SPECIAL ARTICLE

Evidence Based Secondary Prevention of Coronary Artery Disease In The Elderly-2006

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Eighty percent of coronary deaths occur in people above 65 years of age. Fifty percent of deaths in persons above 85 years of age is due to coronary artery disease.

The overall aging of the population and the improvement in survival of patients with coronary artery disease has been creating a growing large population of elderly adults who are elegible for secondary prevention.

Multiple clinical trials and research trials have revealed evidence based information confirming the usefulness and effectiveness of secondary prevention of coronary artery disease in the elderly patient. The secondary prevention beneficial results have been obtained by addressing and controlling the predisposing items recognized a coronary risk factors.

Secondary preventive measures, including lifestyle modifications and pharmacotherapy, modifying risk factors in elderly patients, have been shown to reduce morbidity and mortality from coronary artery disease.

Evidence based data on prevention in elderly patients with coronary artery disease concerning smoking cessation, treatment of hypertension, control of hyperlipidemia, improved dietary patterns, physical activity, moderation in alcohol intake, management of diabetes, weight management, use of antiplatelet agents, beta blockers and renin-angiotensin-andosterone blockers is summarized.

Emphasis has been given to AHA/ACC consensus statements on the prevention of coronary artery disease.

Key words: Coronary artery disease, Secondary prevention, Evidence based data, Risk factors, Lifestyle changes, Medications

Coronary artery disease (CAD) is the leading cause of mortality in the United States with more than 80 percent of the persons 65 years of age or older dying from this condition (1). The presence of obstructive coronary artery disease at autopsy approaches 50% in elderly women and 70-80% in elderly men. Although octogenarians constitute 5% of the population in the US, they account for 20% of all hospitalizations for myocardial infarction and 30% of all myocardial infarction related hospital deaths (2). Fifty percent of the deaths in individuals above 85 years of age is due to coronary heart disease[3]. In advanced countries 50% of the cardiovascular health expenditures are in people above 65 years of age.

For many years, primarily from epidemiological studies, multiple factors have been related to the development of coronary artery disease and have been identified as coronary risk factors. The control of risk factors has been studied in multiple studies conducted in samples of populations revealing a decrease in coronary artery disease with risk factors control. Initially most of the scientifically based studies were mainly carried on individuals younger than 65 years of age and there was no objective evidence that the beneficial preventive measures were also efficient in persons 65 years of age or older.

Finally, in the last 15 years, different studies have been carried on concerning control of coronary risk factors in people above 65 years of age demonstrating the effectiveness of these measures in the prevention of coronary artery disease in the elderly.

In this article we will summarize the main findings concerning evidenced based information available in 2006 for scientifically based prevention of coronary artery disease in the elderly. Increasing evidence has accumulated over the past two decades indicating that elderly individuals with CAD can benefit greatly from secondary prevention.

Different terms are available in the medical literature to describe populations by age groups. By elderly, most publications generally refer to individuals 65 years of age or older. It is clear that most industrialized societies are

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aging and that the prevalence of elderly persons is increasing rapidly. Newer terminology have been presented in the literature such as old elderly and "oldest old elderly" to differentiate groups within the 65 to 90 age bracket. As reference for this article we will use the definition presented in Table 1 . The information presented will be oriented to the preventive measures that have been found to be useful and worthwhile in patients 65 years of age or older.

The Elderly ¿How to define it?	
Middle age	40 to 60 years
Mature	≥ 55 years
Seniors	≥ 60 years
Elderly	≥ 65 years
Young – Old	65-75 years
Median –Old	> 75 years
Oldest - Old	≥ 85 years

Table 1. How to define elderly patients

Risk Factors for Coronary Heart Disease

The Risk Factors for Coronary Heart Disease have been identified and amplified primarily in the last 40 years with significant epidemiological coronary artery disease studies conducted in different populations in multiple countries in the world including among those the Framingham Heart Study, the Puerto Rico Heart Health Study and the Honolulu Heart Study (4).

The main coronary risk factors as we identify them today are summarized in Table 2 prepared by Pyorala K. et al (5).

According to their origin risk factors are considered to be of three types: those depending of the lifestyle, those that are modifiable and a third group consisting of non-modifiable factors.

