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Treatment of NSTEMI (Non-ST Elevation Myocardial Infarction)

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Abstract Non-ST elevation myocardial infarction (NSTEMI) is a recognized diagnostic entity that has an unacceptable mortality rate when it goes unrecognized. Following diagnosis, initial treatment with analgesics, nitrates and anti-platelet agents forms the initial approach. New anti-platelet agents such as ticagrelor and prasugrel need to be clearly understood. Simultaneously, risk stratification for ischaemia and bleeding of each such patient into mild, moderate and severe helps determine the course of further treatment that will be provided to the patient. The major decision is the need for and timing of early coronary angiography to determine the anatomy of the culprit vasculature and the decision for coronary revascularization, either by the percutaneous approach or coronary artery bypass grafting. It is at this stage that the need for and type of anticoagulation will require decision making. Choices include fondaparinux, the heparins, bivalirudin and inhibitors of the coagulation cascade.

Keywords Non-ST elevation myocardial infarction · Cardiac biomarkers · Risk stratification · Clopidogrel · Ticagrelor · Percutaneous coronary intervention

Introduction

Coronary artery disease (CAD), by far the commonest variety of cardiovascular disease, includes a spectrum of conditions ranging from silent angina, stable and unstable angina pectoris, acute myocardial infarction, heart failure and sudden death. The first four of these are referred to as "acute coronary syndromes" (ACS). Though chest pain is the commonest symptom in patients with ACS, the diagnosis is contingent on the electrocardiogram (ECG), which identifies two groups of people, viz. those with persistent ST-segment elevation of more than 20 min duration (ST-elevation myocardial infarction or STEMI), and without persistent ST-segment elevation (including patients with persistent or transient ST-segment depression, T wave inversions, flat T waves or pseudo-normalization of T waves or no ECG changes at all), after a diagnosis of non-cardiac chest pain has been excluded. This paper will focus on this latter group of patients, especially those with non-ST elevation myocardial infarction (NSTEMI). The annual incidence of NSTEMI varies significantly between countries, with a mean global annual incidence of about 3 per 1,000 population [1].

Pathophysiology of Acute Coronary Syndromes

The disease begins gradually with accumulation of atherosclerotic plaques in the coronary arteries until one of these either ruptures or erodes at the luminal surface. The acute thrombus formed over the diseased plaque may be associated with coronary vasoconstriction and critical reduction of blood flow to the distal myocardium. This may be accompanied by endothelial dysfunction, accelerated atherothrombosis and further myocardial injury. NSTEMI lesions have lesser coronary stenosis with a thin overlying fibroatheroma, a large plaque burden, small luminal cross-sectional area or some combination of these [2] than STEMI lesions.

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Diagnosis of NSTEMI

The diagnosis of NSTEMI requires the following:

1. *History*: Chest pain, the leading symptom, typically presents as retrosternal discomfort, heaviness or pressure sometimes radiating to the left arm, neck or jaw, and lasting several minutes or occasionally persistent. There may be accompanying dyspnea, diaphoresis, nausea or vomiting and occasionally palpitations and syncope. Atypical symptoms include epigastric discomfort, sharp chest pains, or increasing breathlessness and are more common in older patients (≥75 years age), women, diabetic patients, and those with uraemia or functional decline. Atypical symptoms can lead to under-diagnosis, hence requiring a high index of suspicion. The symptoms may be aggravated by exertion and anaemia and relieved by rest or taking of nitrates. Risk factors for NSTEMI are similar to that for STEMI.
2. *Physical Examination*: This involves looking for complications of CAD such as heart failure and arrhythmias, precipitating conditions such as anaemia or thyroid problems or identifying non-ischaemic cardiac or non-cardiac causes of chest pain, such as pulmonary embolism, aortic dissection, pneumothorax and others.
3. *Electrocardiogram*: Features on the ECG suggesting NSTEMI include ST-segment depression or transient elevation and/or T-wave changes. However, the presence of a normal or inconclusive ECG at presentation does not exclude NSTEMI. Diagnosis may be enhanced by comparing with previous ECGs, if available, or repeat ECGs at 3–9 h after presentation or even at 24 h, at discharge, or immediately on symptom recurrence. Occasionally changes may be picked up with additional chest leads at V_7–V_9 and V_{3R}–V_{6R}. Transient bundle branch block during occurrence of symptoms signals ongoing coronary ischaemia.
4. *Cardiac Biomarkers*: Elevation of cardiac markers is crucial for a diagnosis of NSTEMI, distinguishing this from unstable angina. They have a role in risk stratification. The range of cardiac biomarkers becoming available is growing. In addition to the traditional creatine kinase MB isoenzyme (CKMB) and myoglobins which are less specific for cardiac muscle damage, troponins (both Trop-T and Trop-I) have been used as standard biomarkers over the last few years. In NSTEMI patients, cardiac troponin elevation occurs from myocardial damage secondary to distal embolization of platelet-rich thrombi from the site of a ruptured or eroded plaque. Troponins, when released into the circulation, usually rise at least 3 h after symptom onset. Other life-threatening causes of chest pain, e.g. dissecting aortic aneurysms, pulmonary embolism and patients with renal failure may also demonstrate elevated troponin levels. The recent introduction of highly-sensitive or ultrasensitive troponin assays [3, 4, 5••, 6•, 7, 8, 9•] has allowed earlier detection of myocardial damage in patients presenting with chest pain. The addition of a second sample of these newer assays 2–3 h after the first further increases their sensitivity.

