Aspects on implementation of coronary heart disease prevention in clinical practice

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- I did it my way

to Maria and Erik

Abbreviations

ACE	Angiotensin converting enzyme
ACS	Acute coronary syndrome
AMI	Acute myocardial infarction
BMI	Body mass index
CABG	Coronary artery bypass grafting
CC	Conventional care
CHD	Coronary heart disease
CVD	Cardiovascular disease
ESC	European Society of Cardiology
HbA_{1c}	Haemoglobin A_{1c} (glycosylated haemoglobin)
HDL	High density lipoprotein
LDL	Low density lipoprotein
PCI	Percutaneous coronary intervention
PAP	Positive at provocation
SCORE	Systematic coronary risk evaluation
SPP	Secondary prevention programme
STD	ST depression

List of papers

I. Stagmo M, Westin L, Carlsson R, Israelsson B. Long-term effects on cholesterol levels and the utilisation of lipid-lowering drugs of a hospital-based programme for secondary prevention of coronary heart disease. J Cardiovasc Risk 2001;8:243-8

II. Stagmo M, Israelsson B, Brandström H, Lingfors H et al. The Swedish National Programme for Quality Control of Secondary Prevention of Coronary Artery Disease - results after one year. Eur J Cardiovasc Prev Rehabil 2004;11:18-24

III. Kotseva K, Stagmo M, Wood D. Treatment potential for cholesterol management in patients with coronary heart disease in fifteen European countries: findings from the EUROASPIRE II study. Manuscript

IV. Stagmo M, Juul-Möller S, Israelsson B. Fifteen-year risk of major coronary events predicted by Holter ST-monitoring in healthy middle-aged men. Eur J Cardiovasc Prev Rehabil. In press

Contents

Introduction

Background

Coronary heart disease (CHD) is the major cause of death and premature disability in Europe [1]. In Sweden, almost 50% of all deaths are attributed to heart disease, the majority of these being CHD. Mortality and morbidity in CHD also carry a substantial economic burden on many countries. According to the latest European Heart Networks statistical report, it was estimated that the cost for CHD in the European Union was €22,955,623,781 in 2003 [2]. In Sweden alone, direct costs were estimated at €633,003,788 in the same year. If indirect costs such as loss of productivity were to be included the figures would be substantially higher. Even more important than fiscal considerations are the negative effects on quality of life and general wellbeing in patients suffering from CHD [3,4]. Although mortality rates for CHD are declining in Western European countries, the opposite is true in other parts of the world such as Eastern Europe and the Far East [5]. Even in areas with falling death rates from CHD, an ageing population together with improved prognosis due to more effective treatment of acute disease can actually increase the number of CHD patients in the future [6].

Risk factors for CHD

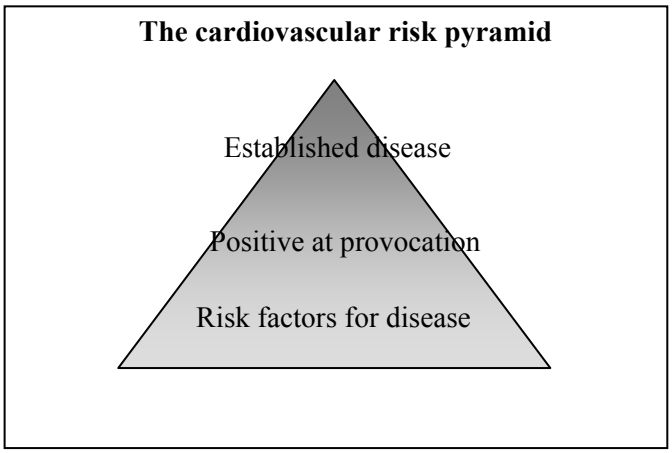
Over the last decades, scientific knowledge regarding pathophysiological mechanisms linking risk factors to coronary atherosclerosis, inflammation, plaque rupture and thrombosis have become clearer [7]. Many risk factors have been linked to the development of CHD [8]. However, risk factors do not contribute equally to the development and progression of disease. In many cases, risk factors are clustered together in a deleterious way [9]. It has been stated that about 80% of major CHD events in middle aged men can be attributed to three, potentially modifiable, risk factors: cholesterol levels, blood pressure, and cigarette smoking [10]. Furthermore, it has recently been shown that nine common and potentially modifiable risk factors account for about 90% of the population attributable risk for CHD in both men and women in different geographical areas [11]. These risk factors are: smoking, hypertension, alcohol consumption, physical activity, blood lipoproteins, diabetes, obesity, low fruit consumption, and psychosocial factors. This case-control study might possibly overestimate the numbers to a certain extent but it is very different from previous belief, which estimated that only about half of the risk for CHD could be attributed to well-known and traditional risk factors.

There is substantial scientific evidence that lifestyle interventions and risk factor modification can reduce cardiovascular mortality and morbidity in subjects both

with and without previous CHD. A comprehensive overview of important risk factors for CHD is beyond the scope of this thesis but can be found in the European Society of Cardiology's (ESC) guidelines for prevention of cardiovascular disease [12].

CHD prevention and risk stratification

Prevention of CHD includes all actions taken, whether lifestyle changes, pharmacological or interventional procedures, which decreases the risk of subsequent heart disease. Risk factors for CHD are not additive but rather act synergistically [13]. Thus, the combined effects of two or more risk factors are greater than the sum of each individual risk. The traditional view has been to regard prevention of first time CHD as primary prevention and prevention of further disease progression and death in patients with established CHD as secondary prevention. This dichotomous view is increasingly being replaced with the concept of absolute risk of having a CHD event over a certain time period, for example ten years. This includes assessment of the combined effect of multiple risk factors. The absolute risk level at which intervention is warranted is arbitrary and can change over time, depending on new scientific knowledge and economical prerequisites.



Cardiovascular risk can be considered a continuum from low- to high-risk depending on risk factor accumulation and concomitant disease. At the top of this virtual risk pyramid are patients with known and established CHD. At the base of the pyramid is the very large group of healthy subjects with a varying risk factor burden for CHD.

Between these groups are subjects without overt disease but who can be proven to have silent coronary heart disease with different kinds of provocations, such as exercise testing or stress echocardiography, i.e. “positive at provocation” (PAP). It would be preferable to identify not only patients with overt disease but also patients at high risk for disease, such as those PAP, or subjects with an exceptionally high aggregation of risk factors. If adequate, well-working, preventive therapies were implemented for these groups, morbidity and mortality in CHD could be expected to decrease substantially. It has been estimated that applying known secondary prevention measures such as treatment with aspirin, betablockers, ACE-inhibitors, and lipid-lowering agents to all eligible patients could reduce the relative risk of recurrence of events by 80% [14].

ESC guidelines for CHD prevention (from ref. 13)

1. Smoking cessation.
2. Increased physical activity, preferably 30-45 min, 4 to 5 times weekly at 60-75% of the average maximum heart rate.
3. Making healthy food choices with an increased intake of fruit and vegetables, whole grain, cereals and bread, low-fat dairy products, fish, and lean meat. Oily fish and omega-3-fatty acids are considered particularly protective. A total fat intake of no more than 30% of the daily energy intake and an intake of saturated fat not exceeding 1/3 of the total fat intake.
4. Avoiding and reducing overweight. Overweight is defined as BMI ≥25 kg/m^2 or subjects with an increased waist circumference (men >102 cm and women >88 cm).
5. Adequate blood pressure control. In patients with increased risk for CHD blood pressure should be <140/90 mmHg. In patients with diabetes or exceptionally high risk for CHD blood pressure should be <130/80 mmHg.
6. Adequate glycaemic control. In patients with type 2 diabetes treatment goals are HbA_{1c} ≤6.1% and fasting venous glucose ≤6.0 mmol/l.
7. Adequate lipid control. In general, total cholesterol should be <5.0 mmol/l, LDL-cholesterol <3.0 mmol/l. However, in patents with established CHD or diabetes, treatment goals should be lower: total cholesterol <4.5 mmol/l and LDL-cholesterol <2.5 mmol/l. HDL-cholesterol <1.0 mmol/l in men and <1.2 mmol/l in women or fasting triglycerides >1.7 mmol/l are markers of increased risk and should be used to guide the choice of therapy.
8. Adequate use of other prophylactic drugs such as aspirin and other antiplatelet drugs, betablockers and ACE-inhibitors where appropriate.