Some of these risk factors are considered non-modifiable as there is no way to alter them. It is accepted that coronary artery disease is more frequent in advancing age. In men it increases from age 45 on and in women from age 55 on. The later start of the postmenopausal disease in women is related to the onset of menopause as it is known that with the decrease in estrogen production the serum LDL-cholesterol increases favoring the deposition of lipids on the coronary arteries. Other non-modifiable risk factors are a family history of coronary artery disease as well as a personal history of the condition.

The factors related to lifestyle are diet, tobacco smoking, excess alcohol consumption and physical inactivity. Data concerning these risk factors as well as samples of evidenced based preventive measures to be instituted concerning lifestyle modifications in the elderly will be summarized.

There have been many advances in the control and management of modifiable risk factors. These include elevated blood pressure, elevated total (LDL) cholesterol, low HDL cholesterol, diabetes mellitus and obesity. We will discuss the salient therapeutic and preventive measure available in 2006 to deal with these factors in the elderly.

Based upon the information generated by multiple studies and clinical trials, the American Heart Association (AHA) in conjunction with the American College of Cardiology (ACC) with the endorsement of the National Heart, Lung and Blood Institute have developed joint statements and guidelines for secondary prevention for patients with coronary artery disease for all age groups, including the elderly (6-8). The recommendations presented represent the major practice guidelines to be followed by practicing physicians and health care professionals in order to modify existing risk factors in order to avoid recurrence or complications of coronary artery disease.

Risk Factors for Coronary Heart Disease		
Lifestyle	**Modifiable**	**Non-Modifiable**
Diet	Elevated total (LDL) cholesterol	Age
Tobacco smoking	Elevated blood pressure	Sex
Excess alcohol consumption	Low HDL cholesterol	Family history of CHD
Physical inactivity	Elevated triglycerides	Personal history of CHD
	Diabetes mellitus	
	Obesity	
	Thrombogenic factors	

Table 2. Evidence based risk factors for Coronary Artery Disease (5)

Measures for Secondary Prevention

Those measures taken to alter risk factors so as to avoid the development of a cardiovascular disease in a healthy individual are called primary prevention measures. The measures taken to prevent complications, recurrences or death in an individual that already has cardiovascular disease are called secondary prevention measures. Both primary and secondary

prevention measures in coronary artery disease are based upon risk factor modification by either non-pharmacologic or pharmacologic interventions that modify risk factors. The preventing measures to be instituted must be derived from evidenced base data obtained in clinical trials and clinical studies.

Smoking Cessation

There is ample clinical evidence showing that maintenance of the smoking habit after a patient has suffered a myocardial infarction or is submitted to coronary artery-bypass surgery is accompanied by deleterious effects on the cardiovascular system. In 1978 Sparrow et al informed that cessation of smoking caused a 25 to 50% reduction in mortality in one year in patients who had suffered a myocardial infarction (9). An article by Wilhelmsen in 1996 revealed the experience of cessation of smoking in six different studies with a reduction of mortality. Data from the Coronary Artery Surgery Study (CASS) registry indicate that smoking cessation reduces both morbidity and mortality rates in those patients over the age of 70 who have undergone CABG Surgery (10). The decrease in relative risk for myocardial infarction and death encountered in those patients over 70 years of age was similar to that seen in younger individuals.

The interventions available to promote smoking cessation include physician counseling, support groups, replacement of nicotine and other pharmacologic measures (11).

Control of Elevated Blood Pressure

Evidence accumulated for many years have demonstrated that arterial hypertension conveys a risk for increased morbidity and mortality from coronary artery disease. The higher the blood pressure the higher the prevalence of coronary artery disease.

Since 1985 there have been multiple publications of observational studies as well of analyses of randomized controlled trials and meta-analyses evaluating the treatment of hypertension in patients older than 60 years of age. The targets for lowering blood pressure are similar for patients of all ages: <140/90 mmHg. In patients with diabetes type 2, chronic renal disease or heart failure a level of less than 130/80 mmHg is recommended (8).

