Acute Coronary Syndrome Unstable angina

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Definition

- Worsening of ischemic symptoms in patients with stable coronary artery disease

Braunwald classification

Adapted from Braunwald E. Circulation 1989; 80:410

Clinical circumstances

Class A - Secondary unstable angina (in the setting of anemia, infection, fever, etc)

Class B - Primary unstable angina

Class C - Post-MI angina

Unstable Angina: 3 Classes

A	B	C
Develops in presence of extracardiac condition that intensifies myocardial ischemia (secondary UA)	Develops in the absence of extracardiac condition (primary UA)	Develops within 2 weeks after acute myocardial infarction (postinfarction UA)

Braunwald Classification of Unstable Angina Severity: 3 forms

- I. New onset (UA de novo) of severe angina or accelerated angina; no rest pain
- II. Angina at rest within past month but not within preceding 48 hr (angina at rest, subacute UA)
- III. Angina at rest within 48 hr (angina at rest, acute UA)

Ethiology

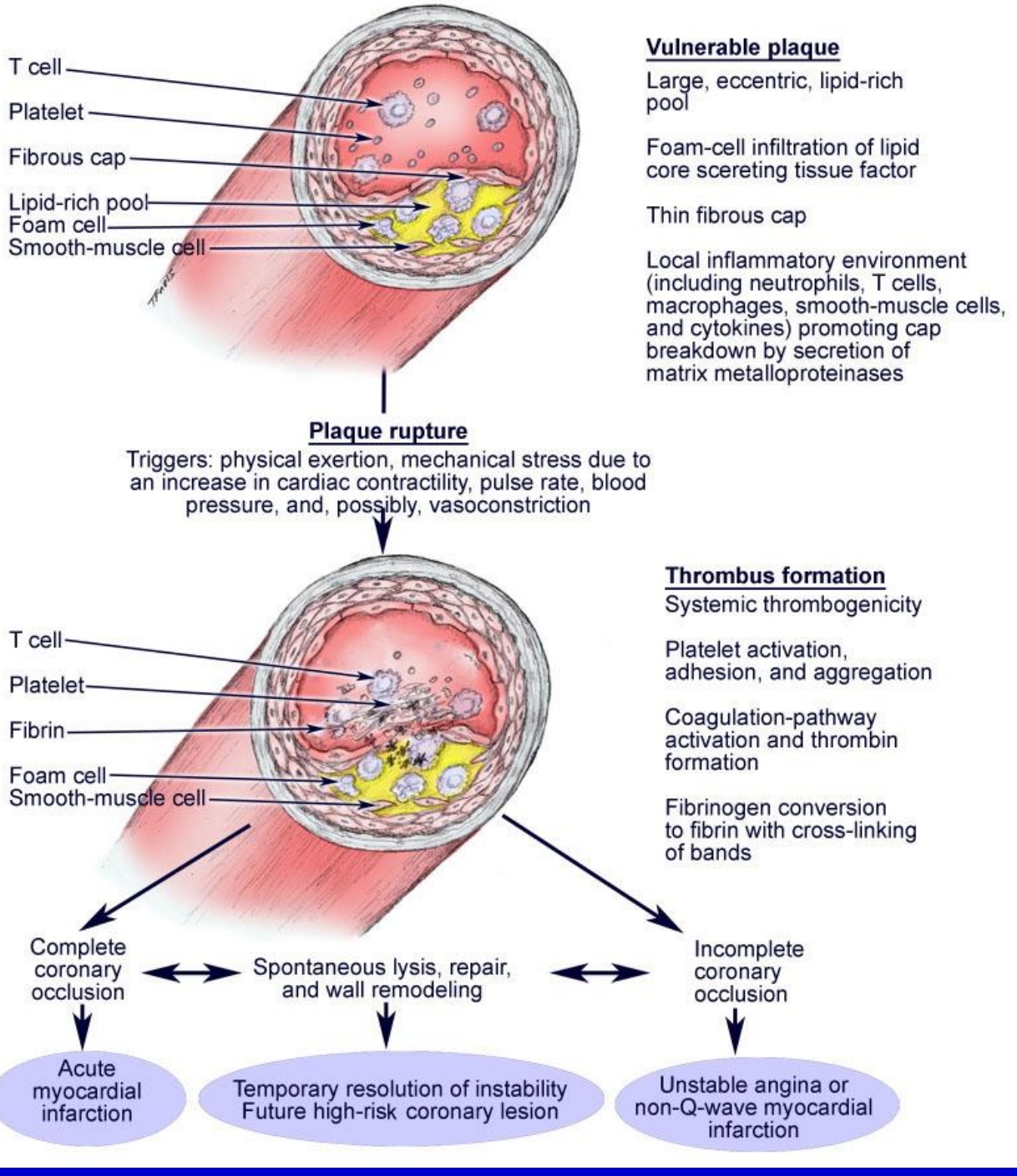
- triggered by such obvious extrinsic factors such as severe anemia, thyrotoxicosis, acute tachyarrhythmias, hypotension, and drugs capable of increasing myocardial oxygen demand: secondary UA
- no obvious external trigger can be identified:Primary UA

