

Acute Coronary Syndrome:

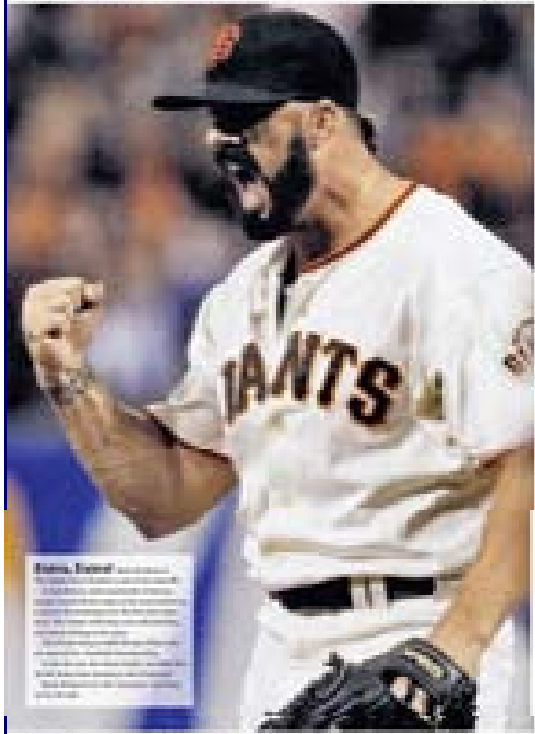
Thoughts on primary and secondary treatment

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Director, Chest Pain Center
University of Michigan Medical Center
Ann Arbor, MI.*

San Francisco Chronicle

GIANTS CLINCH

After a wild ride of a season, it can be played for the first time since 2003



Tim Lincecum celebrates after pitching a scoreless eighth inning to help the Giants clinch the NL West title.

Case 1

- **67 year old male**
- **h/o HTN**
- **Family h/o CAD (father had MI at 46 y/o, brother had MI at 56 y/o)**
- **Current smoker (1/2 PPD)**
- **Meds: Amlodipine, ASA 81 mg QD**
- **BMI: 31, not physically active**

Case 1

■ Exam:

- 142/74, HR 88, RR 16

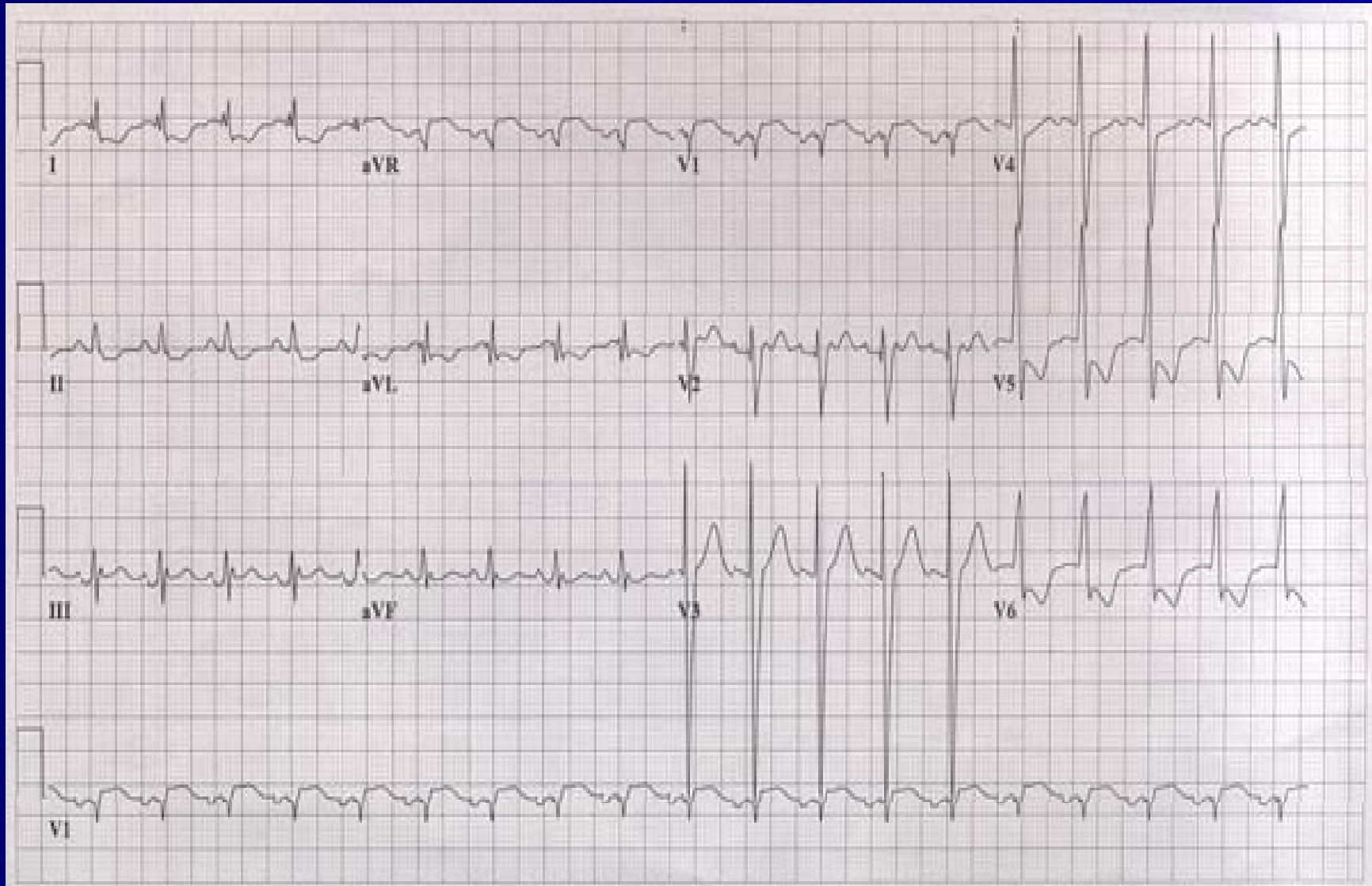
■ Screening Labs:

- Total C: 201
- LDL-c: 134
- HDL: 35
- Trig: 255
- FBS: 138
- HA1c: 5.5
- SCr 1.4
- Hg 12.2

Case 1

- Pt. calls office and related c/o exertional CP for the last 4 – 6 days.
- Pt advised to take his daily ASA (if he hasn't already), and go directly to an ED for further evaluation.

