Point of View

Research on Unstable Coronary Syndromes

Unstable Angina

A Classification

Eugene Braunwald, MD

The establishment of a prognosis and the approach to the treatment of many diseases is aided greatly by a logical classification. For example, classification of a wide variety of neoplasms by anatomic extent, microscopic appearance, and the presence of special markers now forms the basis for selecting appropriate therapy. In cardiology, the classification of patients with acute myocardial infarction and congestive heart failure has been of enormous value in following the progress and in selecting therapy of individual patients and in comparing the outcome of similar patients treated at different locations and at different times. The purpose of this article is to provide a classification of unstable angina. This classification is designed to facilitate communication about these patients, to aid in the decision regarding diagnostic measures and therapy of individual patients, and to provide a more precise basis for including patients in and for evaluating the outcome of clinical trials.

Unstable angina is a complex condition. Early in this century, the clinical-pathologic features of two of the principal manifestations of ischemic heart disease—acute myocardial infarction and chronic stable angina—had already been well described. It has taken much longer to define a syndrome that is intermediate in severity between these two conditions. In 1923, Wearn described, in a group of 19 patients with acute myocardial infarction confirmed at necropsy, attacks of angina pectoris that may precede myocardial infarction and serve as warnings of the presence of coronary artery disease. In 1937, Sampson and Eliaser and Feil separately described a syndrome consisting of severe, prolonged anginal pain that often led to acute myocardial infarction, and they termed it “impending acute myocardial infarction.” Other terms that have been used for this condition include “preinfarction angina,” “crescendo angina,” “status anginosus,” “accelerated angina,” “acute coronary insufficiency,” and “intermediate coronary syndrome”; the term most frequently used now, “unstable angina,” was used by Fowler and Conti et al in 1971. This large number of designations, as well as the lack of a clear, agreed-upon definition, reflects the ambiguity that has continued to be associated with this “catch-all” syndrome. Unstable angina probably consists of a number of conditions, all characterized by severe transient myocardial ischemia.

Unstable angina is very common and often quite serious; it is responsible for more than 750,000 hospitalizations annually in the United States and thus ranks among the most frequent causes of hospitalization in this country. More than 70,000 of these hospitalized patients develop myocardial infarction, and some die suddenly. An unknown, but probably large, number of patients with unstable angina are not hospitalized but are treated at home. Many patients with unstable angina do not develop serious complications, but after recovery from the acute episode, they are left with chronic stable angina of varying severity. A minority of patients recover without developing either complications or chronic angina. In addition, a substantial percentage of patients who develop acute myocardial infarction, ranging from 30% to 60% in most series, experience a prodrome of unstable angina before reaching the hospital. A significant percentage of patients with acute myocardial infarction develop unstable angina in the early postinfarction period.

There is currently intense interest in elucidating the pathogenesis of unstable angina. Maseri has emphasized that both increased myocardial oxygen demand in the presence of severely restricted coronary reserve and dynamic stenosis caused by coronary vasoconstriction may be responsible. Coronary arteriographic examinations have revealed that rapid progression of coronary stenosis often precedes the development of unstable angina and that this stenosis is frequently caused by eccentric, irregular lesions often associated with filling defects thought to be caused by coronary thrombi. Angioscopic studies at operation have revealed that many patients with unstable angina have disrupted, fissured plaques often associated with mural thrombi; the latter finding has been confirmed by pathologic examination. Also, evidence exists that abnormal coro-
Classification of Unstable Angina

<table>
<thead>
<tr>
<th>Severity</th>
<th>Clinical circumstances</th>
</tr>
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<tbody>
<tr>
<td>1. New onset of severe angina or accelerated angina; no rest pain</td>
<td>A. Develops in presence of extracardiac condition that intensifies myocardial ischemia (secondary UA)</td>
</tr>
<tr>
<td>II. Angina at rest within past month but not within preceding 48 hr (Angina at rest, subacute)</td>
<td>IA</td>
</tr>
<tr>
<td>III. Angina at rest within 48 hr (Angina at rest, acute)</td>
<td>IIA</td>
</tr>
</tbody>
</table>

Braunwald Classification of Unstable Angina

Patients with UA may also be divided into three groups depending on whether UA occurs 1) in the absence of treatment for chronic stable angina, 2) during treatment for chronic stable angina, or 3) despite maximal anti-ischemic drug therapy. These three groups may be designated by subscripts 1, 2, or 3, respectively.

In this clinical classification, angina is evaluated relative to the patient’s previous experience. These subgroups allow the clinician to evaluate the response to therapy, which is of major importance.

To separate patients with unstable angina into a manageable number of meaningful and easily understood subgroups based on the severity, the presumed precipitating cause, and the presence of electrocardiographic changes, a clinical classification of this condition is proposed (Table 1). This classification focuses on three important aspects of unstable angina: 1) the severity of the clinical manifestations, 2) the clinical circumstances in which unstable angina occurs, and 3) whether or not the symptomatic ischemic episodes are accompanied by transient electrocardiographic changes. The classification can be made before obtaining the above-mentioned specialized laboratory tests, and once the tests are performed, the results may then be used to supplement the clinical information and the standard electrocardiogram. This classification of unstable angina is based on two premises: 1) the patient’s symptoms are actually caused by myocardial ischemia, and 2) in patients with prolonged ischemia, the diagnosis of acute myocardial infarction is excluded by electrocardiography or serum enzyme determinations. Often, this exclusion must be retrospective.