Patogenesis

- the outcome of a complex interplay involving coronary atherosclerotic plaque and resultant stenosis, platelet-fibrin thrombus formation, and abnormal vascular tone

Unstable Plaque

- Fissure or rupture in its fibrous cap
- Plaque fissure leading to unstable angina or acute MI may occur not only at sites of severe atherosclerotic stenosis, but even more commonly at minimal coronary stenoses


T cell
Platelet
Fibrous cap
Lipid-rich pool
Foam cell
Smooth-muscle cell
Vulnerable plaque
Large, eccentric, lipid-rich pool
Foam-cell infiltration of lipid core scereting tissue factor
Thin fibrous cap
Local inflammatory environment (including neutrophils, T cells, macrophages, smooth-muscle cells, and cytokines) promoting cap breakdown by secretion of matrix metalloproteinases
Plaque rupture
Triggers: physical exertion, mechanical stress due to an increase in cardiac contractility, pulse rate, blood pressure, and, possibly, vasoconstriction
T cell
Platelet
Fibrin
Foam cell
Smooth-muscle cell
Thrombus formation
Systemic thrombogenicity
Platelet activation, adhesion, and aggregation
Coagulation-pathway activation and thrombin formation
Fibrinogen conversion to fibrin with cross-linking of bands
Complete coronary occlusion
Spontaneous lysis, repair, and wall remodeling
Incomplete coronary occlusion
Acute myocardial infarction
Temporary resolution of instability
Future high-risk coronary lesion
Unstable angina or non-Q-wave myocardial infarction

Dynamic Obstruction - THROMBOSIS

- thrombosis by exposing platelets to the thrombogenic components of plaque
- this leads to platelet attachment, aggregation, platelet thrombus formation, and the exposure of tissue factor, an abundant procoagulant in the plaque, which interacts with clotting factor VII
- The ensuing cascade of events results in the formation of thrombin, which contributes to further platelet aggregation, fibrin formation, and vasoconstriction

VASOCONSTRICTION

- Paradoxical vasoconstrictor response to a variety of stimuli: flow changes, exercise, vasoactive substances (eg, acetylcholine, platelet aggregates, thrombin
- This abnormal vasomotor response has been observed well before the development of full-blown atherosclerosis; it has also been seen in patients with risk factors for coronary artery disease but no overt atherosclerosis

Symptoms and Signs in UA

- Retrosternal chest pain or such pain surrogates as a burning sensation, feeling of indigestion, or dyspnea
- Radiation in the neck, jaw, teeth, arms, back, or epigastrium

