Coronary Artery Disease (CAD) — Atherosclerotic Plaque, the six areas of consensus, and the four areas of controversy

See online here

Coronary artery disease is considered the leading cause of death worldwide. It occurs as a result of atherosclerotic changes of the coronary arteries with subsequent narrowing of the vessels preventing their dilation. The atherosclerotic plaque is a sticky yellowish deposit formed within 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 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, and
- Chronic inflammation.

Nitric oxide (NO) production is decreased within the damaged and dysfunctional endothelium. It 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, chemokines and upregulate the adhesive molecules, for instance, VCAM-1, ICAM-1, and monocyte chemoattractant protein 1 (MCP-1). The net result is an 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 the fibrous cap. A strong fibrous cap stabilizes the plaque. A weak fibrous cap makes the plaque vulnerable to rupture.

Plaque rupture

An increased infiltration of inflammatory cells into the plaque, smooth muscle cell apoptosis, and proteolytic degradation of the matrix transforms 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 in the systemic circulation.

The Six Areas of Consensus in Coronary Artery
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 less than 100 mg/dl in patients with CAD to avoid further growth of the atherosclerotic plaque. These drugs work by inhibiting the 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 administration of 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 (JNC) for hypertension recommends a blood pressure goal of less than 140/90 mmHg 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, cardiac contraction, and reduce the myocardial oxygen demand; thus, they have both negative inotropic and chronotropic effects.
- **ACEIs and ARBs** exert their effects of the renin-angiotensin-aldosterone pathway and inhibit angiotensin II receptors, respectively. They are preferred in the patients with diabetes mellitus with an added advantage of preventing the diabetic nephropathy.
- A 20% reduction in mortality has been recorded, especially with the use of ACEIs in patients with MI, 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 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 the platelet aggregation. Aspirin reduces the vaso-occlusive events by 10—20%.

**Smoking**

Smoking is one of the important modifiable risk factors in the etiology of a CAD. The smokers have 6-times of an increased 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. The replacement therapy provides a baseline nicotine level in circulation for those who are addicted to smoking, while, at the
same time, sparing the patient the adverse effects of other smoke components such as tar and carbon monoxide.

**Timely intervention**

Timely intervention can save the patients with CAD.

*Time is muscle.*

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, increase in exercise activities, and lifestyle modifications as an addition to prescribing appropriate medications to cater for the disease.

All the above methods help in the reduction of major ischemic coronary events (MACE), 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 **co-ordinated, 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:

1. Baseline patient assessment.
2. Nutritional counseling and dietary modification.
3. Aggressive risk factor management with control of **hypertension**, diabetes, and smoking.
4. Psychological and vocational counseling.
5. Exercises.

**Likelihood of Coronary Artery Disease**

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

- **Conventional risk factors** such as advanced age > 45 years, 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.
The CAD-associated deaths in 1970 were about 448 per 100,000 people, which have 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:

- Primary and secondary control of atherosclerotic risk factors.
- Introduction of evidence-based treatment with the three 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 vessels CAD and left ventricular dysfunction or left main coronary artery disease.

Earlier studies revealed that coronary artery bypass graft is the only procedure shown to prolong life and reduce mortality. Angioplasty did not show a similar efficacy, 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 an equal efficacy of pharmacological therapy and revascularization in patients with CAD, thus, the three alternatives can be considered effective in the management of CAD.

Cardiac catheter insertion

The bias towards revascularization as the most effective therapy led to a 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 the pharmacological therapy is also effective in the management of CAD; therefore, there is no urgency to institute a catheter placement.

Revascularization

The assumption that in elderly patients, the risks of the revascularization procedure outweigh the benefits has led to withholding of 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 the primary and secondary interventions should be applied to all the 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. The deaths arising from this condition can be controlled since it is a highly preventable disease 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


**Legal Note:** Unless otherwise stated, all rights reserved by Lecturio GmbH. For further legal regulations see our legal information page.