Case 1



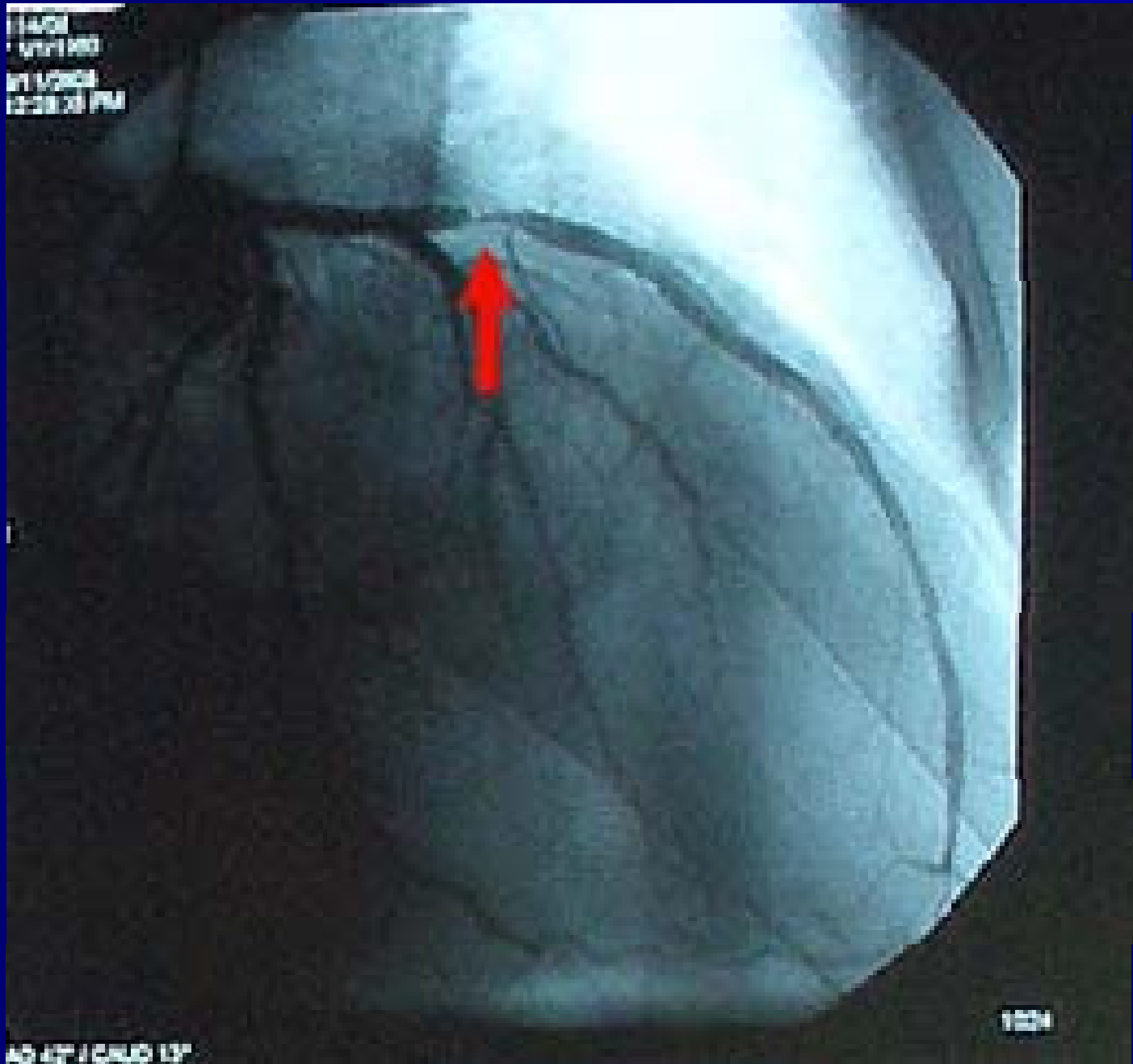
Case 1

- **Physical Exam (ED)**
 - Currently CP free
 - Hemodynamically stable
 - O₂ sat normal
- **Started on IV heparin, given ASA 162 mg (pt. took 162 mg before arriving)**
- **Troponins drawn:**
 - 0 hour: < 0.10
 - 6 hour repeat: 0.82

Case 1

- **Decision made to pursue invasive strategy:**

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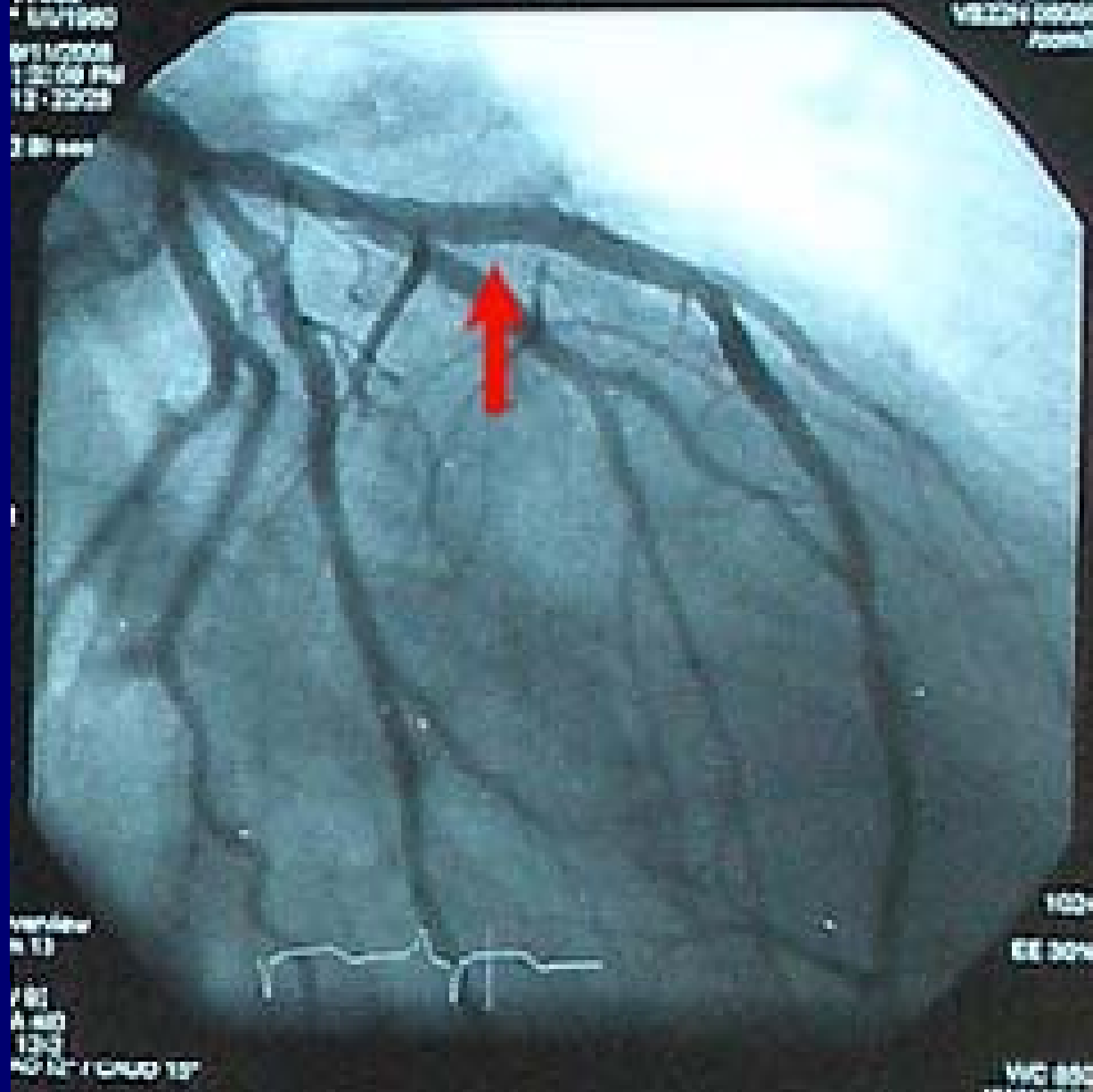


