I Preventive Cardiology

1 Prevention of Cardiovascular Disease

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Cardiovascular disease (CVD) remains the leading cause of death in industrialized nations and its incidence is increasing in developing countries. The lifetime risk for the development of coronary heart disease (CHD) for men at age 40 remains at nearly 50%. Given this large risk, clinical and public health approaches to combat the development of CVD are essential. CVD accounts for over 800 000 deaths each year in the United States alone, with the majority resulting from coronary artery disease (CAD). In addition, over 17 million Americans have known or asymptomatic CHD. As the annual economic costs associated with heart disease morbidity and mortality exceed $500 billion, strong efforts are required for adequate screening and prevention.

Prevention of Coronary Heart Disease

- As the prevalence of CHD is high worldwide, the prevention of even a small proportion of disease has an enormous effect.
- **Primary prevention** refers to risk reduction in a population *without* known heart disease.
- **Secondary prevention** refers to risk reduction in a population *with* known heart disease.
- Understanding CHD risk factors has allowed for better screening guidelines and preventive measures.
- There are four major categories of risk factors (Table 1.1):
  - Predisposing factors (e.g. age, sex)
  - Risk-modifying behaviors (e.g. smoking, exercise)
  - Metabolic risk factors (e.g. hyperlipidemia, diabetes)
  - Disease markers (e.g. coronary calcium score).

Table 1.1 Conventional risk factors for CHD

Risk factor	Modifiable	Notes
Smoking	Yes	Ischemic heart disease accounts for 35–40% of all smoking-related deaths
Hypertension	Yes	Each increment in systolic BP of 20 mmHg or in diastolic BP of 10 mmHg *doubles* the risk of CVD
Hyperlipidemia	Yes	A 10% increase in serum cholesterol is associated with a 20–30% increase in CHD incidence
Diabetes	Yes/no	Age-adjusted rates of CHD in diabetics are 2–3 times higher than in those without diabetes
Family history of premature coronary disease	No	

Smoking

Cigarette smoking accounts for nearly 400 000 deaths annually. There are nearly 1 billion smokers worldwide. Even one to four cigarettes a week can increase the risk of myocardial infarction (MI) and all-cause mortality. Smoking increases risk by several mechanisms including:

- Increasing blood pressure (BP)
- Increasing sympathetic tone
- Reducing myocardial oxygen supply
- Elevating the level of oxidized low-density lipoprotein (LDL) cholesterol
- Impairing endothelium-dependent coronary artery vasodilation
- Increasing inflammation, platelet aggregation, and thrombosis.

Smoking cessation is the single most important intervention in preventive cardiology. Reductions in smoking improve outcomes, including reducing risk of MI and cardiovascular mortality.

Physicians should assess smoking status in all patients, recommend quitting smoking to all smokers, and offer support and referral to smoking cessation programs.

Bupropion, varenicline, and nicotine replacement therapy (NRT) have all been shown to increase success rates for quitting.

EVIDENCE-BASED PRACTICE

Mortality risk reduction associated with smoking cessation in patients with CHD

Context: Health policy-makers need to understand where to focus resources in smoking cessation.

Goal: To conduct a systemic review to determine the magnitude of risk reduction achieved by smoking cessation in patients with CHD.

Method: Twenty studies were included for quantitative review of efficacy of smoking cessation in patients diagnosed with CHD.

> **Results:** Despite many differences in patient characteristics, including age, sex, type of coronary disease, smoking cessation resulted in a 36% relative risk reduction in mortality for patients with CHD.
> **Take-home message:** Smoking cessation is associated with a large reduction in risk of all-cause mortality for patients with CHD. The risk reduction is consistent regardless of age, sex, and other patient characteristics.

Hypertension

Hypertension (HTN) is an often-overlooked and silent risk factor for heart disease. Over 70 million Americans have HTN (see Chapter 3).

Most epidemiologic studies have indicated that both systolic and diastolic BP elevation contribute to an increased risk of heart disease. This risk is especially important in elderly patients and patients with a known history of CHD.

HTN, as defined by the Joint National Committee on Prevention, Detection, Evaluation and Treatment of Hypertension in its seventh report, is:
- Two or more BP readings above 140/90
- Readings must be done on two or more separate office visits.

Each increment in systolic BP of 20mmHg or in diastolic BP of 10mmHg *doubles* the cardiovascular risk.

Hyperlipidemia

Several clinical trials have established that lipid-lowering measures are effective in reducing cardiovascular morbidity and mortality (see Chapter 2).

The goals for lipid therapy (Table 1.2) are based on the presence or absence of CHD, as well as the number of risk factors present for the development of CHD.

