Acute coronary syndrome - current perspectives

Dr. Asha Mahilmaran

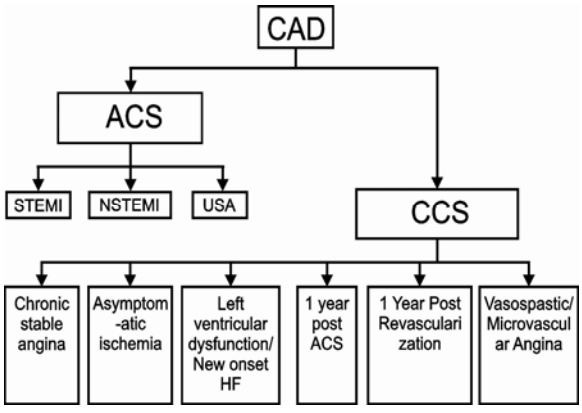
Senior Interventional Consultant Cardiologist, Apollo Hospitals, Chennai.

Acute coronary syndromes (ACS) are the commonest cause of chest pain in emergency departments and the most malignant presentation of coronary artery disease, causing one-third of deaths in the adult population world wide[1].ACS refers to conditions causing acute myocardial ischemia, and the spectrum includes ST-elevation myocardial infarction (STEMI),Non-ST Elevation myocardial infarction (NSTEMI), and unstable angina[2].

Definition

ACS refers to CAD's acute presentations and includes a spectrum of STEMI,NSTEMI, and unstable angina. They are caused by plaque rupture and overlying thrombosis, causing complete or partial occlusion of the coronary artery.

Coronary artery disease is now classified into two types by the European society of cardiology as an acute coronary syndrome and chronic coronary syndrome (CCS).CCS includes all stable CAD presentations, chronic stable angina, asymptomatic ischemia detected on routine testing, new-onset heart failure, one year after ACS, Revascularization, microvascular disease, and vasospastic angina[3].



Etiology

The Etiology of ACS is predominantly atherosclerotic. Three important pathophysio-logical causes are leading to ACS

1. Plaque rupture-More commonly, non-stenotic lesions with large lipid pool and thin fibrous cap are prone to rupture, which activates platelet adhesion and thrombus formation is Inflammation with macrophage infiltration. The plaque tears expose lipid pool to blood, exposing highly thrombogenic tissue factor, collagen resulting in thrombus formation. This thin cap fibro atheroma (TCFA) and plaque rupture is the dominant mechanism in close to 45% of cases.
2. plaque erosion-Plaque erosion without rupture is the cause of ACS in about 30% of cases, more common in young age and women. OCT-based studies have shown that this group responds well to conservative medical management without percutaneous angioplasty.
3. Calcific nodule-In about 8% of cases, the underlying mechanism is a calcific nodule producing critical stenosis. More common in diabetes and old age[4].

Other Etiologies include coronary vasospasm, cocaine abuse

Coronary embolism due to infective endocarditis, myxoma, Left ventricular thrombus, Iatrogenic during cardiac catheterization.

Spontaneous coronary dissection (SCAD)-is a rare non-atherosclerotic cause in 0.1-0.4% of ACS.SCAD is more common in young women with no coronary risk factors. It has been reported in the postpartum period, severe emotional or physical exertion, and association

Address for communication: Apollo hospitals, Number 21, Greams lane, Chennai-600021, India.
Email id-drashamahil@gmail.com

with connective tissue disorders and fibromuscular dysplasia. A sudden disruption of intima from the outer vessel wall causes intramural hematoma and leads to a thrombus containing false lumen and a true compressed lumen. Conservative management is preferred in uncomplicated cases as most spontaneous dissections heal.[5]

Coronary arteritis, compression by myocardial bridges are some rare causes

Risk factors for ACS

Hypertension

Diabetes

Dyslipidemia

Smoking, Tobacco use

Physical inactivity

Obesity

Family history of Premature CAD

Age, male sex, postmenopausal women

Pregnancy-induced hypertension, Gestational diabetes, Preeclampsia, Eclampsia

Rheumatoid arthritis, other connective tissue disorders

Psoriasis

COVID infection

Clinical Presentation.