Symptoms and Signs

- In some patients, particularly the elderly, dyspnea, fatigue, diaphoresis, light-headedness, a feeling of indigestion
- The pain of unstable angina typically lasts 15–30 minutes; it can last longer in some patients. The clinical presentation of unstable angina can take any one of several forms

Physical Examination

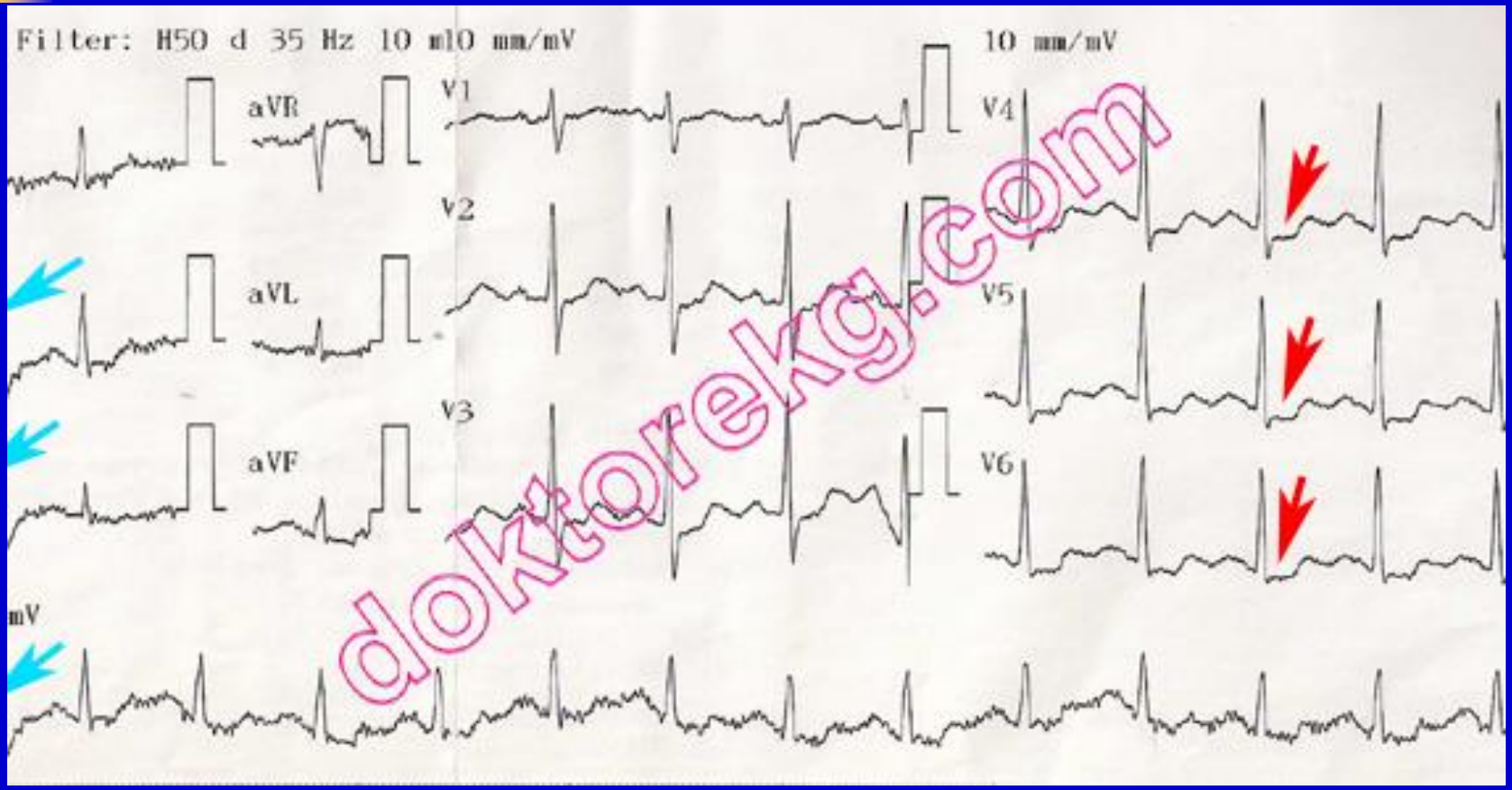
- No physical finding is specific for unstable angina, and when the patient is free of pain the examination may be entirely normal