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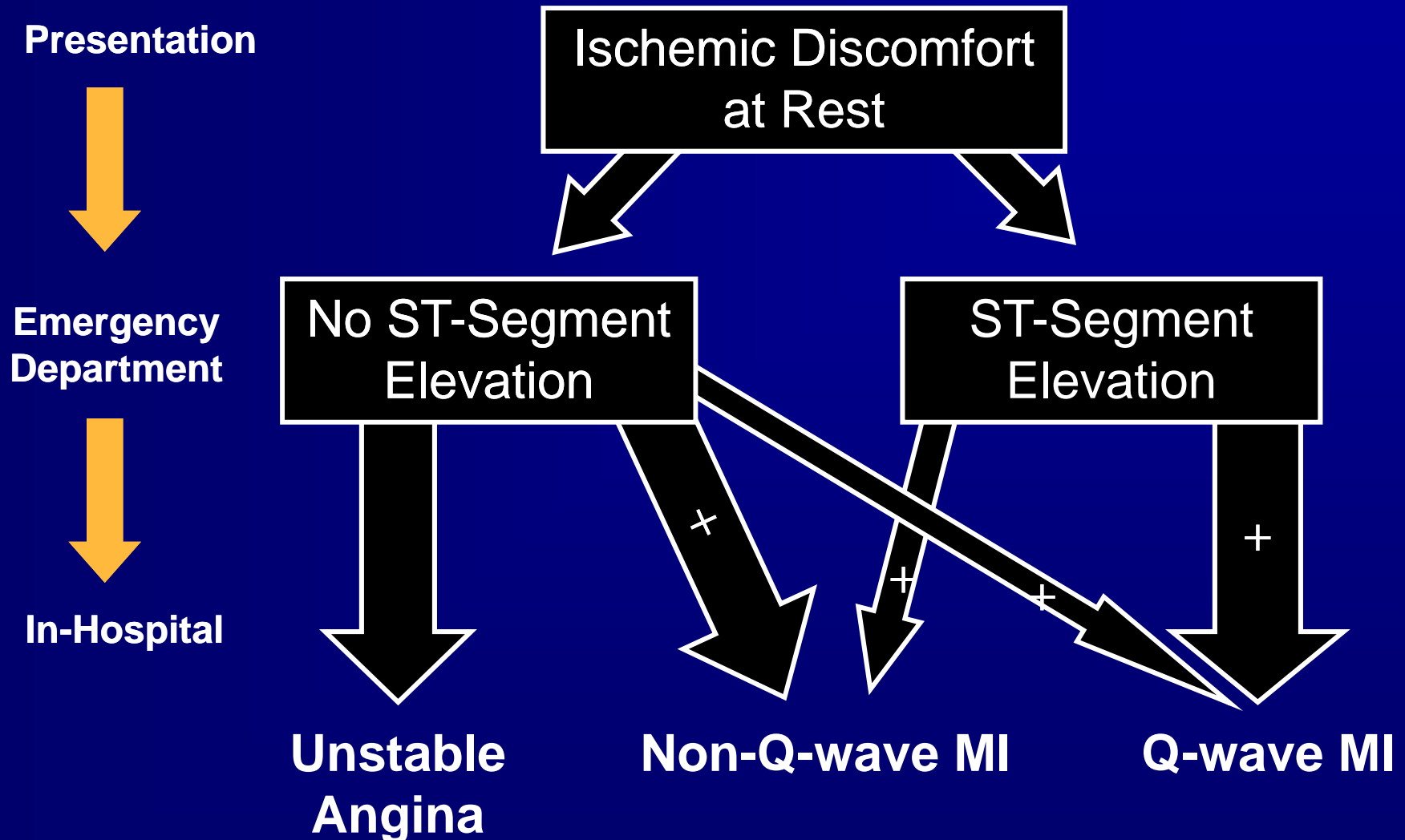
Case 1

- Pt d/c day 3
- Atorvastatin 80 mg QD
- Plavix 75 mg. QD for 12 months
- ASA 325 mg QD for 3 months, then can decrease to 81 mg QD
- Metoprolol Succinate 50 mg QD
- Zetril 20 mg QD
- Norvasc discontinued

Evidence Based Data



Spectrum of Acute Coronary Syndromes



(⊕ : positive cardiac biomarker)

Variables Used in the TIMI Risk Score

- Age \geq 65 years
- At least 3 risk factors for CAD
- Prior coronary stenosis of \geq 50%
- ST-segment deviation on ECG presentation
- At least 2 anginal events in prior 24 hours
- Use of aspirin in prior 7 days
- Elevated serum cardiac biomarkers

The TIMI risk score is determined by the sum of the presence of the above 7 variables at admission. 1 point is given for each variable. Primary coronary stenosis of 50% or more remained relatively insensitive to missing information and remained a significant predictor of events. Antman EM, et al. *JAMA* 2000;284:835–42.
TIMI = Thrombolysis in Myocardial Infarction.

Causes of UA/NSTEMI*

- Thrombus or thromboembolism, usually arising on disrupted or eroded plaque
 - Occlusive thrombus, usually with collateral vessels†
 - Subtotally occlusive thrombus on pre-existing plaque
 - Distal microvascular thromboembolism from plaque-associated thrombus
 - Thromboembolism from plaque erosion
- Non-plaque-associated coronary thromboembolism
- Dynamic obstruction (coronary spasm‡ or vasoconstriction) of epicardial and/or microvascular vessels
- Progressive mechanical obstruction to coronary flow
- Coronary arterial inflammation
- Secondary UA
- Coronary artery dissection§

*These causes are not mutually exclusive; some patients have 2 or more causes. †DeWood MA, et al. *N Engl J Med* 1986;315:417-23. ‡May occur on top of an atherosclerotic plaque, producing missed-etiology angina or UA/NSTEMI. §Rare. Modified with permission from Braunwald E. *Circulation* 1998;98:2219-22. Anderson JL, et al. *J Am Coll Cardiol*. 2007;50:e1-e157, Table 3.

