Coronary Artery Disease: Atherosclerotic Plaque, The 6 Areas of Consensus, and the 4 Areas of Controversy

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,” or lipid accumulation, and “sclerosis,” or thickening. It is a chronic inflammatory process characterized by the accumulation of lipids, inflammatory cells, fibrous material, and calcium within the...
Atherosclerotic plaque is a sticky deposit formed within the arterial intima that causes narrowing and blockage of the arterial lumen, causing cardiovascular disease (CAD; see image).

**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 that form the **lipid core**. They release growth factors, cytokines, and chemokines, and upregulate adhesive molecules such as vascular cell adhesion protein 1, intercellular adhesion molecule 1, and monocyte chemoattractant protein 1. The net result is increased monocyte attraction and macrophage recruitment to the site, magnifying the
endothelial damage and dysfunction.

Smooth muscle cells, however, 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, thereby showering emboli into the systemic circulation (see image).

![Image: Late complications of atherosclerosis. By: Npatchett. License: CC BY-SA 4.0](image)

**The 6 Areas of Consensus**

**Evidence-based pharmacological treatment** is effective in cases of CAD. Recent studies emphasize that the standard treatment for patients with CAD should include the following medications.

**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 HDL levels by administering nicotinic acid. This raises HDL levels by 15%–30%, in addition to lowering LDL levels.
- 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 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 heart rate and cardiac contraction and reduce myocardial oxygen demand. Thus, they have both negative inotropic and chronotropic effects.
- **Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (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 ACE inhibitors in patients with myocardial infarction, CAD, and reduced ejection fraction.

**Antiplatelet Therapy**

- Injury to the vulnerable plaque activates the platelets resulting in their aggregation and thrombus formation at that site. This can be avoided through the administration of antiplatelet therapy.
- **Aspirin** irreversibly inhibits both cyclooxygenase-1 and -2 enzymes. It prevents the production of prostaglandins as well as thromboxane, and thereby reduces platelet aggregation. It also 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 of smoking. 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; 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 patient’s adherence to the interventions. The physician should advocate for smoking cessation, an increase in exercise, and lifestyle modifications in addition to appropriate medications.
All of these methods help reduce major ischemic coronary events, morbidity, and mortality in patients with CAD.

**Cardiac Rehabilitation**

Cardiac rehabilitation improves outcomes for patients with CAD. 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. 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
- Exercise

**Likelihood of Developing CAD**

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

- **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 C-reactive protein, lipoprotein A, homocysteine, fibrinogen, B-type natriuretic peptide, chronic inflammatory conditions, left ventricular hypertrophy, and abnormal ankle-brachial index

**Trend Toward Improvement**

There is a trend toward improvement of mortality in patients with CAD. Due to the aggressive approach and efficacy of medications, the burden of CAD is sharply declining.

CAD–associated death in 1970 was about 448 per 100,000 people; by 2005, this had fallen to 144 per 100,000. As well, CAD was the leading cause of cardiac disease–related deaths in 1970; this was no longer true by 2005. This change is directly attributed to the following factors:

- Primary and secondary control of atherosclerotic risk factors
- Introduction of evidence-based treatment with the 3 major classes of drugs (lipid-lowering, antihypertensives, and antiplatelets)
- Lifestyle changes, such as dietary modifications, increased physical activity, and smoking cessation

**The 4 Areas of Controversy**

**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 Bypass Angioplasty Revascularization Investigation (BARI) trial showed that both interventions have similar efficacy and can be used to reduce mortality from CAD.

As well, the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (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 toward revascularization as the most effective therapy led to the creation of the second controversy, which notes that, in all patients with CAD, a catheter should be inserted in anticipation of revascularization.

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

**Revascularization**

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

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

**A Disease of the Elderly**

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

All primary and secondary interventions should be applied to all persons at risk for CAD, no matter their age.

**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 can help give patients with CAD a long and productive life. Elderly patients should be treated with similar methods as their younger counterparts.

**References**


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