

Acute Coronary Syndrome: Mending the Broken Heart

How should patients with acute coronary syndrome (ACS) be assessed, and what is the common treatment?

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Acute coronary syndrome (ACS) describes a set of clinical presentations with a similar underlying pathophysiology. This description encompasses unstable angina (UA), non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI). In each case, the underlying problem is due to disruption of an atherosclerotic plaque and subsequent thrombus formation. This results in a reduction or cessation of blood flow to the myocardium.

The ultimate presentation depends on a number of factors, including:

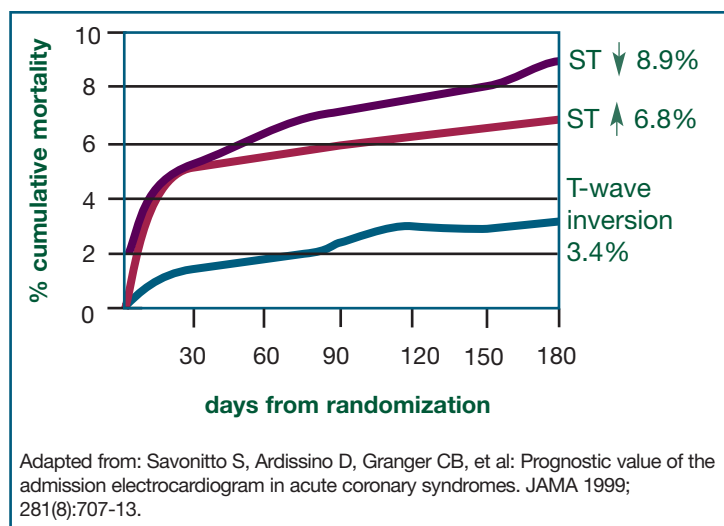
- extent of thrombus formation;
- degree to which blood flow is diminished;
- acuity with which the process has developed; and
- extent of collateral blood flow present within the coronary circulation.

Traditionally, UA and NSTEMI are grouped together due to overlap in terms of symptoms, electrocardiogram (ECG) findings, and treatment. The distinction between these two entities can be

subtle, but, by and large, depends on demonstrating the presence (NSTEMI) or absence (UA) of myocardial necrosis.

How can patients be clinically assessed?

When patients present with chest pain, their risk of future events can be determined based on clinical features, ECG findings, and cardiac markers (Table 1). This risk assessment is stratified into low-, moderate-, and high-risk categories. Risk assessment is not static, and needs



Adapted from: Savonitto S, Ardissino D, Granger CB, et al: Prognostic value of the admission electrocardiogram in acute coronary syndromes. JAMA 1999; 281(8):707-13.

Figure 1. Long-term mortality risk as a function of ST depression.

to be reviewed during initial evaluation, and throughout hospitalization. Several studies have shown that higher risk is associated with a worse prognosis, both in hospital, and on one-year followup.

What role do ECG findings play?

Electrocardiographic changes have prognostic significance, and are important in determining whether a chest pain syndrome is due to ischemic causes. In some cases, the ECG remains normal even when symptoms are due to an ischemic origin. However, in most cases, there are some minimal or subtle changes. Dynamic changes are most indicative of active ischemia, and it is therefore necessary to obtain serial ECGs during assessment. Occasionally, the first changes occur 18 to 24 hours after symptom onset. The most sensitive change is dynamic ST-depression, which is most strongly associated with outcome (Figure 1). T-wave inversion is often due to ischemia, but it is less specific; it may manifest with numerous non-ischemic causes (Table 2).

About the author ...

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Are troponins significant?

Troponin is an integral component of all muscle types. Troponins I and T are specific to cardiac myocytes. In the appropriate clinical setting, their presence is a very sensitive indicator of cardiac necrosis. Troponin assays, either qualitative or quantitative, are supplanting the use of creatine kinase and creatine kinase myocardial band for routine evaluation of patients presenting with chest pain.

Adverse outcomes have been shown to be associated with increasing troponin levels. Patients presenting with low levels of troponin

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Table 1

TIMI risk score for UA/NSTEMI

<u>Historical</u>	<u>Points</u>	<u>Risk of cardiac events (%) by 14 days in TIMI 11b*</u>		
		Risk score	Death or MI	Death, MI, or urgent revascularization
Age ≥ 65	1			
≥ 3 CAD risk factors (FHx, HTN, HC, DM, active smoker)	1			
Known CAD (stenosis ≥ 50%)	1	0-1	3	5
ASA use in past 7 days	1	2	3	8
Presentation		3	5	13
Recent (≤ 24 hours) severe angina	1	4	7	20
Elevated cardiac markers	1	5	12	26
ST deviation ≥ 0.5 mm	1	6-7	19	41

Risk score = Total points (0-7)

*Entry criteria: UA or NSTEMI defined as ischemic pain at rest within past 24 hours, with evidence of CAD (ST segment deviation or +marker)

Legend: TIMI: Thrombolysis in myocardial infarction
 FHx: Family history
 HC: Hypercholesterolemia
 ASA: Acetylsalicylic acid
 UA: Unstable angina
 CAD: Coronary artery disease
 HTN: Hypertension
 DM: Diabetes mellitus
 MI: Myocardial infarction
 NSTEMI: Non-ST-elevation myocardial infarction

Adapted from: Antman EM, Cohen M, Bernink 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(7):835-42.

elevation, without any other high-risk features, are initially managed appropriately with a comprehensive regimen. Then, during their hospitalization, patients are risk stratified with an exercise test, and their left ventricular function is assessed. Troponins may be elevated for reasons other than ischemia (Table 3). This should be kept in mind, particularly in the setting of atypical chest pain or serially normal cardiograms, especially when levels are low.