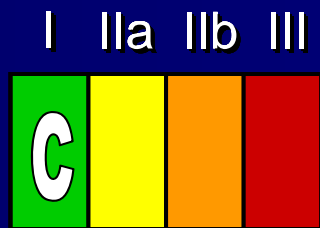
Updated Guidelines

Classes of Recommendations

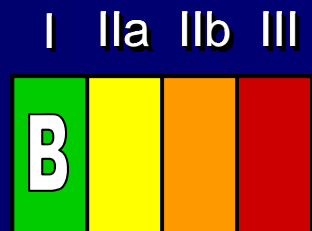
I	IIa	IIb	III	
X				Intervention is useful and effective
	X			Evidence conflicts/opinions differ but leans towards efficacy
		X		Evidence conflicts/opinions differ but leans against efficacy
			X	Intervention is not useful/effective and may be harmful

Identification of Patients at Risk of UA/NSTEMI

New
Section

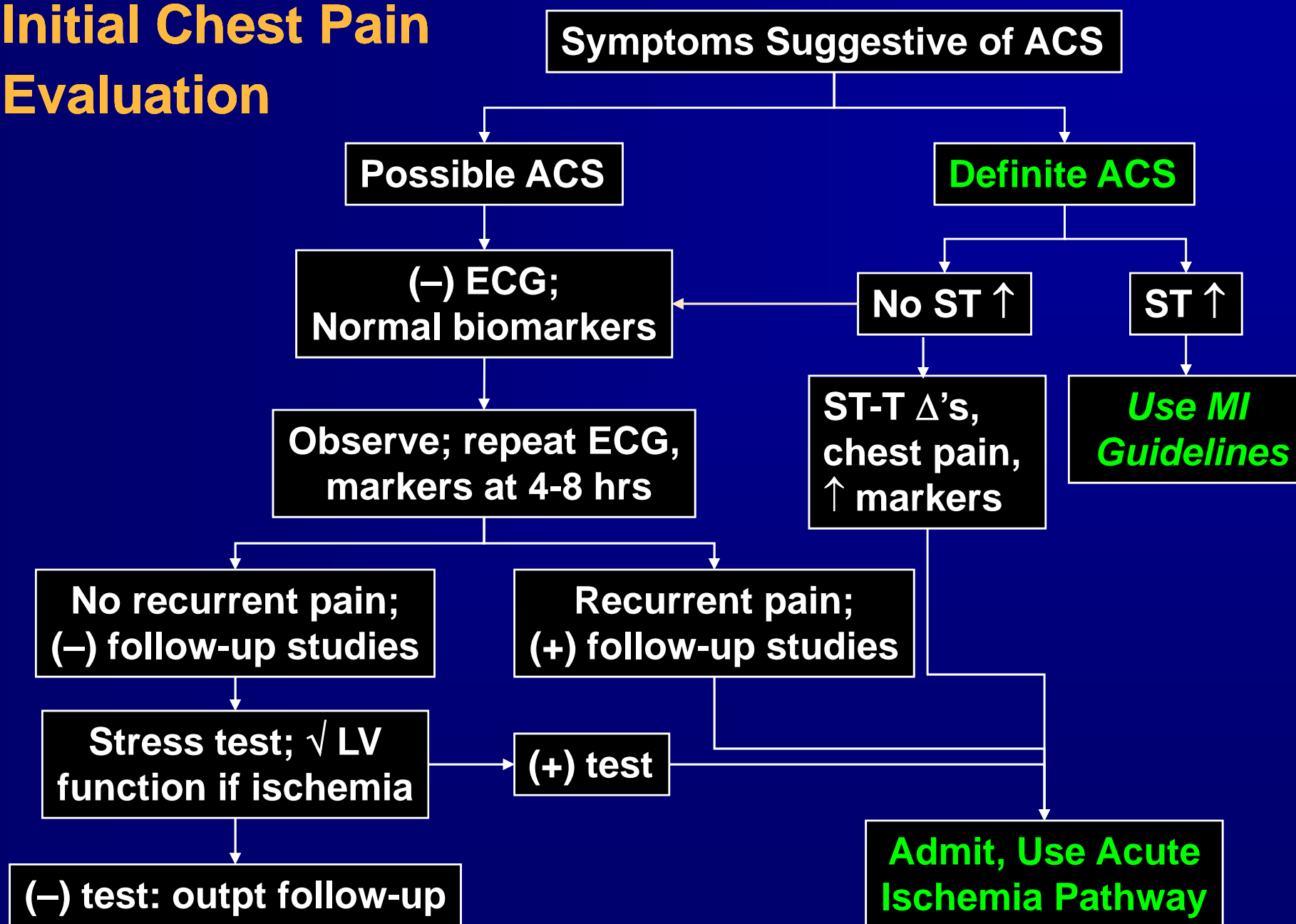


Primary care providers should evaluate the presence and status of control of major risk factors for coronary heart disease (CHD) for all patients at regular intervals (approximately every 3 to 5 years).