Newer cardiac biomarkers [10••] are being tested in clinical trials for their incremental value and cost-effectiveness. One promising example is Copeptin (C-terminal pro-vasopressin) which is released very early soon after onset of symptoms [11–13, 14••, 15] and has demonstrated myocardial damage within an hour of symptom onset. Combinations of biomarkers may provide greater sensitivity for earlier diagnosis of NSTEMI.

Relief of Ischaemic Pain

Pain relief is one of the most pressing needs of the patient. In acute coronary ischaemia, the increased heart rate, higher blood pressure or high preload result in decreased myocardial oxygen supply and increased myocardial oxygen demand. This oxygen imbalance results in ischaemic pain. The objective of anti-ischaemic drugs is to reverse these processes and secure pain relief. Drugs that have been demonstrated to benefit symptoms and promote good outcomes are:

Nitrates: Their venodilator effects decrease myocardial oxygen demand by lowering myocardial preload and left ventricular end-diastolic volume, and at the same time increase myocardial oxygen supply by dilating coronary arteries and increasing coronary collateral blood flow. Nitrate use favours lesser increase in cardiac biomarker levels [16•]. When given intravenously, nitroglycerine allows titration of dose until symptom relief or occurrence of side effects. Caution is needed when administering nitrates to patients on phosphodiesterase-5 inhibitors (e.g., sildenafil) because of likely severe vasodilatation and hypotension.

β-Blockers: While the CRUSADE registry [17] registered a significant 34 % reduction (3.9 vs 6.9 %, $p < 0.001$) in in-hospital mortality with acute β-blocker administration, a systematic review conducted some years later [18•] did not demonstrate any such benefit if given within the first 8 h of presentation. Current recommendation [19•] includes introducing β-blockers within 24-h of diagnosis in those without signs of low-output heart failure or major risk factors for cardiogenic shock.

Calcium Channel Blockers: These are for patients already on nitrates/β-blockers, those for whom β-blockers are contraindicated [20], and those with coronary vasospasm.

Angiotensin Converting Enzyme (ACE) Inhibitors: Oral ACE inhibitors (if not contraindicated) may be given within 24 h of presentation for NSTEMI patients with pulmonary venous congestion or left ventricular ejection fraction (LVEF) ≤40 % or in the absence of hypotension. If ACE inhibitors are contraindicated, an angiotensin receptor blocker (such as losartan, telmisartan or valsartan) may be used [21].

Morphine: Data from the CRUSADE registry [22] demonstrated higher mortality in patients requiring morphine. While this may have been owing to a higher level of pain in such patients, the use of intravenous morphine in NSTEMI would be mainly for those with chest pain refractory to nitrates and presuming other anti-anginal therapy is also underway.

Risk Stratification in NSTEMI

The objective of risk stratification in patients with NSTEMI is to identify those at high risk for further ischemic events or adverse outcomes. The initial assessment is to detect patients at immediate high risk. Subsequent evaluation is to identifying patients who will benefit from an early invasive strategy at 4–48 h and, finally, at predicting who are at increased risk after discharge [23••].