A review article published in 1995 summarized the effects of antihypertensive treatment in a total of 12,483 hypertensive (systolic and diastolic) elderlies from 5 studies conducted in different populations in the United States, England, Sweden and Europe confirming the coronary artery preventive effect obtained in the elderly by the treatment and control of hypertension (12). It was demonstrated a reduction of 20% in total mortality, 33% of cardiovascular mortality, 40% in non-fatal stroke and 15% in coronary events including myocardial infarction and sudden death (13).

Systolic hypertension, defined as a systolic blood pressure of at least 140 mm Hg and a diastolic blood pressure of less than 90mm Hg, is an important health issue that primarily affects elderly persons. Systolic blood pressure rises almost linearly between the ages 30 and 80 years, whereas diastolic blood pressure rises until approximately age 50, levels off, and then declines (14). It has been extensively reported that arterial stiffness increases with aging principally in the central arteries so causing aortic stiffness which is considered the main factor in the development of systolic hypertension (15). Isolated systolic hypertension is a distinct pathophysiological entity in which the rise in systolic blood pressure is mainly due to a decrease in the elasticity of the large arteries and is not necessarily accompanied by a rise in mean arterial blood pressure or in peripheral resistance (16). The prevalence of isolated systolic hypertension averages 8 % in sexagenarians and exceeds 25% beyond 80 years of age (17).

Multiple studies conducted in different institutions and countries correlating systolic hypertension in the elderly with cardiovascular outcomes have demonstrated that it increases cardiovascular mortality, coronary artery disease, myocardial infarction, congestive heart failure and stroke. For this reason the practicing physicians and cardiologists must be aware of the importance and advances concerning the management of the presence of systolic hypertension in older patients.

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC7) states than in the older persons (those ≥60 years) systolic hypertension is a more important cardiovascular risk factor than diastolic hypertension and that control of systolic hypertension in the elderly is of paramount importance (18).

The effects of antihypertensive drug treatment in patients with systolic hypertension and its value in the secondary prevention of coronary artery disease and other vascular outcomes have been evaluated in a meta-analysis of clinical trials. The studies, patients and age of patients included in such meta-analysis appear in Table 3.

It is a metanalysis of outcome in trials of 15, 693 patients >65 years of age and above followed up for 3.8 years. It included the Systolic Hypertension in Elderly Program (SHEP)(19), Systolic Hypertension in Europe Trial (Syst-Eur)(20), Systolic Hypertension in China Trial (Syst-China) (21), European Working Party on High Blood Pressure in the Elderly (EWPHE) (22), the trial on Hypertension in Elderly Patients in Primary Care (HEP)(23), the Swedish

Metanalysis of Systolic Hypertension		
	Total Patients	Average Age
SHEP	4,736	72
SYST-EUR	4,695	70
SYST-CHINA	2,394	67
EWPHE	172	73
HEP	349	70
STOP	268	76
MRC1	428	62
MRC2	2,651	70

Table 3. Metanalysis of 15,693 elderly patients with Systolic Hypertension

Trial on Old Patients with Hypertension (STOP)(24), and the Medical Research Council Trials in mild hypertension (MRC)(25), and in older adults (MRC **2**)(26). It showed a beneficial effect of the treatment of systolic hypertension on cardiovascular outcomes. It revealed a decrease in total mortality of 13%, cardiovascular mortality in 18%, occurrence of fatal and non fatal events in 26%, stroke in 30% and coronary events in 23% (27). Recent trials have evaluated different anti-hypertensive regimes in older persons all demonstrating the beneficial effects with no overall differences in total mortality (28-31).

The SHELL Study on systolic hypertensives in the elderly documented similar benefits in treating hypertension in three old age groups (i.e.) 60 to 69 years, 70 to 79 years and e" 80 years of age (32).

Control of Blood Lipids

Multiple studies have demonstrated the value of lipid lowering therapy for primary and secondary prevention of coronary artery disease.

In the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) new policies concerning the evaluation and management of high blood cholesterol were recommended (33). These include intensive treatment of patients with coronary artery disease and emphasize upon the importance of instituting primary prevention in persons with multiple risk factors. Adults with coronary artery disease should get a lipoprotein profile and be classified by the LDL cholesterol level.

The NCEP has established categories of cardiovascular disease risk based on the levels in mg/dL of total cholesterol and LDL cholesterol in serum samples. It recommends management based upon the LDL-cholesterol level as the primary target of therapy.

