Acute Coronary Syndromes: The Degree and Morphology of Coronary Stenoses
Valentin Fuster, MD, PhD, FACC
New York, New York

Angiographic Morphology and the Pathogenesis of Unstable Angina Pectoris
by J. A. Ambrose, S. L. Winters, A. Stern, A. Eng, L. E. Teichholz, R. Gorlin, V. Fuster (3)

ABSTRACT
In 110 patients with either stable or unstable angina, the morphology of coronary artery lesions was qualitatively assessed at angiography. Each obstruction reducing the luminal diameter of the vessel by 50% or greater was categorized into one of the following morphologic groups: concentric (symmetric narrowing); type I eccentric (asymmetric narrowing with smooth borders and a broad neck); type II eccentric (asymmetric with a narrow neck or irregular borders, or both); and multiple irregular coronary narrowings in series. For the entire group, type II eccentric lesions were significantly more frequent in the 63 patients with unstable angina (p less than 0.001), whereas concentric and type I eccentric lesions were seen more frequently in the 47 patients with stable angina (p less than 0.05). Type II eccentric lesions were also present in 29 of 41 arteries in patients with unstable angina compared with 4 of 25 arteries in those with stable angina (p less than 0.0001) in whom an "angina-producing" artery could be identified. Therefore, type II eccentric lesions are frequent in patients with unstable angina and probably represent ruptured atherosclerotic plaques or partially occlusive thrombi, or both. A temporary decrease in coronary perfusion secondary to these plaques with or without superimposed transient platelet thrombi or altered vasomotor tone may be responsible for chest pain in some of these patients with unstable angina.


Review
The best method for predicting future acute coronary events in patients with coronary artery disease has been difficult to determine. For instance, is the severity of coronary artery stenosis a good predictor of future acute coronary events? Past research has indicated that it is not. In the late 1980s, Ambrose et al. (1) and Little et al. (2) carried out retrospective studies of patients with acute myocardial infarction
(AMI) or unstable angina who had serial angiograms both before and after the acute event. In the Ambrose study, 23 patients were evaluated. Forty-eight percent of vessels that ultimately occluded and caused infarctions had less than 50\% stenosis before the acute event, and only 22\% of the infarct-related arteries were greater than 75\% obstructed. Little and associates found a similar result. In their study, coronary arteries that became totally occluded and resulted in myocardial infarction (MI) had usually not been severely stenosed previously. The culprit artery in most cases had been less than 50\% stenosed before the acute event. Several subsequent investigations confirmed that in the majority of patients with AMI, the culprit vessel had been only mildly stenosed before the acute coronary event.

Does the morphology of the coronary lesion help determine the clinical status or risk of subsequent occlusion? The historical article highlighted in this issue of the Journal was published by Ambrose et al. (3) in 1985, and it suggested that morphology does assist the cardiologist in detecting high-risk lesions. The study was undertaken in order to assess the qualitative appearance of coronary lesions in patients with either stable or unstable angina. One hundred and ten patients with either stable or unstable angina underwent cardiac catheterization. Significant lesions were categorized into four groups: a) concentric; b) type I eccentric (asymmetric narrowing with smooth borders and a broad neck); c) type II eccentric (asymmetric with a narrow neck or irregular borders, or both); and d) multiple irregular coronary narrowing in series. In all patients an attempt was made to localize the culprit artery that produced the chest pain syndrome. This artery was identified in 60\% of the study patients. The artery was designated the “angina-producing” artery if it was found in patients with one-vessel disease, if it was localizable by reversible thallium perfusion defects upon exercise testing, or if reversible ST-T changes were detected on an electrocardiogram during an anginal episode. The result of this study was that the type II eccentric lesions were significantly more frequent in the patients with unstable angina than in those with stable angina. This finding was demonstrated in the entire group as well as in the sub-group of patients in which the angina-producing artery could be identified. The result of this study was important because it suggested that the trigger of acute coronary syndromes might be rupture of an atherosclerotic plaque with subsequent thrombus formation, thus forming the irregular borders seen on the angiogram.

A recent study by Tousoulis et al. (4) returned to the issue of identifying the lesion most likely to progress to complete occlusion. In their study, they analyzed both the severity of stenosis and the morphology of coronary artery lesions in patients with stable angina who later progressed to AMI. They found by analyzing serial angiograms that the lesions that subsequently completely occluded and caused clinical events were less than 50\% stenosed in 58\% of patients, thus confirming again that the degree of stenosis is not a good predictor of subsequent occlusion and MI. Tousoulis and colleagues found that stable lesions were more likely to have a smooth morphology and that the lesions that progressed to cause infarctions were more likely to be of a more complex morphology. The authors concluded that stenosis morphology was more predictive of future events than stenosis severity. It is worth noting that, although complex lesions do seem to increase the risk of future MIs, many such lesions remain stable for years.

Ambrose et al. found that non–Q-wave MI was more likely to occur in coronary arteries having lesions that were greater than 70\% stenosed. Tousoulis et al. (4) found similar results, but other investigators have not always confirmed this finding. There is clearly a tendency for severely stenosed coronary arteries to stimulate collateral circulation. These vessels may contribute to the occurrence of a non–Q-wave MI when the culprit artery becomes totally occluded, as opposed to an extensive Q-wave infarction when such collaterals are not present (5).

An important challenge today is how to identify the minor or silent plaques that carry a high risk of thrombosis. As revealed by pathological examination, these plaques usually contain a large lipid core and a thin fibrous cap with an abundance of inflammatory cells. Angiography, despite its demonstrated usefulness and ability to identify the underlying degree of stenoses (and even their morphology in patients with coronary artery disease), is limited in its ability to identify these vulnerable plaques. Other techniques may be useful in the future for identifying these lesions. Intravascular ultrasound and angioscopy can identify the presence of thrombosis and, in some cases, the lipid-rich vulnerable plaques themselves. However, their ability to predict subsequent coronary events needs further evaluation. In addition, these techniques are invasive and may not be practical on a routine basis in patients with stable coronary artery disease. Magnetic resonance imaging is offering some promising new developments in the evaluation of ischemic heart disease. As this technique develops, it may be able to characterize the components of a plaque in terms of lipid, fibrous and thrombotic material. Another noninvasive technique that may be used for detecting high-risk, vulnerable plaques is electron beam (ultrafast) computed tomography. This test is best at diagnosing the degree of calcium content in coronary arteries; however, although calcium content may be correlated with coronary artery disease, its ability to predict plaque vulnerability has yet to be demonstrated by clinical studies.

The treatment of stable coronary disease must be aimed at stabilizing these vulnerable plaques, which are at risk of becoming a site for acute thrombosis. Plaque stabilization and improvement of endothelial function are best accomplished by lipid-lowering medication in the appropriate patient population. Antithrombotic agents are useful in decreasing thrombus formation and, thus, preventing acute
occlusion and subsequent potentially life-threatening clinical events. More research in this area is needed in order to discover how best to identify and treat those patients with stable coronary artery disease who are at increased risk for MI.

Acknowledgment
I thank Dr. Deborah Gersony for her valuable assistance in preparing the manuscript.

REFERENCES
5. Little WC, Applegate RJ. Coronary angiography before myocardial infarction: can the culprit site be prospectively recognized? Am Heart J 1998;136:368–70.