The most typical presenting symptom is chest pain, a compressive, crushing type of heaviness over the left precordium radiating to the back, left arm, jaw, or upper abdomen. Localized pain is usually not due to ACS. Pain can be present only in the left arm, jaw, or throat, or epigastric region, when a diagnosis can be missed if not suspected.

Pain can also be present over the right chest, arm, or shoulder, or neck. Pain is often associated with diaphoresis. Pain can be at rest or on exertion. Patients can also present with breathlessness, palpitation, fatigue, nausea, and vomiting. Atypical symptoms are more common in the elderly, diabetics, and women.

The clinical examination may be normal. Bradycardia or tachycardia are both poor prognostic markers. Hypotension can be present due to myocardial dysfunction, shock. Hypertension can be due to catecholamine surge, cardiac murmurs, gallop rhythm can be present due to acute left ventricular failure. Peripheral vascular disease can be associated with absent pulses, bruits. Pedal edema can be due to heart failure or associated renal dysfunction.

A brief focused history is recommended, eliciting causal risk factors of smoking, diabetes, hypertension, family history of premature CAD, time of onset and nature of chest pain, prior MI, revascularization, other vascular diseases, and bleeding risk

Diagnosis

Two important tests in diagnosis are ECG and biomarker troponin assay

ECG

Persistent ST elevation > 20minutes confined to coronary distribution is suggestive of **STEMI**

Initial ECG can be Non-diagnostic; serial ECGs can be more revealing.

NSTEMI patients may present with transient ST elevation, ST depression, T wave inversion, flat T waves, pseudo normalization, or normal ECG.

AHA recommends time to ECG of 10 minutes or less

Biomarkers

The most important biomarker in the diagnosis is **troponin**. The high sensitivity troponin is the recommended rule in and rules out test at 0, 1 hour; if the patient is presenting 3 hours after chest pain, if the patient presents early after chest pain, it is recommended to do the 0 and 2-hour test. The patient's symptoms are suggestive, and the initial value of troponin is high, the patient will be triaged as ACS. The initial troponin is not very high, but the second test's

delta change is high, the patient will be treated as ACS. If both the test results are normal, ACS is ruled out. If the risk factors present, GRACE score >140, irrespective of the troponin test patient, should undergo an invasive coronary angiogram. In low to intermediate-risk patients, stress imaging or CT coronary angiography can be done.

NT PRO BNP is useful in the prognosis of ACS patients and may be of added value.

An echocardiogram should be used early to look for left ventricular function, regional wall motion abnormality. It is also useful to look for an alternative diagnosis like aortic stenosis, Hypertrophic cardiomyopathy, aortic dissection, pulmonary embolism, and pericardial effusion.

Biochemical parameters include blood sugars, renal parameters, blood count, lipid profile.

X-ray Chest PA view is helpful to look for lung congestion, cardiomegaly and to look for alternative etiology of chest pain such as pneumonia, pleural effusion, or pneumothorax.

Coronary angiogram should be done within 2 hours in high-risk ACS within 24 hours in most others or within 2-3 days. In low-risk patients, it is recommended to follow up with stress imaging or CT coronary angiogram.

Prognosis

The poor prognostic markers of ACS are hemodynamic instability, arrhythmias, advanced age, diabetes, chronic kidney disease, Transient ST elevation, marked

ST depression, ST elevation in lead AVR, high troponin values, NT pro-BNP, and previous revascularization history.

The GRACE risk score is the preferred risk calculation score as recommended by ESC guidelines 2020

The GRACE risk score is calculated from a nomogram based on age, systolic pressure, serum creatinine, cardiac arrest, ST deviation, KILLIP class, troponin positivity, and predicting in-hospital and six-month mortality rate. Validation of GRACE score in Indian patients in a study by Prabhu Desai et al.[7]showed lower systolic pressure, ST-segment deviation, and cardiac biomarker positivity to be a significant predictor of adverse events, and a GRACE score >217 was predictive of multivessel disease.