The NCEP identifies 3 categories of risk that modify the goals and modalities of LDL-lowering therapy. Table 4 illustrates these categories of risk and shows the corresponding LDL-cholesterol goals for each risk category. The practicing physician is expected to be aware of the 2001 new NCEP report and guidelines concerning how to handle their patients with elevated cholesterol including those with and those without coronary artery disease as well as those with diabetes. Maximum LDL cholesterol for CAD patients should be 100 mg/dL.

Three categories of Risk that Modify LDL-Cholesterol Goals	
Risk Category	**LDL Goal**
CHD and CHD equivalents	< 100 mg/dL
Multiple (+2) risk factors	< 130 mg/dL
0-1 risk factors	< 160 mg/dL

Table 4. LDL-cholesterol goals based upon three risk categories.

The LDL-cholesterol lowering therapy available today consists of two modalities; therapeutic lifestyle changes (TLC) and drug therapy.

The essential features of therapeutic lifestyle changes are: diet with a reduced intake of saturated fats to <7% of total calories; total fat intake of no more than 30 % of the total calories; and a cholesterol intake of less than 200 mg/day; weight reduction therapy for overweight or obese patients; and increased physical activity. Regular physical activity reduces very low-density lipoproteins (VLDL) levels, raises HDL cholesterol, and in some persons lowers LDL-cholesterol levels.

The second modality of lipid lowering therapy consists of drug management. All patients in which drug therapy is instituted should also be kept on TLC therapy. Clinical trials, primarily with statins, have been able to confirm the effectiveness of the use of cholesterol lowering drug therapy in individuals that have had coronary artery disease or myocardial infarction (secondary prevention) or individuals with hypercholesterolemia without the presence as yet, of cardiovascular disease (primary prevention). The studies conducted have included a significant number of elderly subjects to demonstrate the usefulness of drug therapy in the aged. The current recommendation for those patients with coronary artery disease is to target the serum LDL-cholesterol level to < 100mg/dL. Table 5 presents the main studies on the use of statins on older patients with coronary artery disease.

It summarizes the earlier and recent studies concerning the use of statins for the secondary prevention of coronary artery disease in elderly patients.

The earlier lipid lowering drug intervention trials oriented to secondary prevention of CHD have been: the Scandinavian Simvastatin Survival Study known as 4S (34),

Statins in Secondary Prevention						
	4S	**CARE**	**LIPID**	**HPS**	**PROSPER**	**TNT**
Subjects	1,021	1,283	3,514	10,697	5,804	10,001
Follow-up years	5.4	5	6.1	5.5	3.2	4.9
Age (years)	65-75	65-75	65-75	66-80	70-82	mean 61
LDL Cholesterol	↓36%-	↓32%	↓25%		↓34%	-
LDL Cholesterol Level	-	-	-	65mg/dL	-	77mg/dL
Statin	Simva	Prava	Prava	Simva	Prava	Prava Atorva
Date	1994	1998	1998	2002	2002	2005

Table 5. Main studies concerning use of statins in elderlies with coronary artery disease.

the Cholesterol and Recurrent Events trial known as CARE (35), and the Long Term Intervention with Pravastatin in Isehemic Disease study known as LIPID (36).

The **4S** trial used Simvastatin 20-40 mg daily or placebo therapy in 4,444 men and women with CHD and hypercholesterolemia with a follow up of 5.4 years. It included 1,021 patients aged 65 to 75 years. Patients older than 65 years of age taking simvastatin had reductions in total mortality, total CHD deaths and major coronary events paralleling those in patients younger than 65 (34).

In the **CARE** trial, patients with CHD and an average total cholesterol level of 209 mg/dL, received pravastatin or placebo with a follow up of 5 years. It included 1283 patients aged 65 to 75 years. Older patients in CARE benefited as much as younger ones from pravastatin therapy (35).

In the **LIPID** Study 9014 men and women with myocardial infarction or unstable angina pectoris were randomized to pravastatin 40mg daily or placebo. Mean follow up was 6.1 years. It included 3514 patients in the 65 to 75 years age group. There was a reduction in total mortality, non-fatal myocardial infarction and coronary death for individuals on pravastatin therapy. The benefits of the drug therapy extended to the subgroup of patients older than 65 years as well as the younger ones (36).