Patients at the top of the risk pyramid, i.e. with known disease, will probably be taken care of by the health care facilities, either hospital-based or in primary care. Different countries have different organisations regarding this, but the Swedish view has for many years been to refer much of the follow-up of CHD patients to the primary health care after initial hospital treatment. Subjects with silent disease, i.e. PAP, will probably receive a similar follow-up once they are identified. Regarding subjects without disease, but with a high risk due to a malignant accumulation of risk factors, the situation is quite different. This group needs to be identified and risk factors measured before any treatment can be administered. In Sweden this responsibility rests mainly on initiatives taken by primary care physicians and nurses who often are fully occupied with treating overt disease and in many cases are not able to undertake screenings of healthy subjects.

Screening for CHD risk factors in all subjects who come into contact with the health care system has been advocated by some as a way of identifying individuals at risk for CHD [15,16]. The effectiveness of this so-called "opportunistic" screening has however been put in question and a more selective approach has been suggested [17]. Another proposed way of identifying high-risk subjects is community health screening, for example certain age cohorts, in order to identify individuals at risk. Community health screening and risk factor treatment has proven successful in reducing CHD in some studies [18-20]. A review of trials has shown positive effects of lipid screening in subjects over 35 years of age and in younger subjects with additional risk factors for CHD [21]. Even so, these methods are rarely possible due to practical or financial reasons. When it comes to subjects with low-medium risk the situation becomes even more complex. Even though many of these subjects do not need pharmacological treatment, their risk for future CHD can be markedly influenced by lifestyle changes. Smoking cessation, making healthy food choices, and increased physical activity could have a strong impact on mortality and morbidity in CHD if applied to an entire population. However, it would be very difficult for the health care system to take responsibility for this as cost and time consumption would be too high. Since prevention of CHD is an important task for society as a whole, responsibility for this lies not only with the medical profession or the health care system. Promotion of a healthy lifestyle is a political matter expressed all the way from the care of pregnant women, through the school system, the availability of sports facilities, etc. Taxation of tobacco and alcohol and tax deductions for the costs of physical exercise and training are other ways of working towards this goal. In Sweden the Board of Health and Welfare and the National Institute of Public Health monitor and evaluate health polices. Other important actors are schools, social- and occupational health services. In several countries, school projects have started aiming at laying foundations for a healthy

lifestyle early in life [22]. In Sweden, the Heart and Lung Foundation has been collaborating with primary schools in educating teachers and pupils about prevention of CHD and the benefits of a healthy lifestyle; the "Pelle Pump" project, based on the British Heart Foundation's "Artie Beat" campaign.

Different approaches to CHD prevention

The approach to prevention of CHD can be made from at least two different angles: The high-risk approach and the population approach [23]. The high-risk approach identifies and treats people at high risk for future CHD. This is probably the natural approach for most clinical physicians who deal with individual patients and who might not always consider the statistical risk for future events in the population as a whole. It is well known that preventive effort in CHD on an individual basis, whether primary or secondary, is most efficient when applied to high-risk groups. However, the majority of CHD events occur among subjects with lower levels of absolute risk since the number of subjects with low-moderate risk is much greater than the number of high-risk individuals, hence the argument for the population approach. Thus, seemingly modest improvements in risk factors can have major impact on disease on a population level [24]. Due to the relatively low absolute risk at any given moment, this also means that a preventive measure that brings substantial benefits to the community appears to offer little to each individual. This may adversely affect motivation of the population at large, a fact known as the "prevention paradox" [25].

There are, however, problems with both strategies. One problem is how to identify subjects at risk who are not routinely seen by health professionals. Another is how to obtain clinically relevant and long-lasting effects on risk factor treatment and lifestyle behaviour both to patients with known disease and asymptomatic high-risk individuals.

Guidelines

The volume of scientific knowledge regarding prevention of CHD is large; a statement illustrated by the fact that a Medline search on "prevention and coronary heart disease" in March 2005 yielded >20.000 hits. It is obvious that this amount of data cannot be fully studied, appraised, and applied by clinically active health care professionals. Scientific evaluation, condensation, and dissemination of this knowledge into the clinical medical community are of course of paramount importance. Therefore, several national and international organisations consisting of leading experts in the field of CHD prevention have issued guidelines regarding CHD. The European Society of Cardiology's view is that guidelines should present

relevant evidence on a particular issue in order to help physicians to weigh the benefits and risks of a particular diagnostic or therapeutic procedure and that they should be helpful in everyday clinical practice. The latest European guidelines regarding CHD prevention were issued in 2003 [12]. In Sweden, as well as in several other countries national and local guidelines have been developed [26]. All these guidelines state that since CHD is a multifactorial disease, a holistic view regarding risk factor evaluation and treatment must be taken. The medical profession has a wide armamentarium of treating risk factors for CHD as well as acute or chronic manifestations of the illness. The benefits of smoking cessation, increased physical activity, and change in dietary habits as well as pharmacological therapy with platelet inhibitors, lipid lowering agents, betablockers, and ACE-inhibitors in different subsets of patients with CHD have long been well known. The additional use of invasive procedures such as percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) should, according to the guidelines, be used as appropriate to relieve symptoms and in some cases reduce risk of subsequent cardiovascular events. The evolving evidence regarding risk factor evaluation and treatment has lead to recommendations in the ESC guidelines regarding priorities for CHD prevention in clinical practice [12]. The Swedish Board of Health and Welfare has, together with the medical profession, prioritised most interventions and treatments for heart diseases on a scale from 1-10 in order to aid politicians, health care administrators, and physicians in the allocation of economical resources in the best way [27].

Prioritised groups for CHD prevention in the ESC guidelines (from ref. 13)

1. Patients with established CHD, peripheral or cerebral atherosclerotic disease.
2. Asymptomatic individuals who are at high risk of developing atherosclerotic cardiovascular disease (CVD) because of:
   a) Multiple risk factors resulting in a 10-year risk of ≥5% now (or if extrapolated to age 60) for developing a fatal CVD event
   b) Markedly raised levels of single risk factors: cholesterol ≥8 mmol/l, LDL-cholesterol ≥6 mmol/l, or blood pressure ≥180/110 mmHg
   c) Diabetes type 2 and diabetes type 1 with microalbuminuria
3. Close relatives of:
   a) Patients with early onset atherosclerotic disease
   b) Asymptomatic individuals at particularly high risk