Management

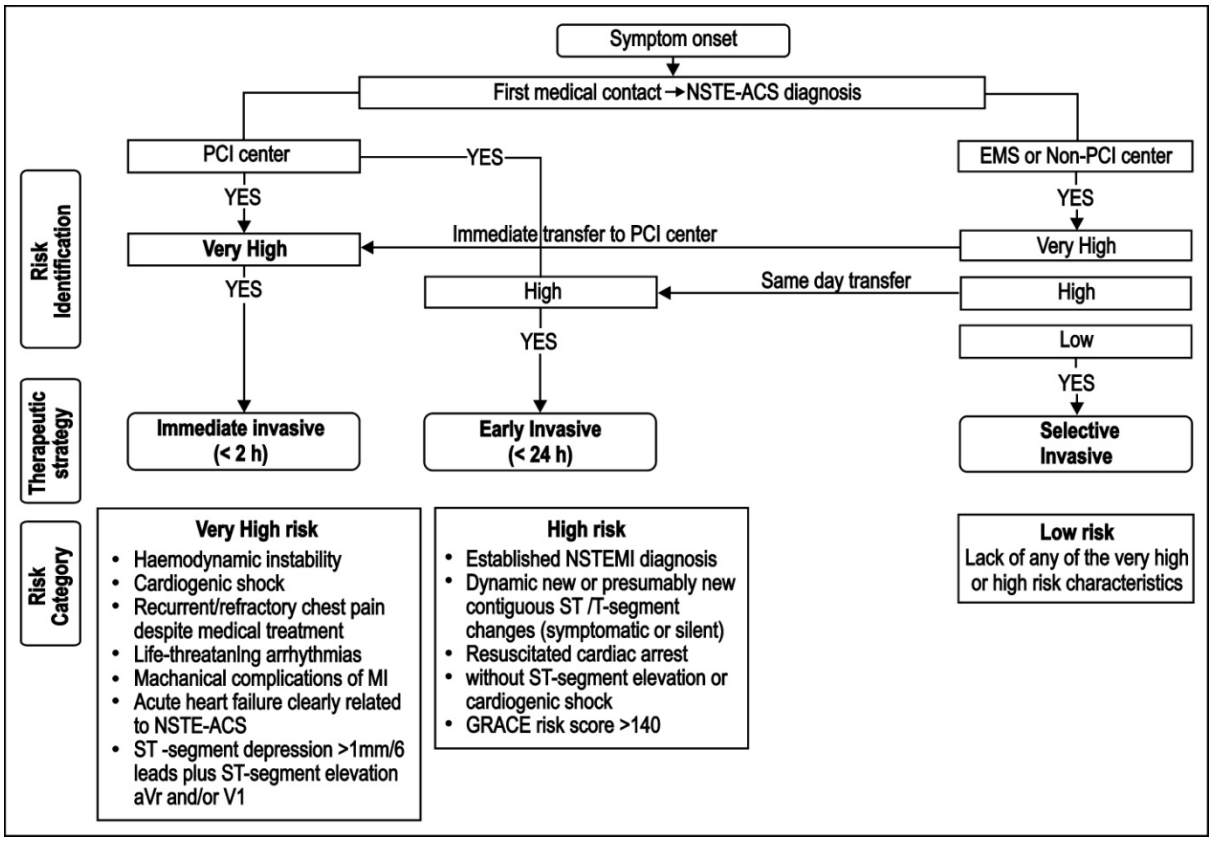
Medical Management

The initial management includes pain relief with nitrates; intravenous nitroglycerine is used in ongoing chest pain. Nitrates should be used cautiously in patients with inferior wall infarction, where it can produce profound hypotension.