On diagnosis of NSTEMI, a decision is required on the level of acute ischaemic and bleeding risk for the patient (high, intermediate or low). Such risk determinations aid decision making on available treatment options. Some common or promising risk stratification scoring systems [24] are:

- Thrombolysis in Myocardial Infarction (TIMI) score [25, 26] includes age ≥65 years, ≥3 CAD risk factors (high cholesterol, family history, hypertension, diabetes mellitus, smoking), prior CAD, aspirin in the past 7 days, at least two angina-related events in the previous 24 h, ST-segment deviation and elevated cardiac biomarkers (CKMB or troponin).
- Global Registry of Acute Coronary Events (GRACE) Score [27], which uses age, heart rate, systolic blood pressure, creatinine level, Killip class, cardiac arrest at admission, elevated cardiac markers and ST segment deviation.
- Platelet glycoprotein IIb/IIIa in unstable angina: receptor suppression using integrilin therapy (PURSUIT) [28, 29] scoring uses age (as a decade), gender, symptomatic class within the last 6 weeks, presence of heart failure symptoms, and ST depression on ECG.
- History, ECG, age, risk factors and troponin (HEART) [30] scores begin with zero, one or two points, depending on the extent of the abnormality. The HEART score is the sum of these five factors.

Some scoring systems for bleeding risk that may be used in the early assessment of NSTEMI include:

- *C*an *R*apid risk stratification of *U*nstable angina patients *S*uppress *AD*verse outcomes with *E*arly (CRUSADE implementation of the ACC/AHA guidelines) bleeding score [31] which considers baseline patient characteristics (female sex, history of diabetes, peripheral vascular disease), admission clinical variables (heart rate, systolic blood pressure, signs of CHF), and admission laboratory values (hematocrit, calculated creatinine clearance) to estimate the patient's likelihood of having an in-hospital major bleed event.
- *A*cute *C*atheterization and *U*rgent *I*ntervention *T*riage strateg*Y* (ACUITY) [32], an integer-based risk score that includes age, gender, serum creatinine levels, white cell count, anaemia, clinical presentation and use of antithrombotic medications, with weightage given to different levels of these seven variables.

With such available stratification systems, risks may be categorized into one of three groups with predicted six-monthly mortality, viz. low (0–3.0 %), intermediate (3.0–6.0 %) and high-risk (9.0 % and above) [33••]. Primary criteria for high-risk categorization includes relevant rise or fall in cardiac biomarker levels, and/or dynamic ST- or T-wave changes. Secondary criteria include diabetes mellitus, renal insufficiency (with eGFR of less than 60 mL/min/1.73 m^2), left ventricular ejection fraction ≤40 %, early post-infarction angina, recent percutaneous coronary intervention (PCI) procedures, prior coronary artery bypass grafting and intermediate to high risk stratification scores.

Early Management of NSTEMI

Risk-level determination allows one to offer advice regarding a variety of treatment procedures, viz. need for a variety of anti-platelet agents, glycoprotein IIb/IIIa inhibitors (GP23I) and anticoagulants, and allow rational discussion of a choice of early invasive versus conservative management. Figure 1 below outlines a schema for such decision making.

Antiplatelet Therapy

Measures to reduce the dominant role of platelet activation and aggregation in the formation and propagation of an arterial thrombus, form a major therapeutic objective in the management of these patients. Antiplatelet agents should be administered once the diagnosis of NSTEMI is likely

or definite. Three classes of antiplatelet agents will be discussed, viz. aspirin, $P2Y_{12}$ receptor antagonists and glycoprotein IIb/IIIa receptor antagonists.

Aspirin

Aspirin (between 150 and 325 mg per oral) should be administered [34–41] as soon as possible after presentation, provided no contraindications (e.g., allergy, active bleeding, current peptic ulceration, recent neurosurgery or haemorrhagic stroke) [42] exist to its use. Aspirin should be continued indefinitely at a daily maintenance dose of 75–150 mg. Aspirin therapy reduces the risk of a vascular event. Efficacy is not increased with higher maintenance doses, which carry a greater risk of gastrointestinal intolerance. The drug should be offered to all patients with NSTEMI, unless contraindicated.

$P2Y_{12}$ Receptor Inhibitors

The thienopyridines were the first group of $P2Y_{12}$ receptor inhibitors used in NSTEMI.