The problem of implementation

Unfortunately, it has become increasingly apparent that the knowledge of CHD prevention, stated in guidelines and treatment recommendations, is not always translated into clinical practice. Several implementation studies both in the United States and in Europe have consistently shown that patients at high risk for CHD are inadequately treated regarding important risk factors such as cessation of smoking, dyslipidaemia and elevated blood pressure [28-33]. The EUROASPIRE II study, performed between 1999 and 2000, showed that even in patients with established CHD both lifestyle- and pharmacological treatment of risk factors were inadequate [30]. As an example, only 58% of the patients achieved the stated goal for total cholesterol (<5.0 mmol/l) despite a relatively high use of lipid-lowering drugs (61%), 21% still smoked and only 50% had an adequately controlled systolic blood pressure (<140 mmHg). There were also marked differences in treatment and achievement of treatment goals in the 15 European countries that participated in the study, despite the common guidelines outlined above. It is worth noting that the study consisted of one or at the most a few centres per participating country and that the results were not necessarily representative of each country. Long term adherence to lifestyle or pharmacological treatment to prevent CHD was unfortunately low, as has been shown in several other studies. Studies have shown that one third of the patents with diagnosed hypertension discontinued their medication after three years [34]. Furthermore, discontinuation of antihypertensive treatment occurs early after initiation and varies markedly with different classes of antihypertensive drugs, probably reflecting different side-effects [35]. The EUROASPIRE II study further showed that even in patients diagnosed with CHD, 21% of the study population were still smoking 1.4 years after the index event [30]. Another example comes from Gothenburg in Sweden where *From Attebring et al*. have shown that even in patients with diagnosed CHD a large proportion still had increased levels of potentially modifiable risk factors, such as smoking and elevated lipid levels [36].

Furthermore, studies have shown that regarding the use of lipid-lowering agents, discontinuation in clinical practice is much greater than that reported in clinical trials [37-39]. There is also evidence that discontinuation of for example statin therapy in hyperlipidaemia can be harmful and result in an increased CHD event rate [40]. Early administration of lipid-lowering agents preferably within the first 24 hours after a coronary event, but certainly before discharge has in several studies been shown to yield higher long-term adherence and a lower frequency of disease relapse [41-43]. It has also been shown that the speciality of the treating physician can have impact on both the degree of measurement and treatment of risk factors for CHD. Several

studies have shown that cardiologists and internists measure and treat cholesterol to a higher degree than general practitioners [31,44,45].
Not only physicians but also patients influence treatment. A survey among the European public has shown that the public have markedly low knowledge of the relationship between important risk factors for CHD, such as high serum cholesterol and subsequent disease [46]. Among patients with known CHD, knowledge about risk factors and the nature of CHD is associated with a greater adherence to lifestyle changes and medication [47]. Several studies have shown that factors such as age, low socioeconomic status, and a sense of non-influence negatively affect adherence to prevention programmes [48,49].

The value of prevention programmes
There has long been conflicting evidence of the effectiveness of primary prevention programmes for CHD. A Cochrane analysis on effectiveness of primary prevention programmes using counselling and education did not show any effect on mortality [50]. Other studies have shown effect on mortality and morbidity in primary prevention as stated earlier [18-20,36]. A study from Stockholm has shown that a comprehensive cardiovascular prevention programme and a structured non-pharmacological treatment was successful in reducing cardiovascular risk in middle-aged men with slightly to moderately increased risk factors for CHD [51]. In patients undergoing PCI, a comprehensive behaviourally orientated programme aimed at lifestyle changes, risk factor modification and rehabilitation has shown positive long-term effects on subsequent coronary events [52].
Apart from prevention programmes, there have been several suggestions to increase long-term adherence to preventive measures and medications. Early initiation of medication, preferably during hospital stay is one way of improving treatment as has been shown in patients after CABG [53]. A British study tried postal prompts to patients and general practitioners at two weeks and three months after hospital discharge for CHD containing information about lowering the risk for another CHD event through lifestyle change and medication. This study could not show any significant improvement in risk factor management [54]. However, an American study on regular physician prompting, via mail or telephone, did show improved lipid treatment over a three-year period [55].
Different kinds of intervention programmes for CHD have been tried in Sweden and in other European countries. These have, in several cases, shown positive long-term effects on risk factor management as well as mortality and morbidity in CHD. Furthermore, studies have shown that a short term cardiac rehabilitation programme after an acute CHD event had lasting effects on treatment to target levels for

cholesterol, as well as positive effects on body anthropometrics, exercise capacity, and quality of life up to two years [56,57]. There is growing evidence that nurse-led clinics for prevention of CHD can have long-lasting effects on risk factor levels for CHD as well as being cost effective in a primary care setting [58-61].

The concept of benchmarking

In order to assess the quality of secondary prevention in relation to guidelines different tools for benchmarking have been suggested. The ESC's EUROASPIRE and Euro Heart Surveys are examples of quality control tools in routine medical practice. However, to measure and describe the quality of preventive work does not automatically transform into improved implementation. This is clearly shown in the comparison between the EUROASPIRE I and II trials. There was regrettably very little improvement in patient care between the two surveys (EUROASPIRE I in 1995/96 and EUROASPIRE II in 1999/2000) despite new guidelines being published [62]. The Swedish Board of Health and Welfare states that measuring quality is not enough. Benchmarking against "best practice" is important but has to be followed by a learning and development process in order to change local practice if necessary [26]. This creates a continuous learning circle of clinical practice, measurement, benchmarking, and change in practice.

Identification of high-risk individuals

A major problem in implementation of CHD guidelines is identifying and treating subjects at risk. In order to determine the risk for CHD of an individual patient, several multifactorial risk models have been developed. The ESC's task force for prevention of CHD advocates the use of the recently developed Systematic Coronary Risk Evaluation (SCORE) risk charts [63]. This model is developed for risk stratification in asymptomatic subjects and takes into account the heterogeneity in CHD mortality in different European regions. Another major difference compared to previously used risk score systems, such as Framingham data, is that risk is now defined as the absolute 10-year probability of developing a fatal cardiovascular event. A 10 year risk of ≥5% now, or extrapolated to the age of 60, is seen as a significant increase in risk and thus warrants intervention according to ESC guidelines [12]. Physicians are advised to use the SCORE risk chart as an aid to identifying high-risk subjects and apply appropriate preventive interventions in these subjects. It is however evident that this risk chart only takes into account a few, albeit major, risk factors for CHD such as age, smoking habits, gender, total cholesterol, and blood pressure and thus cannot predict all cardiovascular events. Several methods to increase the predictive accuracy of prediction of CHD have been

suggested. Provocation tests such as exercise tests have been shown to predict further CHD events. Transient ST-segment depression (STD) is a marker for coronary ischemia [64]. Two well-established methods of measuring STD are exercise- and ambulatory ECG (Holter monitoring). Exercise ECG testing has been shown to predict cardiovascular mortality not only in patients with coronary artery disease but also in asymptomatic subjects [65-67]. Apart from exercise ECG and Holter monitoring, several other methods for increasing the power to predict coronary events have been suggested. Stress echocardiography and myocardial scintigraphy have shown relatively good sensitivity in detecting CHD [68]. Specifically, myocardial scintigraphy has been shown to predict silent myocardial ischemia in 20% of asymptomatic diabetic subjects [69].

Several blood markers for increased CHD risk have been proposed. C-reactive protein (CRP) has been shown to correlate with future coronary events in both men and women in a primary prevention setting, probably as a marker for inflammatory activity in vulnerable coronary plaques [70,71]. B-type natriuretic peptide (BNP) levels are predictors of future coronary events in patients with acute coronary syndromes [72]. Furthermore, in acute coronary syndromes both Troponin T and CRP have been shown to be independently correlated to 30-day mortality but of these two, only Troponin T is associated with an increased risk for myocardial infarction [73]. Another way of predicting future coronary events is to estimate the coronary plaque burden, either indirectly, through ultrasonically measuring carotid intima-media thickness (IMT) or more directly with electron-beam computerised tomography (EBCT) [74]. New non-invasive methods such as multislice detectored computerised tomography and magnetic resonance angiography, are currently being developed for visualising plaques in the coronary arteries [75,76]. It is hitherto not clear how well these methods work in clinical practice.

