Coronary Artery Disease (CAD) —
Atherosclerotic Plaque, The Six Areas of Consensus, And the Four Areas of Controversy

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Coronary artery disease is considered a leading cause of death worldwide. It occurs as a result of atherosclerotic changes in the coronary arteries with subsequent narrowing of the vessels, preventing their dilation. The atherosclerotic plaque is a sticky yellowish deposit formed with the arterial intima. As a result, mismatch between myocardial oxygen supply and demand occurs. In many cases, it remains asymptomatic. Acute retrosternal anginal chest pain is the cardinal symptom. Management involves primary and secondary measures, medical treatment, or even revascularization.
Overview

Atherosclerosis is a combination of the words ‘athero’ meaning lipid accumulation and ‘sclerosis’ meaning thickening. It is a chronic inflammatory process characterized by the accumulation of lipids, inflammatory cells, fibrous material, and calcium within the arteries.

The atherosclerotic plaque is a sticky deposit formed within the arterial intima, which causes the narrowing and blockage of the arterial lumen.

Artherosclerotic Plaque

Plaque formation

The process of plaque formation is insidious and begins with endothelial damage secondary to multiple risk factors; the most important of which are:

- Diabetes
- Smoking
- Hyperlipidemia
- Raised homocysteine
- Chronic inflammation

Nitric oxide production is decreased within the damaged and dysfunctional endothelium. This is followed by the accumulation of low-density lipoproteins and later macrophages within the vessel wall.

Plaque growth
Macrophages engulf fat molecules and form foam cells that accumulate in the plaque-forming the lipid core. They release growth factors, cytokines, and chemokines, and upregulate adhesive molecules, for instance, VCAM-1, ICAM-1, and monocyte chemoattractant protein 1 (MCP-1). The net result is increased monocyte attraction and macrophage recruitment to the site, magnifying the endothelial damage and dysfunction.

Smooth muscle cells, on the other hand, stabilize the plaque by forming a fibrous cap. A strong fibrous cap stabilizes the plaque. A weak fibrous cap makes the plaque vulnerable to rupture.

**Plaque rupture**

Increased infiltration of inflammatory cells into the plaque, smooth muscle cell apoptosis, and proteolytic degradation of the matrix transform a stable plaque into a vulnerable plaque.

The vulnerable plaque has an increased risk of disruption/rupture resulting in thrombus formation, vascular occlusion, and clinical symptoms of ischemic injury. The formed thrombus may also rupture further to shower emboli into the systemic circulation.

![Late complications of atherosclerosis](https://example.com/late-complications.png)

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The Six Areas of Consensus in Coronary Artery Disease

**Evidence-based pharmacological treatment** is effective in coronary artery disease (CAD). Recent studies emphasize that the standard treatment for patients with CAD should include:
Lipid-lowering drugs

- Statins are administered with a target serum LDL of < 100 mg/dL in patients with CAD to avoid further growth of the atherosclerotic plaque. These drugs work by inhibiting cholesterol synthesis. Common adverse effects include rhabdomyolysis, myalgia, and renal injury.
- After achieving the target LDL level, the next step is to raise the HDL levels by administering nicotinic acid which raises HDL by 15–30% in addition to lowering the LDL.
- Other lipid-lowering drugs include ezetimibe and fibrates.
- Lipid-lowering drugs reduce mortality by > 15% in primary patients and by up to 40% in patients with a previous history of myocardial infarction.

Antihypertensive medications

- The joint national committee for hypertension recommends a blood pressure goal of < 140/90 mm Hg in patients < 50 years of age. Different classes of drugs are available to achieve this goal.
- Cardioselective β blockers (atenolol, bisoprolol) decrease the heart rate and cardiac contraction, and reduce myocardial oxygen demand; thus, they have both negative inotropic and chronotropic effects.
- ACEIs and ARBs exert their effects on the renin-angiotensin-aldosterone pathway and inhibit angiotensin II receptors, respectively. They are preferred in patients with diabetes mellitus, with an added advantage of preventing diabetic nephropathy.
- A 20% reduction in mortality has been recorded, especially with the use of ACEIs in patients with myocardial infarction, coronary artery disease, and reduced ejection fraction.

Antiplatelet therapy

- An injury to the vulnerable plaque activates the platelets resulting in their aggregation and a thrombus formation at that site. This can be avoided by the administration of antiplatelet therapy.
- Aspirin irreversibly inhibits both COX-1 and COX-2 enzymes. It prevents the production of prostaglandins, as well as thromboxane, and hence reduces platelet aggregation. Aspirin reduces vaso-occlusive events by 10–20%.

Smoking

Smoking is one of the important modifiable risk factors in the etiology of CAD. Smokers have 6 times the risk of developing CAD in the first 5 years. Smoking damages the endothelium, which is the initial event in plaque formation. The risk of CAD decreases rapidly to 50% after the first year of smoking cessation and the risk falls to the level of a non-smoker in 15 years.

