ROLE OF VARIOUS RISK FACTORS ASSOCIATED WITH CARDIOVASCULAR DISEASES

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Article Received on: 10/03/13 Revised on: 09/04/13 Approved for publication: 11/05/13

DOI: 10.7897/2230-8407.04511

IRJP is an official publication of Moksha Publishing House. Website: www.mokshaph.com

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ABSTRACT

Coronary Artery Disease (CAD) is the leading cause of cardiovascular mortality world wide. Increasing rate of CAD mortality and projected rise in CAD mortality for 2020 in the developing world necessitates immediate prevention and control measures. Cardiovascular disease (CVD) is generally due to reduced blood flow to the heart, brain or body caused by atheroma or thrombosis. It is increasingly common after the age of 60, but rare below the age of 30. Plaques (plates) of fatty atheroma build up in different arteries during adult life. These can eventually cause narrowing of the arteries, or trigger a local thrombosis (blood clot) which completely blocks the blood flow. Despite scientific evidence that evidence based drug therapy reduce mortality in patients with established CAD, these therapies continue to be underutilized in patients receiving conventional care. It is essential to identify and manage risk factors for coronary artery diseases and to implement unique and creative approaches to stimulate better adherence to practice guidelines, to improve the quality of care given to patients with CAD. Reduction of SBP, DBP, heart rate, and body fat%, total cholesterol, triglycerides and LDL after regular yogic practices is beneficial for cardiac and hypertensive patients. Emphasis focusing on conventional risk factors, lifestyle modifications, smoking cessation, reduction of central obesity through dietary modification and exercise, can be proved to be the key interventions for preventing CAD.

KEYWORDS: Coronary Artery diseases, Hypertension., Hyperlipidaemia, Risk Factors.

INTRODUCTION

Coronary Artery Disease is a collective term given to symptomatic manifestations of reduced blood flow in narrowed coronary arteries (those which supply the heart muscles).¹ Cardiovascular disease (CVD) can be thought of as a continuum that begins with the presence of cardiovascular risk factors and proceeds via progressive vascular disease to target organ damage, end-organ failure, and death. This concept has led to two important proposals: first, that intervention anywhere along the chain of events can disrupt the pathophysiologic process and thus confer cardiovascular protection; and second, because many cardiovascular events share the same etiology, it is essential to assess and treat a patient's total cardiovascular risk rather than to consider risk factors in isolation. The incidence of CAD varies greatly between countries and within them, but in all, the mortality from this cause rises rapidly with age. The worldwide prevalence of cardiovascular risk factors is increasing. Hypertension, which was identified in a recent World Health Organization (WHO) report as among the most important preventable causes of premature death, which is predicted to increase around 1.56 billion people by 2025.⁴ The development of concept of 'risk factors' and their relationship to the incidence of coronary artery disease evolved from prospective epidemiological studies in the united states and Europe. These studies demonstrated a consistent association between characteristics such as increase in the concentration of plasma cholesterol, the incidence of cigarette smoking, hypertension, clinical diabetes, obesity, age or male gender, and the occurrence of CAD.⁵

Coronary Artery Diseases represents a continuum of disease pathologies and its subsequent risks.¹ CAD can be classified as Chronic CAD and Acute Coronary syndromes (ACS)

Chronic CAD is almost always secondary to coronary arteriosclerosis leading to an oxygen supply and demand mismatch and a stable pattern of coronary ischemia.

Acute Coronary Syndrome (ACS) is acute myocardial ischemia, which is usually, but not always caused by atherosclerotic CAD and is associated with an increased risk of cardiac death and myonecrosis. It encompasses acute Myocardial Infarction (both resulting in ST elevation or non-ST elevation) and Unstable Angina. Unstable Angina (UA) is usually secondary to reduced myocardial perfusion resulting from coronary artery atherothrombosis. In this event however the non-occlusive thrombus that developed on a disrupted atherosclerotic plaque does not result in any biochemical evidence of myocardial necrosis.

Non-STEMI represents a clinical condition presenting very similarly to UA but with evidence of myonecrosis by some form of cardiac markers, without ST elevation on ECG. STEMI represents the most lethal form of ACS, one in which a completely occlusive thrombus results in total cessation of coronary blood flow in the territory of the occluded artery and the resultant ST-segment elevation on the ECG.¹ The major manifestation of CAD is angina, which is sometimes called angina pectoris, is chest pain that is caused by inadequate coronary blood flow to the myocardium. When coronary blood flow cannot deliver sufficient oxygen to support cardiac oxidative metabolism (reduced oxygen supply/demand ratio), the myocardium becomes hypoxic. This triggers pain receptors within the heart, which lead to the classical presentation of chest pain and the sensation of substernal heaviness or pressure.

