Management of the acute coronary syndromes

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ABSTRACT

The clinical presentation with an acute coronary syndrome (ACS), is an indication of a serious event (atherosclerotic plaque rupture) occurring in the patient's coronary artery. This rarely resolves spontaneously and requires early recognition and appropriate management to prevent to further progression with life threatening consequences. The acute coronary syndromes include:
• Unstable angina (UA)
• Non-ST-segment elevation myocardial infarction (NSTEMI)
• ST-segment elevation myocardial infarction (STEMI)

This article will be focussing on the management of patients with UA and NSTEMI in general private practice who are hemodynamically stable. *(SA Fam Pract 2004;46(9): 16-20)*

Pathophysiology of the unstable plaque.

A basic knowledge of the underlying processes which may transform a stable plaque into an unstable plaque with all its consequences makes it easier to understand the disease and its management.[1,2]

Atherosclerosis is a systemic disease affecting the intima of large– and medium-size arteries (aorta, carotid, coronary, peripheral) with secondary changes occurring in the underlying media and adventitia in the more advanced stages of the disease. An atherosclerotic plaque may be non-flow-limiting but still has the potential to rupture causing a thrombus extending into the plaque as well as into the lumen. The extent of diameter stenosis on angiography is however misleading and not indicative of the plaque's potential to rupture. Rupture of the fibrous cap, lead to exposure of thrombogenic parts of the atherosclerotic plaque with subsequent activation of the clotting cascade and platelet adhesion, activation and aggregation. Plaques that rupture tend to be large, to demonstrate outward remodelling, have a large lipid core often occupying ≥40% plaque volume, show inflammatory cell infiltration of the fibrous cap and adventitia, posses a thin cap depleted of smooth muscle cells and have increased neovascularity.

The rate of progression is not linear and unpredictable. Plaque rupture may be sudden and spontaneous without any obvious trigger or may follow a particular event like extreme physical activity, emotional trauma, and exposure to illicit drugs, cold exposure or any other stressful event. The lipid core contains prothrombotic oxidised lipids and is impregnated with tissue factor derived from macrophages. This make the lipid core materials highly thrombogenic when exposed to circu-lating blood. Plaques of smokers contain more platelet factor and inflammatory cells (macrophages) than plaques of non-smokers, contributing to the high thrombotic state of smokers.

Thrombi can be present on atherosclerotic plaques without rupture of the fibrous cap when superficial intimal erosion is present. The precise mechanism in this scenario is unknown but is more common in young victims of sudden cardiac death, in smokers and in women.

It is clear from the above that stabilisation of the plaque and maintaining the integrity of the endothelial barrier is of critical importance. There is angiographic proof that risk factor modification leads to reduced new lesion formation, less lesion progression and sometimes even actual regression. Surprisingly, the magnitude of clinical event reduction is far greater than that accounted for by the relatively small changes in stenosis severity. This may be due to reduced propensity for plaque rupture and thrombosis by changing the composition of the plaque (plaque stabilisation).

ACUTE CORONARY SYNDROMES IN PRACTICE

Clinically the ACS's are a continuum ranging from unstable angina pectoris, N-STEMI and STEMI. Unstable angina is classically defined as:
- angina pectoris occurring at rest (or with minimal exertion),
- angina occurring in a crescendo pattern
- being severe and of new onset
- post-infarction angina.

Patients presenting with unstable angina or in N-STEMI may present with no ST-segment changes or ST-

Table I: The TIMI Risk Score for UA/NSTEMI

Characteristics	Points
Historical	
Age ≥65 yrs	1
≥3 Risk factors for CAD	1
Known CAD (stenosis ≥50%)	1
Aspirin use in past 7 days	1
Presentation	
Recent (24 h) severe angina	1
ST-deviation ≥0.5 mm	1
Cardiac markers	1
Risk Score = Total Points	(0-7)

segment depression, and the final distinction between the two entities are the presence or absence of biomarkers. Patients with UA have normal CK, CK-MB and troponin while all these are elevated in N-STEMI patients. Both groups may have the same clinical presentation and electrocardiographic abnormalities (no changes or varying degree of ST segment depression).

Once the diagnosis of an ACS has been made, further management will depend on the severity of the patient's symptoms. Patients with angina at rest or continuing chest pain, with arrhythmias, with new ECG changes or those who are hemodynamically unstable, should immediately be admitted to hospital and referred to a cardiologist as soon as they are stable enough to be transported. Patients with typical chest pain and ST-segment elevation on the presenting ECG have STEMI and besides the usual symptomatic and supportive treatment, they should be considered for urgent reperfusion (thrombolysis or primary angioplasty if available).

When confronted with a patient presenting with UA or N-STEMI, the first step is to stratify the patient into a low- or high-risk group. Certain clinical parameters identify patients who are at risk and are obtained from the patient's history and clinical presentation. The TIMI risk score is particular useful and can easily be applied in clinical practice (table I).[3] It is a simple way in which a doctor can estimate risk for serious com-plications and whether more aggressive therapy is indicated or not. Patients with UA or non-STEMI should be graded as low risk (0 to 2 points) intermediate (3 to 4) of higher risk (5 to 7). The higher the risk, the more aggressive the treatment should be and referral to a cardiologist should be as soon as the patient is stable or even earlier if the patient remains symptomatic despite optimal therapy. Note that apart from the cardiac markers, the other information is based on the patient's history and clinical presentation.