Aims of this thesis

General aims

CHD is a major burden for society and its subjects and medical research is constantly striving to develop improved prevention, detection, and treatment options. Our aims were to find more effective ways of implementing this knowledge in clinical practice and to more accurately identify subjects at risk for CHD.

Specific aims

- To assess if a mainly nurse-led, structured, hospital-based, one-year secondary prevention programme for CHD, addressing both lifestyle change and pharmacological risk factor intervention, could have long-lasting effects on lipid levels and the use of lipid-lowering drugs four years after referral to primary health care.

- To assess the feasibility to implement a quality control programme which incorporates regular feedback of treatment goals vis-à-vis local guidelines and an increased patient co-operation in order to improve the quality of secondary prevention of CHD.

- To assess the reasons behind the failure of reaching treatment goals set in European guidelines for serum lipids in the EUROASPIRE II study.

- To assess if ST-analysis of long-term ECG registration (Holter) could be used to identify asymptomatic subjects at high-risk for subsequent CHD as a complement to conventional risk factor analysis.

Presentation of the manuscripts

Paper I

Aims

The aim of this study was to assess if a one-year, hospital-based, secondary prevention programme could have long-term positive effects on serum lipids and the use of lipid-lowering drugs in patients with CHD four years after referral to primary care facilities.

Methods

Between the years 1989 and 1991, all 395 patients between 50 and 69 years of age, treated at the University Hospital, Malmö, Sweden with acute myocardial infarction or after coronary artery bypass surgery were screened for participation in the study. After exclusion of 154 high-risk patients following prespecified exclusion criteria, the remaining 241 patients were included in the study. After discharge from hospital, all patients underwent a 4-6 week follow-up programme consisting of two visits to a specialist nurse and one visit to a cardiologist. During this period the patients received information on risk factors for CHD as well as lifestyle advice regarding CHD prevention. Conventional risk factors such as serum lipids and blood pressure were measured. The 241 patients were randomised to either referral to conventional care (CC) or to a secondary prevention programme (SPP) for further follow-up. CC could mean general practitioners or cardiologists in private practice. The SPP consisted of a one-year follow-up programme with regular visits and prespecified goals for risk factor intervention. These goals were: serum cholesterol <5.2 mmol/l, serum triglycerides <1.5 mmol/l, blood pressure <160/90 mmHg, HbA_{1c} <5.3% and smoking cessation. The programme constituted of on average two visits to a cardiologist and four visits to a specialist nurse. Thorough and repeated information on the nature of CHD, the importance of risk factor intervention and lifestyle changes such as making healthy food choices and smoking cessation was given. After this year the SPP ended and all patients were referred to primary care follow-up for another four years. Five years after the index event all patients in both the SPP and CC group were re-examined and lipid levels and the use of lipid-lowering therapy were investigated.

Results

Baseline characteristics were similar in both groups. The five-year participation rate was similar in both groups; 75% and 72% in the CC and SPP group, respectively. Total mortality did not differ between the groups, being 15% in the CC group and 14% in the SPP group. Both total- and LDL-cholesterol were significantly lower after one year in the SPP group compared with baseline values. This difference was largely maintained after five years. In the CC group there was no difference in serum lipids during the five-year follow-up. There was also a significantly higher use of lipid-lowering drugs in the SPP group after one, and five years (68% and 52%, respectively), compared to the CC group (24% and 32%).

Conclusions

This study shows that a structured, hospital-based, secondary prevention programme during one year with defined targets for risk factor intervention and a high use of lipid-lowering drugs can have favourable effects on serum lipids even four years after the termination of the programme. A higher use of lipid-lowering drugs and higher doses of drugs as well as lifestyle changes and motivation to drug adherence can be factors explaining this outcome. Furthermore, it seems feasible to entrust this follow-up mainly to specialist nurses with physician backup.

Paper II

Aims

The aim of the study was to present results from the Swedish National Programme for Quality Control on Secondary Prevention. This was an attempt to improve implementation of preventive measures for patients with CHD through increased patient involvement and continuous feedback to both patients and treating physicians regarding risk factor levels.

Methods

Guidelines for the prevention of CHD have been developed both in Europe and in the United States. However, several surveys have shown that these guidelines are poorly implemented in clinical practice. In order to increase implementation and provide an instrument of monitoring secondary prevention work on a national and local level, the Swedish Societies of Cardiology and Family Medicine started the Swedish National Programme for Quality Control on Secondary Prevention in 1998. The programme consisted of 51 of Sweden's 79 health care districts. Each district consisted of one or more hospitals and surrounding primary care facilities. At hospital discharge, patients with a diagnosis of AMI, CABG or PCI were included in the programme and provided with a diary, the "heart booklet". The diary included a brief presentation of risk factors for CHD and explained the potential benefits of lifestyle changes. The diary was filled in at discharge and at subsequent outpatient visits with each patient's own values for serum cholesterol, LDL-cholesterol, HDL-cholesterol, serum triglycerides, fasting blood glucose, blood pressure, HbA_{1c}, and weight compared to local intervention goals for different risk factors. These measurements were also reported to a central database via prepaid report cards at each visit.

Each year a report on obtained risk factor goals in relation to local prevention programmes and the use of medication was distributed. Mean values for the entire nation as well as every participating health care region in relation to others were given.

Results

Results based on data from one year after the index event showed that a majority of patients reached targets for serum cholesterol (70%), and LDL-cholesterol (71%). Mean values were for total cholesterol 4.6 (±SD 0.9) mmol/l, LDL-cholesterol 2.7 (±SD 0.8) mmol/l. Blood pressure targets were less often achieved, with 58% reaching ESC target for systolic (<140 mmHg) and 81% for diastolic (<90 mmHg)

blood pressure. A large proportion of patients was prescribed preventive drugs; aspirin (96%), betablockers (78%) and lipid-lowering drugs (83%).
A problem with the registry was varying response rates in different districts and a decreasing response rate with increasing time from the index event. Nevertheless, a pilot study has shown relatively good congruence between responders and non-responders regarding risk factors for CHD. It was furthermore evident that a large majority of both patients and participating physicians considered the registry a valuable tool in the work of preventing CHD.

Conclusions
The Swedish Quality Control Programme on CAD was one of the first attempts to assess the implementation of secondary prevention guidelines on a national level. Our data supported the view that the clinical practice of secondary prevention of CAD still needed to be improved and that patients were treated differently in different parts of Sweden.
Whether the programme itself improved management is not clear but compared to other surveys the management was better with respect to lipid management and prescription of drugs for prevention. Limitations of our study due to missing report cards were obvious and the data may have given a better picture than what was really the case. Regardless, the programme identified one possible approach to improve the implementation of guidelines in clinical practice.

Paper III

Aims

The aim of this study was to describe the treatment of hyperlipidemia among CHD patients in the EUROASPIRE II study in relation to contemporary clinical guidelines.

Background

During the last decade the evidence of beneficial effects of cholesterol lowering in patients with CHD has been proven in several clinical trials. This has prompted international guidelines on prevention of CHD to include recommendations on dietary and pharmacological treatment of hyperlipidaemia with set goals on total- and LDL-cholesterol. As new evidence has emerged these guidelines have been changed and treatment goals lowered.