Ticlopidine

Ticlopidine, the first of this group to be used is an adenosine diphosphate (ADP) receptor antagonist. Originally used in patients not tolerating aspirin and later tried in patients requiring dual antiplatelet therapy, reports of increased risk of thrombotic thrombocytopenic purpura (TTP) and neutropenia led to its relative non-use and replacement by clopidogrel. Ticlopidine is usually given orally in 250 mg doses twice daily. It is contraindicated in patients with bleeding disorders, active bleeding and severe liver disease, and needs to be reviewed in those with renal or hepatic impairment, geriatric patients (increased sensitivity), pregnancy, lactation, children, neutropenia and TTP. It may be used in patients allergic to clopidogrel.

Clopidogrel

Clopidogrel, a pro-drug activated in the liver by the CYP2C19 isoenzyme of cytochrome P450, irreversibly inhibits the $P2Y_{12}$ subtype of ADP receptor and also blocks activation of the glycoprotein IIb/IIIa pathway. Platelet

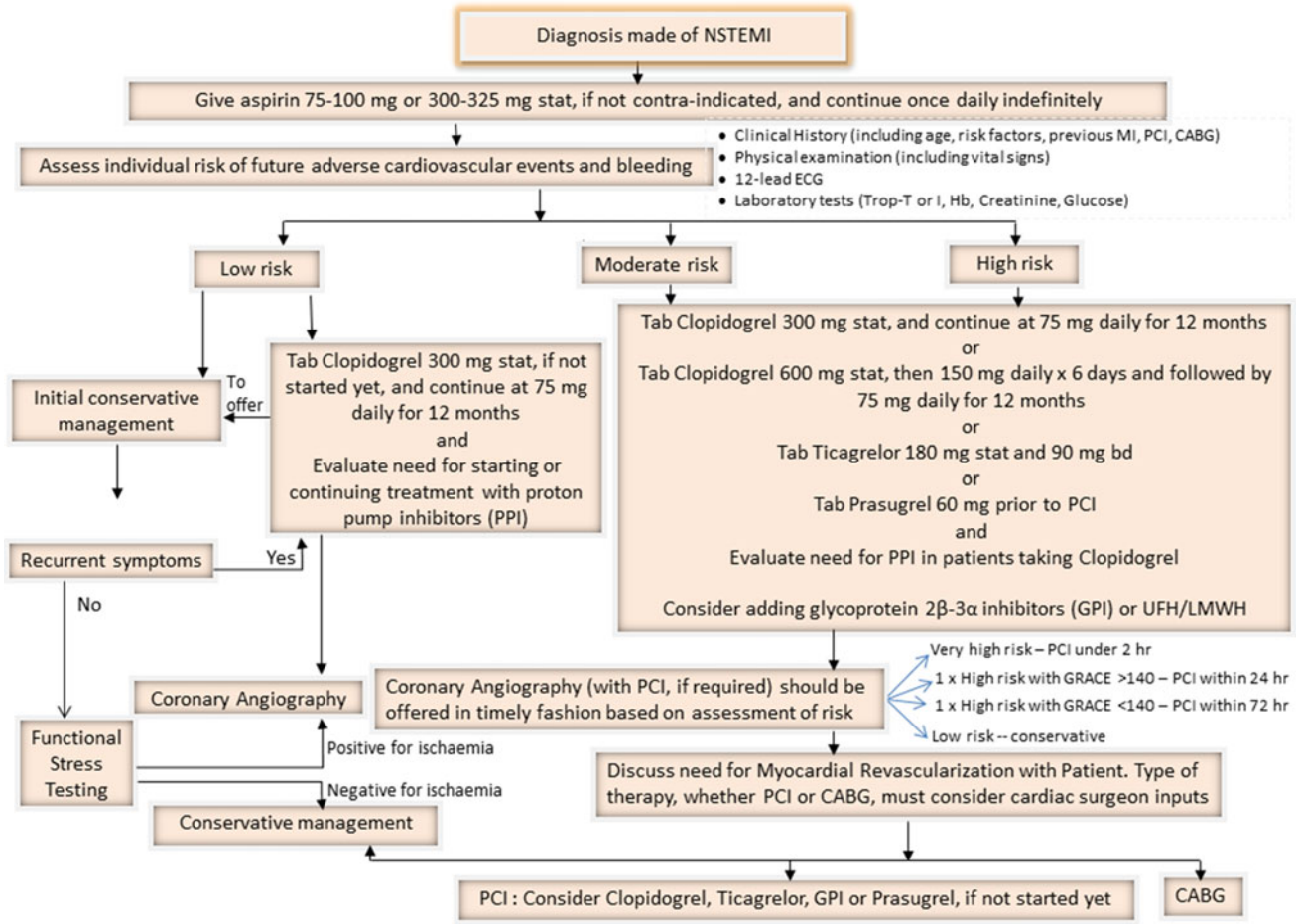

Fig. 1 Schema for early management of NSTEMI

inhibition is evident 2 h after a single dose of oral clopidogrel. Patients with a variant allele for the CYP2C19 isoenzyme have lower levels of active metabolite and are 1.5–3.5 times more likely to die or have complications than those with the high-functioning allele [43–45]. Poor metabolizers apparently make up to about 14 % of the patients and are at high risk of treatment failure. The Food and Drug Administration (FDA) [46] has placed a warning on clopidogrel to make doctors and patients aware of this.

Serious adverse drug reactions associated with clopidogrel include severe neutropenia, TTP and hemorrhage (gastrointestinal and cerebral). Use of NSAIDs is discouraged in those taking clopidogrel, owing to increased risk of gastrointestinal bleeding. Other side effects include diarrhea and rash.

Clopidogrel interacts with many drugs, especially proton pump inhibitors (PPIs) (except possibly pantoprazole), phenytoin, tamoxifen, tolbutamide, warfarin, heparin, enoxaparin, anistreplase, dipyridamole, streptokinase, ticlopidine and urokinase. In November 2009, the FDA announced that clopidogrel should be used with caution in patients on PPIs such as omeprazole and esomeprazole [47].