Diabetes Mellitus

- Diabetic patients have a two- to eight-fold increased risk for cardiovascular events as compared to age-matched nondiabetic individuals.
- Diabetes leads to both macro- and micro-vascular complications in cardiovascular patients.

Table 1.2 Goals for lipid therapy

Risks	Ideal LDL goal (mg/dL)	Non-HDL goal (mg/dL)	Revised goal (mg/dL) for initiation of pharmacotherapy
CHD or equivalent	<100 (or <70)	<130	Regardless of LDL
2+ Risk factors	<130	<160	10-year risk 10–20% >130
			10-year risk <10% >160
0–1 risk factor	<160	<190	>190

- Insulin resistance and the metabolic syndrome are also associated with increased mortality and cardiovascular risk, even long before the onset of clinical diabetes.
- By age 40, CHD is the leading cause of death in both diabetic men and women.
- Data suggest that tight glycemic control can prevent microvascular complications in diabetics (i.e. diabetic retinopathy).
- However, there are very few data suggesting that glycemic control in diabetics can control macrovascular complications.
- Recommendations:
  - For diabetics a multifactorial approach involving diet, exercise, and medications is essential.
  - Target BP is <130/80 mmHg as per the American Diabetes Association (ADA) guidelines.
  - Favored medications for HTN include angiotensin-converting enzyme inhibitors (ACE-Is), beta-blockers, and diuretics.
  - Goal LDL is <100 mg/dL given that diabetes is considered a CHD equivalent.

EVIDENCE-BASED PRACTICE

Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes – the Steno-2 Study

Context: The benefit of an integrated intensive behavior modification and an intensive targeted and tailored polypharmacy in high-risk patients with type 2 diabetes.

Goal: To assess whether a multifactorial treatment approach to diabetics results in lower rates of cardiovascular disease.

Method: Eighty patients with type 2 diabetes and microalbuminuria were randomly assigned to receive conventional treatment in accordance with national guidelines and 80 to receive intensive treatment, with a stepwise implementation of behavior modification and pharmacologic therapy that targeted hyperglycemia, HTN, dyslipidemia, and microalbuminuria, along with secondary prevention of cardiovascular disease with Aspirin (ASA). Intensive, multifactorial treatment resulted in an HbA_{1C} below 6.5%, total cholesterol <175 mg/dL, and BP <130/80 mmHg.

Results: The rates of cardiovascular disease as assessed by cardiovascular death, nonfatal MI, or stroke over the course of 8 years of follow-up in the intensive treatment arm were less than half those found in the conventional treatment arm.

Take home message: A target-driven, long-term, intensified intervention that addresses multiple risk factors in patients with type 2 diabetes and microalbuminuria reduces the risk of cardiovascular and microvascular events by about 50%.

Specific Medications

- **Aspirin:**
  - **Secondary prevention.** Meta-analyses demonstrate that ASA reduces the rate of cardiovascular events by 25% in patients with existing heart disease. This group includes those with a history of MI, coronary artery bypass graft (CABG), angina, stroke, percutaneous coronary intervention (PCI), and peripheral vascular disease.
    – All patients with known CHD should be on ASA
    – For patients with an ASA allergy, other antiplatelet agents should be used.
  - **Primary prevention.** The data for ASA in primary prevention are mixed. It is now thought that those patients without known heart disease, but with a 10-year risk of CHD estimated at >6%, should be on ASA.
- **Beta-blockers:**
  - A number of trials have shown that beta-blockers are effective at reducing cardiovascular events in patients with known CHD.
  - The more effective the beta-blocker is at reducing heart rate, the more effective it is at reducing cardiovascular events.
- **ACE-Is:**
  - ACE-Is reduce the risk of CHD events in patients with known heart disease.
  - This risk reduction is magnified in patients with known left ventricular (LV) dysfunction and in diabetics. In fact, in patients with LV dysfunction, ACE-I treatment reduces total mortality by 26% at 30 days.
- **Statins:**
  - Statin therapy is indicated in any patient with CVD regardless of LDL level.

EVIDENCE–BASED PRACTICE

The Heart Outcomes Prevention Evaluation Study

Context: Benefit of ACE-I on cardiovascular events in high-risk patients.

Goal: To evaluate the role of an ACE-I, ramipril, in patients who are at high risk for cardiovascular events but who do not have LV dysfunction or heart failure.

Method: A total of 9297 high-risk patients with evidence of vascular disease or diabetes plus one other cardiovascular risk factor without LV dysfunction were randomly assigned to receive ramipril (10 mg once per day orally) or matching placebo for a mean of 5 years. The primary outcome was a composite of MI, stroke, or death from cardiovascular causes.

Results: Treatment with ramipril reduced the rates of death from cardiovascular causes by 26%, from stroke by 32%, and from MI by 20%.