Methods

The EUROASPIRE programme was a survey designed to assess the adherence to guidelines in clinical practice. The first survey, performed in 1995/96 showed poor adherence to recommendations regarding lipid lowering in patients with CHD. The second survey was performed 1999/2000. This survey was performed at selected centres in 15 European countries and enrolled 5,556 patients with CHD. Medical records were assessed and clinical examinations of risk factors including serum lipids were performed on average 1.4 years after the index CHD event.

Results

The result of the study showed that although mean value of serum cholesterol was relatively low (5.23 mmol/l), this varied significantly between countries. Fifty-eight percent of the patients did not reach the target of 5.0 mmol/l set up in the guidelines. This also varied significantly between different countries. The use of lipid-lowering drugs was relatively high (61%) in the total population. However, the most frequently used doses of lipid-lowering agents were much lower than the doses with proven effect used in clinical trials. There was an improvement in treatment of hyperlipidemia over time when this study was compared to the first EUROASPIRE survey.

Conclusions

Although the treatment of hyperlipidemia in CHD patients seems to be improving with introduction of new guidelines, a significant number of patients do not reach treatment goals. If the full potential of lipid-lowering therapy was utilised with all eligible patients treated and doses titrated correctly, more patients would benefit in terms of reduced mortality and morbidity in CHD.

Paper IV

Aims

The aim of this study was to assess if Holter monitoring with ST-analysis could be used to predict future major coronary events (MCE) in asymptomatic middle-aged men with a defined aggregation of conventional risk factors for CHD.

Background

Ambulatory ECG monitoring (Holter) with ST-analysis as a measure of myocardial ischemia has in populations with CHD been shown to predict MCE, i.e. death, myocardial infarction or coronary revascularisation. However, there has been conflicting evidence regarding the usefulness of this technique in identification of healthy subjects with increased risk for CHD.

Methods

At an age of 55, 155 asymptomatic subjects in the city of Malmö, Sweden, with known levels of conventional cardiovascular risk factors underwent Holter monitoring for analysis of transient ST-segment depression. Fifteen years after the Holter monitoring, hospital records, diagnosis-, and death registries were reviewed for MCE.

Results

A ST-segment depression of $\geq$1 mm (0.1 mV) was considered significant for myocardial ischemia and was found in 54 of the 155 men. There were no significant differences in risk factors in the two groups at baseline. The 15-year incidence of a first major coronary event was significantly higher in men with ST-segment depression (39%) than in men without ST-segment depression (20%) ($p<0.015$). Holter ECG could predict future MCE with a positive and negative predictive value of 35% and 80%, respectively.

Conclusions

Holter monitoring can be used as a complement to conventional risk factor evaluation in deciding whether or not to treat risk factors for CHD in asymptomatic subjects.

Discussion

The treatment gap (paper I, II, III)

The benefits of an aggressive and sustainable prevention of risk factors for CHD in patients with elevated risk are well known and documented. Despite this, the treatment gap between guidelines and clinical reality is substantial. The reasons for this under-treatment are numerous. A European study to assess attitudes to and implementation of guidelines among general practitioners has shown that an overwhelming majority agrees with the content of guidelines for CHD prevention [77]. However, several barriers to implementation of these guidelines were identified. Thirty-five percent of the physicians regarded lack of time as a hindrance to successful implementation. Furthermore, costs of drugs and poor patient compliance were considered important obstacles to successful implementation of guidelines.

In the RIKS-HIA registry it has been noticed that even on a hospital level, response rate and the implementation of guidelines vary substantially over time (*B Lindahl, administrator of the RIKS-HIA registry, personal communication*). This is probably not connected to changes in prevention programmes, knowledge or resources but rather a change of priorities on the part of the responsible physicians. In order to avoid irrational and non-medical reasons for variations in medical practice and to make prevention programmes more resistant and compliant to guidelines, more focus should probably be placed on organisational aspects.

Specialist nurses and prevention programmes (paper I)

The health care system is differently organised in different countries although the ultimate goal is the same: to bring as much health care to as many people as possible with the limited resources available. Local tradition and health insurance systems could have greater impact on health care delivery than is usually recognised. In Sweden, health care teams consisting of both physicians, specialist nurses, and in some cases physiotherapists, have an opportunity to work together to implement preventive measures in high-risk individuals. Since the 1990's, nurses specialising in CHD prevention have been trained and recruited in Sweden to give patients information about lifestyle modification, education about CHD, and risk factor monitoring. As has been shown both by us and elsewhere, nurse-led clinics with physician backup and a structured risk factor control and intervention programme can have substantial effects on risk factor levels as well as cardiovascular mortality and morbidity [58-60]. The system leaves more time to physicians to occupy themselves with symptomatic and acutely ill patients. Nurses have proven to be well suited for

risk factor monitoring as well as lifestyle counselling. Furthermore, since nurse-led clinics pose a lesser cost than clinics run by physicians, more time can be spent on each patient and education about CHD and the importance of adherence to preventive measures can be stressed. In Sweden, all hospitals treating patients with acute coronary syndromes (ACS) have an organisation with nurses dealing with secondary prevention after the acute event. This is usually in the form of both individual outpatient clinics and group sessions with other patients. In many hospitals, group information about CHD is offered to family members as well.
Our study has shown that a relatively short, comprehensive, mainly nurse-led but physician backed-up, secondary prevention programme yields substantial effects on lipid treatment in CHD patients after one year compared to conventional follow-up. Our group has earlier shown that lifestyle factors such as smoking habits and healthy food choices were positively affected by participation in the prevention programme after one year [78]. Unfortunately, we could not show that these lifestyle effects were maintained four years after the end of the programme. The positive effects on lipid levels and the use of lipid-lowering therapy were, however, significantly better in the intervention group, even four years after the termination of the programme. Thus, as has been confirmed by other studies, it is possible to obtain long term effects on both risk factor profile and to influence mortality and morbidity among CHD patients by organising structured prevention programmes led by specialist nurses [58,59]. One reason why this is not done in some countries could be financial considerations. However, recently published health economic data from Scotland have shown that nurse-led clinics are cost effective compared with most interventions in health care [61]. Another obstacle might be lack of education and training among nurses to handle topics such as dietary advice, risk factor evaluation, and the need for pharmacological intervention. It is a fact that the amount of medical responsibility given to nurses differs between countries. To allow nurses to partake in drug titration and monitoring could in some countries be difficult both for professional and medico-legal reasons. In other countries, like Sweden, it is a well-established practice to give responsibility to nurses to titrate drugs in for example patients with congestive heart failure [79]. It is probably important that programmes relying on nurses are structured and well prepared to facilitate the handling of the issues and to prevent treatment errors.

