Cardiovascular Disease and Health in the Older Patient

Expanded from 'Pathy's Principles and Practice of Geriatric Medicine, Fifth edition edited by Alan J. Sinclair, John E. Morley and Bruno Vellas'

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Contents

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Foreword

The reduction in the age-specific mortality and morbidity from cardiovascular disease in developed countries has been one of the great medical success stories of the last 50 years. A solid foundation of epidemiology coupled with improved understanding of the pathophysiology of cardiovascular disease in general, and atherosclerosis in particular, has been achieved. Approaches to the primary and secondary prevention of cardiovascular disease, as well as medical and interventional procedures for treatment of symptomatic disease, have been developed and validated by randomized controlled trials, giving cardiovascular medicine an unrivalled evidence base of effective interventions. Unfortunately, since most cardiovascular disease is essentially progressive and degenerative, reductions in mortality in middle age have resulted in an increasing population of older individuals with overt or silent cardiovascular disease. Thus the overall prevalence of individuals with cardiac and cerebrovascular disease is rising. Although many of the treatment paradigms applicable to younger patients can be translated to the older patient, the prevalence of comorbidities, frailty and cognitive decline require a more holistic approach to the management of cardiovascular disease in elderly people.

The purpose of this book is to provide the non-specialist reader with an up-to-date review of the epidemiology, pathophysiology and management of cardiovascular disease in older people. Most of the chapters would be found in a textbook of general medicine, but the impact of physiological and pathological ageing and the importance of comorbidity and frailty on clinical management are emphasized throughout. The relative paucity of clinical trial evidence in the over-80s, or in specific groups such as those with cognitive impairment, nursing home residents or the frail, is emphasized, and should stimulate further research. The book concludes with a thoughtful discussion on the scope, limitations and appropriateness of aggressive investigation and management in older subjects.

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May 2012

Introduction

Prevention and treatment of cardiovascular disease in older people is an increasing part of primary and secondary care. Heart disease, stroke and peripheral vascular diseases are increasingly prevalent worldwide, due to increasing numbers of older persons; the persistence of major risk factors including tobacco smoking, hypertension and hyperlipidaemia; and the global epidemic of obesity and diabetes. Optimal management requires recognition of multiple morbidities in elderly patients, and a holistic approach to their management.

This book is based on the chapters in the Section on Cardiovascular Diseases and Health, and chapters on cerebrovascular disease in the Section on Central Nervous System Disorders, from the latest, fifth edition of *Pathy's Principles and Practice of Geriatric Medicine*, edited by Alan Sinclair and colleagues. We hope that these chapters from this standard textbook for geriatricians, together with an additional chapter on tailoring the approach to investigation and management of vascular disease in frail older subjects, will provide a useful resource to general practitioners and hospital clinicians and their teams.

We have performed some further editing to the chapters: principally some updating on recent evidence, and adding references to recent clinical practice guidelines in Europe and North America. Management of cardiovascular disease is a rapidly changing field, and readers may find the following web sites to be useful supplements to this book:

Guidelines International Network (G-I-N): www.g-i-n.net

American Heart Association (AHA): www.heart.org

American Stroke Association (ASA): www.strokeassociation.org

Canadian Heart and Stroke Foundation: www.heartandstroke.ca

American College of Chest Physicians (ACCP): www.chestnet.org

European Heart Association (EHA): www.escardio.org/guidelines

National Institute for Health and Clinical Excellence (NICE): www.nice.org.uk

Scottish Intercollegiate Guidelines Network (SIGN): www.sign.ac.uk

Australian Government, National Health and Medical Research Council: www.nhmrc.gov.au

New Zealand Guidelines Group: www.nzgg.org.nz

Guidance on systems and processes of acute medical care for frail older people is given in the Royal College of Physicians Acute Care Toolkit 3: http://rcplondon.us1.list-manage.com/track/click?u=bc4bee17da1faeabe3a951bca&id=33faac6a13&e=012fdadfb6

We welcome feedback on the usefulness of this book. We thank our colleague chapter authors; Professor Stuart Cobbe for his Foreword; Robyn Lyons and Fiona Seymour and their colleagues at Wiley-Blackwell for the original suggestion and for their efficiency in its production; and as always our families for their support.

