angina and non-Q wave myocardial infarction: results of the TIMI III Registry ECG Ancillary Study. *J Am Coll Cardiol* 1997; 30:133-140.
10. Grailey K and Glasziou PP. Diagnostic accuracy of nitroglycerine as a 'test of treatment' for cardiac chest pain: a systematic review. *Emerg Med J* 2012; 29:173. http://www.ncbi.nlm.nih.gov/pubmed?term=21511974.
11. Simons, M., Cutlip, D., Lincoff, M.A. Antiplatelet agents in acute non-ST elevation acute coronary syndromes. In C.P. Cannon, F. Verheugt (Ed.), (2010). Retrieved from https://www-uptodate-com.ezproxy.library.wisc.edu/contents/antiplatelet-agents-in-acute-non-st-elevation-acute-coronary-syndromes?source=search_result&search=Antiplatelet+agents+in+acute+nonST+elevation+acute+coronary+syndromes&selectedTitle=1%7E150#H4
12. Antithrombotic Trialists's Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high riskpatients. *BMJ* 2002; 324:71. http://www.ncbi.nlm.nih.gov/pubmed/11786451
13. Yusuf S, Zhao F, Mehta SR, et al. Clopidogrel in Unstable Angina to Prevent Recurrent Events Trial Investigators. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med* 2001; 345:494. http://www.ncbi.nlm.nih.gov/pubmed/11519503
14. Cohen M, Demers C, Gurfinkel EP, et al. A comparison of low-molecular-weight heparin with unfractionated heparin for unstable coronary artery disease. Efficacy and Safety of Subcutaneous Enoxaparin in Non-Q-Wave Coronary Events Study Group. *N Engl J Med* 1997; 337:447. http://www.ncbi.nlm.nih.gov/pubmed?term=9250846
15. Goodman, S. G., Cohen, M., Bigonzi, F., et al. Randomized trial of low molecular weight heparin (enoxaparin) versus unfractionated heparin for unstable coronary artery disease. *Journal of the American College of Cardiology* 1997; 36:693-698. http://www.ncbi.nlm.nih.gov/pubmed?term=10987586
16. Antman EM, McCabe CH, Gurfinkel EP, et al. Enoxaparin prevents death and cardiac ischemic events in unstable angina/non-Q-wave myocardial infarction. Results of the thrombolysis in myocardial infarction (TIMI) 11B trial. *Circulation* 1999; 100:1593. http://www.ncbi.nlm.nih.gov/pubmed?term=10517729
17. Cannon, CP and Turpie AG. Unstable Angina and Non-ST-Elevation Myocardial Infarction: Initial Antithrombotic Therapy and Early Invasive Strategy. *Circulation* 2003; 107:2640-2645. http://www.ncbi.nlm.nih.gov/pubmed/12782615
18. Granger CB, Goldberg RJ, Dabbous, et al. Global Registry of Acute Coronary Events Investigators. Predictors of hospital mortality in the global registry of acute coronary events. *Arch Intern Med* 2003; 163:2345. http://www.ncbi.nlm.nih.gov/pubmed/14581255
19. Antman EM, Cohen M, Bernick PJ, et al. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision-making. *JAMA* 2000; 284:83542 http://www.ncbi.nlm.nih.gov/pubmed/10938172
20. Damman P, Hirsch A, Windhausen F, et al. 5-Year Clinical Outcomes in the ICTUS (Invasive versus Conservative Treatment in Unstable coronary syndromes) Trial. *J Am Coll Cardiol* 2010; 55:858-864. http://www.ncbi.nlm.nih.gov/pubmed/20045278
21. Mehta SR, Granger CB, Boden WE, et al. Early versus Delayed Invasive Intervention in Acute Coronary Syndromes. *N Engl J Med* 2009; 360:2165-2175. http://www.ncbi.nlm.nih.gov/pubmed/19458363
22. Updated ESC Guidelines for managing patients with suspected non-ST-elevation acute coronary syndromes. *Eur Heart J* 2011; 32:2909–10.doi: 10.1093/eurheartj/ehr319
23. Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2011; 32:2999–3054. doi: 10.1093/eurheartj/ehr236.
24. New Oral Anticoagulants in Acute Coronary Syndrome: Is There Any Advantage Over Existing Treatments?Andrea Messori,1,* Valeria Fadda,1 Roberta Gatto,1 Dario Maratea,1 and Sabrina Trippoli1
25. Bayer Pharma AG. Xarelto® (rivaroxaban) Available at:http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_Product_Information/human/000944/WC500057108.pdf [accessed 9 June 2015].