Long-term persistence (paper I and II)
Since CHD is a chronic and continuously developing disease, secondary prevention programmes must have enough persistence to overcome this. The natural history of drug treatment and lifestyle change is unfortunately a diminishing adherence over

time. Organisational questions regarding CHD prevention are important also in this context. In countries where cardiologists have long-term contacts with CHD patients the situation is different compared to countries like Sweden, where patients are referred to primary health care physicians for follow-up rapidly after one or perhaps two visits to the hospital's outpatient clinic after an acute CHD event. Studies have shown that cardiologists treat risk factors such as cholesterol to a greater extent than general practitioners do [44,45]. CHD prevention is only a small part of the general practitioners' responsibilities, and it cannot be easy to be constantly up-to date on all different guidelines, from CHD prevention to urinary tract infection or asthma treatment, and to master the entire panorama of diseases from paediatric to geriatric medicine. The interests and knowledge of individual doctors can probably play a pivotal role in the time and effort invested in CHD prevention in this setting. In Sweden, attempts to overcome this have been made by developing local treatment programmes for CHD in co-operation between hospitals and the primary health care. This work started in the 1990's and was inspired and welcomed by the Swedish Board of Health and Welfare. Paper II describes our attempt to disseminate this idea and to monitor the success; the Swedish National Programme for Quality Control on Secondary Prevention. Participation in the project was voluntary and 51 of Sweden's 79 health care regions participated. The idea was to combine patient empowerment and responsibilities with continuous feedback and to benchmark each participating district to constantly improve the quality of secondary prevention. Thus, it was designed more as an instrument for quality development and patient empowerment than a scientific research tool. We have shown that the programme was considered very important both by patients and participating health care professionals. Furthermore, our results have shown that treatment of risk factor levels was relatively successful in Sweden during this time. There was however marked differences in reaching treatment targets between different participating districts. The main problem with the registry was the high dropout rate, especially after responsibility for the patients had been transferred to the primary health care facilities. Because the system was voluntary, this was difficult to avoid but it made the data from the registry more difficult to interpret. Structural problems during this period especially in the primary care system with a shortage of doctors and lack of funds may well have contributed to this. Unfortunately, the project has been put on hold due to lack of funds. Thus, we have to conclude that, although considered important both by patients and the medical profession, the time and place were not right for a general implementation of this programme in Sweden.

Using the right tools (paper III)

One reason why patients do not reach the recommended risk factor levels could be that ambitions and treatment targets are set unrealistically high. The treatment targets recommended in the guidelines could be seen as ideal goals obtained only in closely controlled clinical trials, but difficult to reach in routine clinical practice. Over the last year several studies have shown that a more intensive lipid-lowering treatment yields even greater reduction in mortality and morbidity in patients with established CHD [80,81]. Our third paper addresses the use of lipid-lowering agents in patients with known CHD. Although the use of lipid-lowering drugs was generally high, a large group of patients did not reach the set goal of total cholesterol <5.0 mmol/l. If the new ESC recommendation of <4.5 mmol/l for high-risk subjects was used, even fewer patients would have reached the treatment goal. In the study, three fifths of the population were on a lipid-lowering drug; the overwhelming majority on statins. Despite this, only 58% of the patients reached the target of < 5.0 mmol/l for total cholesterol. Further analyses showed that one reason for this was that in many cases sub-optimal doses and less potent statins were used. The doses used were often much lower than those used in the clinical trials that form the scientific basis of the guidelines. The commercially available statins have different documentation on efficacy and safety. They also have different lipid-lowering potential with lovastatin and fluvastatin lowering cholesterol to a lesser extent than atorvastatin and rosuvastatin, with pravastatin and simvastatin in-between [82,83]. One could argue that the use of drugs and doses that do not have scientifically proven effects on hard endpoints such as mortality and morbidity, are dubious in clinical medical practice. On the other hand, since the concept of lower-is-better concerning cholesterol lowering seems to have been confirmed in the aforementioned studies, the use of drugs with proven benefit but with weaker cholesterol-lowering effect could also be considered a kind of under-treatment. Another reason for not using higher doses or newer, more potent, drugs could be that many doctors adhere to Hippokrates' idea of "*primum est non nocere*" - the most important thing is to do no harm. Indeed, the withdrawal of cerivastatin from the market in 2001, due to an excess of potentially fatal side-effects, may have served as a deterrent from using new drugs to some physicians. In many countries the choice of lipid-lowering agent is also governed by the reimbursement system. This is especially true in countries where the patients' carries a major part of the cost for medication themselves. Over the last few years it has been debated whether total- and LDL-cholesterol should be lowered as much as possible or if a certain percentage decrease is enough, regardless of the initial value. It is worth noting that the treatment targets for both blood pressure and lipids are arbitrarily set and more the results of extrapolations and deductions from both

epidemiological and intervention studies. However, the current trend seems to be in support of those who advocate lowering these treatment targets radically.
It is not an unrealistic scenario that the concept of lower-is-better regarding lipid levels will be adopted in the near future and that the intervention goals are lowered towards 4.0-4.5mmol/l for total cholesterol and 1.8-2.0 mmol/l for LDL-cholesterol. Indeed, this approach has already been suggested by the National Cholesterol Education Programme (NCEP) in the United States [84,85]. If this is to be achieved, the use of higher doses of lipid-lowering agents is needed. In some cases the switch to more potent drugs or combinations of lipid-lowering drugs with different mechanisms of action are needed. One such example is the dual use of a statin to block cholesterol synthesis in the liver and an inhibitor of cholesterol uptake in the intestine. This combination has been shown to be very effective in lowering total- and LDL-cholesterol [86]. However, to date no study with hard clinical endpoints using this combination has been published. Another interesting future development is HDL-elevating drugs, which are at present being evaluated in clinical trials [87].
In conclusion, there seems to be room for both a better utilisation of the current armamentarium for lipid lowering and for new therapeutic options currently under development.

> "The superior doctor prevents disease;
> The mediocre doctor attends to impending disease;
> The inferior doctor treats actual disease."
>
> Chinese proverb

Identifying high-risk individuals (Paper IV)
The rather artificial division of prevention into primary, i.e. subjects not yet overtly sick, and secondary, i.e. patients with known disease, is slowly being replaced by the concept of global and absolute risk. It may very well be that a patient with a history of angina pectoris has lower risk for a subsequent event than a subject with a particularly malign congregation of risk factors who has not yet fallen ill.
In order to address the problem of CHD prevention, several risk score systems which incorporate risk factors and predict the risk for a subsequent event have been developed. Perhaps the best known is the Framingham risk prediction algorithm [88]. This estimates the 10-year risk of CHD based on age, gender, LDL- or total cholesterol, HDL-cholesterol, blood pressure, diabetes, and smoking status.

However, the impact of risk factors for CHD varies between different populations. This could result in an over- or underestimation of the true risk in other populations. As a consequence, several risk models based on European data have been developed. The Prospective Cardiovascular Münster (PROCAM) study included family history and triglyceride levels together with the risk factors used in the Framingham system to predict the 10-year risk for CHD [89]. There is to some extent a consensus that a 10-year risk of 20% or more for a CHD event constitutes high-risk and thus warrants treatment. The ESC's recently published SCORE risk evaluation system has taken a somewhat different approach. This system is based on contemporary CHD data from both high- (northern Europe) and low-risk regions (southern Europe) [63]. The outcome variable is cardiovascular death and an absolute risk of >5% of a fatal CV death on a 10-year basis warrants treatment. Regardless of which risk scoring system one chooses to utilise, the problem of correctly identifying high-risk subjects remains. In a situation with limited resources and an increased focus on cost this has become even more important. Another aspect is that if risk prediction could be made more accurately, one could confidently decide whom not to treat and thereby limit the risk of treatment side-effects. It is not realistic to believe that any risk prediction system, whatever method used, will ever be able to accurately predict all subjects who will face a future CHD event and who will benefit from treatment. However, we have showed that a 48-hour ECG with ST-depression analysis can improve risk stratification of CHD in asymptomatic males at relatively high risk based on conventional risk factors. Especially a negative examination is coupled with a high probability of event-free survival as shown by the negative predictive value of 80%. It is reasonable to believe that STD on Holter monitoring represents a silent stage of CHD. Due to the relatively low positive predictive value we do not believe that this method is warranted in all cases of CHD prevention but should rather be used selectively when there are doubts on behalf of either the patient or the doctor as to whether or not treatment is warranted. We cannot from this study deduce if these results are true in a younger population or in females. The fact that this study has showed a predictive value of ambulatory ECG monitoring where other studies have failed to do so can perhaps be explained by the relatively high-risk population that was examined. When calculated with the SCORE system the 10-year risk for a fatal CHD event was about 10% in the study group, i.e. a risk well over the recommended treatment level of 5%. Thus, by modern recommendations the majority of these subjects would be eligible for preventive treatment.