Diagnostic Studies

- Unstable angina is a common reason for admission to the hospital,
- in a patient with typical effort-induced chest discomfort that is new or rapidly progressive, the diagnosis is relatively straightforward, particularly (but not necessarily) when there are associated ECG changes
- The physician should strongly suspect unstable angina, particularly when coronary artery disease or its risk factors are present

Rest ECG

- ECG abnormalities are common in patients with unstable angina
- The ECG abnormalities tend to be in the form of transient ST-segment depression or elevation and, less frequently, T wave inversion, flattening, peaking or pseudo-normalization (ie, the T wave becomes transiently upright from a baseline state of inversion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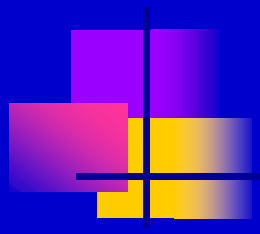


- Therefore, it is not surprising that 40–50% of patients admitted with a clinical diagnosis of unstable angina have no ECG abnormalities on initial presentation

Holter ECG monitoring

- reveals a much higher prevalence of transient ST-T wave abnormalities, of which 70–80% are not accompanied by symptoms (silent ischemia)
- These episodes, which may be associated with transient ventricular dysfunction and reduced myocardial perfusion, are much more prevalent in patients with ST-T changes on their admission tracings (up to 80%) than in persons without such changes
- Frequent and severe ECG changes on Holter monitoring, in general, indicate an increased risk of adverse clinical outcome

Angiography

- More than 90–95% - angiographically detectable atherosclerotic coronary artery disease of varying severity and extent
- The prevalence of single-, two-, and three-vessel disease is roughly equal, especially in patients older than 55 and those with a past history of stable angina
- In relatively younger patients and in those with no prior history of stable angina, the frequency of single-vessel disease is relatively higher (50–60%)

A subset of patients (5–10%) with angiographically normal or near normal coronary arteries