OPTIMAL THERAPY FOR ACS
Pathologically these syndromes are characterised by an erosion or rupture of a plaque with subsequent occlusive or non-occlusive coronary artery thrombosis. The interaction between activated platelets and thrombin is central to the pathogeneses of ACS and adequate antiplatelet and antithrombotic treatments are critical in the management of ACS. This therapy can be initiated by the GP in consultation with a cardiologist.
1. Aspirin: 300mg should be chewed and swallowed if the patient has not been on aspirin. Therapy must be continued indefinitely at a dose of 80-150 mg unless contra indications exist.
2. Clopidogrel: (Plavix®) inhibits adenosine diphosphate receptor mediated platelet activation and is a more potent platelet inhibitor than aspirin. Maximal inhibition of platelet aggregation takes 3 to 5 days after initiation of a standard dose (75mg daily) but occurs within 4-6 hours after the administration of a larger loading dose (300 to 600mg). The use of a high loading dose has been shown to obviate the need for Gp IIb/IIIa inhibitors in low-to-moderate risk patients undergoing PCI.[4] Unfortunately the administration of clopidogrel also increases the risk of serious bleeding and some physicians delay such treatment until the results of coronary arteriography are known and confirmed that by-pass grafting is not necessary. Should the drug be given before surgery, it should be discontinued for 5 to 7 days prior to surgery to avoid serious bleeding.

In patients undergoing percutaneous coronary interventions (PCI), the combination of aspirin and clopidogrel reduces the risk of vessel thrombosis compared with the aspirin alone. Until recently it was given for a period of 8-12 weeks mainly to prevent sub-acute thrombosis of the stented segment. Recent studies have, however, shown that the administration of aspirin and clopidogrel for 9 to 12 months after such a procedure reduces the incidence of major cardiovascular events without increasing the risk of bleeding as compared with aspirin alone. The accepted recommendation is now that all patients should be continued for at least 9 to 12 months on the combination.
3. Heparin: Low molecular weight heparin (LMWH) has replaced unfractionated heparin (UFH) largely due to its ease of use and its predictable anticoagulant effect.[5] The normal dose for enoxaparin (Clexane®) is 1mg/kg subcutaneously 12 hourly. Additional advantages of enoxaparin are:
- less platelet activation than UFH
- less heparin-induced thrombocytopenia
- less rebound ischemia (reoccurrence of ST-segment deviations on discontinuation of the drug) than UFH.

4. Nitrates: (spray, tablets or intravenous) should be given as clinically required. Of note is that in the absence of anginal symptoms, the usefulness of administering nitrates is of doubtful clinical significance.

5. Beta Blockers: In the absence of contra-indications, beta-blockers are extremely useful with favourable symptomatic and prognostic results. Adequate beta-blockade is present when the resting pulse is ± 60 beats/min. Beta-blockers are particularly useful in the presence of hypertension or arrhythmias and the first dose should be given intravenously if there is ongoing chest pain.

6. Statins: The benefits of statin therapy in patients with ACS have been shown in recent trials.[6] In the MIRACL study high doses of statin were given early (24 to 96 hours) after admission to patients presenting with unstable angina or in-STEMI. Death non fatal AMI, cardiac arrest with resuscitation or recurrent myocardial ischemia re-quiring emergency hospitalisation was significantly reduced (16% relative risk reduction with atorvastatin). Similar results were reported with pravastatin 20-40 mg (+ cholestyramine/niacin) with clinical end-points significantly less in the pravastatin group (17%) compared to the placebo group (43%).

Acute lipid lowering may stabilize the unstable coronary plaque but there is a growing body of evidence that statins also exhibit pleotropic effects beyond their lipid-lowering mechanisms that might provide benefit in the immediate period following an ACS. These effects are on the reduction of inflammatory mediators, modulation of the immune system, and reversal of endothelial dysfunction, reduced platelet activity and thrombosis as well as direct coronary plaque stabilizing effects.[5]

7. Glycoprotein IIb/IIIa inhibitors (Gp 2b/3a-I). The efficacy of Gp 2A/3B antagonist has recently been analyzed.[7] These agents should be considered if the troponin levels are positive and ischemic ST-segment abnormalities are present. In patients with negative troponins, no risk reduction was seen. The anti-platelet effects of these drugs are maximal within minutes after the initial bolus. Trials with tirofiban and eptifibatide have shown their efficacy in ACS patients. Treatment with Gp 2a/3b-I increases the risk of bleeding, which is typically muco-cutaneous or involves the access site of vascular intervention and hemoglobin and platelet counts should be monitored.

Take home message:

1. The ACS is not uncommon in GP practice and early diagnosis is critical.
2. Cardiac enzymes and biomarkers are of vital diagnostic and prognostic significance.
3. Aggressive anticoagulant and antiplatelet therapy is indicated.
4. Risk stratification using *The TIMI Risk Score* helps to identify high risk patients who may require earlier referral to a cardiologist.
5. There is no indication for thrombolytic therapy in patients presenting with ACS. ✍

See CPD Questionnaire p.47

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