PRIMARY PREVENTION OF CORONARY ARTERY DISEASE (REVIEW)

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DEFINITION

Primary prevention can be defined as to take steps for prevention of Coronary Heart Disease (CHD) in individuals who don't have CHD.

EPIDEMIOLOGY

Coronary heart disease (CHD) is a major cause of mortality and morbidity around the world. It is increasing in the developing world and in countries belonging to the former Soviet Union. It is estimated that worldwide deaths from CHD will increase 100% in men and 80% in women from 1990 to 2020. The main bulk of this increase will be in Asia, Africa, and Latin America. Disability adjusted life years lost will increase 107% in men and 74% in women worldwide[1]. The causes of this change have been identified as effluence in the society due to control over the environment, resulting in abundant food supply. Furthermore, a decline in infectious diseases resulting in prolonged survival, and technology of transportation providing sedentary life style contribute to the risk factors.

Historical Background:

The concept of prevention has been around for a long time. Medical writings of as early as 2500 BC refer to the practice of prevention. Hippocrates and Osler stressed the importance of prevention of diseases in their writings[2]. The interest in this concept was emphasized in the 33rd Bethesda conference, which specifically focused on CHD and formulated recommendations for prevention of this disease. CHD is the number one killer in USA today.

Five task forces provided in depth reports on preventive cardiology. As the cause of CHD is not known, so the cure cannot be achieved. There are,

however, well-established risk factors associated with it. Major risk factors are hyperlipidemia, diabetes, hypertension, smoking, and obesity. There are some minor risk factors as well like homocysteinemia, Marfan's syndrome, osteogenesis imperfecta, and cocaine addiction. A mass population intervention strategy started in 1970 in North Karelia, Finland, that has the highest mortality rate of CHD in the world, has shown a 50% reduction in CHD mortality [3,4].

Screening of the whole population is not feasible, and only high-risk populations need to be given primary prevention [5].

Screening of Target Population:

Special groups of people at risk should be screened like;

1. Clinical signs of hyperlipidemia, i.e corneal arcus, xanthomas and xanthelesmas
1. Obesity
2. Smoking
4. Family history of premature ischemic heart disease
5. Diabetes Mellitus including impaired glucose tolerance test.
6. Hypertension.
7. Homocysteinemia

Age group

Teenagers of families with premature CHD should be screened for the major risk factors for coronary artery disease. In the general population people from 35 years to 70 are recommended for testing. The risk of CHD below 35 is too low to justify widespread screening, while there is no advantage of intervention above 70 years of age.

Screening tests

The target people should have following tests,

A- ECG

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B- Blood sugar and if required, glucose tolerance test.
C- Lipids
D- Blood pressure check up, taking a history of smoking and of coronary artery disease.

1- Hyperlipidemia

Hyperlipidemia is the main risk factor of CHD amenable to primary prevention.
The most common inherited metabolic disorder causing CHD is heterozygous Familial Hyperlipidemia (FH). It is an autosomal dominant disorder with a prevalence of 1 in 500.There is a defect in low-density lipoproteins (LDL) receptors causing high levels of cholesterol - LDL 6.

Clinical signs

This disease shows signs of manifestation as early as mid 20. Tendon xanthomas over knuckles and Achilles tendons are major sings of this disease. The skin over these is normal. The xanthomata usually manifest in 20 years and increases up to 50 years, some 20% patients will never have these. In age group 20-39 there is fifty-fold increase in mortality as compared to 4 fold increase in mortality in overall 20 -70 years age group 7.

DIAGNOSIS

Simon Broome criterion requires 7
Definitive diagnosis -cholesterol> 7.5 mol/L in an adult (>6.7mmols/l in children under 16) Or LDL cholesterol > 4.9mmols/L in adults
Plus tendon xanthomas in-patient or first or second-degree relative.
Possible FH
Cholesterol >7.5 mol/l in an adult (6.7mmols/l in children under 16). Or LDL cholesterol >4.9mmols/l in adults. Plus family history of MI before 60 years in first-degree relatives. Or cholesterol > 7.5mmol /l in first or second-degree relative.

Triglycerides are not required in this criterion and are expected to lie in normal range. (2.30 mmol/l)or may be increased.

Other inherited hyperlipidemias
1.   Type 3 hyperlipidemia

2.   Familial combined hyperlipidemia

3.   Lipoprotein abnormalities 8.

Lipid measurements
A   Serum triglycerides
B   Total cholesterol

High density lipoproteins(HDL)are measured and LDL can be derived with Friedewald formula.

LDL cholesterol (mmol/l)=total cholesterol-HDL cholesterol-.45*triglycerides (mmol/l)) valid if triglycerides are taken fasting and are <4.0 mmol/l)9.