Clopidogrel is currently the commonest used $P2Y_{12}$ receptor inhibitor in patients presenting with NSTEMI. The recommended loading dose is uncertain, especially in those undergoing PCI. The benefit of higher-dose clopidogrel loading is offset by an increase in major bleeding [48]. Current United States guidelines recommend higher-dose (600 mg loading, 150 mg daily for 6 days and then 75 mg daily for 12 months) than the lower dose of 300 mg loading and 75 mg daily thereafter for those undergoing PCI, because of reduction in myocardial (re)infarction and cardiovascular death at these higher doses in the CURRENT–OASIS 7 Trial [48, 49•] and in stent thrombosis. For those who had a prior loading dose of 300 mg, a supplementary dose of 300 mg is suggested. Doses for patients aged 75 years and above has not been established.

Clopidogrel therapy may be initiated early, such as at the emergency department or even earlier, or delayed until just after cardiac catheterisation when coronary anatomy can be defined and a decision made on whether revascularisation is appropriate. The advantage of early treatment is the potential to reduce ischaemic events. The disadvantage is the potential for increased bleeding in patients who subsequently may require early CABG [50]. The delayed approach avoids the increased bleeding risk. Current consensus is to go for early initiation of higher-dose clopidogrel.

Prasugrel

Prasugrel is chemically similar to and produces more rapid and consistent platelet inhibition than clopidogrel [51]. Response to prasugrel is not affected significantly by CYP inhibitors, including PPIs, or loss-of-function variants of the CYP2C19 gene; nor by reduced ABCB1 function [52]. The recommended loading dose is 60 mg orally administered not later than 1 h once coronary anatomy is defined and a decision made to proceed with PCI. Maintenance therapy is 10 mg daily for at least 12 months. Prasugrel has a lower incidence of cardiovascular death, non-fatal myocardial infarction and stroke when compared to clopidogrel [53] owing to a significant risk reduction for myocardial infarction and lesser stent thrombosis. However, life-threatening bleeding has been noted, especially in patients with a history of cerebrovascular accidents. Greater benefit without increased risk of bleeding is observed in diabetic patients. There is no apparent net clinical benefit in patients >75 years of age and in those with body weight <60 kg.

Ticagrelor

This is a cyclopentyl-triazolo-pyrimidine and reversibly binds to the $P2Y_{12}$ inhibitor with a plasma half-life of 12 h. The degree of $P2Y_{12}$ inhibition depends mainly on the plasma ticagrelor level. The onset of action is rapid compared with clopidogrel. Offset of action is also quicker with faster recovery of platelet function and shorter duration of effect. Ticagrelor increases levels of drugs metabolized through CYP3A, such as simvastatin. Moderate CYP3A inhibitors such as diltiazem increase levels and lengthen duration of ticagrelor effect.

