

# Acute Coronary Syndrome

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## Summary

One of the most powerful manifestations of atherosclerosis is acute coronary syndrome. Acute coronary syndrome (ACS) is an endpoint of atherosclerosis, which results in limited blood flow to the heart muscle resulting in symptoms (i.e., chest pain) and/or hemodynamic decompensation. Acute coronary syndrome requires early recognition and aggressive intervention. A combination of surgical interventions and pharmacologic therapy is used to reopen obstructed coronary vessels and decrease morbidity and mortality related to ACS.

## Key Points

- ACS is a frequent and costly cause of hospital admissions.
- ACS results in significant morbidity and mortality.
- Aggressive early detection and intervention are the hallmarks that predict good outcome in the patients with ACS.
- Revascularization in a patient with ACS reduces hospital mortality by one third.
- Combinations of antiplatelet agents, certain beta-blockers, statins, ACE inhibitors, and other medications are all used to decrease morbidity and mortality after an episode of ACS.

SEVEN MILLION PEOPLE ARE DIAGNOSED with coronary artery disease each year, yet this condition is underdiagnosed.<sup>1</sup> Many patients, particularly women, do not have any classic symptoms to suggest that they have coronary artery disease. Over 500,000 deaths each year are due to coronary heart disease.<sup>1</sup> One person dies every minute of every day from coronary artery disease. Close to 1.5 million hospitalizations from myocardial infarction take place every year.<sup>1</sup> The estimated cost to care for patients with coronary heart disease is \$60 billion a year.<sup>1</sup>

Atherosclerosis is a disease of the blood vessel with deposition of lipids within the vessel wall. ACS occurs when an atherosclerotic plaque ruptures and disrupts blood flow in the coronary vessels. The diagnosis of acute coronary syndrome is extraordinarily prevalent. Over 2 million patients a year are admitted to the cardiac care units of this country with acute coronary syndrome.<sup>1</sup>

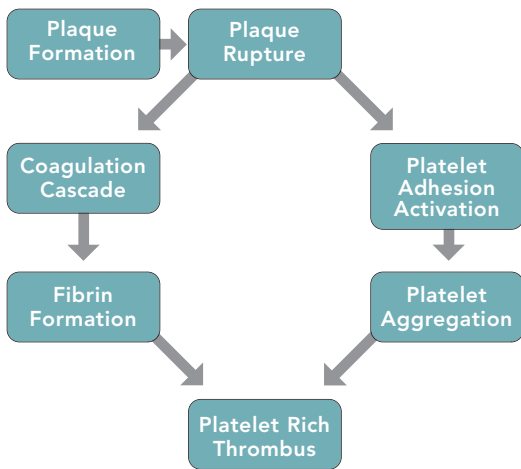
When an atherosclerotic plaque ruptures, the contents leak out and the body's natural response is to reseal the plaque. There is a cascade of events that lead to protecting this disrupted plaque cap. Because this is not a big area, occlusion of the vessel with a

blood clot and material from the plaque occurs. Exhibit 1 illustrates the cascade of events with ACS that ultimately leads to thrombus formation that occludes the artery.

The key variable that predicts whether or not one plaque will lead to an acute coronary syndrome is the amount of the lipid core. Other factors are a low amount of smooth muscle cells covering the plaque, a thin fibrous cap over the plaque, and a high content of inflammatory cells like macrophages in the lipid core.<sup>2</sup> Mild to moderate plaques, which comprise 20-30 percent of the total plaques in a typical patient, have the highest tendency to rupture and cause ACS (Exhibit 2). Different imaging modalities are being utilized every day to find variables that would increase understanding of how significant any given plaque is in its contribution to the risk of ACS.

There are two major types of ACS presentation. One is an ST-segment elevation on electrocardiogram indicating a myocardial infarction (STEMI). About 600,000 hospital admissions occur every year for STEMI. Another group of patients will have non-ST-segment elevation ACS that indicates either unstable angina (UA) or a non-ST elevation myocar-

**Exhibit 1: Acute Coronary Thrombosis**



dial infarction (NSTEMI). This type of presentation accounts for about one and a half million admissions per year.