TREATMENT

1- Dietary Advice
Every body requires a healthy diet. It is an extremely important part of strategy against Coronary heart disease. The main aim is to reduce cholesterol but dietary stuffs labeled low cholesterol are not, all that is required. The main source of cholesterol is saturated fat and diets containing saturated fats are to be reduced. Monounsaturated fats are to be increased and so are intake of fruits and vegetables 10-13. Diet should also contain more fiber, fish , fruits and monounsaturated fats. American Heart Association(AHA) step 1 and step 2 diets recommend < 30% of total calories as fats.

AHA STEP 1 DIET
< 30% of total calories as fats, with8-10 % as saturated fats, polyunsaturated/ saturated fatty acids (p/S) ratio> 1.0 ,cholesterol intake< 300 mg / day and calories intake to achieve desirable body weight.
AHA STEP2 DIET
<30 % of total calories as fat, with < 7% as saturated fat, (P/S ratio >1:4: cholesterol intake < 200 mg / day and calorie intake to achieve desirable weight.

Things to Do
Reduce Fat intake. Saturated fats reduction helps to lower LDL cholesterol and to lose weight. Fats are high in calories but polyunsaturated and monounsaturated fats are to be used .Our foods contain four types of fats.

Saturated fats like butter, cheese, red meat and its products raise LDL cholesterol.

Polyunsaturated fats like Soya bean oil, corn oil, sunflower oil and reduced fats spreads are high in polyunsaturated fats, lower LDL and total cholesterol.

Monounsaturated fats like rapeseed oil olive oil and margarines high in monounsaturated fats raise HDL cholesterol.

Cholesterol rich foods like organ meet i.e. liver spleen kidneys; eggs and shellfish raise blood cholesterol although in small amount.

Eat oily fish like mackerel, salmon. Herring, kipper and sardines, twice a week.

Eat lots of fruits and vegetables. These contain antioxidant vitamins A C and E. These protect the good effects of polyunsaturated fats and stop the deposition of fatty material along the blood vessels.

Physical Exercise 30-45 min brisk walk or any other exercise on most days of a week improves blood lipid levels and reduces weight.

2-Drug Treatment.

 FH patients should be given intensive dietary advice and lipid lowering therapy. The drugs used for lipid lowering should be the statins except in children and in pregnancy. Fibrates and resins may be added if adequate reduction is not achieved.

Desirable levels of total cholesterol and LDL along with other risk factors are given in Framingham points table-1.

Table-1

Estimate of ten years risk (Framingham point score)14

Men	
Age	**Points**
20-34	-9
25-39	-4
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	11
s70-74	12
75-79	13

Total	Points				
Cholesterol	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	0
200-239	7	5	3	1	0
240-279	9	6	4	2	1
> 280	11	8	5	3	1

Total	Points				
Cholesterol	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
Nonsmoker	0	0	0	0	0
Smoker	8	5	3	1	1

HDL (mg/dl)	Points
≥ 60	-1
50-59	0
40-49	1
≤ 40	2

Systolic BP (mmHg)	If Untreated	If Treated
≤ 120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
≥ 160	2	3

10 Years risk for women	
Points Total	**10-years Risk%**
< 9	< 1
9	1
10	1
11	1
12	1
13	2
14	2
15	3
16	4
17	5
18	6
19	8
20	11
21	14
22	17s
23	22
24	27
≥ 25	≥ 30

10 Years risk for men

Points Total	10-years Risk%
< 0	< 1
0	1
1	1
2	1
3	1
4	1
5	2
6	2
7	3
8	4
9	5
10	6
11	8
12	10
13	12
14	16
15	20
16	25
≥ 17	≥ 30

Women

Age	Points
20-34	-9
25-39	-4
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	11
70-74	12
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Cholesterol	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
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240-279	11	8	5	3	2
>280	13	10	7	4	2

Total	Points				
Cholesterol	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
Nonsmoker	0	0	0	0	0
Smoker	9	7	4	2	1

HDL (mg/dl)	Points
≥ 60	-1
50-59	0
40-49	1
≤ 40	2

Systolic BP (mmHg)	If Untreated	If Treated
≤ 120	0	0
120-129	1	3
130-139	2	4
140-159	3	5
≥ 160	4	6

This table calculates risk contribution of age, sex, smoking, BP , total cholesterol and HDL cholesterol ,of a patient on a point score and works out 10-years risk of the patient. This risk category taken with LDL levels can help to decide what steps (i.e. life style modification and or drugs) are to be initiated.

