REVIEW ARTICLE

Implementation of Secondary Prevention Methodologies in Ischemic Heart Disease

ABSTRACT

Ischemic heart disease (IHD) remains a major cause of mortality, morbidity, and disability in the U.S. and other developed countries and is an emerging epidemic in developing countries. As a result of therapeutic and preventive measures to control the IHD pandemic, mortality has declined steadily during the last several decades with consequent gains in life expectancy; however, this decrease in mortality started to plateau in the 1990's.[1,2] Secondary prevention is identifying and treating people with established disease and those at very high risk of developing ischemic heart disease, which involves the treatment and rehabilitation of patients with known ischemic heart disease to prevent future cardiovascular events, including myocardial infarction, stroke, and heart failure.

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Key words

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The secondary prevention patient population includes those with established coronary and other atherosclerotic vascular disease, including peripheral arterial disease, atherosclerotic aortic disease and carotid artery disease.[1] However, one might also consider expanding this to persons with other coronary heart disease risk equivalents, such as those with a >20% 10-year calculated risk of IHD, diabetes, chronic kidney disease, or with significant subclinical coronary atherosclerosis (e.g., high levels of coronary artery calcification). Secondary prevention of coronary artery disease is effective in reducing morbidity and mortality, but deficiencies in implementation and prescription bias have been identified.

In evaluating the patients with preexisting coronary artery disease (CAD) for future risk of cardiovascular events, the value of the medical history, physical examination, 12-lead electrocardiogram, and selected laboratory tests cannot be overlooked. Originally, the Framingham Heart Study[2] has assembled algorithms for determining the 2-year risk of IHD events, stroke, or cerebrovascular disease death in women (Table 1) and men (Table 2) with existing IHD. These tables may be useful for initial risk stratification, but they should be considered only approximate guides for assessing patient risk. Clinical presentation, including the type of chest pain present, as well as the presence of any associated co-morbidities (e.g., diabetes) also figure into the determination of prognosis. Other information about symptoms, coronary anatomy, left ventricular function, or results from exercise and/or nuclear stress imaging testing or newer biomarkers such as brain naturietic peptide (BNP) or troponin levels can provide important information for risk stratification.

Risk Factor Modification and Secondary Prevention Guidelines

Risk factor modification is the foundation of secondary prevention efforts in persons with IHD.[1-3] This comprehensive approach involves lifestyle modification efforts including smoking cessation, diet, and physical activity, pharmacologic therapies to ensure control of blood pressure, lipids and glucose, and the use of cardioprotective drug therapies.

Over the past decade, guideline panels, including those from the American Heart Association (AHA) and American College of Cardiology (ACC)[1] as well as European panels[4], have developed a series of recommendations for therapy and clinical management of risk factors in persons with IHD (Tables 3, Tables 4, Tables 5). Evidence confirms that aggressive comprehensive risk factor management improves survival, reduces recurrent events and the need for interventional procedures, and improves the quality of life in these patients.

Table 1. Risk of Coronary Artery Disease Event, Stroke, or Cerebrovascular Disease Death in Women with Existing Coronary Artery Disease

			Points by HDL-C, mg/dL										
Age	Points	Total-C Mg/dl	25	30	35	40	45	50	60	70	80	SBP mmHg	Points
35	0	160	4	3	3	2	2	1	1	0	0	100	0
40	1	170	4	3	3	2	2	2	1	1	0	110	0
45	2	180	4	3	3	2	2	2	1	1	0	120	1
50	3	190	4	4	3	3	2	2	1	1	1	130	1
55	4	200	4	4	3	3	2	2	2	1	1	140	2
60	5	210	4	4	3	3	3	2	2	1	1	150	2
65	6	220	5	4	4	3	3	2	2	1	1	160	2
70	7	230	5	4	4	3	3	3	2	2	1	170	3
75	7	240	5	4	4	3	3	3	2	2	1	180	3
		250	5	4	4	4	3	3	2	2	1	190	3
		260	5	5	4	4	3	3	2	2	1	200	3
		270	5	5	4	4	3	3	2	2	2	210	4
Other Points		280	5	5	4	4	3	3	3	2	2	220	4
Diabetes	3	290	5	5	4	4	4	3	3	2	2	230	4
Smoking	3	300	6	5	4	4	4	3	3	2	2	240	4
												250	4

Average 2-year Risk in Women with CVD

Total Points	2-year Probability, percent	Age, years	Probability, percent
0	0	35–39	< 1
2	1	40–44	< 1
4	1	45–49	< 1
6	1	50–54	4
8	2	55–59	6
10	4	60–64	8
12	6	65–69	12
14	10	70–74	12
16	15		
18	23		
20	35		
22	51		
24	68		
26	85		

Key: HDL-C, high-density-lipoprotein cholesterol; SBP, systolic blood pressure; CVD, cardiovascular disease.
Source: Califf et al.[2] with permission.