The diagnostic tools outside of symptoms that are most commonly used in the ACS setting are the electrocardiogram and laboratory testing. Troponin assays are a laboratory marker used to diagnose ACS. Troponin, a protein leaked from damaged myocytes, increases in the blood around the time of ACS. The greater the degree of elevation in troponin, the higher the mortality rate in the patient.<sup>3</sup> The degree of troponin elevation also indicates how quickly decisions about therapy must be made. In some cases, levels of creatine phosphokinase (CPK) are also used for diagnosis and to predict rates of mortality in the short and long term.

Patients who are admitted to a hospital with ACS may be risk-stratified according to the Thrombolysis in Myocardial Infarction (TIMI) risk score. There are

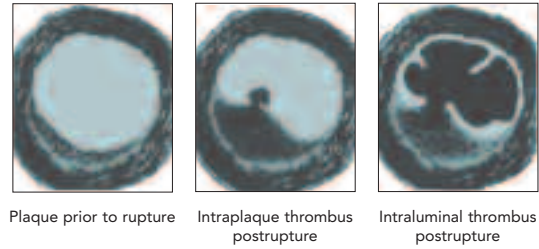
**Exhibit 3: TIMI risk score for UA/NSTEMI - 7 independent predictors<sup>3</sup>**

- Age  $\geq$  65 years
- $\geq$  3 CAD Risk Factors ( $\uparrow$ chol, FHx, HTN, DM, smoking)
- Prior CAD (cath stenosis  $>$ 50%)
- ASA in last 7 days
- $\geq$  2 anginal events  $\leq$  24 hours
- ST deviation
- Elevated cardiac markers (CK-MB or troponin)

UA, unstable angina; NSTEMI, non-ST segment elevation myocardial infarction; CAD, coronary artery disease; chol, cholesterol; FHx, family history; HTN, hypertension; DM, diabetes mellitus; ASA, aspirin; CK-MB, creatinine kinase - myocardial band

**Exhibit 2: Plaque Rupture of Lipid-Rich Plaques**

Mild-to-Moderate Lesions that Rupture are the Most Common Cause of Cardiac Events

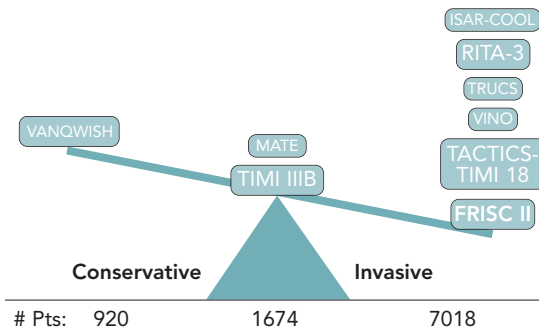


TIMI risk scoring systems for STEMI and NSTEMI/UA. The higher the risk score, the higher the 30-day mortality rate. Risk scores can also be used to identify the need for early intervention. High-risk patients will need more aggressive and early intervention. Exhibit 3 lists the independent factors that comprise the NSTEMI/UA TIMI risk score.

There are data demonstrating that an aggressive approach is better for the individual who is suffering from acute coronary syndrome (Exhibit 4). Of all the different trials that have looked at the ACS population, only one has demonstrated some success with the conservative approach. All the other trials have clearly shown, with several thousand patients, that early aggressive intervention such as catheterizations and coronary vessel stenting works and improves survival.

The aggressive strategy of catheterization and stenting are not all that is necessary. There are many other modes of pharmacologic therapy that will also help sustain the improved survival that we see in patients who undergo coronary angiograms.

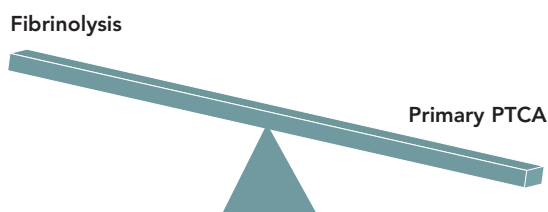
**Exhibit 4:**



VANQWISH, Veterans Affairs Non-Q-Wave Myocardial Infarction Strategies In-Hospital; MATE; TIMI, Thrombolysis in Myocardial Infarction; ISAR-COOL, Evaluation of Prolonged Antithrombotic Pretreatment ("cooling-off" strategy); RITA, Randomized Intervention Trial of Unstable Angina; TRUCS, Treatment of Refractory Unstable Coronary Syndrome; VINO, Value of First Day Angiography; TACTICS, Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy; FRISC II, Fast Revascularization During Instability in Coronary Artery Disease



