Coronary Artery Disease

– Backgrounder –

Coronary artery disease (CAD), also known as ischemic heart disease, is the most common type of heart disease. Globally, CAD is *the* leading cause of death and is predicted to remain so for the next 20 years.[1]

CAD: A global killer

Each year, approximately 3.8 million men and 3.4 million women die from CAD.[2] In 2020, it is estimated that this disease will be responsible for a total of 11.1 million deaths globally.[1]

In both Europe and the USA, CAD is the single most common cause of death. In the USA, someone suffers a coronary event every 26 seconds, and someone dies from one every minute.[3] Overall, CAD was responsible for approximately one in every five deaths in the USA in 1995, with a death rate of 144.4 per 100,000 population.[3-5] Similarly in Europe, CAD is the largest major killer of both men and women. Between 1 in 5 and 1 in 7 European women die from CAD, and the disease accounts for between 16% and 25% of all deaths in European men.[6]

An international epidemic

CAD has been described as an epidemic due to its increasing incidence across the world.[6] Studies suggest that the average age-adjusted incidence rates of CAD per 1,000 person-years are 12.5 for white men, 10.6 for black men and 4.0 for white women.[7] According to American Heart Association (AHA) statistics, 770,000 Americans suffered a new coronary attack in 2008, and a further 430,000 experienced a recurrent attack.[3] An additional 190,000 silent first heart attacks are estimated to occur each year.[3]

Cost burden

In addition to its mortality burden, CAD is a leading cause of morbidity and loss of quality of life. This makes CAD a major public health problem which exerts heavy economic costs. Overall, CAD is estimated to have cost the EU €45 billion in 2003.[8] Over half of these costs (€23 billion) were made up of healthcare expenditure, principally inpatient care. A further third of the total cost burden was due to productivity losses. Approximately one million working years were lost because of CAD mortality, with a total cost of €11.7 billion. An additional 90 million working days were lost because of CAD morbidity.[8]

Causes and consequences

In CAD, the coronary arteries that supply oxygen-rich blood to the heart muscle become hard and narrow as a result of atherosclerosis – a build-up of cholesterol and plaque on the inner artery walls. These fatty deposits reduce blood flow to the heart muscle, depriving it of essential oxygen.[9,10]

The insufficient supply of oxygen to the heart muscle which results from CAD can cause symptoms of chest pain and discomfort known as angina. These brief episodes of oxygen deprivation and angina occur when the lumen of the artery narrows by 65-75%.[6] In more severe cases of CAD where the coronary artery becomes completely blocked, a whole section of the heart muscle can be deprived of oxygen and die.[9] The result is a heart attack (also known as a myocardial infarction). Most heart attacks occur when a blood clot forms in the coronary artery, cutting off the blood supply and causing permanent heart damage.[9] The atherosclerosis associated with CAD increases the risk of these arterial blood clots.[10] Over time, CAD can lead to both heart failure and heart rhythm disorders (arrhythmias).

Signs and symptoms

Patients with CAD may display one or more of the following signs and symptoms:

- Pain or pressure in the chest, arm, jaw, shoulder or neck
- A feeling of tightness, heaviness, squeezing or burning in the chest
- Shortness of breath
- Sweating
- Fatigue
- Reduced exertional capacity.

However, a significant number of people with underlying CAD and heart muscle oxygen deprivation (also known as ischemia) will experience no symptoms. Others will show only very subtle signs such as decreased endurance or energy. As a result, CAD is often a silent disease which progresses undetected until the first effects of ischaemia appear. Symptoms of angina are the most common presentation of CAD. However, the underlying coronary atherosclerosis may also manifest suddenly as an acute heart attack or sudden cardiac death.[6]

Definitive diagnosis of CAD requires a combination of clinical examination, laboratory tests and specific investigations to confirm that the heart muscle is being deprived of oxygen.[6]

Risk factors

CAD develops when certain factors damage the inner layers of the coronary arteries. Key risk factors which have been identified in patients with CAD include:

- Age

- Family history of early heart disease
- Smoking
- High blood pressure
- High amounts of certain fats and cholesterol in the blood
- Physical inactivity
- Being overweight or obese
- Raised levels of sugar in the blood due to insulin resistance or diabetes
- Elevated resting heart rate.

Heart rate and CAD

A large body of evidence from epidemiological studies and clinical trials has shown that elevated resting heart rate is associated with a significantly increased risk of heart attack and death in patients with CAD.[11] Heart rate is a major determinant of oxygen consumption and can precipitate most episodes of ischemia, both symptomatic and silent. One key study found that CAD patients with a high resting heart rate (≥70 beats per minute) were at 46% greater risk of heart attack and 34% more likely to die from cardiovascular causes.[12] Because of this emerging role as a risk factor for CAD, resting heart rate is becoming an important consideration for clinicians when choosing optimal therapy for CAD patients.[6] Lowering the resting heart rate in patients with CAD reduces the heart's oxygen requirements and may have beneficial effects in terms of reducing cardiovascular events.

Medical management of CAD

Current medical management of CAD involves a two-pronged approach – to relieve symptoms and reduce the risk of cardiovascular events. This is combined with lifestyle modification, which is an important step in both preventing CAD and improving the prognosis in patients with stable CAD.

Symptomatic treatment of CAD is intended to reduce angina symptoms and improve exercise capacity and quality of life. Beta blockers and calcium channel antagonists are among the main medicines used to lower heart rate and reduce cardiac work, thus alleviating angina symptoms. Newer treatment options include selective I_f inhibitors which relieve angina symptoms and boost exercise capacity by selectively reducing resting heart rate.

Cardioprotective therapy for CAD is aimed at reducing the risk of heart attack and heart failure, and prolonging life. It can include:[6]

- Antithrombotic therapy (e.g. aspirin) – which prevents blood clots forming in the coronary arteries
- Statins – which reduce cholesterol levels in the blood
- ACE inhibitors – which lower blood pressure and have additional cardiovascular effects

- Beta blockers – which relieve symptoms of angina and also reduce the risk of cardiovascular death and heart attack in patients who have suffered a previous myocardial infarction
- I_f inhibitor – this has anti-anginal effectiveness and may also reduce the risk of coronary events in CAD patients with a high resting heart rate.[13]

Medical procedures are also used in the treatment of CAD. These may include angioplasty to open a blocked or narrow coronary artery or coronary artery bypass grafting (CABG). Despite lifestyle modifications, current treatment options and surgical techniques, cardiovascular disease remains a problem and there exists a clear need for new and effective preventative treatments.

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