PERSPECTIVE

Smoking and cardiovascular disease

COLIN MENDELSOHN MB BS(Hons)

Smoking cessation is an urgent priority for all smokers, especially those with cardiovascular disease. The cardiovascular risks from smoking are substantial but are largely reversible by quitting. Quitting is especially important for smokers with pre-existing cardiovascular disease and GPs are well placed to assist them.

Cigarette smoking is one of the most important modifiable risk factors for cardiovascular disease (CVD)[1] and quitting resolves most or all of the excess risk.[2] In smokers with established CVD, smoking cessation reduces mortality more than any other secondary prevention measure, including the use of statins and aspirin.[3]

Most smokers in Australia want to quit and try repeatedly to do so.[4] However, nicotine dependence is a powerful substance use disorder.[5] Even after an acute coronary event[6] or cardiac surgery,[7] only one in two smokers are able to quit long term.

Counselling and advice from GPs are effective in helping smokers to quit; however, many opportunities are missed due to lack of time, training and confidence to intervene.[8] Misplaced concern about the safety of nicotine replacement therapy (NRT) and varenicline is another barrier to intervention.

This article examines the relationship between smoking and CVD. It explains how smoking causes cardiovascular damage, the clinical effects of smoking, the health benefits of quitting, and some important interactions between smoking and medications used for CVD. Key principles for assisting smokers with CVD to quit are described, with particular reference to the role and safety of stop-smoking medications.

Pathophysiology of smoking

Smoking induces a hypercoagulable state as a result of increased platelet aggregation, raised fibrinogen levels and polycythaemia.[9] The high risk of thrombosis is the main cause of acute cardiovascular events from smoking. After quitting, these changes reverse quickly and the excess cardiovascular risk diminishes.[10]

Smoking also accelerates atheroma formation by disrupting the inner vascular lining (endothelial dysfunction), creating a chronic inflammatory state and causing dyslipidaemia.[9] Atheroma is responsible

Key points

- **Smoking triples the risk of acute myocardial infarction.**
- **Even smoking one to four cigarettes per day is associated with substantial cardiovascular risk.**
- **The cardiovascular risks from smoking are largely reversible by quitting.**
- **Smoking impacts on the action of warfarin, aspirin, clopidogrel and some other medications used for cardiac conditions.**
- **The safety of nicotine replacement therapies in smokers with stable cardiovascular disease has been firmly established.**

CARDIOLOGY TODAY 2013; 3(4): 23-25

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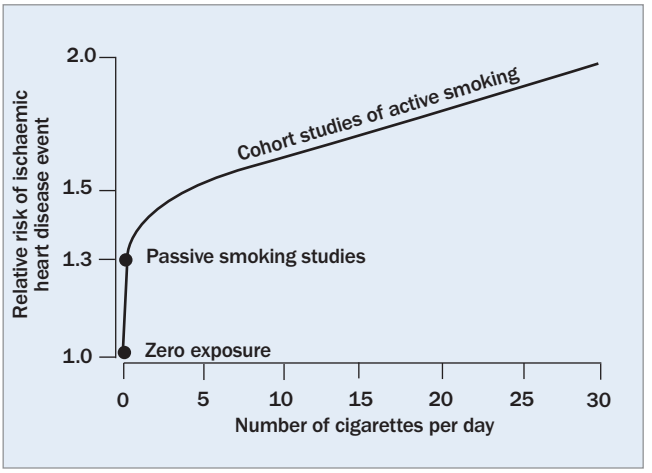

Figure 1. The dose–response relationship between the number of cigarettes smoked and risk of ischaemic heart disease.[11]
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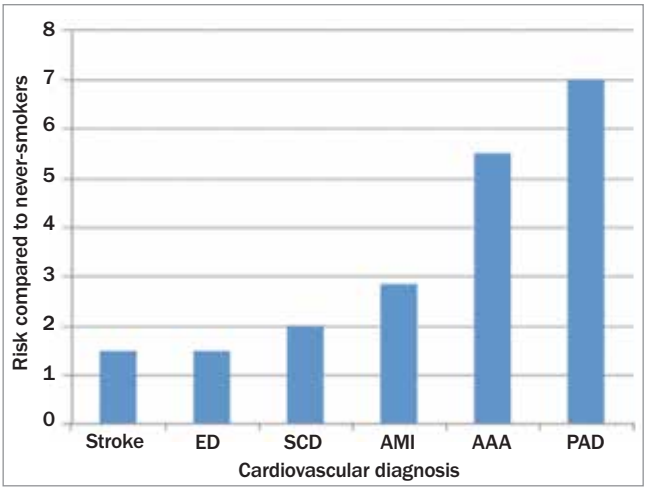

