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Acute Coronary Syndromes: Unstable Angina/Non-ST Elevation Myocardial Infarction

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Coronary artery disease (CAD) affects 13.2 million Americans, including 7.2 million individuals who have had a prior myocardial infarction (MI). In 2003, the estimated direct and indirect health care cost of CAD was an astounding $142.5 billion [1]. The data are sobering, in that every 26 seconds an American suffers a coronary event; or every minute, someone dies from CAD. More than 80% of those who die from CAD are more than 65 years of age [1]. Among patients who have CAD, acute coronary syndrome (ACS) is a major health problem affecting approximately 1.5 million individuals a year [1].

Patients who have CAD may present as having stable angina or ACS. The spectrum of ACS includes ST-segment elevation MI, unstable angina (UA), and non–ST-segment elevation MI (NSTEMI). UA is characterized by the clinical presentation of angina with or without ischemic ECG changes (ST segment depression or new T-wave inversion). NSTEMI is similar to UA but is characterized by positive biomarkers (troponin or creatine kinase-MB [CK-MB]) in the setting of angina or ECG changes. The presence of myonecrosis as evident by positive cardiac markers portends a higher risk than those presenting with just UA. UA and NSTEMI pathophysiologically and clinically are related and initially may be indistinguishable, as biomarkers may not be elevated at presentation.

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Pathogenesis of unstable angina/non–ST-segment elevation myocardial infarction

Myocardial ischemia is the result of a mismatch between oxygen supply and demand and, when prolonged, may lead to myocardial necrosis and infarction. Patients who have UA/NSTEMI typically have obstructive coronary disease; however, ACS may occur in the absence of significant coronary obstruction due to rupture of a nonobstructive plaque, coronary vasospasm, or increased myocardial oxygen demand. Rupture of an atherosclerotic plaque and subsequent formation of a thrombus usually is the triggering event in the pathogenesis of most cases of ACS. Some other causes may lead to coronary ischemia but are relatively rare (Table 1).

Plaque rupture is precipitated by two main mechanisms—physical shear stress to the plaque or inflammatory mediators. Plaques that are prone to rupture have a large lipid core, high macrophage and activated T-lymphocyte density, low smooth muscle cell density, and a thin fibrous cap characterized by disorganized collagen. Rupture of the plaque shoulder, at its junction with the arterial wall, which is mechanically the weakest point, exposes the highly thrombogenic necrotic lipid core to platelets and circulating inflammatory cells, stimulating the formation of acute thrombi [2,3].

With the breakdown of the atherosclerotic plaque, the local milieu becomes prothrombotic because of the exposure of subendothelial matrix to the circulating blood. Platelet surface receptors recognize the vascular matrix components (collagen, von Willebrand factor [vWF], vitronectin, and fibronectin), stimulating platelet adhesion via the glycoprotein (GP) Ib receptor and vWF. After this, there is platelet activation leading to a change in platelet morphology and degranulation of the alpha and dense granules, which release substrates, thromboxane A2 [4], platelet factor 4, factor V [5], P-selectin, vWF, plasminogen activator inhibitor-1, fibrinogen, serotonin, and ADP [6]. These chemotactic and vasoactive substances lead to the recruitment and activation of GP IIb/IIIa receptors on the platelet surface. The activated GP IIb/IIIa receptors are cross-linked by fibrinogen (or vWF), leading to platelet aggregation and formation of the white

Table 1
Causes of unstable angina and non–ST-segment elevation myocardial infarction[a]

1. Nonocclusive thrombus on pre-existing plaque
2. Dynamic obstruction (coronary artery spasm or vasoconstriction)
3. Progressive mechanical obstruction
4. Inflammation or infection
5. Secondary UA

[a] These causes are not mutually exclusive; some patients have ≥ 2 causes.

From Braunwald E. Unstable angina: an etiologic approach to management. Circulation 1998;98:2220; with permission.