Table 2.
Risk of Coronary Artery Disease Event, Stroke, or Cerebrovascular Disease Death in Men with Existing Coronary Artery Disease

			Points by HDL-C, mg/dL										
Age, years	Points	Total-C, mg/dL	25	30	35	40	45	50	60	70	80	SBP (mmHg)	Points
35	0	160	6	5	4	4	3	2	1	1	0	100	0
40	1	170	6	5	5	4	3	3	2	1	0	110	1
45	1	180	7	6	5	4	4	3	2	1	1	120	1
50	2	190	7	6	5	4	4	3	2	2	1	130	2
55	2	200	7	6	5	5	4	4	3	2	1	140	2
60	3	210	7	6	6	5	4	4	3	2	1	150	3
65	3	220	8	7	6	5	5	4	3	2	2	160	3
70	4	230	8	7	6	5	5	4	3	3	2	170	4
75	4	240	8	7	6	6	5	4	4	3	2	180	4
		250	8	7	6	6	5	5	4	3	2	190	4
		260	8	7	7	6	5	5	4	3	2	200	5
		270	9	8	7	6	6	5	4	3	3	210	5
Other Points		280	9	8	7	6	6	5	4	4	3	220	5
Diabetes	1	290	9	8	7	7	6	5	4	4	3	230	6
		300	9	8	7	7	6	6	5	4	3	240	6
												250	6

Average 2-year Risk in Men with CVD

Total Points	2-year Probability, percent	Age, years	Probability, percent
0	2	35–39	< 1
2	2	40–44	8
4	3	45–49	10
6	5	50–54	11
8	7	55–59	12
10	10	60–64	12
12	14	65–69	14
14	20	70–74	14
16	28		
18	37		
20	49		
22	63		
24	77		

Key: HDL-C, high-density-lipoprotein cholesterol; SBP, systolic blood pressure; CVD, cardiovascular disease.
Source: Califf et al.[2] with permission.

Importantly, the revised AHA/ACC guidelines, based on compelling evidence from recent clinical trials and revised practice guidelines from the National Institutes of Health and the AHA/ACC allow for categorization according to classification of recommendation and level of evidence (A through C).[1] The strongest guidelines are those classified as Class I, for which there is evidence or general agreement that the procedure or treatment is beneficial, useful and effective and/or where data are derived from multiple randomized clinical trials or meta-analyses (level of evidence A), whereas weakest are those classified as Class III (not useful/effective and possibly harmful) and/or with a level of evidence of C (only expert consensus, case studies, or standard of care). For instance the initiation of LDL-C lowering drug therapy when the LDL-C >100 mg/dl is given a class Ia recommendation. The guidelines provides the level of recommendations and applicable classifications/ level of evidence for the key components of secondary prevention as outlined in Table 3, including their assessment, treatment goals, and recommended treatment approaches as recommended by the AHA/ACC.

Status of Risk Factor Control and Recommended Treatments

Previous studies have shown that cardiovascular risk factors among IHD patients are poorly controlled,[4] with many exceeding target levels.[5] Previous reports[6] have focused on clinical or hospitalized samples, U.S. population data from free-living U.S. adults with IHD describing the adequacy of recommended treatments and risk factor control are limited. Recent reports from the U.S. National Health and Nutrition Examination Survey have shown barely a third of those with IHD to be at a recommended LDL-C <100 mg/dl with only a sixth at recommended levels of all lipids, and less than half at recommended levels of blood pressure.[8-9] Since major risk factors account for 75% or more of the risk for developing a CVD event,[10] the secondary prevention efforts should focus on achieving optimal risk factor control by all valid approaches. For instance, the daily use of a "polypill" containing an HMG CoA reductase inhibitor (simvastatin 40 mg), 3 blood pressure-lowering medications (diuretic, beta blocker, angiotensin converting enzyme inhibitor at usual doses), folic acid (0.8 mg), and aspirin (75 mg) has been estimated to reduce recurrent cardiovascular events by 88%.[11]