In the PLATO trial [54], ticagrelor (180 mg loading dose and 90 mg twice daily for up to 12 months) reduced death from vascular causes, MI, or stroke to 9.8 % from 11.7 % in the clopidogrel group (HR 0.84; 95 % CI 0.77–0.92; $p = 0.001$). Stent thrombosis was reduced from 1.9 to 1.3 % ($p = 0.01$) and total mortality from 5.9 to 4.5 % ($p = 0.001$). Ticagrelor also reduced early and late mortality following CABG from 9.7 to 4.7 % (HR 0.49; CI 0.32–0.77; $p = 0.01$). Adverse effects include dyspnea (usually transient, occurring within the first week and occasionally persisting until cessation of treatment [54, 55, 56•, 57]) without any deterioration in cardiac or pulmonary function, increased frequency of ventricular pauses, and asymptomatic increases in uric acid [54, 58, 59]. Caution is advised in patients with either advanced sinoatrial disease or second- or third-degree atrioventricular block, unless already treated by permanent pacemaker. The mechanism for the dyspnoea and ventricular pauses remains uncertain.

Glycoprotein IIb/IIIa Inhibitors

GP23I have not demonstrated any reduction in MI or death rates when used in purely medically managed patients

not subjected to coronary revascularization procedures. In patients who had undergone PCI [60••], if GP23Is were maintained during the procedure, significant cardiovascular benefit was observed. There was generally an increase in bleeding complications, though not intracranial haemorrhage. The recommendations for use of these agents would be as follows:

1. Not routinely before coronary angiography if the decision is for an invasive treatment strategy [61].
2. Not for patients on dual anti-platelet therapy if for conservative management, unless the risk of bleeding is low [60••, 61].
3. In high-risk patients eptifibatide or tirofiban may be added to those on aspirin alone or on dual anti-platelet therapy prior to angiography if there is ongoing ischaemia and the risk of bleeding is low [61, 62].
4. They may be withheld until after angiography, when the procedure demonstrates the presence of thrombi and the extent of the disease is clear, biomarker levels are elevated, and there has already been concurrent treatment with a $P2Y_{12}$ inhibitor and a relative lack of factors that contribute to serious bleeding [63, 64].

Anti-coagulant Therapy

Since the initiating event in a myocardial infarction is the formation of a thrombus, reducing pro-thrombotic events would assist in minimizing propagation of the clot formed. In addition to platelet inhibition, processes that counteract conversion of prothrombin to thrombin would naturally decrease the conversion of fibrinogen to fibrin [65, 66]. Together, these two processes may be expected to further inhibit thrombus formation in a coronary vessel. Therefore, anticoagulation is recommended for all patients presenting with NSTEMI, in addition to dual anti-platelet therapy. Selection of anticoagulants should be based on subsequent ischaemic bleeding risk profile. Such anticoagulation should be maintained at least until hospital discharge. Discontinuation of anticoagulant should be considered after completion of an invasive procedure, unless otherwise contra-indicated. During anticoagulation, gastric protection should be considered, especially with PPIs, since the commonest spontaneous bleed in such patients is gastrointestinal. Anti-platelet agents, on the other hand, need to be continued for at least a further 12 months, even without PCI.

Anti-coagulants can be divided into a few groups depending on their mode of action:

a. Heparins, such as unfractionated heparin (UFH) and low-molecular weight heparins (LMWH) have been used in patients with NSTEMI for more than a decade. UFH is proven to reduce the rate of death and MI in multiple trials [65], especially when given in combination with aspirin, though with some increased risk of bleeding. When invasive procedures such as PCI are performed the usual dose given is 70–100 IU/kg body weight, or 50–60 IU/kg if used in combination with a GP IIb/IIIa inhibitor [66]. Dosing should be guided by measurements of activated clotting times (ACT). UFH use should be terminated after removal of the arterial sheath. LMWHs, however, can be administered subcutaneously at a dose of 1 mg/kg every 12 h for at least 2 days until clinical stabilization. The arterial sheath should be removed at least 8 h following a dose of enoxaparin with the subsequent dose another 8 h after sheath removal. Treatment may be continued for up to 8 days. LMWH can be administered without the use of anti-factor Xa monitoring, except in patients with renal failure or obesity. Efficacy rates have generally been similar with both UFH and LMWH while lower bleeding rates have been noted with the LMWHs [67, 68]. Crossover of heparins in the same patient is usually not recommended.
b. Direct inhibitors of thrombin, e.g., bivalirudin. Bivalirudin directly inhibits thrombin by specifically binding both to the catalytic site and the anion-binding exosite of circulating and clot-bound thrombin [69]. It is to be administered at a dose of 0.1 mg/kg IV bolus followed by an infusion at 0.25 mg/kg/h until the PCI procedure is completed. Trials have demonstrated a similar efficacy endpoint when compared to heparins, both given with GP IIB/IIIa inhibitors [32, 70–72] with significant reduction in major bleeding [73].
c. Direct inhibitors of factor Xa such as apixaban, rivaroxaban and otamixaban: while apixaban and rivaroxaban have been used mainly for management of deep vein thrombosis, otamixaban, an investigational anti-factor Xa compound, in intermediate dosages, has been found, in initial studies [74] to offer substantial reduction in major coronary complications such as death and myocardial infarction in patients presenting with NSTEMI, with similar bleeding rate when compared to a combination of UFH and eptifibatide.
d. Indirect inhibitors of factor Xa such as fondaparinux: this is a synthetic, highly sulfated pentasaccharide, with a sequence derived from the minimal antithrombin (AT) binding region of heparin. Fondaparinux binds to AT with a higher affinity than the native pentasaccharide of UFH or low molecular weight heparin, and causes a conformational change in AT that significantly increases the ability of AT to inactivate factor Xa. Fondaparinux is licensed in Europe for treatment of NSTEMI in patients for whom invasive management is not indicated within 2 h of diagnosis. Administration of

the drug is recommended [75, 76, 77•] as soon as possible following diagnosis and continued for up to 8 days or hospital discharge, whichever occurs earlier. Fondaparinux is not yet recommended in patients for whom urgent PCI is indicated.

Coronary Revascularization in NSTEMI

The primary mechanism for occurrence of symptoms is coronary artery blockage. Various grades of patients constitute the spectrum that is NSTEMI. Those with low risk benefit from conservative management, while those at high risk may require an invasive approach. Whichever is taken would depend on the patient's clinical condition, presence of co-morbidities and risk factors, severity of lesions seen on coronary angiography, and a clear understanding of the risks and benefits of invasive versus conservative strategies.

Though routine invasive management has shown reduced overall rates of adverse outcomes compared with selective invasive strategy, it, has also demonstrated an early hazard of death and/or MI during the initial hospitalization for the procedure [78–80]. Two-year survivals and coronary ischaemia rates are significantly better with an early invasive approach [81, 82•] in both men and women. The reductions in cardiovascular death and MI are greater in high-risk groups than in those with low or intermediate risk [60••].

The best timing for invasive evaluation in NSTEMI patients at extremely high risk and who are haemodynamically unstable (those with ongoing chest pain in spite of optimal medical therapy, severe heart failure or life-threatening arrhythmias) is generally immediately after presentation (i.e., less than 2 h) [83••]. For patients with at least one primary high-risk criterion and a GRACE risk score >140, an early invasive strategy within 24 h of presentation would be advisable [84, 85•]. In patients with at least one primary high-risk criterion and a GRACE risk score <140, an invasive strategy is recommended within 72 h after first presentation [60••]. In those at low-risk and without recurrent symptoms, there needs to be non-invasive documentation of inducible ischaemia before a decision is made for invasive evaluation of the patient [60••, 86, 87]. For such patients, routine invasive evaluation is not recommended [60••, 81]. Where angiography is carried out, PCI of non-significant lesions is also not recommended.

Conclusion

Management of patients with NSTEMI is contingent on diagnosis, followed by stratification of risk for adverse cardiac events and major bleeding. Following initial relief of symptoms and haemodynamic optimization, further management revolves around measures to decrease thrombus propagation and re-open significantly blocked coronary vessels, if any. Future areas of NSTEMI management will include more aggressive imaging modalities to define coronary anatomy safely for earlier definitive treatment options.

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