Table-2

Risk category	LDL Goal	LDL level for life style changes	LDL level for drugs
CHD or CHD risk equivalent (10 year risk > 20%)	< 10 mg/dl	> 100 mg/dl	> 130 mg/dl
2+ Risk factors (10 year risk < 20%)	< 130 mg/dl	> 130 mg/dl	> 160 mg/dl
0-1 Risk factor	< 160 mg/dl	> 160 mg/dl	>190 mg/dl

The aim is to bring 10 years risk of a patient < 10% by tackling the modifiable risk factors (i.e. BP, smoking, obesity, diabetes and lipids). All patients with 0-1 risk factor have a 10 year risk < 10% so there risk assessment is not required. If triglycerides are > 500 mg/dl, first lower triglycerides to prevent pancreatitis.

* Very low fat diet (< 15% calories from fat)

* Weight reduction and physical activity

* Fibrates or nicotinic acid

When triglycerdes are < 500 mg/dl turn to LDL lowering therapy. If triglycerdes remains > 200 mg/dl after achieving LDL goal, intensify LDL lowering therapy or add fibrates or nicotinic acid.
Treatment of HDL if < 40 mg/dl

* Achieve LDL goal

* Intensify weight reduction & physical activity

* Achieve triglycerdes goal
* If triglycerdes < 200 mg/dl in CHD or CHD equivalent, consider fibrates or nicotinic acid

Drugs- Statins

Homogentisic acid co enzyme -A reductase inhibitors called statins have undergone many randomized primary prevention trialsWOSCOP, AFCAPS/TexCAPS39, 4S showing reduction in cholesterol and some increase in HDL level in the blood15-17. The statins have class effect and synthetic varieties have no added advantage. Pravastatin does not undergo phase-1 oxidation and instead is metabolized directly by phase -2 sulfation. Pravastatin is preferred in transplant recipients with hyperlipdemia and diabetics who require antifungal therapy for onychmycosis. Myalgia and increase in muscle enzymes in blood should be watched carefully. Cerivastatin was withdrawn from market in August 2001 after 52 deaths due to rhabdomyolysis 18.

The Joint British recommendations fixed the threshold to start statins at serum total cholesterol >=5,0 mmol/L19. The Standard Medical Advisory Committee (SMAC) recommends that people with coronary event rate 0f >= 3% per year, in primary prevention should be given a statin20. Both these committees fixed an ultimate aim of treating all those people with coronary risk of >= 1.5% per year ,if economy affords 19,21.

Other drugs like Fibrates and resins are to be added if desired levels of total cholesterol and triglycerides are not achieved or if there are side effects. A balance between benefits and side effects however is very important, as is the cost effectiveness. The cost effectiveness of statins in primary prevention is less well under stood than secondary prevention of CHD because lower absolute risk of CHD except in high risk patients One hopes that cost of statin will fall with time and with introduction of generic names.

2-OBESITY

It is defined as body mass index(BMI) >=30 kg/ m2. It effects all major risk factors adversely, like hypertension, cholesterol, triglycerides, glucose tolerance and thrombogenesis22,23. Obesity increases the deleterious effects of hyperlipidemia, hypertension or diabetes on coronary artery disease and is required to be tackled independently of these related risk factors 24. Waist circumference >= 88cm in women and >=102cm in men provides an easy estimate of excess weight as it indicates high relative risk.25. It is recommended that 5-10kg initial weight loss will set the patient on path to continue weight loss with enough encouragement. A strategy for weight loss should include diet modifications, exercise and change in life style.. A continuous encouragement is required to maintain the weight ,once lost.

Physical exercise

Sedentary life style is associated with increased risk of coronary heart disease 26. A 45 minutes brisk walk on most days of week appears to give enough benefit for coronary risk27-28. It reduces total cholesterol, LDL and increases HDL cholesterol 29. A study has shown recently that moderate physical exercise decreases mortality 30. Exercise results in a change of life style which can be easily extended to cessation of smoking, improved diet and weight loss, so it can affect coronary risk favorably in more than one way. It should be launched as a group based or community based programme 31.

3- SMOKING

Smoking has an adverse effect on coronary heart disease. It increases risk of coronary heart disease many fold 32. Any number of cigarettes are dangerous and should be stopped forth with .A strong and detailed informatory session and repeated reinforcements will help cessation of smoking.
 Nicotine replacement therapy has been shown to help reduce or stop smoking and can be recommended especially in heavy smokers, who smoke > 10 cigarettes/day 33.

Weight Gain:

Smoking cessation causes weight gain in most people. This makes stoppage of smoking rather problematic. Dietary advice and exercise plan should be started at the same time to keep weight under control 34.

Diet; Diet has an extremely complex relationship with cholesterol and coronary heart disease 35. Cholesterol can be increased even without intake of fatty foods and diet modification reduces coronary mortality even without reducing cholesterol perhaps through reducing thrombosis. Diet reduces cholesterol only upto modest degree ,only 5% 36. So diet although an important component of reducing cholesterol, it s effect should not end there .A Mediterranean diet which includes more fruits and vegetables and less fats has been shown to reduce coronary heart disease 37. A diet high in fruits and vegetable, nuts and grains is highly beneficial 38.