Take home message: ACE-Is significantly reduce the rates of death, MI, and stroke in a broad range of high-risk patients who are not known to have a low ejection fraction or heart failure.

Physical Activity

- One of the most modifiable risk factors for CHD.
- The importance of physical activity should be addressed in clinic visits, for both primary and secondary prevention purposes.
- Energy expenditure of 1000 kcal/week is associated with a nearly 30% reduction in all-cause mortality.
- Exercise improves CHD risk by:
  - Increasing HDL
  - Decreasing LDL
  - Reducing BP
  - Decreasing triglycerides
  - Increasing insulin sensitivity
  - Improving endothelial function.
- **Primary prevention.** The United States Surgeon General recommends at least 30 min/day of moderate-intensity exercise on "most" days (150 min/week).
- **Secondary prevention.** American College of Cardiology (ACC)/AHA guidelines recommend at least 30–60 min of moderate-intensity aerobic exercise on most days.
- Walking is sufficient exercise for most patients and has the fewest barriers to successful adoption.
- Cardiac rehabilitation program use is associated with significant lowering of recurrent event rates and can be a critical resource for practitioners.

Weight Loss

- Obesity continues to be an epidemic in the United States, with a growing proportion of the population now considered to be overweight (BMI 25–29.9) or obese (BMI 30 or higher).
- Obesity may have a small independent association with cardiovascular risk over many years but contributes to risk most strongly by influencing other risk factors.
- Weight loss of only 5–10% can result in significant improvements in BP and lipid profiles.
- Weight loss recommendations should be given to any patient with a BMI >25 according to the North American Association for the Study of Obesity. These involve:
  - Caloric restriction
  - Behavioral therapy
  - Physical activity.

Alcohol Consumption

- Moderate alcohol consumption is associated with reduced risk of MI, stroke, sudden cardiac death, and cardiac death (relative risk reduction of 20% according to meta-analyses of several studies).

- No clinical trial has established that alcohol use causes this association.
- Excess alcohol consumption is related to increased mortality and morbidity.
- Alcohol also has effects, often deleterious, on several other organ systems, including increased BP in some and increased breast cancer risk in women.
- Therefore, recommendations on alcohol use should be individualized to each patient; alcohol intake should not be recommended to non-users for medical purposes.
- Moderate alcohol consumption is classified as 1–2 drinks daily in men and 1 drink daily in women.
- In the absence of a history of alcohol problems, this level of intake can be acceptable in patients who report alcohol use.

Diet

- Six decades of observational and metabolic studies have found an association between diet and risk for CHD, either directly or, more often, through effects on risk factors.
- Dietary effects on CVD risk are complex and can depend on the metabolic context, particularly obesity and the amount of exercise.
- There are few large trials studying the impact of dietary changes and CHD, in part due to design challenges.
- The current consensus recommendation based on all these studies is to promote a diet that is rich in unprocessed foods, including greater intake of fresh fruits and vegetables, whole grains, and fish, with limited amounts of meat and high-fat dairy products.
- Though there are no large clinical trials studying *trans*-fat and the risk of heart disease, there is observational evidence that *trans*-fat intake is associated with higher rates of heart disease; *trans*-fats are found mainly in highly-processed convenience and snack foods.
- No diet program can be applied to all patients. An individualized approach, with possible involvement of a nutritionist, may prove most beneficial.

CLINICAL PEARLS

- CHD is the leading cause of morbidity and mortality in Western nations.
- Prevention of CHD revolves around recognition and modification of clinical risk factors.
- Aggressive lipid-lowering therapy has been shown to reduce CHD mortality and morbidity
- HTN is an often under-recognized clinical entity and requires vigilance on proper BP readings, especially in diabetics.

(Continued)

- Smoking cessation is the single most important intervention to reduce risk of CHD.
- There is a 50% reduction in cardiovascular events within the first 4 years after smoking cessation.
- Remember, buproprion is effective for smoking cessation, but must be avoided in patients at risk for seizures; nicotine replacement therapy, available without prescription, can be combined with bupropion.
- Weight loss, exercise, and diet can improve HTN and reduce cardiovascular risk.
- Obesity contributes to CAD risk factors. The distribution of fat is a more important factor than the total amount of fat.
- Exercise, diet and weight loss, and smoking cessation can increase HDL levels.
- Exercise, caloric restriction, and behavioral modification are the keys to effective weight loss.
- C-reactive protein (CRP), homocysteine, and lipoprotein (a) are novel risk factors associated with CAD. CRP is useful as a tool to identify patients who may benefit from earlier lipid therapy.

Recommended Reading

Clinical Trials and Meta-Analyses

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