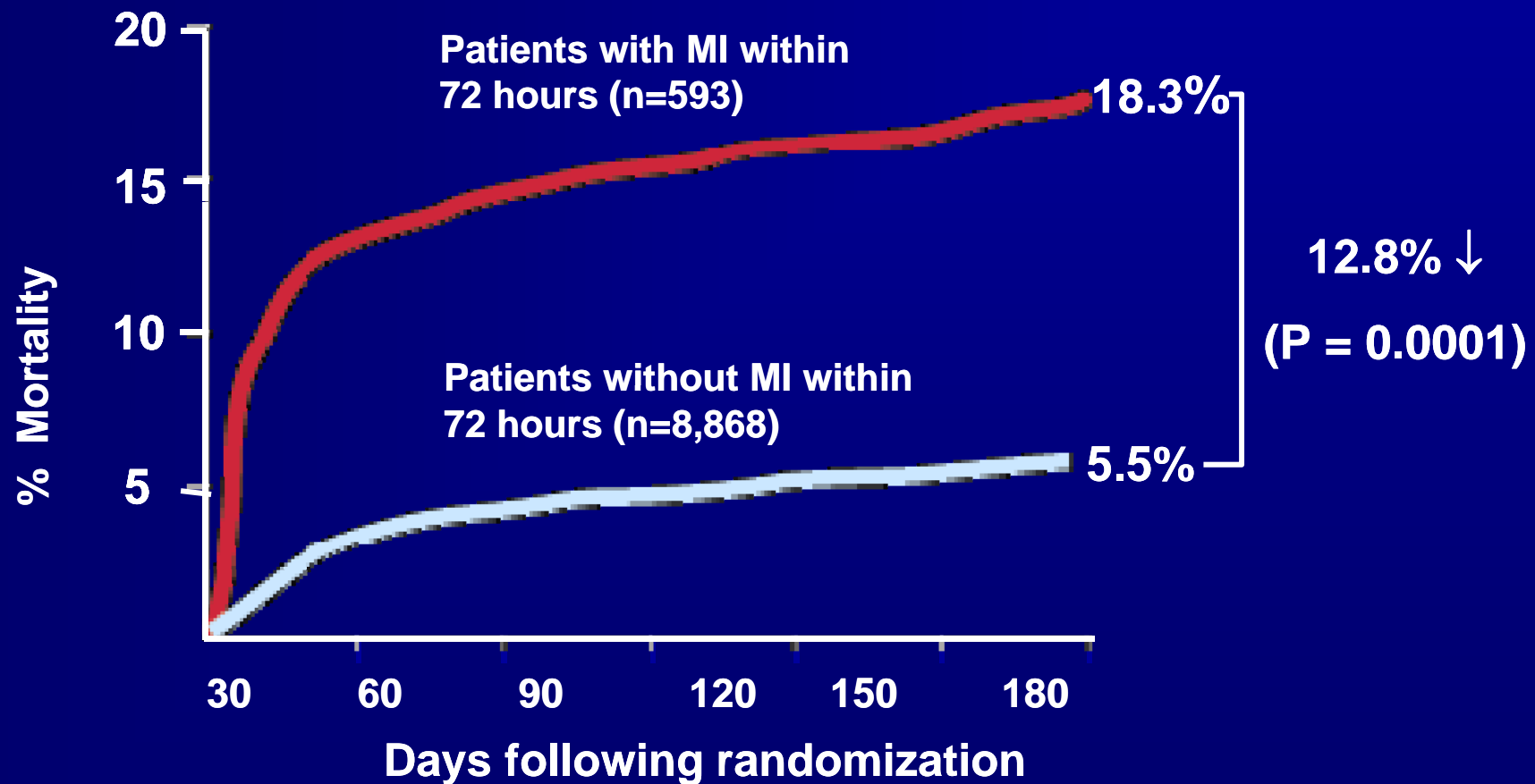


Ten-year risk (National Cholesterol Education Program [NCEP] global risk) of developing symptomatic CHD should be calculated for all patients who have 2 or more major risk factors to assess the need for primary prevention strategies (1,2).

Initial Chest Pain Evaluation



Mortality in Non-ST ↑ ACS Patients With Myocardial Infarction During Hospitalization



Variables Used in the TIMI Risk Score

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TIMI = Thrombolysis in Myocardial Infarction.

TIMI Risk Score

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

At Admission (in-hospital/to 6 months)

At Discharge (to 6 months)

Age ▾

HR ▾

SBP ▾

Creat. ▾

CHF ▾

SI Units

Cardiac arrest at admission

ST-segment deviation

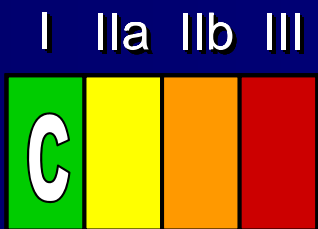
Elevated cardiac enzymes/markers

Probability of	Death	Death or MI
In-hospital	<input type="text" value="--"/>	<input type="text" value="--"/>
To 6 months	<input type="text" value="--"/>	<input type="text" value="--"/>

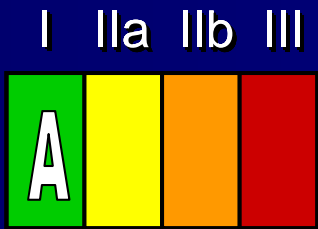
Reset

Lipid Management

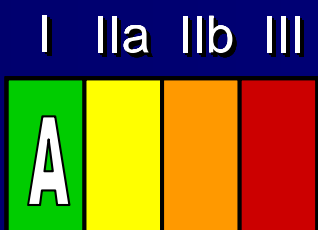
Major Changes



Lipid management should include assessment of a fasting lipid profile for all patients, within 24 h of hospitalization.

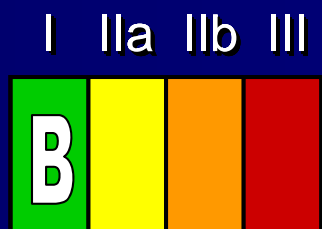
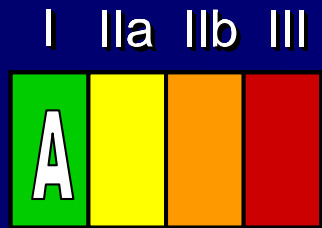


Statins, in the absence of contraindications and regardless of baseline LDL-C and diet modification, should be given to post-UA/NSTEMI pts, including post-revascularization pts.



For hospitalized patients, lipid-lowering medications should be initiated before discharge.

Lipid Management



For UA/NSTEMI patients with elevated LDL-C (≥ 100 mg per dL), cholesterol-lowering therapy should be initiated or intensified to achieve an LDL-C < 100 mg per dL.

Further titration to less than 70 mg per dL is reasonable. (Class IIa, Level of Evidence: A)

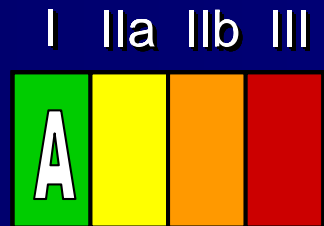
Therapeutic options to reduce non-HDL-C are recommended, including more intense LDL-C-lowering therapy.

*Non-HDL-C = total cholesterol minus HDL-C

Pravastatin Or atorVastatin Evaluation and Infection Therapy–Thrombolysis In Myocardial Infarction 22 (PROVE-IT TIMI 22)

- 4,162 patients within 10 d of ACS
- 40 mg pravastatin vs 80 mg atorvastatin daily
- ↓ All-cause death, MI, UA requiring hosp, revasc & stroke @ 2 y by atorvastatin
 - Median LDL-C ↓ (62 vs 95 mg/dL)

Blood Pressure Control



*New BP
Levels*

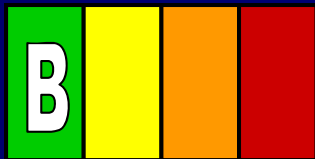
Blood pressure control according to JNC 7 guidelines* is recommended (i.e., BP < 140/90 mm Hg or < 130/80 mm Hg if the patient has diabetes mellitus or chronic kidney disease).

*Chobanian AV, et al. JAMA 2003;289:2560-2572.

JNC 7 = 7th report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure.

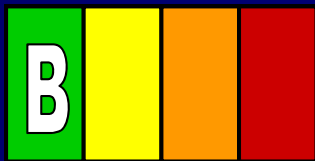
Diabetes Mellitus

I IIa IIb III



Diabetes management should include lifestyle and pharmacotherapy measures to achieve a near-normal HbA1c level of $< 7\%$.

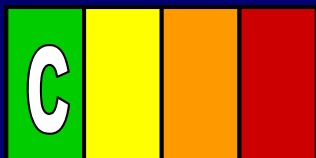
I IIa IIb III



Diabetes management should also include the following:

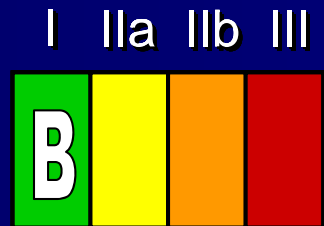
- a. Vigorous modification of other risk factors (e.g., physical activity, weight management, BP control, and cholesterol management) as recommended should be initiated and maintained.

I IIa IIb III



It is useful to coordinate the patient's diabetic care with the patient's primary care physician or endocrinologist.

Smoking Cessation

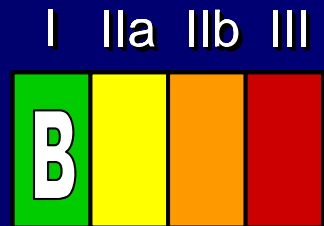


Smoking cessation and avoidance of exposure to environmental tobacco smoke at work and home are recommended.