Implementation of Prevention Guidelines

Lifestyle, risk factos, and therapeutic goals set by recommendations of Joint European Societies for coronary disease prevention in clinical practice are not realized by most patients throughout Europe.[12-18] Many national multicenter studies showed results similar to those in EUROASPIRE I (1995/96), EUROASPIRE II (1999/2000), and EUROASPIRE III (2006/2007).[3-19]

The comparison between these EUROASPIRE surveys demonstrates a substantial gap between the standards set in the CVD prevention guidelines in clinical practice. These surveys, show that lifestyle trends in patients with IHD are growing cause for concern.[14-11] Other surveys have also reported inadequate risk factors management and underuse of prophylactic drug therapies in patients with IHD in Spain (PREVESE I and II, in 1994 and 1998,[20-21] France (PREVENIR,1998 and 1999, Usik 1998 and 2000),[22] Republic of Srpska/Bosnia and Herzegovina(ROSCOPS I,II,III) in 2000, 2003[24] and 2007 , Croatia (TASPIC-CRO) in 1998[23] and 2003, and Serbia in 2008/2009[25]. What is abundantly clear from these European surveys is that drug therapies are simply not sufficient and they have to be combined with the professional support to make lifestyle changes and also manage their risk factors more effectively. Simply giving a drug prescription is not enough. Patients need to understand the nature of their disease and how to manage it through achievin a healthy lifestyle and adhering to cardioprotective drug therapies over the long term. Most importany of all, adverse lifestyle trends in the general population calls to attention the urgent need for a societal strategy for CVD prevention. They illustrate how difficult it is for individual patients to change their behavior, despite the development of life-threatening disease, given that their unhealthy life-styles are shared by an ever-increasing proportion of the adult population. To help patients to quit smoking, adopt a healthy diet and increase physical activity requires sustained professional support. Yet only third of patients with coronary disease access cardiac rehabilitation programs in Europe. All patients with coronary disease as well as those at high risk of development CVD should be able to access preventive cardiology programs.[11-15]

The results of the management program of the cardiac hospitalizations for atherosclerosis (CHAMP) at UCLA carried out in two different groups of 256 and 302 patients also showed that a hospital-based strategy of RF increases the rates medication at discharge, from 6% for statins prior to implementation of the program in the years 1990-93 to 86% after running the program. One year after discharge 58% of patients reached LDL-cholesterol levels less than 100 mg/dl compared with only 6% of patients in the previous period. Many persons with IHD in the United States in 2005-2006 remain short of American Heart Association and American College of Cardiology recommended goals for BP, lipids and if diabetic, A1C. Vulic et al. recently reported treatment rates for recommended treatments (ACE/ARBs, beta-blockers and lipid-lowering medication) are higher than reports from previous investigations in clinical populations that have examined IHD patients.[26] These studies demonstrate that under conventionally guided management, regardless of the health care delivery system, an unacceptably large number of IHD patients are left untreated by cardioprotective drugs. This low rate of patient adherence to therapy, undoubtedly, is a significant contributor to the large number of patients not being treated with evidence-based therapy on an outpatient basis. The underuse of cardioprotective drugs in patients with

Table 3.
Components of Secondary Prevention

Cigarette smoking cessation
Blood pressure control
Lipid management to goal
Physical activity
Weight management to goal
Diabetes management to goal
Antiplatelet agents / anticoagulants
Renin angiotensin aldosterone system blockers
Beta blockers
Influenza vaccination

(Adapted from Smith et al.[1])

Table 4.
What Are the Objectives of Secondary CVD Prevention?