Conclusions

There are several ways to improve implementation of scientific knowledge and contemporary guidelines regarding CHD prevention into clinical practice. It can be concluded from this study that:

- A structured, one-year, hospital-based secondary prevention programme after CHD, mainly led by specialist nurses with physician backup, can positively influence the use of lipid-lowering drugs and serum cholesterol levels several years after the end of the programme.

- A quality control system based on patient empowerment and education with continuous feedback to patients, nurses, and physicians seems to be welcomed by both patients and participating health care professionals. However, our system based on voluntary participation and report cards was not successful at this time due to a high dropout rate especially after the patients were referred to primary health care facilities.

- Reasons why ESC targets for serum lipids were not met in the EUROASPIRE II study were that too few patients received lipid-lowering drugs, and that of those who did receive such treatment many were treated with sub-optimal doses. If more CHD patients are to fully benefit from lipid-lowering therapy and reach the target levels for serum cholesterol both higher doses and more effective drugs must be used.

- There is a need for new and improved methods of targeting individuals at high risk for CHD even before overt disease in order to start adequate treatment. It is also desirable to find methods of identifying subjects at low risk for disease. Holter ECG with ST-analysis can be one method of improving risk prediction regarding CHD in asymptomatic subjects.

We found that a structured programme for secondary prevention mainly run by nurses could be a useful tool for secondary prevention in patients with CHD. These initial efforts resulted in benefits on lipids even several years after the termination of then programme. The idea of nurse-led clinics has subsequently been implemented in all hospitals in Sweden. Since secondary prevention is a long-term undertaking and needs to be of good quality for the remainder of the patient's life, we introduced the idea of the "heart booklet" and the Swedish National Programme for Secondary Prevention as a tool towards this goal. However, this initiative failed since the

dropout rate turned out to be too high to warrant prolonged economic support. Similar to our shortcomings, long term follow-up in other parts of Europe has also been mostly unsuccessful as was seen in EUROASPIRE II.

Finally, since the idea of absolute risk is gaining ground over primary- and secondary prevention, better tools for risk stratification of asymptomatic subjects have to be introduced. Since the reason for the low activity is said to be lack of time or other resources, those subjects with high accumulated risk and who will also be positive at provocation (PAP) should be identified in the first time run.
In order to bridge the treatment gap between treatment guidelines and the clinical reality many good forces need to co-operate. New scientific knowledge and treatment guidelines need to be rapidly distributed to the medical community. Physicians need to be encouraged to continually update their medical knowledge. This includes participation in post-graduate training as well as international and national meetings and conferences. There has to be an increased co-operation between different parts of the health service, such as hospital- and primary care, in order to reduce differences in treatment. One way of obtaining this goal is the development of joint treatment programmes. Prevention programmes for CHD should be implemented and one way to achieve this is to allow them to be nurse-led with physician backup. Clear treatment goals for risk factors should be set up, both concerning the target levels and the time within which they should be reached. Both pharmacological and non-pharmacological treatment should be used to its full capacity in order to decrease the risk for future CHD. The patients should be more actively involved in their own disease and treatment in order to increase compliance and treatment effect. Subjects without clinically overt disease but with a high risk for future events should be identified and treated adequately.

Clinical implications

In the future, important new knowledge regarding CHD prevention has to be implemented more rapidly and thoroughly than has been seen in clinical practice in the past. Processing and disseminating national and international guidelines into local programmes should be requested by authorities financing health services, since such an interest would probably increase commitment to the goals at all levels of the health care system. The medical community must be persuaded to utilise all tools at their disposal in order to treat risk factors for CHD optimally, both regarding lifestyle changes and pharmacological risk factor treatment. In order to secure a continuing learning and improvement process the health authorities should demand quality control and monitoring of success. Indeed, in the United Kingdom this is already being implemented inasmuch as funding being partly coupled to treatment success on a local basis. Robust, easy-to-use, quality control programmes are tools to help accomplishing these goals. For several years the RIKS-HIA registry regarding hospital treatment of acute coronary syndromes has been in operation. Quite recently a registry for secondary prevention within the RIKS-HIA population (SEPHIA) was launched. This registry is administered by hospitals and includes patients below the age of 75 who have suffered an AMI and the patients will be followed up to one year after the index event.
The prevention of CHD is a major task that urges us to focus on those parts of the population that are most likely to benefit the most from intervention, i.e. high-risk subjects. Thus, improved risk stratification tools are important. Holter ECG with ST-analysis is one among many possible tools.

Finally, prioritisation of patients with overt symptoms often leaves the physician short of time to deal with preventive medicine. This thesis and other studies have shown that nurses safely and effectively could be entrusted with the responsibility and opportunity to handle parts of the important task of preventive cardiology. Thus we believe that, in order to implement risk factor treatment for CHD in the community, specialist nurses interested in CHD prevention should be trained and deployed also in the primary health care system. A model for this is the often well organised nurse-led monitoring and treatment of patients with diabetes, which take place at out-patient clinics in both hospital and primary care facilities. If this idea turns out to be impossible because of shortage of resources within the primary health care organisation, CHD patients could be re-evaluated by secondary prevention nurses at hospital clinics on an annual or biannual basis.

Summary in Swedish

Praktiska synpunkter på genomförandet av förebyggande behandling rörande sjukdomar i hjärtats kranskärl

Sjukdomar i hjärtats kranskärl omfattande bland annat kärlkramp och hjärtinfarkt är den viktigaste orsaken till sjukdom och död i Sverige. Kranskärlssjukdom innebär åderförkalkning och tilltäppning av ett eller flera av de blodkärl som förser hjärtmuskeln med blod. En successiv tilltäppning av ett kranskärl medför symptom som ofta yttrar sig som bröstsmärta vid ansträngning, kärlkramp, p.g.a. nedsatt blodflöde till hjärtat. En akut tilltäppning av ett kranskärl medför att en del av hjärtmuskeln dör p.g.a. brist på blod. Detta yttrar sig vanligen som akut påkommen bröstsmärta, ofta utan relation till arbete, och kallas hjärtinfarkt. De bakomliggande orsakerna till återförkalkningssjukdomen börjar bli allt mer kända. Det finns ärftliga faktorer som påverkar risken att drabbas. Även ålder och manligt kön ökar risken för kranskärlssjukdom. Förutom dessa faktorer finns det ett flertal påverkbara riskfaktorer som i varierande grad påverkar risken för framtida kranskärlssjukdom. Exempel på dessa är rökning, högt blodtryck, låg fysisk aktivitet, höga blodfetter (kolesterol) och blodsockerhalt. Det är bevisat att påverkan på dessa riskfaktorer i rätt riktning, både livsstilsfaktorer såsom rökstopp, ökad fysisk aktivitet, och en hälsosam kost, samt med läkemedelsbehandling mot såväl förhöjda kolesterolvärden som högt blodtryck, gör att risken att drabbas av kranskärlssjukdom i framtiden minskar avsevärt.
För att underlätta för såväl sjukvården som för patienterna publiceras det behandlingsrekommendationer med målvärden rörande behandlig av dessa riskfaktorer. För patienter med känd kranskärlssjukdom (kärlkramp, tidigare hjärtinfarkt, tidigare ballongvidgning eller bypassoperation av kranskärlsförträngningar) liksom för individer som ännu inte är sjuka men som har en ökad riks att drabbas gäller för närvarande följand riktlinjer: Absolut rökstopp. kolesterolvärde <5,0 mmol/l, LDL-kolesterol (”det onda kolesterolet”) <3,0 mmol/l, och ett blodtryck <140/90 mmHg. För patienter med kraftigt ökad risk såsom diabetiker gäller ännu lägre gränsvärden. Trots dessa riktlinjer visar det sig att relativt många patienter inte når dessa målvärden.