*Cessation
Emphasized*

Follow-up, referral to special programs, or pharmacotherapy (including nicotine replacement) is useful, as is adopting a stepwise strategy aimed at smoking cessation (the 5 As are: Ask, Advise, Assess, Assist, and Arrange).

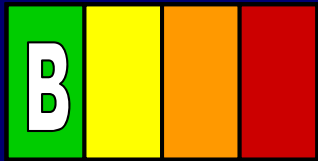
Weight Management



Weight management, as measured by body mass index (BMI) and/or waist circumference, should be assessed on each visit. A BMI of 18.5 to 24.9 kg per m² and a waist circumference (measured horizontally at the iliac crest) of < 40 inches for men and < 35 inches for women is recommended.

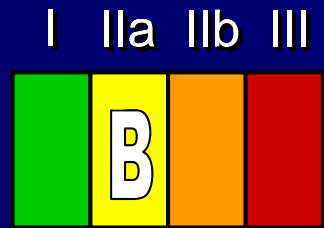
Physical Activity

I IIa IIb III

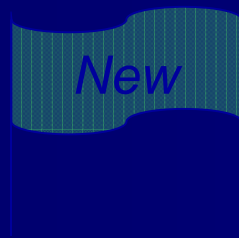


Cardiac rehabilitation/secondary prevention programs are recommended for patients with UA/NSTEMI, particularly those with multiple modifiable risk factors and/or those moderate- to high-risk patients in whom supervised exercise training is particularly warranted.

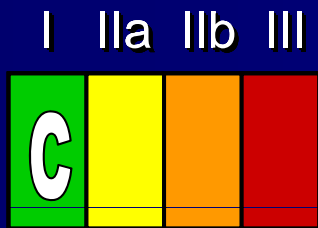
Depression



It is reasonable to consider screening UA/NSTEMI patients for depression and refer/treat when indicated.

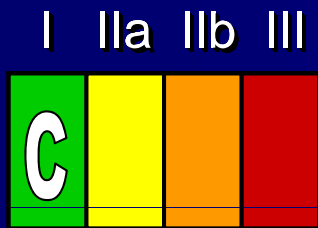


Clinical Assessment

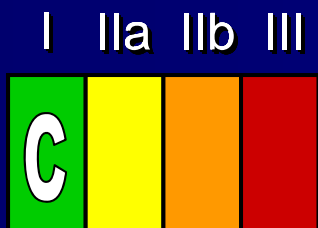


Patients with symptoms that may represent ACS should not be evaluated over the telephone, but should be referred to a facility that allows evaluation by a physician and the recording of a 12-lead ECG and biomarker determination (e.g., an emergency department [ED] or other acute care facility).

Early Risk Stratification

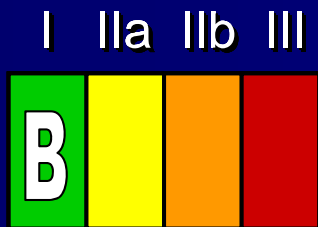


A rapid clinical determination of the likelihood risk of obstructive CAD (i.e., high, intermediate, or low) should be made in all patients with chest discomfort or other symptoms suggestive of an ACS and considered in patient management.

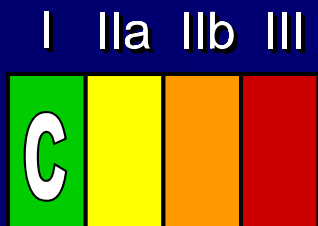


Patients who present with chest discomfort or other ischemic symptoms should undergo early risk stratification for the risk of cardiovascular events (e.g., death or [re]MI) that focuses on history, including anginal symptoms, physical findings, ECG findings, and biomarkers of cardiac injury, and results should be considered in patient management.

Early Risk Stratification

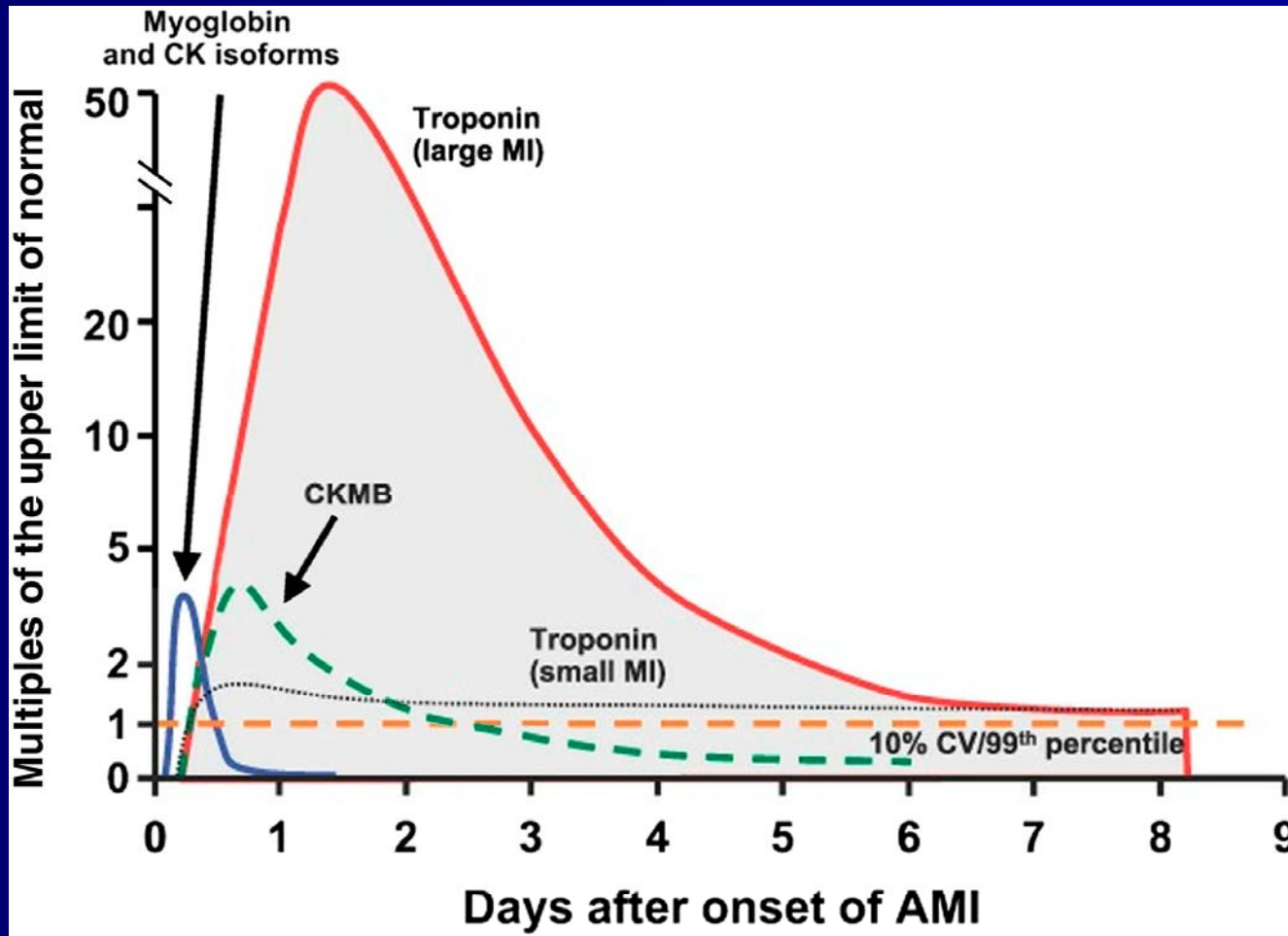


Patients with negative cardiac biomarkers within 6 h of the onset of symptoms consistent with ACS should have biomarkers remeasured in the time frame of 8 to 12 h after symptom onset. (The exact timing of serum marker measurement should take into account the uncertainties often present with the exact timing of onset of pain and the sensitivity, precision, and institutional norms of the assay being utilized as well as the release kinetics of the marker being measured.)