DJS and GDOL, Glasgow
April 2012

CHAPTER 1
Epidemiology of Heart Disease

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Introduction

Epidemiology is defined as the study of occurrence and distribution of disease in human populations. Epidemiological research can be used to study benefits of interventions to prevent and decrease the burden of disease or to predict requirements for trained healthcare professionals, caregivers for disabled or older people, and service planning. Coronary heart disease (CHD) is an important cause of morbidity and mortality. Incidence and prevalence of CHD both rise steeply with increasing age. The older population is growing and the world's population ≥60 years old is estimated to reach 2 billion by 2050 (three times that in 2000). The development and progression of atherosclerosis is not just a function of ageing but is determined by the distribution of cardiovascular (CV) risk factors related to specific lifestyles. Heart disease may affect quality or quantity of life or both. As the population suffering from heart disease becomes older, their functional ability becomes more important. Mortality cannot be the only outcome relevant to older people: quality of life, cognitive and functional capacities are equally important endpoints. While CHD is a major cause of mortality, other heart diseases may have a significant impact on quality of life due to limitation of exercise tolerance. This chapter discusses epidemiological features of the most common heart diseases affecting older people including CHD, heart failure, valvular heart disease and rhythm disorders (Box 1.1).

Coronary heart disease

The CHD epidemic started in the 1950s affecting firstly Western countries. Prior to the 1920s CHD was not common and caused only <10% of all deaths in the United States. However, by the 1950s this had escalated to

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Box 1.1 Common heart diseases in older people

- Coronary heart disease
- Heart failure
- Valvular heart disease
  Degenerative valve disease
  Infective valve disease
- Rhythm disorders
  Atrial fibrillation
  Sudden cardiac death

>30% and it is now the leading cause of death. While its mortality has fallen by 50%, its incidence has decreased to a lesser extent. Mortality from CHD has also decreased among elderly people, but information on changes in incidence in the elderly population is limited. The main reasons for the decline in morbidity and mortality are due to changes in risk factors as well as improvement of treatment. Survival after myocardial infarction has improved and significant advances have also been made in the surgical and medical treatment of CHD.

Risk factors and prevention

Major risk factors for atherosclerosis have been well established. Epidemiological studies concluded that the causes for this epidemic are genetic factors, age, smoking, hypertension, obesity, diabetes and cholesterol. Variations in disease occurrence in different nations still remain far from being fully explained.

Genetics

It is believed that CVD results from many genes, each with a relatively small effect working alone or in combination with other modifier genes and/or environmental factors. Familial hypercholesterolaemia[1] and hyperhomocysteinaemia[2] are well-described examples. Telomere length is another genetic factor associated with CV health and ageing. Telomere attrition is associated with elevated blood homocysteine and increased endothelial cell inflammatory markers and may underlie early origins of CVD. The identification and characterization of genes that enhance prediction of disease risk and improve prevention and treatment of atherosclerosis need further genetic epidemiological studies.

Age and sex

Prevalence of CHD increases with age from 2% for males and 0.5% for females at age 40–44 to peak at 18% and 12% respectively at age 85–89.

Median age at onset is 67.5 years for males and 77.5 years for females. Lifetime risk is 35% for males and 28% for females. CHD accounts for 22% of male deaths and 17% female deaths at all ages. Epidemiology of CHD is changing from a fatal disease of middle-aged men to a more chronic condition of elderly women. CHD is intimately related to normal ageing in that its incidence continues to increase indefinitely with age. In a prospective study to investigate the influence of increasing age on incidence of CVD in 22 048 male physicians aged 40–84 who were free of major disease, incidence of CVD continued to increase to age 100 over 23 years of follow-up.[3] Beginning at age 80, CVD was more likely to be diagnosed at death. The remaining lifetime risk of CVD at age 40 was 34.8%, 95% confidence interval (CI), 33.1–36.5% and at age 90 was 16.7% (95% CI, 12.9–20.6%). These findings suggest that people aged ≥80 may be living with a substantial amount of undiagnosed CVD. Additional research is needed to determine if continued screening and detection of CVD up to and beyond age 80 might help improve health in later life.