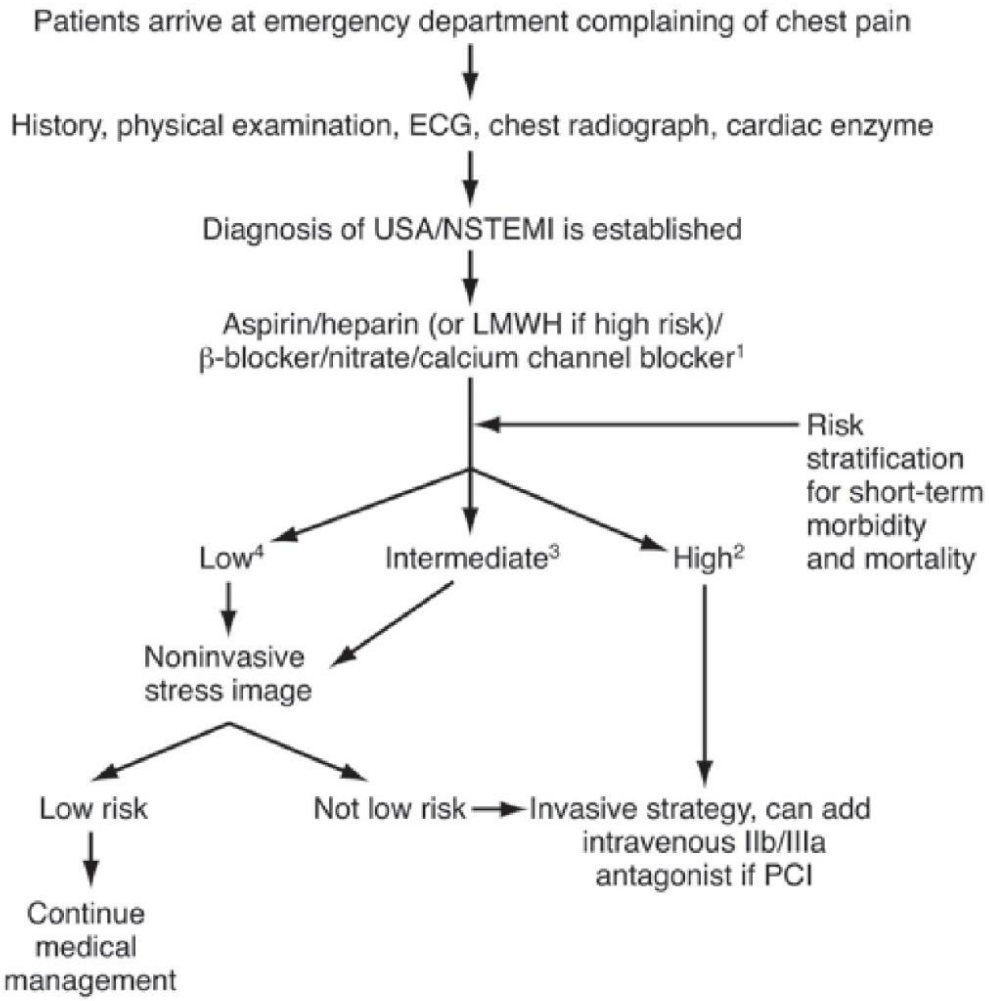
- may have noncardiac symptoms masquerading as unstable angina
- the clinical syndrome X (ischemic symptoms with angiographically normal arteries and possible microvascular dysfunction)
- primary vasospastic syndrome of Prinzmetal (variant) angina.

Stress Tests

- Any form of provocative testing (exercise or pharmacologic stress) is clearly **contraindicated** in the acute phase of the disease because of the inherent risk of provoking a serious complication

Other Laboratory Findings

- Blood levels of myocardial biomarkers - not elevated in unstable angina
- if they are elevated without evolution of Q waves, the diagnosis is generally a non–Q wave myocardial infarction (or NSTEMI)


Patients arrive at emergency department complaining of chest pain
History, physical examination, ECG, chest radiograph, cardiac enzyme
Diagnosis of USA/NSTEMI is established
Aspirin/heparin (or LMWH if high risk)/
β-blocker/nitrate/calcium channel blocker[1]
Risk stratification for short-term morbidity and mortality
Low[4]
Intermediate[3]
High[2]
Noninvasive stress image
Low risk
Not low risk
Invasive strategy, can add intravenous IIb/IIIa antagonist if PCI
Continue medical management

High risk features

- accelerating ischemic symptoms in preceding 48 h
- rest pain > 20 min
- presence of clinical congestive heart failure
- advanced age (> 75 years)
- new bundle-branch clock or rest angina with transient ST-segment changes > 0.5 mm
- sustained ventricular tachycardia or marked elevation of cardiac enzyme

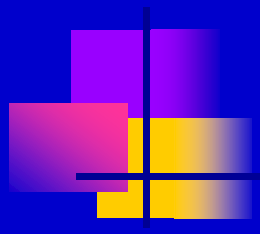
Intermediate risk features

- history of prior MI/PVD/CABG/CVA/aspirin use
- resolved prolonged rest angina (> 20 min), rest angina (< 20 min) relieved with rest or sublingual nitroglycerin
- age > 70 years
- T-wave inversion > 2 mm
- presence of pathologic Q wave
- slightly elevated cardiac enzyme

Low-risk features do not have the clinical features

- have new-onset class III or IV angina in the past 2 weeks without prolonged
- (> 20 min) rest angina
- normal or unchanged ECG
- normal cardiac enzyme
- CABG, coronary artery bypass grafting