Three recently published lipid lowering trials including coronary heart disease elderly patients have been: the Heart Protection Study known as HPS (37), the Prospective Study of Pravastatin in the Elderly at Risk known as PROSPER (38) and Treating to New Targets Study known as TNT (39).

The HPS trial used 40 mg of Simvastatin vs placebo in 10, 697 coronary heart disease elderlies aged 65-80 years followed up for 5.5 years. All cause mortality was 13% lower in the statin group, coronary death was 18% lower and a combined end point of non fatal myocardial infarction or coronary death was 27% lower. Of the individuals randomized 5,806 were at least 70 years of age at study entry and 1,263 individuals were aged 75-80 years (37).

The PROSPER study used Pravastatin vs placebo in 5,804 persons (men a women) aged 70-82 years followed up for 3.2 years obtaining a 15% lower end point (coronary death, non fatal myocardial infarction) in the pravastatin group (38).

The TNT study included 10,001 coronary patients, receiving atorvastatin, average age 61, followed for 4.9 years. It showed a highly significant reduction in events and expanded the benefit of more intensive statin therapy to patients with stable coronary artery disease (39).

The three studies HPS, PROSPER and TNT revealed a significant reduction in coronary events confirming the efficacy of statins in the secondary prevention of coronary artery disease demonstrating a reduction of all cause mortality, coronary artery disease mortality and myocardial infarction in the elderly individuals.

The findings from these and additional lipid reduction trials involving thousand of patients have resulted in new optional therapeutic targets outlined in the 2004 National Heart, Lung and Blood Institute's Adult Treatment Panel (ATP) III report (40). These changes include optional lower target cholesterol levels for high risk CHD patients. After the 2004, report mainly based upon the TNT (39) and the Incremental Decreased in End Points through Aggressive Lipid Lowering (IDEAL) study (41), it is considered that level of <100 mg dL should be for all patients with CAD and that it is reasonable to treat aimimg for a LDL-cholesterol of <70mg/dL.

Preventive and Therapeutic Life Style Changes

Diet

Patients must be aware of the deleterious effect that an inadequate diet could have upon his coronary artery disease including the additional negative effects if the patient concurrently suffers from overweight, arterial hypertension and dyslipidemia.

Certain basic principles should be mastered by each patient and the immediate family members that reside with him in order to maintain a healthy diet. A healthy diet should a have distribution of total calories per day based upon a body mass index (BMI) of 25kg/m^2 with a distribution of intake of approximately 23-25% total calories from fat; 50-60% from carbohydrates and 15% from proteins. Saturated fats should be reduced to <7% of the total calories, poli unsaturated fats up to 10% and monounsaturated fats up to 20%. Cholesterol food intake

should be less than 200 mg per day particularly if there is an increased serum level of cholesterol. The daily intake of fiber should be around 20 to 30 grams per day. Emphasis should be on an increased consumption of fresh fruits, vegetables and low-fat dairy products.

For patients who concurrently have hypertension a reduction of salt consumption is indicated. The reasonable level is a salt ingestion of no more than 6.0 grams of salt consumed per day. There is evidence of the usefulness of sodium reduction in the treatment of hypertension in older patients (42).

Epidemiologic studies have demonstrated that populations that consume 1 to 2 drinks of alcohol per day develop less coronary heart disease than the individuals that do not consume alcohol (43). Consumption of alcohol at larger quantities per day has deleterious effects upon hypertension and coronary artery disease. Besides, these subjects are as well bound to develop problems caused by alcohol consumption such as cirrhosis of the liver and others. Moderation on alcohol consumption is mandatory. Limit the consumption to no more than two drinks (1oz or 30 ml of alcohol e.g. 24oz of beer, 10oz of wine or 3oz of 80 proof whiskey) per day in men and to no more than one drink per day in women.

The daily total amount of calories, its distribution and its composition is a very important consideration when dealing with weight control and management while dealing with obesity and coronary artery disease.

Obesity

Obesity is a risk factor for the development of second coronary events in older men and women with CHD (44). This is primarily due to the prominent association with dyslipidemia, hypertension, and insulin resistance in older overweight individuals (45). Weight loss has the potential to act as a risk reduction intervention in this population.