Ethnicity and race

Prevalence of CHD and related risk factors vary among different ethnic groups. The pattern of this variation is complex, and could be related to genetic or socioeconomic differences. For example, populations of African descent living in Europe and the United States have a higher incidence of stroke and lower incidence of CHD than in their white counterparts. They have higher rates of hypertension, which may explain their high rate of stroke. Similarly, in China mortality from CHD is still lower than in Western countries while mortality due to stroke is several times higher largely due to the high prevalence of hypertension. The lower rate of CHD may be explained by low rates of other risk factors including smoking.[4] In the Indian subcontinent CVD is expected to increase rapidly and it will be the host of >50% of cases of heart disease in the world within the next 15 years. Risk factors for this epidemic are similar to those elsewhere in the world; however, ~50% of CHD-related deaths occur in people <70 years compared with only 22% in the West. Also Asians living in Western countries have a 50% greater premature mortality risk from CHD than the general population.

Diet

Dietary factors are related to the risk of CHD through several biological mechanisms. For example: (i) Fish consumption provides cardio-protective benefits through favourable effects on lipid profile, threshold for arrhythmias, platelet activity, inflammation, endothelial function, atherosclerosis and hypertension. Consumption of fish 1–2 times per week or at least 5–10% of energy from polyunsaturated fatty acids reduces the risk of CHD

in older people relative to lower intakes.[5] (ii) Antioxidants present in fruit and vegetables improve endothelial function, inhibit platelet activation and lower blood pressure. (iii) High salt consumption is directly related to hypertension, myocardial infarctions and strokes. Modest reductions in salt lower systolic blood pressure by at least 2 mmHg reducing the prevalence of hypertension by 17%, cardiac events by 30% and overall mortality by 20%. Older people will gain the greatest advantage from lowering their salt intake, most likely because they are more salt sensitive. (iv) Alcohol intake has a U-shaped relationship with the risk of CHD. 'Moderate drinking' defined as one drink for women and two drinks for men per day reduces the risk of CHD by 25%. Data relating to multivitamin use and the risk of CVD are inconsistent. Broader adherence to recommendations for daily intake of fruit, vegetables, low salt, alcohol in moderation and fish may take away 20–30% of the burden of CVD and result in one extra life-year if started early by the age of 40 years.[6]

Cholesterol

Cholesterol is a risk factor for CVD in the middle aged but appears to be less potent at older ages. However, dietary cholesterol is more detrimental in people with diabetes, regardless of age, because of dyslipidaemia and increased insulin resistance. In the Health, Aging and Body Composition Study of 1941 community-dwelling elderly people aged 70–79, there were no significant associations between dietary fats and CVD risk, hazard ratio (HR) 1.47, 95% CI, 0.93–2.32 for the upper versus lower tertile, p for trend 0.10 after 9 years of follow-up. However, dietary cholesterol was associated with increased CVD risk among older people with diabetes (3.66, 1.09–12.29).[7] Possible reasons for these results are attenuated association between lipids and CV risk among older people, differences in baseline CV risk between old and young, or selective survivorship of older people leading to a population sample less vulnerable to environmental factors such as dietary fat.

