



Disease Background

Cardiovascular Disease

What is cardiovascular disease?

- Cardiovascular disease (CVD) is a collective term describing a wide range of disorders affecting the blood vessels, and the various organs that they supply with blood and oxygen (most importantly the heart and brain).
- A large proportion of conditions that fall under this term are based on an underlying pathology that comprises of gradual blockage of blood vessels due to the development of deposits of lipids in the blood vessel wall, and the aggregation of platelets (a type of blood cell central to clotting) at the site of the lipid deposit.
- This process is known as 'atherosclerosis' and the growing deposit in the vessel wall as an atherosclerotic 'plaque'.

The impact of CVD

- CVD is the leading cause of death around the globe, affecting men, women, and all ethnic groups; yet it is largely a preventable disease.¹ An estimated 17.1 million people worldwide died from CVD in 2004, which represents 29% of all global deaths.¹
 - Of these deaths, an estimated 7.2 million were due to coronary heart disease (CHD) and 5.7 million were due to stroke.
- According to the World Health Organization, global CVD deaths are predicted to reach approximately 23.6 million by 2030,¹ and it is estimated that CVD will surpass infectious diseases to become the largest cause of disability worldwide by 2020.²
- This increase in the prevalence of CVD is partly due to an aging population but is also the result of economic, social, and cultural changes that have led to increases in risk factors for CVD. This is particularly pronounced in developing countries where the majority of the world's population lives.
- CVD also places a significant burden on world healthcare systems and economies.
 - Represents the main cause of the disease burden in Europe (23% of all illness and death) with an annual cost to the EU economy of €192 billion.³
 - CVD (including CHD and stroke) is estimated to cost the US \$475.3 billion in 2009.²



CVD – arterial blockage, oxygen starvation and end-organ damage

- The clinical symptoms of CVD can be explained by two broad pathologies based on the development of the atherosclerotic plaque. Both result from atherosclerotic restriction of blood supply, leading to oxygen starvation, cell death, end-organ damage and, ultimately, partial or complete end-organ failure. This may occur by one of two routes:
 - **Gradual blockage**
 - As the blood vessels gradually become blocked, patients will experience painful symptoms, usually on exertion when the need for oxygen increases.
 - The blockage of one or more coronary arteries in the heart is known as *coronary heart disease* (CHD) and the painful symptoms are referred to as *angina*, while in the large arteries of the arms and legs both the arterial blockage and the symptoms are known collectively as *peripheral vascular disease*.
 - Ultimately this gradual blockage of major vessels can lead to significant cardiovascular (CV) events such as myocardial infarction (MI; heart attack), when part of the heart is sufficiently starved of oxygen that it can no longer function properly.
 - **Abrupt blockage**
 - Atherosclerotic plaques are often unstable and fragments may break away and enter the blood stream.
 - If such a fragment lodges in a smaller blood vessel in another organ it can cause a sudden blockage that abruptly interrupts the oxygen supply to part or that entire organ.
 - If this blockage occurs in the brain, it can cause a stroke.

From risk factors to heart attacks and strokes – the CV continuum

- CVD is often referred to as forming part of the CV continuum that describes heart failure, MI, and stroke as late complications of an underlying, inter-dependent series of disease processes that are triggered by a range of CV risk factors.⁴⁻⁶
 - The final life threatening endpoints of CVD are therefore dependent on the long-term presence of risk factors and underlying pathological processes.
- The CV continuum provides a link between risk factors and the development (often decades later) of severe disease; implicit to this is the concept that effective treatment at any stage will significantly decrease the risk of progression to more severe disease.



- This has allowed physicians to develop approaches to disease management that attempt to identify those at risk throughout the continuum, and delay CVD progression by targeting and managing risk factors.
- Management of CV risk factors is central to this concept. It is estimated that approximately 75% of CVD worldwide is associated with risk factors including obesity, physical inactivity, and smoking.¹
 - In developed countries at least one third of CVD is attributed to smoking, alcohol, high blood pressure, raised cholesterol and obesity.¹

Risk factors fall into two categories:

- Potentially modifiable by lifestyle change - obesity, smoking and physical inactivity, mild hypertension (raised blood pressure), elevated blood sugar (predictive of diabetes) and mild hyperlipidemia (elevated blood lipid levels)
- Modifiable by therapeutic intervention – e.g. hypertension, diabetes and hyperlipidemia
- Management of risk is prioritized in those patients who have already shown signs of significant CVD, such as post-MI, where effective treatment can radically reduce the risk of further, potentially fatal, episodes.

Drug treatment to address underlying mechanisms and reduce risk

- There are three major classes of drug that are used either alone, or in combination to reduce CV risk in those patients who already have evidence of clinical risk factors:
 - Antihypertensives – reduce blood pressure either alone or with a combination of more than one antihypertensive agent. In patients with additional risk factors or complications, combination therapy with different types of antihypertensive agents is needed to get to target blood pressure.
 - Statins – reduce levels of lipids that are associated with atherosclerosis.
 - Antiplatelet agents, such as low-dose aspirin – reduce platelet aggregation and thus inhibit formation of atherosclerotic plaques or enlargement of existing plaques. Antiplatelet agents can either be used alone or in combination for:
 - Prevention of a primary event – to minimize the impact of contributing risk factors before a CV event such as a heart attack has occurred
 - Prevention of a secondary event – to prevent the recurrence of a CV event, such as after a first heart attack.



European and US guideline recommendations for CV event prevention

- As part of a multifactorial treatment approach, guidelines from Europe and the United States recommend low-dose aspirin for the prevention of first and recurrent CV events in at-risk individuals with specific recommendations for individuals with type 2 diabetes or hypertension.⁷⁻⁹
- As with all treatment guidelines, the decision to use low-dose aspirin should continue to be based on an assessment of the potential benefits and risk of side-effects in individual patients.

References

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