Unfortunately, a recommended approach to weight reduction in the elderly has not been declared because of the paucity of data on the impact of exercise and diet on obesity in the elderly. The available literature suggests a small role for exercise alone (46). This probably is caused by the low levels of physical activity usually achieved by older patients with CHD. It is advisable to recommend more frequent and more prolonged periods of walking as an adjunct to dietary therapy in obese elderly patients with CHD.

When approaching obesity it is worthwhile to asses the body mass index and waist circumference of the patients. The goals should be a body mass index of 18.5 to 24.9 Kg/m^2 and the waist circumference <40 inches for men and < 35 inches for women measured horizontally at the level of the iliac crest.

Physical Inactivity

Physical inactivity has been recognized to be a risk factor for the development of coronary artery disease.

The prescription of exercise training for increasing physical activity in elderly patients with cardiovascular disease have been advocated as part of a multidisciplinary approach to secondary prevention. A standardized exercise program improves functional capacity and reduces activity-related symptoms. These changes in improved functional capacity occur as early as 12 weeks after training initiation, and modest improvement persists with extended participation (47). Despite lower absolute functional levels and smaller improvements in measures of exercise capacity, elderly patients derive significantly greater benefit in total functional scores and quality of life from increased physical activity than younger patients (48). In addition, exercise training positively impacts other CHD risk factors such as obesity, hypertension, and insulin resistance, even in patients older than 75 years. The ability of exercise training to reduce morbidity and mortality rates has not been well established for elderly patients, but limited data suggest some benefit. In the British Regional Heart Study, which enrolled 5,934 men with known CHD (mean age, 63 years), light to moderate physical activity in the form of regular walking, frequent recreational activities (e.g., gardening), or once-weekly sporting activities (e.g., jogging, swimming), was associated with a significant reduction in all-cause mortality over the five years of follow-up (49).

The Iowa Women's Health Study (40,417 women; mean age, 62 years), concluded that there was an inverse association between physical activity and all-cause mortality in postmenopausal women over the 7 year follow up (50). The Cardiovascular Health Study (5201 men and women; mean age, 73 years) suggested that the level of physical activity was an independent predictor of 5 year mortality (51).

The exercise prescription should not be limited to participation in structured programs, but should include occupational, leisure, and daily life activities. The program should promote all aspects of physical conditioning and encourage socialization in an effort to improve quality of life. Particular attention should be paid to the avoidance of high-intensity exercises that can adversely affect the knees and shoulders. The exercise recommended should be individualized, taking into consideration comorbidities such as arthritis and peripheral vascular disease. Increasing the frequency and duration of exercise sessions should take precedence over increasing the intensity of the activities, with an emphasis on strength training to promote independence in activities of daily living.

For all patients it is important for the physician to assess the risk with a physical activity history and an exercise

test. Patients should be encouraged to perform 30 to 60 minutes of aerobic activity such as walking all days of the week. When dealing with high risk patients such as a recent acute coronary syndrome or heart failure the exercise program should be medically supervised.

Preventive Measures in Diabetics with Coronary Artery Disease

The concurrence of diabetes mellitus is a powerful predictor for the development of secondary coronary events in elderly patients with coronary artery disease (52). The prevalence of insulin resistance and diabetes mellitus increases with age (53). Diabetic patients require an orderly and periodic supervision of the management of the diabetes in order to maintain it under control. The recommended therapeutic interventions are similar across all age groups and include dietary counseling, pharmacologic therapies (insulin and or glucose lowering medications) and life style modifications including exercise and weight control. Appropriate hypoglycemic therapy to achieve near-normal fasting plasma glucose levels with a goal of glycosylated hemoglobin (HbAlc) of <7% (7). In elderly patients, the lifestyle modifications leading to loss of body fat have a positive impact on insulin and glucose metabolism.

Performance of exercise improves insulin resistance and glucose control in healthy elderly persons. Diabetic patients need to be informed about the short hypoglycemic effects of exercise. Frequent fingerstick measurements before and after performance of exercise help to guide the therapy.

In diabetic patients with coronary artery disease vigorous modifications of other risk factors such as physical activity, weight management, blood pressure control and cholesterol management are strongly recommended.