Exercise

Although few studies have been conducted in elderly people, most have reported physical activity to be beneficial in preventing premature mortality but with some concerns about adverse effects especially in frail elderly individuals with comorbidities. Physical activity may trigger sudden death and may have a higher risk of injury. However, in a Japanese study of 10 385 elderly (aged 65–84), most of whom were under treatment for pre-existing disease, every physical activity was associated with a reduced risk of all causes and CVD mortality after seven years of follow-up. Hazard ratios (95% CI) for CVD mortality among participants with $\geq$5 days of physical activity per week for the total sample and those with pre-existing

diseases were 0.38 (0.22–0.55) and 0.35 (0.24–0.52) respectively, compared with no physical activity. In spite of possible adverse effects, this study indicated that elderly people with a pre-existing disease benefit from any level of physical activity in a dose–response relationship to mortality.[8]

Obesity

Obesity is a risk factor for CHD, poor health and excess mortality. Thresholds for normal weight or obesity defined as body mass index (BMI) were primarily based on evidence from studies in younger adults. In older people the relationship between weight and CV risk is more complex. It remains unclear whether overweight and obese cut points are overly restrictive measures for predicting mortality in older people. In a study to examine all cause and cause-specific mortality associated with underweight (BMI $<18.5\,kg\,m^{-2}$), normal weight (BMI 18.5–24.9), overweight (BMI 25.0–29.9), and obesity (BMI $>$ or $=$ 30.0) in an elderly cohort of 4677 men and 4563 women aged 70–75, mortality risk was lowest for overweight participants after 10 years of follow-up. Risk of death for overweight participants was 13% less than for normal weight participants (HR 0.87, 95% CI, 0.78–0.94). Minimum mortality risk was found at a BMI of 26.6 (95% CI, 25.7–27.5) in men and 26.26 (95% CI, 25.5–26.9) in women. Risk of death was similar for obese and normal weight participants (HR 0.98, 95% CI, 0.85–1.11).[9] It appears that extreme obesity is harmful but overweight older people are not at greater mortality risk, and there is little evidence that dieting in this age group confers any benefit.

Smoking

Smoking is a major modifiable risk factor for CVD and causes 11% of all CVD-related mortality. Smoking contributes to the pathogenesis of CHD through promotion of atherosclerosis, triggering of coronary thrombosis, coronary artery spasm, cardiac arrhythmias and the reduced capacity of blood to deliver oxygen. The magnitude of the burden produced by smoking increases rather than decreases with ageing. While relative risk for smoking on CHD is similar in elderly and middle-aged people, there is a twofold increase in excess absolute risk in older people. Benefits of cessation for older smokers are similar in magnitude to those of younger smokers who quit. The risk of CHD drops by 50% one year after smoking cessation and approaches that of a person who has never smoked within 3–4 years, even in individuals older than 60 years. Smoking cessation is highly cost-effective and should be viewed as a therapeutic rather than just a preventive intervention regardless of age.[10]

The prevalence of cigarette smoking in older people in the United Kingdom has declined substantially over the past 40 years, from around 1-in-3 of the over 60s smoking in the early 1970s to a stable level of 1-in-8

from around 2004 onwards. In general a lower proportion of older people are smokers compared to younger age groups.[11]

There are some important attitudinal differences to smoking in old age compared to younger people. Older smokers are less likely to accept that smoking is bad for their health, and doctors are less likely to provide smoking cessation advice to older patients despite evidence that smoking cessation is just as feasible in old age.[12]

Observational data suggests that there are substantial potential benefits for older people from stopping smoking. Compared to older continued smokers, matched ex-smokers have better mobility, greater walking speed and grip strength, reduced prevalence of chronic ill-health, better quality of life scores, reduced risk of cognitive decline and dementia, and reduced risk of death from lung cancer, stroke and cardiovascular disease.[13]

Socioeconomic factors

There is an inverse relationship between socioeconomic status (SES) and prevalence of CV risk factors. People with lower SES tend to adopt unhealthier behaviours, such as smoking and unhealthy dietary habits, and seem to have an increased prevalence of CV risk factors resulting in socioeconomic inequalities in CV health. Although there is a strong social class gradient in CHD risk in middle age, the evidence in old age is limited. In a population-based study of 3761 British men aged 60–79 years there was a graded relationship between social class and CHD incidence after 6.5 years of follow-up. The HR for CHD incidence comparing social class V (unskilled workers) with social class I (professionals) was 2.14 (95% CI, 1.06–4.33; p for trend = 0.11) after adjustment for behavioural factors. Absolute difference in CHD risk between highest and lowest social classes was 4%. Socioeconomic inequalities in CHD persist in elderly people and are at least partly explained by behavioural factors. Improving behavioural factors (especially smoking) could reduce these inequalities by one third.[14]