High dose statins 40-80 mg atorvastatin, 20-40 mg rosuvastatin should be initiated early.

Antiplatelet therapy with dual agents - Clopidogrel is loading 600 mg followed by 75 mg once daily or ticagrelor 180 mg loading followed by 90 mg twice daily, and aspirin 325 mg loading followed by 75 mg daily is recommended in medical management. DAPT therapy is continued for one year and can be extended beyond in patients with high ischemic risk and low bleeding risk. Beta blockers and ACE inhibitors also should be initiated. Beta-blockers are contraindicated in patients with pulmonary edema and cardiogenic shock. Low molecular weight heparin, fondaparinux, or unfractionated heparin may be used until revascularization or clinical stabilization.

The patients with very high and high risk should proceed to a cath lab for coronary angiogram within 2-24 hours, respectively. For patients who are planned for an early angiogram, the recommendation is to start antiplatelet agents after the coronary anatomy is known, and it is preferred to give prasugrel for ACS PCI rather than ticagrelor based on the recent ISAR REACT trial. Clopidogrel is given only if there is a contraindication for the use of the other two agents, GPIIB/IIIA Agents like tirofiban or



eptifibatide are used only in bailout situations in the cath lab[6].

Invasive strategy

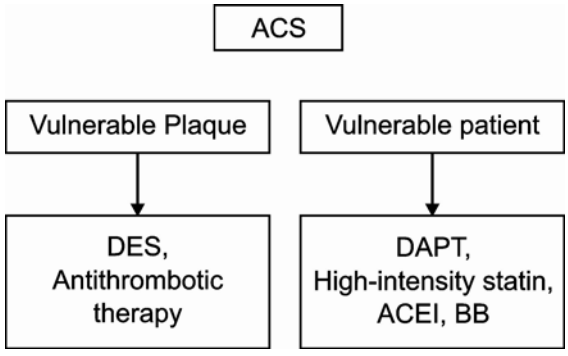
Timing of invasive coronary angiogram

An early invasive approach is recommended in all the high-risk patients; the timing of angiogram should be immediate in very high risk and within 24 hours in high-risk patients[6].

Multivessel PCI can be done at the same index PCI or staged depending on the complexity of the anatomy and clinical situation. Fractional flow reserve (FFR) can be used to assess the significance of the non -culprit artery

Patients with anatomy not suitable for PCI may undergo early CABG, and these patients should be continued on DAPT with Clopidogrel and aspirin for one year. Ticagrelor with aspirin increases bleeding risk and no difference in MACE rates.

An important concept in the management of ACS is that there is a vulnerable local plaque responsible for ACS, but it is a systemic disease with multiple plaques, Inflammation, endothelial dysfunction, and multiple CV risk factors.



ACS in special subsets

ACS in the elderly

Elderly people are not subjected to invasive strategy in many cases; in the European registry, only 28-30% of those aged >75 undergo a coronary angiogram, and in the US, it is even lower at 17% for men and 11% for women. Real

world studies have shown lesser revascularization and angina with an invasive strategy; mortality difference not significant. In STEMI, PPCI is the standard of care. Elderly are more prone to bleeding complications, avoid prasugrel in those > 75 years of age, a radial approach preferred, and Primary PCI preferred over lysis in STEMI. Half dose tenecteplase, avoidance of clopidogrel loading, and enoxaparin help reduce the intracranial bleeding risk[8].

ACS in women

Women tend to have more unstable angina than STEMI. Women tend to complain of pain in the neck, back, or throat more often; younger women in the premenopausal group may present with no chest pain and breathlessness and fatigue, whereas postmenopausal women more often present with chest pain. Women tend to present ten years later than men, present more often with heart failure, tend to have worse prognosis due to delayed presentation, under-diagnosis, and under treatment. They are more prone to vascular complications, radial spasm, and bleeding complications. Non-obstructive CAD and plaque erosion rather than plaque rupture is more common. Women with positive troponin benefit more from an invasive strategy. Younger women have more risk factors like DM, hypertension, obesity, COPD, and the previous stroke, have worse outcomes due to delay and missed diagnosis, and a greater incidence of co-morbidities. Women are less likely to be advised coronary angiogram, receive guideline-directed therapy. The gender-related bias and differences have been understood and addressed with improvement in outcomes in women [9,10].