No smoking
Healthy food choices
Physical activity: 30 min of moderate activity a day
Body mass index (BMI) <25 kg/m2 and avoidance of central obesity
Blood pressure under 130/80 mmHg if feasible
Total cholesterol <4.5 mmol/l (~175 mg/dl) with an option of <4 mmol/l (~155 mg/dl) if feasible
LDL cholesterol <2.5 mmol/l (~100 mg/dl) with an option of <2 mmol/l (~80 mg/dl) if feasible
Fasting blood glucose <6 mmol/l (~110 mg/dl) and glycosylated haemoglobin (HbA1c) <6.5% if feasible

(Source: European Guidelines on CVD Prevention Fourth Joint European Societies Task Force on Cardiovascular Disease Prevention in Clinical Practice 2007; reproduced with permission from Graham et al.[13])

IHD represents a major clinical practice and public health mismanagement issue.

Adherence to lifestyle advice about diet, exercise and smoking cessation following acute coronary syndrome (ACS) has a substantial effect on lowering the risk of further events, according to a study of more than 18,000 patients.[27] According to an accompanying editorial, this marked improvement in cardiovascular morbidity and mortality seen with lifestyle modification in the ACS population is "a novel and compelling finding". The editorial adds that such results "should raise a new level of focus on the timely initiation of behavioral modification after MI, similar to what is currently done with acute pharmacological intervention". It was striking in the study that at 30 days following ACS, 96.1% of subjects had been prescribed antiplatelet drugs and 78.9% statins- while around one-third of smokers were still smoking, and adherence to neither diet nor exercise recommendations was reported by 28.5%.

Multiple studies of the use of these recommended therapies in appropriate patients continue to show that many patients in whom therapies are indicated are not receiving them in actual clinical practice. The AHA , ACC and ESC urge that in all medical care settings where these patients are managed that programs to provide practitioners with useful reminder hints based on the guidelines, and continuously assess the success achieved in providing these therapies to the patients who can benefit from them be implemented. Data from a national samples of people with IHD show that a substantial majority were not optimally treated for BP, lipids, and HbA1c, but better in comparison with previous reports.[24-26] Further research into identification of patient and provider factors, resulting in suboptimal treatment, is needed. Further education of patients and providers in the appropriate use of multiple or combination treatments to appropriately treat risk factors to goal is also needed. General practitioners are in a unique position to provide ongoing advice, support and counseling to such patients with established IHD, who require life-long risk factor control and treatment management. Table 6 lists ten important strategies for improving effectiveness of behavioral interventions.

Conclusions

Patients with established heart disease or CVD risk equivalents are at high risk for acute coronary events. Multiple randomized clinical trials have documented the valuable clinical benefits of aggressive risk factor modification for the prevention of recurrent events and mortality. Guidelines established by European, American, and other societies have described the assessment, goals, and management strategies for key areas of secondary prevention including smoking cessation, blood pressure control, lipid management, physical activity, weight management, diabetes management, antiplatelet therapy, renin-angiotensin system blockade, beta-blockade, and most recently, influenza

vaccination. Aggressive and comprehensive management of all established risk factors should be initiated for most high-risk patients without delay. Close monitoring to ensure adherence to prescribed therapies and lifestyle modifications is crucial for the success of secondary prevention strategies. Further clinical trials will help establish the role of monitoring and treatment of newer emerging risk factors and biomarkers in secondary prevention efforts.

Table 5.
When to Prescribe Cardioprotective Drugs in Addition to Those Used to Treat Blood Pressure, Lipids and Diabetes

Aspirin or other platelet modifying drugs are recommended in all patients at high risk of occlusive arterial disease unless there are specific contraindications.
Beta-blockers after myocardial infarction and, in carefully titrated doses, in those with heart failure.
ACE inhibitors are indicated in all patients, unless there are contraindications, for the following reasons: (i) treatment of left ventricular dysfunction with or without over heart failure.
Anticoagulants in those at increased risk of thromboembolic events, particularly atrial fibrillation.

Table 6.
Ten Strategic Recommendations to Enhance the Effectiveness of Behavioral Counseling

Develop a therapeutic alliance
Counsel all patients
Ensure that patients understand the relationship between behavior and health
Help patients to assess the barriers to behavior change
Gain commitments from patients to behavior change
Involve patients in identifying and selecting the risk factors to change
Use a combination of strategies including reinforcement of patient's own capacity for change
Design a lifestyle modification plan
Monitor progress through follow-up contact
Involve other healthcare staff wherever possible

(Source: European Guidelines on CVD Prevention Fourth Joint European Societies Task Force on Cardiovascular Disease Prevention in Clinical Practice 2007. Reproduced with permission from Graham et al.[13])

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