Hypertension

Hypertension is a major risk factor for CVD in older adults. It reduces life expectancy by 7 years. Prevalence of hypertension is 20% in developed countries. However, prevalence is significantly higher in older people affecting 70% of those >80 years. Black Americans develop hypertension earlier in life and it tends to be more severe than in the white population. There is a strong but complex association between blood pressure (BP) and age. Up to 50 years of age, systolic and diastolic BP rise in tandem. After age 50, systolic BP continues to rise, whereas diastolic BP tends to fall. Below age 50, diastolic BP is the major predictor of CHD risk, whereas above age 60, systolic BP is more important. There is also an enhanced risk for CHD associated with increased pulse pressure. The risk of a fatal CHD event

doubles for every 20/10 mmHg increment above 115/75 mmHg. Absolute risk of adverse outcomes increases with age reaching 16-fold higher for persons 80–89 years than for those 40–49 years. A 10 mmHg reduction of systolic BP would predict a 50–60% lower risk of stroke death and a 40–50% lower risk of CHD death. In very old individuals (≥85 years old) the association between hypertension and mortality is weaker and treating hypertension reduces risk of death by 21%, risk of stroke by 30% and risk of cardiac failure by 64%. The target for BP is <140/90 mmHg in general and <130/80 mmHg in individuals with diabetes or chronic kidney disease. Evidence that excessive lowering of diastolic BP in older hypertensive individuals with wide pulse pressures may compromise cardiac outcomes (J curve) is inconsistent and no consensus exists regarding the minimum safe level of diastolic BP in these individuals.[15]

Diabetes mellitus

Diabetes has been recognized as an independent major CV risk factor. In spite of various known metabolic and microvascular complications of diabetes, cardiovascular disease remains the most common cause of death in diabetic persons of all age groups affecting around 65–80%. Increased risk of CVD in diabetes is not fully explained by traditional risk factors and could be related to increased insulin resistance. Risk of CHD and myocardial infarction rises by 30% and 14% respectively for every 1% increase in HbA1c. Whether hyperglycaemia itself is a risk for CHD is not very clear.

Metabolic syndrome

Metabolic syndrome is a constellation of central obesity, impaired fasting glucose, hypertension, high triglycerides and low HDL cholesterol. Pathophysiology of metabolic syndrome includes decreased physical activity and increased inflammation. In older people vitamin D deficiency,[16] leading to increased parathyroid hormone and insulin resistance, in combination with low testosterone, leading to increased waist:hip ratio, are other contributing factors. Metabolic syndrome affects >40% of persons >60 years old and is more common in men. Comparative utility of metabolic syndrome versus its individual components for predicting adverse outcomes in older populations is not well established. In an Italian study of 2910 subjects aged ≥65 years, metabolic syndrome was associated with increased all-cause mortality in all subjects (HR 1.41, 95% CI, 1.16–1.72, $p < 0.001$), in men (1.42, 1.06–1.89, $p < 0.017$), and in women (1.47, 1.13–1.91, $p < 0.004$). It was also associated with increased CV mortality in all subjects (1.60, 1.17–2.19, $p < 0.003$), in men (1.66, 1.00–2.76, $p < 0.051$), and in women (1.60, 1.06–2.33, $p < 0.025$). Among metabolic syndrome components, all-cause mortality is better predicted by high glucose in all subjects (1.27, 1.02–1.59,