Figure 2. Risk of cardiovascular disease from smoking.[14]

Abbreviations: AAA = abdominal aortic aneurysm; AMI = acute myocardial infarction; ED = erectile dysfunction; PAD = peripheral arterial disease; SCD = sudden cardiac death.

for the more long-term cardiovascular effects of smoking. Oxidant gases and carbon monoxide are the main agents that are responsible for these changes.[10] Nicotine appears to play only a small role in the development of CVD. Its effects include minor haemodynamic effects such as a raised heart rate, a transient rise in blood pressure and increased cardiac contractility.[9,10]

Increased risk of cardiovascular disease

Being a current smoker triples the risk of acute myocardial infarction (odds ratio [OR], 2.95) compared with a nonsmoker.[2] The risk increases as more cigarettes are smoked per day. People who smoke over 40 cigarettes per day have a nine-fold increased risk compared with nonsmokers. However the dose–response curve may not be linear at low doses and the risk increases sharply from smoking none to five cigarettes per day (see Figure 1).[11] People who smoke one to four cigarettes per day have almost three times the risk of dying from ischaemic heart disease compared with never smokers (relative risk [RR], men 2.74; women 2.94).[12] This observation may be explained by the effect of smoking on platelet aggregation, which appears to occur at low doses.[11]

Cutting down the number of cigarettes smoked per day may not lower cardiovascular risk proportionally.[13] Smokers may compensate by smoking the remaining cigarettes more intensely to maintain their usual blood nicotine level and avoid nicotine withdrawal.

Secondhand (passive) smoke causes a disproportionate increase in the risk of CVD, as predicted by the dose–response curve (Figure 1). For example, living with a spouse who smokes increases the risk of death from ischaemic heart disease by 30%.[11]

Smoking also increases the risk of other vascular diseases to different orders of magnitude (Figure 2).[14] The risk is highest for peripheral arterial disease[15] and abdominal aortic aneurysm,[16] and lowest for cerebrovascular disease.[17] Women who take the oral contraceptive pill and smoke have a synergistically increased risk of myocardial infarction and stroke.[18]

Maternal smoking during pregnancy increases the risk of CVD in the offspring during childhood and even adulthood. Offspring of smoking mothers have higher rates of cardiac risk factors, including obesity, type 2 diabetes, hypertension, and lower HDL levels.[19]

Benefits of quitting

Smoking cessation almost completely eliminates the excess risk of CVD from past smoking. Physiological changes are evident within weeks after quitting, including a rapid resolution of the thrombotic state.[10]

In people who smoke 20 or more cigarettes per day, the excess risk of acute myocardial infarction is halved after about three to five years of quitting.[2] The risk declines more slowly after that, and a small residual risk still remains after 20 years.[2] Light smokers (<10 cigarettes per day) return to the risk level of the never smoker within about three years of quitting. Smokers who quit before the age of 35 years reverse all their excess risk of smoking-related disease.[20]

In patients with pre-existing CVD, smoking cessation reduces total mortality by 36% compared with continuing to smoke.[21] This compares favourably with the risk reduction from other secondary preventative strategies such as use of statins (29%), ACE inhibitors (23%), β-blockers (23%) and aspirin (15%).[3] Cessation also reduces the risk of stent or graft thrombosis and revascularisation.[10] Smoking cessation is also associated with a substantial reduction in risk of stroke,[22] peripheral arterial disease[23] and erectile dysfunction.[24]

It has been speculated that postcessation weight gain could attenuate the cardiovascular benefits of quitting. However, a recent study found that the weight gain after quitting had only a minimal effect on cardiovascular risk.[25]

Drug interactions with smoking

Chemicals in cigarette smoke accelerate the metabolism of a number of medications for CVD by inducing the hepatic enzyme CYP1A2. As a result, blood levels of these drugs are lower in smokers and may rise after quitting.

Smokers taking warfarin require a 13% higher dose than non-smokers.[26] Close monitoring of the international normalised ratio is recommended after quitting smoking as blood levels of the drug rise and a dose reduction may be required. Other drugs for cardiac conditions metabolised by CYP1A2 include propranolol, flecainide and verapamil.