Treatment



- During this early in-hospital phase, therapy is primarily aimed at stabilizing the patient by stabilizing the culprit coronary lesion and thus preventing a recurrence of myocardial ischemia at rest and progression to myocardial infarction

General Measures

- Intensive or intermediate care unit
- Bed rest with continuous monitoring of cardiac rate relief of anxiety with appropriate reassurance and, if necessary, anxiolytic medication
- A 12-lead ECG should be repeated if it is initially unrevealing or if any significant change has occurred in symptoms or clinical stability
- Serial cardiac biomarkers evaluation should be performed to rule out an acute myocardial infarction

NITRATES

- Nitrates are generally considered one of the cornerstones of therapy
- They tend to relieve and prevent ischemia by improving subendocardial blood flow in the ischemic zone through their vasodilator actions, predominantly on the large epicardial vessels, including the stenotic segments and the coronary collaterals

ANTIPLATELETS

- Aspirin has been shown to reduce the risk of developing myocardial infarction by about 50% in at least four randomized trials
- The protective effect of aspirin in unstable angina has been comparable, in the dosage range of 75–1200 mg/day
- However, because of the potential for gastrointestinal side effects, low doses of aspirin (75–81 mg/day) are preferable
- A lower dose should be preceded by a loading dose of 160–325 mg on the first day in order to initiate the antiplatelet effect more rapidly

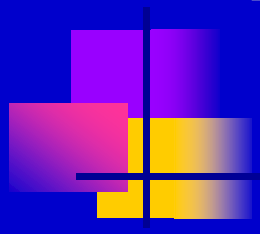
Ticlopidine and Clopidogrel

- They have been shown to be comparable to aspirin in reducing the risk of developing acute myocardial infarction in unstable angina
- Both drugs have delayed onset of full antiplatelet effect, hence they are not suitable in acute cases
- Because they are more expensive than aspirin and carry a 1% risk of agranulocytosis and, rarely, thrombotic thrombocytopenia purpura, ticlopidine and clopidogrel should be used only when a patient cannot tolerate aspirin due to hypersensitivity or major gastrointestinal side effects

Anticoagulants
Unfractionated Heparin
Low-Molecular-Weight Heparin

- The protective effect of intravenous unfractionated heparin (UFH) in treating unstable angina has been demonstrated in randomized trials
- During short-term use, the risk of myocardial infarction in unstable angina is reduced by about 90%, and ischemic episodes are reduced by about 70%

β-BLOCKERS



Metoprolol

Bisoprolol

Carvrdilol

Statins

- Simvastatin
- Atorvastatin
- Rozuvostatin

Definitive Management

- **Catheter-Based Interventions** – Endovascular interventions such as percutaneous coronary angioplasty, atherectomy, and laser-assisted angioplasty are commonly performed in patients with unstable angina to reduce the critical stenosis in the culprit artery or in multiple coronary arteries.

Acute complications

- death (0–2%)
- abrupt closure (0–17%)
- acute myocardial infarction (0–13%)
- and the need for urgent coronary artery bypass surgery (0–12%), than in patients with stable angina
- The risk is especially great when the procedure is performed soon after the onset of symptoms, in the absence of prior treatment with heparin, or in the presence of an angiographically visible intracoronary thrombus
- The 3- to 6-month restenosis rate with these interventions is 17–44%

Coronary Artery Bypass Surgery

- myocardial revascularization in patients with unstable angina is relatively superior to medical therapy for controlling symptoms and improving effort tolerance and ventricular function

Indication

- for patients with unstable angina who do not stabilize with aggressive medical therapy or for whom angioplasty is unsuccessful
- is followed by acute complications not amenable to additional catheter-based intervention
- It is also applicable to patients who have severe multivessel or left mainstem coronary artery disease, particularly when left ventricular function is also impaired