Medications in Secondary Prevention of Coronary Artery Disease in Elderly patients

Antiplatelet Agents

Aspirin has been the most frequently used antiplatelet agent in the secondary prevention of coronary artery disease.

The Antiplatelet Trialists Collaboration Overview of trials of antiplatelet medications analyzed in 1994 trials with 54,000 patients at high risk (angina, myocardial infarction, stroke, bypass and angioplasty) and aspirin was found to reduce in 25% the risk of myocardial infarct, stroke or cardiac death. It was effective in elderly patients (54). The Cooperative Cardiovascular Project including 10,018 elderly medicare patients above 65 years of age (1,590 of them 85 years of age or older) showed that those receiving aspirin had a 22% lower mortality rate at 30-day follow-up (55) see Table 6. Daily aspirin is a secondary prevention measure that should be used by all these patients.

Aspirin in Acute Myocardial Infarction

Age Years	Total Patients	On Aspirin	Without Aspirin
65-74	4,320	2,824	1,496
75-84	4,108	2,456	1,652
ee85	1,590	859	731
Total	10,018	6,139	3,879

30 day mortality was 22% lower in those on Aspirin

Table 6. Effect of Aspirin in 10,018 elderly medicare beneficiaries with acute myocardial infarction

On a recent study conducted on 118,999 medicare patients 65 years of age or older of which 78,975 were on daily aspirin, multivariate analysis including multiple risk factors, revealed a decrease in mortality after one and 6 months follow up in those that received aspirin (56).

A study on Aspirin use in the Women Health Study included 39, 876 women ≥45 years of age followed for a period of 10 years. The study included 4,097 women at ≥65 of age. The elderly group only showed its preventive value by a decrease in the recurrence of myocardial infarction which was not observed in the younger age group (57). The AHA/ACC guidelines for Secondary Prevention for Coronary Disease recommend to start aspirin 75 to 162 mg per day and continue indefinitely in all CHD patients unless contraindicated. For patients undergoing coronary artery bypass grafting aspirin is recommended within 48 hours after surgery (8).

In patients with acute coronary syndrome or percutaneous coronary intervention the use of clopidogrel 75mg/day in combination with aspirin is recommended for a period up to 12 months (8).

Beta Blockers

Since 1981, the BHAT Study and other beta-blockers studies have shown that beta-blockers are indicated as a secondary preventive measure in patients with myocardial infarction (58). Recently, a study of 3,737 patients with acute myocardial infarction older than 65 years, of which 1,392 were 65 to 74 years of age, 1744 were 75 to 89 years of age and 601 were age 85and above, showed a reduced mortality rate at 2 years for those using beta-blockers (59). These results confirm the usefulness of b-blockers in the

elderly patient with MI. All patients who have had a myocardial infarction should be on secondary prevention of beta-blockers irrespective of age.

Renin-Angiotensin-Aldosterone System Blockers

ACE Inhibitors-ACE indicates angiotensin-converting enzyme.

The benefit of the use of angiotensin converting enzyme (ACE) inhibitors treatment in patients with heart failure are now well established, and all patients with heart failure and left ventricular systolic dysfunction should receive an ACE inhibitor. Trials have also investigated the late use of ACE inhibitors after myocardial infarction. Three of them have revealed significant favorable results (60). The SAVE (Survival and Ventricular Enlargement) trial consisted of 2,231 patients, aged 21-80 years with myocardial infarction under captopril or placebo and showed a 19% reduction in cardiac deaths at 3-year follow-up of those treated (61). The AIRE (Acute Infarction Ramipril Efficacy) trial consisted of 1,986 subjects, mean age 65 years, with myocardial infarction under Ramipril or placebo. It showed a 27% reduction in cardiac deaths at 1.5 years (62). The TRACE (Trandolapril Cardiac Evaluation) trial included 1,749 patients, mean age 68 years, with myocardial infarction under Trandolapril or placebo resulted in a 22% reduction in cardiac death at 2 years (63). The risk of reinfarction was reduced in the three studies.