I denna avhandling har jag försökt utröna varför många patienter med kranskärlssjukdom inte når målvärden för blodfetts (kolesterol) -nivåer samt undersöka hur man kan organisera sjukvården på så sätt att man kan förbättra detta så mycket som möjligt. Jag har också utvärderat ett nytt sätt att på friska förutsäga

vem som i framtiden kommer att drabbas av kranskärlssjukdom för att på så sätt kunna sätta in förebyggande behandling i tid.

Uppsats I

Denna uppsats utvärderade ett program för uppföljning och behandling av riskfaktorer hos patienter med etablerad kranskärlssjukdom. Patienterna följdes under ett år efter sjukhusvistelsen på en speciell mottagning där sköterskor och läkare tillsammans behandlade patienten efter ett bestämt program. Man lade ner mycket vikt på att programmets målvärden för blodfettsbehandling skulle nås både med kost och mediciner. Efter ett år avslutades programmet och patienterna remitterades vidare till primärvården på sedvanligt sätt. Fyra år senare undersökte patienterna igen avseende blodfetter. Det visade sig att de patienter som genomgått det speciella programmet även fyra år efter att det avslutades hade lägre blodfetter och en högre andel blodfettsänkande medicinering än kontrollpatienterna som inte genomgått detta program. Slutsatsen är att ett kortvarigt, men intensivt, program för blodfettsänkning kan ha långsiktiga positiva effekter på blodfettsnivåer hos patienter med kranskärlssjukdom.

Uppsats II

I denna uppsats utvärderades ett hjälpmedel för läkare, sköterskor och patienter för bättre följsamhet till gällande riktlinjer för behandling av riskfaktorer för kranskärlssjukdom, det så kallade kvalitetssäkringsprojektet för kranskärlssjukdom. Femtioen av Sveriges 75 sjukvårdsdistrikt deltog i projektet. Vid utskrivning från sjukhus fick varje patient en egen bok, den så kallade hjärtboken. Denna innehöll kortfattad och lättbegriplig information rörande riskfaktorer för kranskärlssjukdom riktat till patienterna. Vidare fanns patientens egna nivåer av blodfetter, blodtryck, blodsocker och vikt sant medicinering noterade liksom de målnivåer som rekommenderades. Vid varje besök inom sjukvården efter utskrivning skulle patientens riskfaktornivåer införas i boken och jämföras med föregående värden och med målvärdena. Vidare skulle ett rapportblad inskickas till registrets databas. Varje år presenterades en rapport om hur väl riskfaktorer för kranskärlssjukdom behandlades både i hela riket och i de olika sjukvårdsdistrikten. Målen med registret var flera. Dels hoppades vi att hjärtboken skulle medföra en ökad kunskap och ett ökat intresse hos den enskilda patienten rörande sina riskfaktorer. Det har visat sig att patienter som är välinformerade och har kunskap om sina egna riskfaktorer också i större utsträckning når de uppsatta behandlingsmålen. Vidare hoppades vi att den kontinuerliga återrapporteringen av hur väl behandlingsmålen uppnåddes skulle kunna leda till ett kontinuerligt förbättringsarbete i de olika sjukvårdsdistrikten.

Rapporterna visade att behandlingsmålen för kranskärlssjukdom i många fall uppnåddes relativt väl i landet som helhet. Dock fanns det fortfarande utrymme för förbättringar. Det fanns också stora geografiska skillnader i hur väl behandlingsmål rörande riskfaktorer för kranskärlssjukdom uppnåddes. Både patienter och sjukvårdspersonal betraktade hjärtboken som ett värdefullt redskap i behandlingen. Trots detta tvingades vi avbryta projektet p.g.a. att bortfallet, d.v.s. antalet rapporter som inte skickades in, var allt för stort vilket medförde att finansieringen upphörde.

Uppsats III

Denna uppsats, som var en del av ett större sameuropeiskt projekt, syftade till att utröna varför patienter med etablerad kranskärlssjukdom inte når de målvärden rörande blodfettsbehandling som de europeiska riktlinjerna rekommenderar. EUROASPIRE II- studien genomfördes i 15 europeiska länder och i denna studie undersöktes 5556 patienter med känd kranskärlssjukdom, i genomsnitt 1.4 år efter den akuta sjukdomsepisoden. De europeiska riktlinjerna rörande blodfettsänkning säger att dessa patienter bör ha ett kolesterolvärde <5,0 mmol/l samt LDL- kolesterol (”det onda kolesterolet”) < 3,0 mmol/l. Undersökningen visade dock att mer än hälften av patienterna inte nådde dessa målvärden. För att undersöka varför så var fallet analyserade vi användandet av blodfettsänkande läkemedel bland dessa patienter. Det visade sig att endast 61% av patienterna hade någon form av blodfettsänkande behandling. Vidare såg vi att de flesta patienter som hade blodfettssänkande läkemedel var behandlade med för låga doser av dessa mediciner. Om fler patienter hade förskrivits blodfettsänkande läkemedel och dessa hade använts i rätt dosering hade säkerligen många fler patienter förbättrat sina kolesterolvärden och på så sätt ytterligare minskat sin risk att drabbas av framtida kranskärlssjukdom

Uppsats IV

I denna uppsats undersökte vi 155 friska medelålders män utan känd kranskärlssjukdom men med en måttlig ansamling av riskfaktorer (blodfetter, rökning och högt blodtryck) med en 48 timmars långtidsregistrering av hjärtats elektriska aktivitet med en bärbar EKG apparat. Femton år senare jämförde vi utfallet av denna registrering med insjuknande i kranskärlssjukdom och död hos dessa patienter. Det visade sig att patienter med en viss EKG-förändring, s.k. ST-sänkning, som kan vara ett tecken på oupptäckt kranskärlssjukdom, hade betydligt högre risk att drabbas av framtida kranskärlssjukdom än patienter utan denna EKG-förändring, trots att andra riskfaktorer för kranskärlssjukdom som kön, ålder, blodtryck, rökning och blodfetter var lika i båda grupperna. Således skulle

långtidsregistrering av EKG med ST-analys kunna var en metod att mera säkert identifiera friska individer med ökad risk att drabbas av kranskärlssjukdom i framtiden. Det krävs dock mer forskning rörande denna och andra metoder innan man med säkerhet kan förutsäga vem som är i riskzonen att drabbas av kranskärlssjukdom.

Sammanfattningsvis anser jag att även om behandlingen av riskfaktorer för kranskärlssjukdom hos patienter och individer med ökad risk i många fall är god så skulle denna kunna förbättras ytterligare genom en del relativt enkla åtgärder. Detta skulle i sin tur kunna leda till minskad sjuklighet och dödlighet i kranskärlssjukdom. Denna avhandling har visat att sköterskebaserade mottagningar under en begränsad tid och utnyttjande av den fulla potentialen av både livsstils- och läkemedelsbehandling samt i vissa fall noggrannare metoder att identifiera högriskpatienter är medel nå detta mål.

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