$p < 0.037$) and in women (1.61, 1.16–2.24, $p < 0.005$) and by low HDL cholesterol in women (1.48, 1.08–2.02, $p < 0.014$), whereas CV mortality is better predicted by high glucose (2.17, 1.28–3.68, $p < 0.004$) and low HDL cholesterol (1.78, 1.07–2.95, $p > 0.026$) in women.[17] In a similar US study of 4258 older people ≥65 years free of CVD, those with metabolic syndrome had a 22% higher mortality, relative risk (RR) 1.22, 95% CI, 1.11–1.34 compared with persons without metabolic syndrome after multivariable adjustment. Higher risk with metabolic syndrome was confined to persons having an elevated fasting glucose level >6.1 mmol l^{-1} (RR 1.41, 95% CI, 1.27–1.57) or hypertension (RR 1.26, 95% CI, 1.15–1.39) as one of the diagnostic criteria of metabolic syndrome. Persons having metabolic syndrome without high fasting glucose or metabolic syndrome without hypertension did not have higher risk (RR 0.97, 95% CI, 0.85–1.11 and 0.92, 0.71–1.19, respectively). Persons having both hypertension and high fasting glucose had 82% higher mortality (RR 1.82, 95% CI, 1.58–10.9).

In older people individual components of metabolic syndrome predict CVD mortality with equal or higher HR when compared with metabolic syndrome. Therefore, these findings suggest that the metabolic syndrome concept is a marker of CVD risk, but may not have any more advantage in predicting cardiac risk than its individual components.[18]

Frailty and disability

Frailty is a geriatric syndrome of increased vulnerability to stress factors due to decline in function in multiple interrelated systems. Frailty is distinct from related concepts of (i) comorbidity: the burden of coexisting medical illnesses, and (ii) disability: the limited ability for self-care (Figure 1.1). Frailty reflects biological rather than chronological age leading to substantial variability in the outcomes of older people. The relationship between frailty and CVD is mutual; frailty may lead to CVD just as CVD may lead to frailty. In other words frailty is associated with CVD as a risk factor and as an outcome. Around 7% of the US population >65 years and 30% of octogenarians are frail. Domains to define frailty include mobility, strength, balance, motor processing, cognition, nutrition, endurance and physical activity. Frailty reduces a patient's ability to maintain homeostasis in the face of acute stress, predicts mortality and heralds transition to disability. In a systematic review of frailty in patients with CVD, nine studies were included encompassing 54 250 elderly patients with a mean follow-up of 6.2 years. In community-dwelling elders, CVD was associated with an odds ratio (OR) of 2.67 to 4.1 for prevalent frailty and an OR of 1.47 for incident frailty in those who were not frail at baseline. Gait velocity (a measure of frailty) was associated with an OR of 1.61 for incident CVD. In elderly patients with documented severe CHD or heart failure, the prevalence of

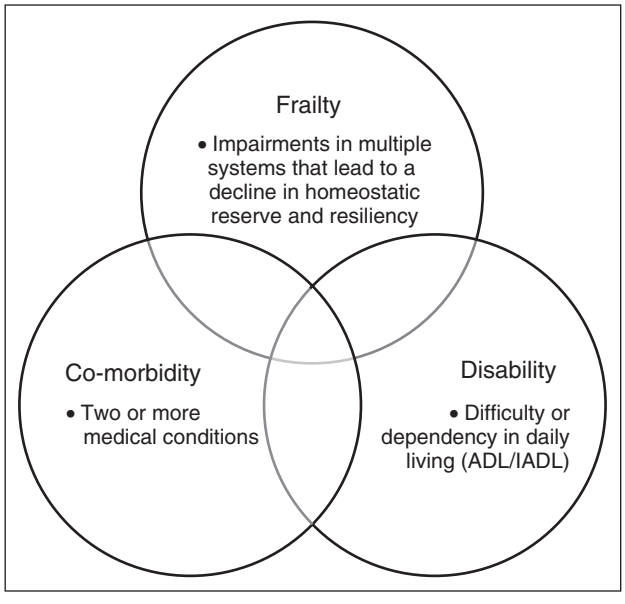

Figure 1.1 Overlap between frailty, comorbidity and disability. ADL, activities of daily living (basic self-care tasks); IADL, instrumental ADL (household management tasks). Reprinted from Afilalo *et al*.[19] Copyright 2009, with permission from Elsevier.