Troponins become positive four to six hours after an ischemic episode. Therefore, serial measure-

ments should be carried out to ensure that an initial negative result has not been misinterpreted.

What medications are used in ACS?

Plaque disruption, with platelet aggregation and thrombus formation, is the underlying pathogenesis in ACS. This has led to the development of medical regimens aimed at minimizing or

Table 2

Non-ischemic causes of T inversion

- Pericarditis
- Myocarditis
- Acute Rt heart strain (e.g., PE)
- Exacerbation of COPD
- Underlying hypertrophic cardiomyopathy

Rt: Right

PE: Pulmonary embolism

COPD: Chronic obstructive pulmonary disease

Table 3

Non-ischemic causes of troponin elevation

- Sepsis
- Pulmonary embolism
- Pericarditis
- Cardioversion
- Cardiopulmonary resuscitation
- Cardiomyopathy
- Myocarditis
- Rhabdomyolysis
- Severe renal failure

detering these processes from progressing. While acetylsalicylic acid (ASA) and unfractionated heparin have both proven to reduce events and improve outcomes, extensive studies have been carried out with newer agents to define their role in management.

ASA

All patients should receive ASA on presentation. Daily therapy should continue, unless there are absolute contraindications, such as anaphylaxis. The usual dose is 81 mg/day to 325 mg/day.

Clopidogrel

Recent studies have shown improved outcomes when clopidogrel is started early during hospitalization, and continued for up to nine months. There is a benefit to patients whether they are managed conservatively, or go on to angiography and percutaneous transluminal coronary angioplasty (PTCA). For patients requiring bypass surgery, clopidogrel

should be stopped at least five days prior to surgery because of an increased bleeding risk. Dosing is 300 mg orally, followed by 75 mg/day.

Beta blockers

Beta blockers reduce myocardial oxygen demand, and raise the threshold for ventricular fibrillation. In general, beta blockers with stimulant activity (ISA) should be avoided. Caution is required for patients with significant reactive airway disease, brittle diabetics, and those with excessive bradycardia. In many questionable cases, however, beta blockers are still well-tolerated, and can be monitored closely when started at low doses during in-hospital treatment.

Intravenous (IV) nitrates

Although they have not been shown to affect outcome, IV nitrates are effective for pain relief during acute ischemia. Ongoing pain despite high-dose nitrates may require further evaluation, and possible angiography, especially in high-risk patients with ongoing ECG changes.



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Unfractionated heparin vs LMWH

Heparin is a very effective anticoagulant whose role in ACS has been well-established, with demonstrated improvement in cardiac events. However, there are drawbacks to heparin therapy, including: platelet activation; significant protein binding (which results in inconsistent dosing, thus necessitating frequent monitoring); and an increased risk of bleeding.


Low-molecular-weight heparins (LMWHs) have much more consistent anticoagulant activity. Hence, LMWHs can be administered without the need for monitoring. They have a longer half-life, and can be administered once or twice daily. Aside from being more convenient, LMWHs are also associated with a lower bleeding risk, and they cause less platelet activation. The LMWH enoxaparin has been studied most extensively in the setting of ACS. The usual dose is 1mg/kg every 12 hours.

In head to head comparisons with unfractionated heparin, there was an improvement in the composite end point of death, myocardial infarction, need for urgent revascularization, and severe bleeding. Intermediate- and high-risk patients presenting with ACS should receive anticoagulation therapy. Either unfractionated heparin or LMWH can be used, but current recommendations favour the use of LMWH.

Glycoprotein (GP) IIb/IIIa inhibitors

The GP IIb/IIIa inhibitors are potent agents which, in the presence of all usual stimuli, block the final common step of platelet aggregation. There are two general types of inhibitors:

- abciximab, which is an antibody directed against the receptor; and
- eptifibatid and tirofiban, which are small molecules that inhibit the receptors.

At present, only eptifibatid and tirofiban are indicated in the setting of ACS. These agents are initiated on presentation, particularly in patients presenting with high-risk features, but also in those with intermediate risk. Although these agents can be used when a conservative strategy is contemplated, in most cases they will be initiated with the anticipation of proceeding to early angiography. 

Suggested Reading

1. Braunwald E, Antman EM, Beasley JW, et al: ACC/AHA guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction. *J Am Coll Cardiol* 2002; 40(7):1366-74.

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