There are three types of angina: Prinzmetal's variant angina, chronic stable angina, and unstable angina. All three forms are associated with a reduction in the oxygen supply/demand ratio. Variant (Prinzmetal's) angina results from coronary vasospasm, which temporarily reduces coronary blood flow (i.e., produces ischemia by reducing oxygen supply; "supply ischemia"), thereby decreasing the oxygen supply/demand ratio. Enhanced sympathetic activity (e.g., during emotional stress), especially when coupled with a dysfunctional coronary vascular endothelium (i.e., reduced endothelial

production of the vasodilators nitric oxide and prostacyclin) can precipitate vasospastic angina. Chronic stable angina is caused by chronic narrowing of coronary arteries due to atherosclerosis. When a coronary artery is narrowed beyond a critical value (critical stenosis), the myocardial tissue perfused by the artery will not receive adequate blood flow (i.e., the tissue becomes ischemic and hypoxic), particularly during times of increased oxygen demand (e.g., during physical exertion). The relative ischemia occurs when the oxygen demand increases, so this is referred to as "demand ischemia." This will lead to anginal pain during physical exertion. The pain usually is associated with a predictable threshold of physical activity. Other conditions that cause myocardial oxygen demand to increase, such as a large meal or emotional stress, can also precipitate pain. Unstable angina is caused by transient formation and dissolution of a blood clot (thrombosis) within a coronary artery. The clots often form in response to plaque rupture in atherosclerotic coronary arteries; however, the clot may also form because diseased coronary artery endothelium is unable to produce nitric oxide and prostacyclin that inhibit platelet aggregation and clot formation. When the clot forms, coronary flow is reduced, leading to a reduction in the oxygen supply/demand ratio ("supply ischemia"). If the clot completely occludes the coronary artery for a sufficient period of time, the myocardium supplied by the vessel may become infarcted (**acute myocardial infarction**) and become irreversibly damaged.⁶

Risk Factors

A risk factor may be defined broadly as "any habit or trait that can be used to predict an individual's probability of developing that disease." A risk factor so defined may be a causative agent or condition that can be used to predict an individual's probability of developing that disease.⁵ Modifiable risk factors for CVD—which include hypertension, smoking, abdominal obesity, abnormal lipids, and diabetes mellitus, as well as stress, low consumption of fruits and vegetables, and lack of regular physical activity—are the major contributors to cardiovascular morbidity and mortality and account for more than 90% of all myocardial infarctions (MI).²⁻³

Non-modifiable risk factors are those that cannot be changed and Modifiable risk factors that can be changed if the individual is willing to alter lifestyle, habits, diet, etc.

Non-modifiable risk factors :

Gender : Where morbidity from CHD in males is twice that in females and the condition occurs approximately 10 years earlier in men compared with women. Endogenous oestrogen is protective in women, but after the menopause the incidence of CHD rises steeply and parallels that seen in men. The use of oral contraceptives increases the risk of CHD approximately threefold with some evidence that the risk with the newer third generation preparations may be less.

Family History: A family history of CHD in a first-degree relative aged less than 70 years is an independent risk factor for the presence of CHD. Family aggregation of CHD suggests a genetic predisposition to the condition. **Age:** Risk of CHD increases with increase in age. It is more prevalent above the age of 65. Fifty-five percent of heart attacks occur in people age 65 or older.

Modifiable risk factors

Diabetes mellitus: Diabetes have more severe, aggressive, complex and more diffuse CHD than do age-matched controls. In general, coronary disease develops at a younger age than in the non-diabetic patients. The risk of developing CHD in the patient with NIDDM is two to four times higher than the general population and does not appear to relate to either the severity or duration of the diabetes. Diabetes, although an independent risk factor for CAD, is also associated with the presence of abnormalities of lipid metabolism, obesity, systemic hypertension and an increase in thrombogenesis (increased platelets adhesiveness and elevated levels of fibrinogen). **Systemic hypertension:** The risk of CHD is directly related to BP: for each 5mmHg, reduction in diastolic BP the risk of CHD is reduced by approximately 16%. Hypertension may contribute to its development in two ways: by accelerating the development of arterial disease and by increasing the workload of the left ventricle. **Smoking:** The risk of developing CHD from smoking is dose related with those smoking 20 or more cigarettes daily having a risk of two to three times that of the general population of developing a major coronary event. The role of smoking in the pathogenesis of CHD is complex and includes:

- Promotion of atherosclerosis
- Increase in thrombogenesis and vasoconstriction (including coronary artery spasm)
- Increase in Blood Pressure and Heart rate
- Increase in myocardial oxygen demand
- Reduction in oxygen carrying capacity

The risk of developing CHD from smoking falls to 50%1 year after smoking cessation and to normal within 4 years of quitting the habit.¹⁸

Obesity: There is an interrelationship between weight, and elevated BP, raised blood cholesterol, non-insulin dependent diabetes mellitus and low levels of physical activity. A high waist-to Hip ratio (common in South Asian Men) has been linked to coronary artery disease.