Margarines and other foods enriched with plant sterol and stenol esters enhance the LDL lowering effect of die,. by reducing absorption of cholesterol from the gut.

Alcohol: A moderate amount of alcohol intake reduces coronary risk by increasing HDL cholesterol. It is very difficult to keep alcohol intake at this level and increased intake causes hypertension, sudden death and a host of other cardiovascular and non-cardiac problems39,40.

4- Familial coronary heart disease

Coronary artery disease(CAD) has a strong familial component 41. Twin studies have identified genetic contribution to CAD that is more prominent in premature forms of the disease (.P-CAD)42. Many studies have supported for the independent genetic defects to be at work in familial forms of CAD.A positive family history has been reported as an independent risk factor 43,44. Defects in myocardial perfusion 45, endothelial dysfunction 46, and ECG abnormalities 47 have been found in healthy first - degree relatives of patients of P-CAD. These associations have been shown to persist after adjustment for classic risk favctors.In some first degree relatives of patients of P_CAD , metabolic abnormalities like hyperlipidemia.48,49,small, dense low density lipoprotein particles50, and hypertension51have been found suggesting that P-CAD in afflicted sibling pairs may be mediated in part by a familial, possibly genetic predisposition to these intermediate traits. A study of" Risk factors and Family CAD" has reported recently that classic , remediable risk factors are highly prevalent in patients with familial P-CAD , hence ,casting doubt that a major contribution of genes acting in the absence of these risk factors is unlikely 52. This calls for removal of these risk factors along with genetic counseling.

5-Diabetes Mellitus

Diabetes is a major risk factor for coronary artery disease. The metabolic and lipid abnormalities present in diabetics ,place them at par with patients who have coronary artery disease as for as risk stratification of coronary heart disease is concerned. Diabetics even if they don't have any evidence of vascular disease, their mortality and morbidity are much higher than age matched non-diabetics. Very strict control of diabetes reduces to some extent, the risk of coronary heart disease.

A special group of patients of metabolic syndrome are also at high risk of ischemic heart disease. These patients are candidates of intensive preventive and life style modification measures. The syndrome contains any 3 of the following 53.(table-3)

Abdominal obesity	waist circumference
Men	>102cm or 40 inches
Women	>88cm or35 inches
Triglycerides`````	>150mg/dl
HDL cholesterol	
Men	<40mg/dl
Women	<50mg/dl
BP	$\geq 130/\geq 85$ mmHg
Fasting glucose	≥ 110mg/dl

Hormone Replacement Therapy

Hormone replacement therapy reduces risk of CHD in women. Estrogen reduces LDL and raises HDL by 15% 54. It also improves endothelial function and has a beneficial effect on coagulation system55,56. Estrogen whether given alone or in combination with progesterone protects from CHD 57,64, along with protection against endometrial carcinoma in the presence of uterus.

6-Hypertension

Hypertension is a leading risk factor for CHD. Many community projects like The North Karelia Project

(1972-1997) have proved a significant decline in CHD due to control of hypertension, cholesterol and smoking. North Karelia remains a world leader in community health promotion 65. The Franklin Cardiovascular Health Program (1974- to the present) is serving 23 communities with objective to reduce cardiovascular deaths. This project has documented risk - factor reduction by detection, medical treatment and control of hypertension and has brought significant reduction in cardiovascular mortality 66. The contribution of hypertension towards CHD as risk factor is covered in Framingham score table. Hypertension should be treated so that 10 year risk of CHD comes down to < 10%.

7- Homocysteinemia:

Homocystein is an amino acid whose levels in the blood have been correlated with an increased risk for cardiovascular disease 67,68,69. Supplementing one's diet with folic acid, a vitamin, can reduce homocystein levels easily and effectively70. Vitamin B6 and B12 can also be used in combination with folate to achieve the same purpose.

However, it has not yet been shown that supplementation with these vitamins has any impact on reducing clinical cardiovascular events. Trials are underway to investigate this relationship 67.

SUMMARY

In conclusion there are three broad key groups of patients who require intensive primary prevention for CHD. The first group includes patients of 10 year CHD risk > 20% on Framingham scoring table (Table 1). The second group is of diabetic patients. The metabolic and lipid abnormalities in diabetics ,place them at high risk of CHD. These two groups are considered to be CHD risk equivalents. That is, their 10 year risk is similar to 10 year risk of an individual with CHD. A third group of patients known as of metabolic syndrome,(table-3) is also at markedly high risk of CHD and requires intensive primary prevention. The measures to bring down 10 year risk of CHD in these three groups include life style modifications and drugs. The life style modification include an array of steps to target diet, weight, smoking, physical activity, lipids and BP. These life style changes are to be employed prior to

or along with drug therapy to achieve optimal goal of primary prevention.

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