All three trials are quoted in the American Heart Association/American College of Cardiology Practice Guidelines recommending ACE inhibitor therapy after acute myocardial infarction. The ACE inhibitor reduced total mortality by 19%, cardiovascular mortality by 21%, and the recurrence of ischemic events requiring revascularization was reduced by 25% over a follow-up period of 42 months. Fifteen per cent of the patients included were over 70 years of age.

The 2006 update of the AHA/ACC Guidelines for Secondary Prevention for Patients with Coronary Disease indicate that ACE inhibitors should be started and continued indefinitely in all patients with a left ventricular ejection fraction ≤ 40% and in those with hypertension, diabetes or chronic kidney disease unless contraindicated[8].

Angiotensin Receptor Blockers

The 2006 AHA/ACC report recommends to use angiotension receptor blockers in patients who are intolerant of ACE inhibitors and have heart failure or have had a myocardial infarction with left ventricular ejection fraction ≤40%. Also, is recommended for other patients who are ACE inhibitor intolerant (8).

Aldosterone Blockade

The 2006 AHA/ACC report recommends to use of aldosterone blockade in post myocardial infarction patients, without significant renal dysfunction or hyperkalemia, who are already receiving therapeutic doses of an ACE inhibitor and beta-blocker, have a left ventricular ejection fraction of ≤40% and have either diabetes or heart failure (8).

Conclusions

Secondary prevention intervention measures to impact and control risk factors of coronary artery disease in the elderly are summarized in Table 7.

Secondary Prevention of CAD in the Elderly

Lifestyle modifications

Behavior	Goal
Smoking	Cessation
Physical activity	30-60 min. daily activity
Weight management	BMI. 18.5-24.9 Kg/m²
	Waist:
	≤40 inches (men)
	≤35 inches (women)
Dietary	Moderate sodium, alcohol consumption
	Emphasis on fruits, vegetables, low fat dairy

Drug Treatment

Drug	Recommendations
Antiplatelet agents	Aspirin 75-162 mg/d
	Consider clopidogrel-ACS
B. Blockers	All post MI patients
ACE inhibitors	MI patients ejection fraction de ≤40%
Statins	Use LDL cholesterol level and risks
Antihypertensives	All hypertensive patients, ≥140/90

ACS-Acute Coronary Syndrome; **MI**-Myocardial Infarction

Table 7. Presents in outline form the lifestyle modifications and drug treatments indicated for secondary prevention of coronary artery disease in the elderly.

Preventive measures include lifestyle modifications and drug treatment. Lifestyle modifications are important concerning cigarette smoking, physical activity, obesity, weight management, moderation in alcohol and salt intake and improved dietary patterns. Drug treatment conveys use of antiplatelet agents (aspirin, clopidogrel), beta blockers, statins, antihypertensive agents and ACE inhibitors.

Special attention to be given to the presence of hypertension, abnormal blood lipids and elevated blood glucose. Evidence based information available today confirms that secondary prevention intervention measures are as effective in elderly coronary artery disease patients as observed in the younger ones.

Resumen

El 80% de las muertes coronarias ocurren en personas mayores de 65 años de edad. El 50% de las muertes en las personas mayores de 85 años de edad se debe a la enfermedad de las arterias coronarias. El envejecimiento de la población y el mejoramiento en la sobrevivencia de los pacientes con enfermedad coronaria ha estado creando una población creciente de adultos añosos que son elegibles para la prevención secundaria.

Múltiples ensayos clínicos y de investigación han provisto información basada en evidencia sobre prevención secundaria de la enfermedad coronaria en el envejeciente mediante el control de los factores de riesgo.

La prevención secundaria incluyendo la modificación de estilos de vida y la farmacoterapia modificando factores de riesgo ha reducido la morbilidad y mortalidad de la enfermedad coronaria en el añoso.

Información basada en evidencia en el envejeciente sobre cesar de fumar, tratamiento de la hipertensión arterial, control de la hiperlipidemia arterial, mejoramiento de patrones dietéticos, actividad física, moderación en el consumo de alcohol, manejo de la diabetes y la obesidad, el uso de antiplaquetarios, bloqueadores beta y bloqueadores de renina-angiotensina-aldosterona se resume en este escrito. Se le ha dado énfasis a los pronunciamientos de consenso emitidos conjuntamente por la AHA/ACC sobre enfermedad coronaria y su prevención.

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