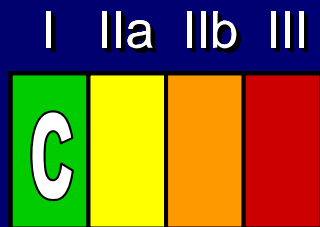
The initial evaluation of the patient with suspected ACS should include the consideration of noncoronary causes for the development of unexplained symptoms.

Timing of Release of Various Biomarkers After Acute Myocardial Infarction



Shapiro BP, Jaffe AS. Cardiac biomarkers. In: Murphy JG, Lloyd MA, editors. *Mayo Clinic Cardiology: Concise Textbook*, 3rd ed. Rochester, MN: Mayo Clinic Scientific Press and New York: Informa Healthcare USA, 2007:773–80.
Anderson JL, et al. *J Am Coll Cardiol* 2007;50:e1–e157, Figure 5.

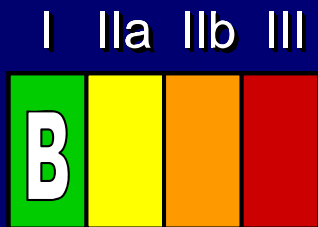
Immediate Management



The history, physical examination, 12-lead ECG, and initial cardiac biomarker tests should be integrated to assign patients with chest pain into 1 of 4 categories:

- 1) a noncardiac diagnosis
- 2) chronic stable angina
- 3) possible ACS
- 4) definite ACS.

Immediate Management

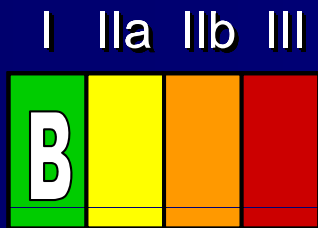


Patients with probable or possible ACS but whose initial 12-lead ECG and cardiac biomarker levels are normal should be observed in a facility with cardiac monitoring (e.g., chest pain unit or hospital telemetry ward), and repeat ECG (or continuous 12-lead ECG monitoring) and repeat cardiac biomarker measurement(s) should be obtained at predetermined, specified time intervals*.

*See Section 2.2.8 in Anderson JA, et al. *J Am Coll Cardiol* 2007;50:e1-e157.

Early Hospital Care

Anti-Ischemic Therapy

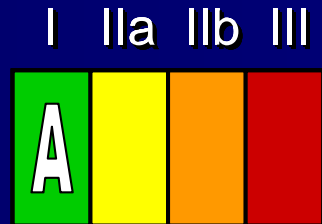


Oral beta-blocker therapy should be initiated within the first 24 h for patients who do not have 1 or more of the following:

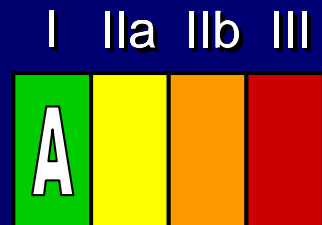
- 1) signs of HF
- 2) evidence of a low-output state
- 3) increased risk* for cardiogenic shock
- 4) other relative contraindications to beta blockade (PR interval greater than 0.24 s, second or third degree heart block, active asthma, or reactive airway disease).

*Risk factors for cardiogenic shock (the greater the number of risk factors present, the higher the risk of developing cardiogenic shock): age greater than 70 years, systolic blood pressure less than 120 mmHg, sinus tachycardia greater than 110 or heart rate less than 60, increased time since onset of symptoms of UA/NSTEMI. Chen ZM, et al. *Lancet* 2005;366:1622–32.

Antiplatelet Therapy



Aspirin should be administered to UA/NSTEMI patients as soon as possible after hospital presentation and continued indefinitely in patients not known to be intolerant of that medication.

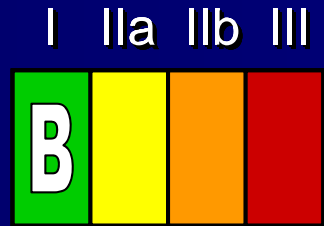


Clopidogrel (loading dose [LD] followed by daily maintenance dose) should be administered to UA/NSTEMI patients who are unable to take ASA because of hypersensitivity or major gastrointestinal intolerance.



*Some uncertainty exists about optimum dosing of clopidogrel. Randomized trials establishing its efficacy and providing data on bleeding risks used a loading dose of 300 mg orally followed by a daily oral maintenance dose of 75 mg. Higher oral loading doses such as 600 or 900 mg of clopidogrel more rapidly inhibit platelet aggregation and achieve a higher absolute level of inhibition of platelet aggregation, but the additive clinical efficacy and the safety of higher oral loading doses have not been rigorously established.

Antiplatelet Therapy



In UA/NSTEMI patients with a history of gastrointestinal bleeding, when ASA and clopidogrel are administered alone or in combination, drugs to minimize the risk of recurrent gastrointestinal bleeding (e.g., proton-pump inhibitors) should be prescribed concomitantly.

Selection of Initial Treatment Strategy: Initial Invasive Versus Conservative Strategy

Invasive

Recurrent angina/ischemia at rest with low-level activities despite intensive medical therapy

Elevated cardiac biomarkers (TnT or TnI)

New/presumably new ST-segment depression

Signs/symptoms of heart failure or new/worsening mitral regurgitation

High-risk findings from noninvasive testing

Hemodynamic instability

Sustained ventricular tachycardia

PCI within 6 months

Prior CABG

High risk score (e.g., TIMI, GRACE)

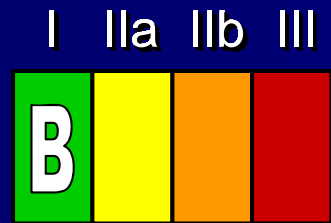
Reduced left ventricular function (LVEF < 40%)

Conservative

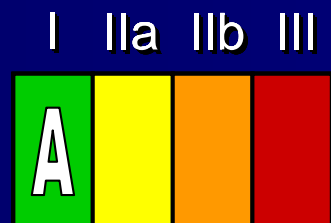
Low risk score (e.g., TIMI, GRACE)

Patient/physician presence in the absence of high-risk features

Initial Conservative Versus Initial Invasive Strategies



An early invasive strategy* is indicated in UA/NSTEMI patients who have refractory angina or hemodynamic or electrical instability (without serious comorbidities or contraindications to such procedures).