Classification

Severity

Class I. New onset severe or accelerated angina. Patients with new onset (<2 months in duration)
exertional angina pectoris that is severe or frequent (≥3 episodes/day) or patients with chronic stable angina who develop accelerated angina (that is, angina distinctly more frequent, severe, longer in duration, or precipitated by distinctly less exertion than previously) but who have not experienced pain at rest during the preceding 2 months.

Class II. Angina at rest, subacute. Patients with one or more episodes of angina at rest during the preceding month but not within the preceding 48 hours.

Class III. Angina at rest, acute. Patients with one or more episodes of angina at rest within the preceding 48 hours.

In classes II and III, manifestations described in class I may also occur. Unstable angina is no longer considered to be present when a patient has been asymptomatic or suffers angina that has been stable for more than 2 months.

Clinical Circumstances in Which Unstable Angina Occurs

Class A. Secondary unstable angina. Patients in whom unstable angina develops secondary to a clearly identified condition extrinsic to the coronary vascular bed that has intensified myocardial ischemia. Such conditions reduce myocardial oxygen supply or increase myocardial oxygen demand and include anemia, fever, infection, hypotension, uncontrolled hypertension, tachyarrhythmia, unusual emotional stress, thyrotoxicosis, and hypoxemia secondary to respiratory failure.

Class B. Primary unstable angina. Patients who develop unstable angina pectoris in the absence of an extracardiac condition that has intensified ischemia, as in class A.

Class C. Postinfarction unstable angina. Patients who develop unstable angina within the first 2 weeks after a documented acute myocardial infarction.

Electrocardiographic Changes

If an electrocardiogram has been recorded during an episode of chest pain, the presence or absence of transient ST-T abnormalities is noted. (The presence of such abnormalities is associated with more severe underlying disease.33–36)

Intensity of Treatment

For research purposes, especially clinical trials, it may be helpful also to classify patients by the intensity of treatment as follows: 1) unstable angina occurring in the absence of or with minimal antianginal therapy; 2) unstable angina occurring in the presence of appropriate therapy for chronic stable angina (the administration of conventional oral doses of antianginal drugs, i.e., β-adrenergic blockers, long-acting nitrates, and calcium antagonists); and 3) unstable angina occurring in the presence of maximally tolerated doses of all three categories of anti-ischemic drugs, including intravenous nitroglycerin.49

These three levels of treatment may be designated by the subscripts 1, 2, and 3.

Discussion

This classification of unstable angina, which should be tested prospectively, permits the grading of patients with unstable angina from the mildest to the most severe condition. An example of the mildest form would be a patient with chronic stable angina who develops marked intensification of exertion-induced angina pectoris after blood loss and who has no ST segment or T wave changes during angina. This patient would be in class IA without transient electrocardiographic changes (I, accelerated angina; A, secondary unstable angina). At the other end of the spectrum is the patient who experiences recurrent angina at rest with transient ST segment depressions several days after an acute myocardial infarction. This patient would be in class IIC with transient electrocardiographic changes (class III, angina at rest, acute; C, postinfarction unstable angina).

Unstable angina is a dynamic condition, and patients may initially be in one class and move to another as the underlying disease changes or as response to treatment occurs. For example, a patient with the new onset of severe and frequent exertional angina without an apparent provocative extracardiac condition is in class IB. If that patient then developed an episode of angina at rest, he would be in class IIB. If no pain occurred for 48 hours, he would be in class IIB.

The classification of the intensity of treatment may be used as follows. A patient with a history of primary unstable angina at rest during convalescence from a myocardial infarction who is receiving no anti-ischemia therapy is in class IIC1. If episodes of pain persist despite treatment with usual doses of antianginal agents, the patient would advance to IIC2; if during treatment with intravenous nitroglycerin the episodes disappeared for more than 48 hours, the patient would be classified as IIC3.

Although the proposed classification of unstable angina is clinical, it can be related to the underlying disease. Angioscopic observations performed during operation suggest a good correlation between the presence of nonocclusive thrombi and the recent occurrence of angina at rest.25 Such thrombi usually undergo rapid spontaneous lysis and therefore become less prevalent with the passage of time. Thrombolytic or anticoagulant therapy may therefore be of great value in patients in class III, of less value in class II, and of little value in class I. The precipitation of unstable angina by changes in conditions extrinsic to the coronary artery bed that have intensified ischemia (class A) is compatible with fixed, severe coronary obstruction, and the presence of a fissured plaque or thrombus need not be presumed (but cannot, of course, be excluded).

Unstable angina secondary to an increase in myo-
cardial oxygen needs or abnormal coronary vasoconstriction generally responds to bed rest, mild sedation, and vigorous treatment with multiple anti-ischemic drugs; failure to respond to such vigorous therapy suggests total or subtotal coronary occlusion, sometimes by a thrombus.

It is hoped that this classification will aid in the clear description of and communication about patients with unstable angina, in the elucidation of the natural history and prognosis of the various subgroups, in the precise definition of patients selected for clinical trials so that therapy can be evaluated in comparable patients, and ultimately in the development of treatment regimens that are appropriate for each subgroup.

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Braunwald Classification of Unstable Angina 413
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