Smoking may also inhibit the antiplatelet effect of aspirin and it may be necessary for smokers to take larger than normal doses.[27] Paradoxically, smoking improves the effectiveness of clopidogrel (a prodrug) by accelerating its metabolism to the active metabolite.[28] The efficacy of clopidogrel may be substantially reduced after quitting as the enhanced antiplatelet effect from smoking is lost.

Treatment

A diagnosis of a cardiac condition is a teachable moment when the smoker is more motivated to quit and there is a window of opportunity for GPs to intervene.[29] Optimal treatment consists of a combination of counselling and pharmacotherapy.[30]

Even brief advice of less than a minute from a doctor can substantially increase the chance of quitting.[31,32] Higher quit rates are achieved when more time is spent on counselling and when follow-up visits are provided.[31]

A Cochrane review found that psychosocial interventions, such as behavioural counselling, are effective in helping people with coronary heart disease to stop smoking if they are sustained for at least a month (OR, 1.66).[33] Patients who continue to smoke in the face of known CVD are likely to be highly addicted,[10] and may need more intense counselling.[34] Further detail on psychosocial counselling is described elsewhere.[30,33] Referral options are available for doctors who do not have the time to provide further support (see the box on this page).

It is important to emphasise to patients that they need to quit completely, as cutting down may not reduce cardiovascular risk proportionately.[13] Patients, especially those with pre-existing CVD, should also be advised to avoid secondhand smoke in view of the disproportionate risk from exposure to even very small amounts of smoke.[11]

Pharmacotherapy

Nicotine replacement therapy

Despite concerns from many smokers and doctors, the safety of NRT in smokers with stable CVD has been firmly established. A number of studies have found no increased incidence of adverse cardiovascular events compared with placebo,[35,36] and the use of NRT in this setting is supported by the Australian smoking cessation guidelines.[30] Nicotine is absorbed more slowly from NRT than from smoking cigarettes and reaches lower peak plasma levels, resulting in less intense cardiovascular effects.[10]

There is also growing evidence for the safety of NRT in smokers with acute coronary syndromes,[37-39] and its use can be considered under medical supervision if patients are unable to abstain from smoking without it.[30,39-41] NRT appears just as effective in patients with CVD as in those without.[42] The use of any form of NRT is always safer than continuing to smoke.[43]

Referral options for patients wanting to quit smoking

Australian Association of Smoking Cessation Professionals (AASCP)

Members of AASCP are accredited smoking cessation specialists using evidence-based advice and support to help smokers quit. GPs can search for a local provider on the association website at www.aascp.org.au. Members are GPs, nurses, psychologists, drug and alcohol workers and pharmacists.

Quitline

Provides proactive telephone support Australia-wide by trained counsellors.
Phone number: 137 848.

Smoking clinics

A limited number of smoking cessation clinics and services are also available at some hospitals and community health centres.

Varenicline

Concerns about the cardiovascular safety of varenicline in the general population were raised by a meta-analysis in 2011.[44] A subsequent, more comprehensive meta-analysis[45] and a US Food and Drugs Administration review[46] both found no significant increased risk of adverse cardiovascular events. Varenicline was also demonstrated to be safe and effective in a study of smokers with stable CVD (OR, 3.14 at 12 months).[47]

Bupropion

Bupropion has been found to be safe and effective in patients with stable coronary artery disease in an outpatient setting (OR, 2.78 at 12 months).[48]

Conclusion

Smoking cessation is an urgent priority for all smokers, especially those with CVD. The cardiovascular risks from smoking are substantial but are largely reversible by quitting.

Smoking is a substance use disorder and most smokers need help to quit. Smokers with CVD are likely to be more nicotine dependent and may need more intensive treatment and support. Pharmacotherapy plays an important role in treating nicotine dependence. Based on the evidence so far, any cardiovascular risks from medication are likely to be small and are far outweighed by the benefits of quitting.

Smoking is now viewed as a chronic medical illness. The smoker needs to be re-engaged and assisted at regular intervals. The GP is well placed to assist smokers in quitting or at least refer them for further help when the opportunity arises. **CT**

References

A list of references is included in the website version (www.medicinetoday.com.au) of this article.

COMPETING INTERESTS: Dr Mendelsohn has received funding for teaching, consulting and travel from Pfizer Australia Ltd, GlaxoSmithKline and Johnson & Johnson Pacific.

CARDIOLOGY TODAY 2013; 3(4): 23-25

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