Exhibit 7:



- |                     |                       |
|---------------------|-----------------------|
| • Reduces mortality | • Lower mortality     |
| • Well studied      | • Anatomic definition |
| • Widely available  | • Avoids hemorrhage   |

Twenty four hours after presenting with an MI, patients will have their heart function measured to determine if they have suffered significant enough injury to their myocardium that they have depressed systolic function (i.e., an ejection fraction less than forty percent). In patients whose ejection fractions are forty percent or greater, the role of anti-platelet agents, ACE inhibitors and statins is well studied. The use of beta-blockers, though commonly prescribed, is poorly supported by the data. The need for beta-blockers post-MI in the face of an ejection fraction greater than 40 percent is a matter of debate.

For patients with ejection fractions less than 40 percent, the standard therapy is determined based on whether the patient is symptomatic or asymptomatic. Anti-platelet agents, ACE inhibitors and statins are standard therapy for asymptomatic patients. Only one beta-blocker, carvedilol (Coreg®), has been studied in this patient population. It appears to improve survival in this type of patient. The symptomatic patient, whose ejection fraction is less than forty percent, should receive anti-platelet, carvedilol, ACE inhibitor, and statin therapy in order to improve post-MI survival. One additional medication, eplerenone (Inspra®), has been shown to improve morbidity and mortality when added to these other therapies in patients who have heart failure and a reduced ejection fraction after an MI.

There are several revascularization strategies to restore adequate blood flow to the heart in the face of significant atherosclerosis and ACS. These include the placement of stents in the coronary arteries, angioplasty, and thrombolytic therapy. Thrombolytics include alteplase (Activase®), reteplase (Retevase®), and tenecteplase (TNKase®). These agents dissolve the blood clots, which are causing artery occlusion in ACS.

One interesting finding with thrombolytics is there is a ceiling of benefit. Not all patients get a sustained benefit because of hemorrhage. Hemorrhage with thrombolytics is not just a stroke. The plaque inside the arteries is susceptible to hemorrhage. Bleeding within the plaque structure will cause an expansion of the plaque itself and further disruption of the coronary artery blood flow.

In addition to hemorrhage, there are other limitations with thrombolysis. With thrombolytic therapy, 20 percent of the patients' artery remains closed.<sup>10</sup> Five to 10 percent of patients will re-occlude within twenty-four hours of their presentation.<sup>11,12</sup> Re-infarction occurs in about 5 percent of patients.<sup>13</sup> Each of these events decreases the benefits of thrombolysis on mortality.

When balancing which strategies to use that may make a difference in these ACS patients long-term, it is now being recognized that despite the fact that thrombolytic therapy reduces mortality, is well studied, and is widely available, aggressive interventional options lower mortality, define the coronary anatomy to its fullest, and avoid the one reason why a plateau is reached with thrombolytics - hemorrhage (Exhibit 7).<sup>14</sup> Thrombolytics are a good therapy option when emergent angioplasty is not available, but patients should not receive this therapy because it is "easier," rather than trying to get them to a cardiac catheterization suite, where they can have aggressive, definitive revascularization. Thrombolytic therapy is not used in NSTEMI because it has been shown to actually be harmful.

The key determinant to impacting morbidity and mortality for a person who has ACS is how quickly they receive cardiac catheterization to reopen the blocked artery. The threshold for major mortality benefit is ninety minutes from the time the patient walks in the door.<sup>15</sup> Once two hours passes, there is a marked increase in mortality because more muscle cells have been allowed to die resulting in greater impairment of systolic heart function. Aggressive and rapid catheterization of high-risk patients with ACS makes a significant difference in hospital mortality. If a patient does not get appropriate blood flow to the coronary artery reestablished, the hospital mortality is 18.5 percent.<sup>16</sup> Reestablishment of blood flow results in 6.6 percent mortality.<sup>16</sup> Revascularization of the patient and the in hospital mortality is one third less.

## Conclusion

The morbidity and mortality in patients with ACS is extraordinarily high. Using different clinical prog-

nostic and diagnostic parameters can help make early diagnosis, which is critical if morbidity and mortality are to be impacted. Aggressive evidence based medical and revascularization strategies are absolutely essential to maximally decrease morbidity and mortality from ACS. **JMCM**

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