ACS in Diabetes

Diabetes is an important comorbid condition that increases the mortality rates, and a higher incidence of heart failure, renal failure, cardiogenic shock, and multivessel disease is more common. About 40% of ACS patients have DM in the GRACE registry[11].Diabetics had a higher incidence of previous CVD and multiple major CV risk factors. Diabetics was associated with a two-fold higher risk of all-cause death and a 1.5 fold higher risk of MACCE in a large study of 23,880 patients from China[12].

ACS with Chronic kidney disease

ACS in patients with kidney disease is challenging as they tend to have more multivessel and calcific lesions, and the risk is related to elevated creatinine. Contrast-induced nephrotoxicity should be minimized by using low osmolality contrast and the use of imaging guidance by IVUS to reduce contrast use.

ACS and COVID

COVID infection can cause type 2 MI due to hypotension, hypoxia. Procoagulant and proinflammatory states in COVID infection also predispose to ACS in patients with preexisting CAD. Troponin elevation and myocarditis may also occur as part of COVID infection. Higher thrombus burden and poorer outcomes have been noted in COVID ACS. A higher incidence of stent thrombosis has also been reported. Patients with STEMI and high-risk NSTEMI with a low probability of COVID should go to the lab for invasive management. Patients with COVID infection and STEMI can undergo thrombolysis, and NSTEMI is conservatively managed. If the patient is hemodynamically unstable, the decision to intervene will be based on a multidisciplinary approach and extent of COVID respiratory disease and expected outcomes. Proper PPE and protection of cardiac catheterization lab staff are important[13,14].

ACS with cardiogenic shock and mechanical complications

ACS with cardiogenic shock complicates 7% of STEMI and less often with NSTEMI. They carry high mortality and morbidity. Early mechanical cardiac support (MCS) is needed in severe cases with IABP, IMPELLA, ECMO, or left ventricular, right, or biventricular support devices in addition to revascularization by PCI of culprit vessel or CABG. Mechanical complications like papillary muscle rupture and severe mitral

regurgitation, ventricular septal rupture need MCS and early surgery. Device closure of VSR has also been done with varied outcomes and high mortality.

ACS in Patients needing anticoagulation

ACS may occur in patients on a chronic anticoagulant for chronic atrial fibrillation or mechanical prosthetic valve. Patients on warfarin with INR higher than 2.5 should be taken for intervention without additional heparin, preferably through the radial route. Patients on NOACS can be taken up for intervention, will need heparin during PCI. Triple therapy with anticoagulant, aspirin, and p2y12 inhibitor should be limited to 1 week followed by p2y12 inhibitor with anticoagulant stopping the aspirin. Clopidogrel is the safest antiplatelet agent in a dual or triple therapy, and potent drugs such as ticagrelor and prasugrel are better avoided with anticoagulant therapy.

Conclusion

Acute coronary syndromes are the leading cause of cardiac emergencies leading to significant morbidity and mortality. High sensitivity troponin and ECG, bed side ECHO is important in diagnosis and prognostication. A GRACE risk score is useful in risk stratification. Routine invasive strategy is preferred in all high-risk patients. Stress imaging, CT coronary angiography is useful in low-risk patients for further risk assessment. PCI with DES and DAPT with a potent antiplatelet agent of prasugrel, ticagrelor preferred with low dose aspirin for a standard duration of one year. Extended or truncated regimens are recommended based on ischemic or bleeding risk. High dose statins, ACEI, and beta-blockers are important in the management of ACS patients. Ezetimibe and PCS K9 inhibitors are to be added to reach lipid goals if not achieved with statins alone.

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