frailty was 50–54%, and this was associated with an OR of 1.62 to 4.0 for all-cause mortality after adjusting for potential confounders (Table 1.1). It is likely that underlying abnormalities in haematological, inflammatory and metabolic systems in frail older patients are linked to increased CV risk. Compared with non-frail counterparts, frail patients had significantly higher levels of factor VIII, D-dimer, C-reactive protein, leukocytes, fibrinogen, glucose, low vitamin D and low haemoglobin. The close correlation between frailty and biomarkers of inflammation and thrombosis resembles the correlation between CVD and these same biomarkers. This common biological pathway may explain why frailty and CVD are interrelated at clinical level. Reasons to consider frailty in older people with CVD include its early identification and anticipation of care after major cardiac events. There is overlap of frailty with comorbidity and disability. Unintended weight loss, disability in activities of daily living and presence of multiple comorbid conditions in a complex cardiac patient should alert physicians to the possibility of associated frailty. Screening of frailty may include simple tests, such as grip strength, gait speed or quadriceps strength. Early recognition of frailty will need comprehensive geriatric assessment combined with multidisciplinary interventions to slow or reverse functional decline, improve physical performance and quality of life.[19] Disability, on the other hand, is a common condition in older people and has been associated with

Table 1.1 Association between cardiovascular disease and frailty.

Study	Variable
	Prevalent frailty in elders with CVD
Zutphen Elderly Men's Study	OR 4.1 (95% CI, 1.8–9.3)
CHS	OR 2.79 (95% CI, 2.12–3.67)
Beaver Dam Eye Study	OR 2.67 (95% CI, 1.33–5.41)
WHI-OS	OR 3.36 (95% CI, 3.09–3.66)
WHAS I and II	OR 2.72 (95% CI, 1.72–4.30)
	Incident frailty in elders with CVD
WHI-OS	OR 1.47 (95% CI, 1.25–1.73)
	Incident CVD in frail elders
HABC Study	HR 1.61 (95% CI, 1.05–2.45)
	Mortality in frail elders with severe CVD
Cacciatore *et al*.	HR 1.62 (95% CI, 1.08–2.45)
Purser *et al*.	OR 4.0 (95% CI, 1.1–13.8)

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prevalent CHD and shorter longevity. It is less clear whether disability is a risk factor for atherosclerosis development or a prognostic factor for CHD outcome. In a French multicentre prospective population-based cohort of 9294 subjects free of CVD (aged ≥65 years), the mean level of CV risk factors increased gradually with severity of disability. After a median follow-up of 5.2 years, 264 first coronary events, including 55 fatal events, occurred. After adjustment for CV risk factors, participants with moderate or severe disability had a 1.7 times (95% CI, 1.0–2.7) greater risk of overall CHD than non-disabled subjects, whereas those with mild disability were not at greater CHD risk. An association was also found with fatal CHD, for which risk increased gradually with severity of disability (HR 1.7, 95% CI, 0.8–3.6 for mild disability, 3.5, 1.3–9.3 for moderate to severe disability, p for trend = 0.01). This result reflected a specific association between disability and fatal but not with non-fatal CHD. The lack of association between disability and non-fatal CHD suggests that disability has little impact on atherosclerosis development. In other words disability even of mild severity has more to do with prognosis rather than with occurrence of CHD (Figure 1.2). However, this prognostic function of disability could be related to the possibility that disabled subjects suffering from an acute event might be treated less aggressively, too frail to cope with a vascular event and likely to die, or simply disability is associated with severe CHD with a worse prognosis. Therefore, in this population, promotion of regular physical activity seems appropriate, because physical activity has been associated with less severe acute coronary syndrome, lower in-hospital mortality, better short-term prognosis and less disability.[20]