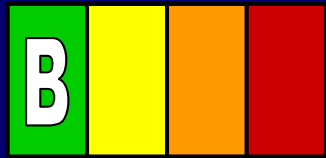


An early invasive strategy* is indicated in initially stabilized UA/NSTEMI patients (without serious comorbidities or contraindications to such procedures) who have an elevated risk for clinical events.

*Diagnostic angiography with intent to perform revascularization.

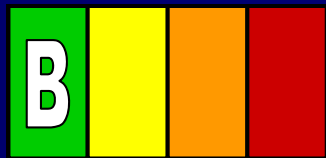
Risk Stratification Before Discharge

I IIa IIb III



Prompt angiography without noninvasive risk stratification should be performed for failure of stabilization with intensive medical treatment.

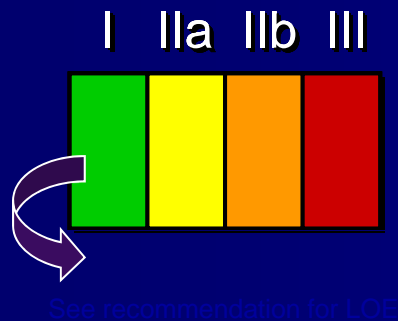
I IIa IIb III



A noninvasive test (echocardiogram or radionuclide angiogram) is recommended to evaluate LV function in patients with definite ACS who are not scheduled for coronary angiography and left ventriculography.

IIa → I

Antiplatelet Therapy



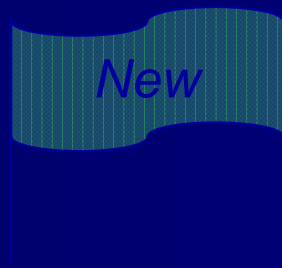
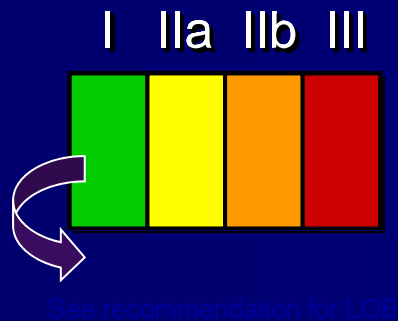
For UA/NSTEMI patients treated medically without stenting, aspirin* (75 to 162 mg per day) should be prescribed indefinitely (*Level of Evidence: A*)

clopidogrel† (75 mg per day) should be prescribed for at least 1 month (*Level of Evidence: A*) and ideally for up to 1 year. (*Level of Evidence: B*)

*For ASA-allergic patients, use clopidogrel alone (indefinitely), or try aspirin desensitization.

†For clopidogrel-allergic patients, use ticlopidine 250 mg by mouth twice daily.

Antiplatelet Therapy

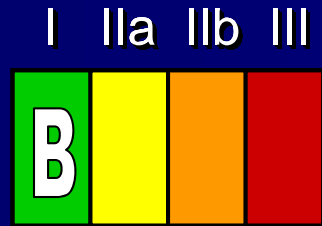


For UA/NSTEMI patients treated with bare-metal stents, aspirin* 162 to 325 mg per day should be prescribed for at least 1 month (Level of Evidence: B), then continued indefinitely at a dose of 75 to 162 mg per day (Level of Evidence: A)

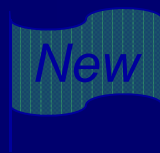
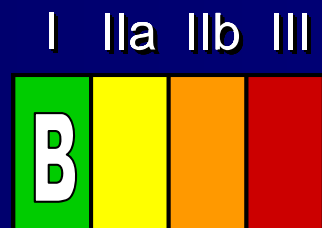
Clopidogrel should be prescribed at a dose of 75 mg per day for a minimum of 1 month and ideally for up to 1 year (unless the patient is at increased risk of bleeding; then it should be given for a minimum of 2 weeks). (Level of Evidence: B)

*For ASA-allergic patients, use clopidogrel alone (indefinitely), or try aspirin desensitization.

Antiplatelet Therapy



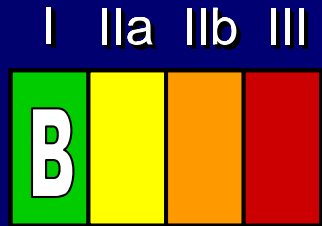
For UA/NSTEMI patients treated with drug-eluting stents (DES), aspirin 162 to 325 mg per day should be prescribed for at least 3 months after sirolimus-eluting stent implantation and 6 months after paclitaxel-eluting stent implantation then continued indefinitely at a dose of 75 to 162 mg per day.



Clopidogrel 75 mg daily should be given for at least 12 months to all post-PCI patients receiving DES.

*For ASA-allergic patients, use clopidogrel alone (indefinitely), or try aspirin desensitization.

Cardiac Rehabilitation



Cardiac rehabilitation/secondary prevention programs, when available, are recommended for patients with UA/NSTEMI, particularly those with multiple modifiable risk factors and those moderate- to high-risk patients in whom supervised exercise training is warranted.

Hospital Care

Conservative vs. Invasive Strategies

I IIa IIb III

I	IIa	IIb	III
A			

Early invasive strategy in high-risk patients with any of the following:

- *Recurrent ischemia, despite meds*
- *Elevated Troponin I or T*
- *New ST-segment depression*
- *New CHF symptoms*
- *High-risk stress test findings*
- *LV dysfunction (EF < 40%)*
- *Hemodynamic instability, sustained VT*
- *PCI within 6 months, prior CABG*

Discharge/Post-Discharge Medications

I IIa IIb III

A			
A			
B			
B			
A			
A			

ASA, if not contraindicated

Clopidogrel, when ASA contraindicated

Aspirin + Clopidogrel, for up to 9 months

β-blocker, if not contraindicated

Lipid ↓ agents + diet, if LDL >130 mg/dL

ACE Inhibitor: CHF, EF < 40%, DM, or HTN

Risk Factor Modification

	I	IIa	IIb	III	
B					Smoking Cessation Counseling
B					Dietary Counseling and Modification
B					Cardiac Rehabilitation Referral
A					HTN Control (BP < 130/85 mm Hg)
B					Tight Glycemic Control in Diabetics

Case Review using TIMI risk score assessment

Variables Used in the TIMI Risk Score

- Age \geq 65 years
- At least 3 risk factors for CAD
- Prior coronary stenosis of \geq 50%
- ST-segment deviation on ECG presentation
- At least 2 anginal events in prior 24 hours
- Use of aspirin in prior 7 days
- Elevated serum cardiac biomarkers

The TIMI risk score is determined by the sum of the presence of the above 7 variables at admission. 1 point is given for each variable. Primary coronary stenosis of 50% or more remained relatively insensitive to missing information and remained a significant predictor of events. Antman EM, et al. *JAMA* 2000;284:835–42.
TIMI = Thrombolysis in Myocardial Infarction.

Case 1

- 67 year old male