Smoking cessation can be achieved by psychological counseling, coupled with nicotine replacement therapy, such as varenicline/bupropion treatment. Replacement therapy provides a baseline nicotine level in circulation for those who are addicted to smoking, while sparing the patient the adverse effects of other smoke components, such as tar and carbon monoxide.

Timely intervention

Timely intervention can save patients with CAD.
The efficacy of all interventions is based on the physician’s aggressiveness and the patients’ adherence to the interventions. The doctor should advocate for smoking cessation, an increase in exercise, and lifestyle modifications as an addition to appropriate medications to cater for the disease.

All of the above methods help in the reduction of major ischemic coronary events, morbidity, and mortality in patients with CAD.

**Cardiac rehabilitation**

Cardiac rehabilitation improves outcomes for patients with CAD and has been recommended.

The American heart association recommends cardiac rehabilitation with coordinated, multifaceted interventions designed to optimize a cardiac patient’s physical, psychological, and social functioning, in addition to slowing or reversing the progress of the disease altogether. The events that entail rehabilitation include the following:

- Baseline patient assessment
- Nutritional counseling and dietary modification
- Aggressive risk factor management with control of hypertension, diabetes, and smoking
- Psychological and vocational counseling
- Exercises

**Likelihood of Coronary Artery Disease**

The likelihood of developing CAD can be predicted by scoring the patient based on various risk factors. This is only an estimate and is not an accurate statistic. The risk factors for CAD include:

- **Conventional risk factors**, such as age > 45 years, a family history of CAD, and African American descent
- **Modifiable risk factors**, such as hypercholesterolemia, hypertension, cigarette smoking, diabetes mellitus, obesity, physical inactivity, and mental stress
- **Non-traditional risk factors**, such as a raised CRP, lipoprotein A, homocysteine, fibrinogen, BNP, chronic inflammatory conditions, left ventricular hypertrophy, and abnormal ankle-brachial index

**Trend towards improvement**

There is a trend towards improvement of mortality in patients with CAD. Due to the aggressive approach and efficacy of medications, the burden of CAD is on a sharp decline.

CAD-associated death in 1970 was about 448 per 100,000 people and had fallen to 144 deaths per 100,000 people in 2005. Moreover, an interesting change in statistics is that CAD was the leading cause of cardiac disease-related deaths in 1970, which is no longer the case in 2005. This change is directly attributed to the following:

- Primary and secondary control of atherosclerotic risk factors
- Introduction of evidence-based treatment with the 3 major classes of drugs, i.e., lipid-lowering drugs, antihypertensives, and antiplatelet drugs
- Lifestyle changes, such as dietary modifications, increased physical activities and smoking cessation
The Four Areas of Controversy in Coronary Artery Disease

The efficacy of revascularization

The efficacy of revascularization in patients with CAD has been controversial.

Studies show that revascularization is the only effective therapy in patients with 3-vessel CAD and left ventricular dysfunction or left main coronary artery disease.

Earlier studies revealed that coronary artery bypass graft (CABG) is the only procedure shown to prolong life and reduce mortality. Angioplasty did not show similar efficacy, thus creating a controversy. However, the BARI trial showed that both interventions have similar efficacy and can be used to reduce mortality from CAD.

Moreover, the COURAGE study showed that pharmacological therapy and revascularization had equal efficacy in patients with CAD. Thus, the 3 alternatives can be considered effective in the management of CAD.

Cardiac catheter insertion

The bias towards revascularization as the most effective therapy led to creation of the second controversy that, in all patients with CAD, a catheter should be inserted in anticipation for revascularization.

However, current studies reveal that pharmacological therapy is also effective in the management of CAD. Therefore, there is no urgency to institute catheter placement.

Revascularization

The assumption that in elderly patients the risks of the revascularization procedure outweigh the benefits has led to withholding the procedure in elderly patients.

Studies have shown that elderly people respond well to revascularization. Moreover, there are even lower mortality rates with CABG in the elderly population compared to other interventions. Thus, the restoration of cardiac function is more important than age.

Coronary artery disease is a disease of the elderly population

Chronic CAD was initially thought to be a disease of the elderly. Recent autopsies have shown a changing trend with younger people acquiring the disease. The disease is now common in young males.

All primary and secondary interventions should be applied to all persons at risk for CAD irrespective of their age.

Conclusion

In conclusion, CAD is one of the leading causes of death worldwide, affecting people of all sexes, races, and ages. Since it is a highly preventable disease, it can be controlled with primary and secondary interventions that reduce morbidity and mortality.

Effective therapy and lifestyle modifications achieve further control to give patients with CAD a long and productive life. Elderly patients should also be treated with similar methods as their younger counterparts.
References


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