Dyslipidemia: There is a direct relationship between the risk of CHD and levels of blood cholesterol. Low levels of LDL cholesterol are implicated in CHD, there is an inverse relationship between HDL levels, and the incidence of CHD.

The role of triglycerides as a risk factor for CHD is controversial. Increased levels of lipoprotein (a) are an independent risk factor for CHD. The function of this protein is unclear but it has been implicated in familial CHD risk and can be found in atherosclerotic plaque in association with fibrinogen.

Behavioral risk factors: Stress, either physical or mental, is a risk factor for CHD. Coronary prone behavior (Type A Personality) includes aggression, competitiveness, hostility, cynicism, desire for recognition and achievement, sleep disturbances, road rage etc. Both anxiety and depression are important predictors of CHD.

Coagulation and fibrinolytic factors: A number of thrombogenic elements may influence the incidence of CHD, including levels of fibrinogen, endogenous fibrinolytic activity, blood viscosity and the levels of factors V11 and V111.

Homocysteine: A large amount of epidemiologic data suggests a graded relationship between homocysteine (HC) levels and coronary vascular disease. Endothelial dysfunction and a proatherogenic state are consequences of an increased HC. Until ongoing randomized trials conclusively resolve the question of whether intervention with folic acid and B vitamins are beneficial, no definite recommendation for therapy can be made. Nevertheless, the apparent absence of

an adverse effect of such therapy makes it reasonable to administer folic acid with B vitamins in selected high-risk subjects, especially those with renal disease or the elderly.

Management Of Coronary Artery Disease

The management of coronary artery disease (CAD) involves the practice of preventive cardiology, i.e. Primary prevention (preventing the first coronary event) and secondary prevention (preventing subsequent myocardial infarctions (MI) or other vascular events).

It was the identification of CAD risk factors in industrialized nations in the last century that lead to successful implementation of primary and secondary preventive measures.

The primary prevention strategies focus on preventing exposure to known CAD risk factors in individuals who have not manifested any signs of having CAD. Tobacco control, healthful dietary practices, and promotion of exercise are areas to be targeted for primary prevention.

The secondary prevention when the individuals have already had manifestations of CAD, such as myocardial infarction, secondary prevention must be undertaken, to try to reduce the incidence of further ischemic events.⁷

Treatment Modalities

Treatment of cardiovascular disease includes lifestyle changes, together with various approaches such as⁸

Pharmacological management: The primary goal in the management of CAD is to restore the balance between oxygen supply and oxygen demand in Myocardium. Four major factors that determine oxygen requirements in cardiac tissue are. Firstly the Preload the volume of blood returned to the heart through the vena cava and in the heart before it beats Then after load resistance to blood flow including opening of aortic valves and pushing blood through the arteries (peripheral vascular resistance or PVR) Then contractility, the forcefulness with which the heart contracts . Then the heart rate is the major determinant of cardiac output. The major manifestation of CAD is anginal pain which results from a temporary imbalance between the ability of the coronary arteries to supply oxygenated blood to cardiac muscle and the oxygen requirements of the tissue. Therefore, in order to alleviate the pain, it is necessary to improve this ratio. This can be achieved by either of two ways by Increasing blood flow (which increases oxygen delivery or supply) **Coronary vaso dilators** : Eg Calcium Channel Blockers, Nitrodilators . The Antithrombotic drugs Eg Anti Coagulats, Thrombolytics.

Decreasing oxygen demand (i.e., by decreasing myocardial oxygen consumption)Vaso dilators (reducing preload and afterload): Eg Nitrodilators, Calcium Channel Blockers .Cardiac depressants (reduce heart rate and contractility) Eg β Blockers, Anti arrhythmics^[9]. Drugs for the management of coronary artery disease are the Anti thrombotic drugs

which include Anti Platelets, Anti Coagulants, Thrombolytics.

The Anti anginals include Nitrates, Beta Blockers, ACE Inhibitors, Calcium Channel Blockers whereas the Lipid lowering drugs include Statins, Fibrate, Niacin, Ezetimibe, Bile acid sequestrants .

The Antithrombotic drugs are antiplatelet agents are medications that block the formation of blood clots by preventing the clumping of platelets.¹⁰⁻¹² The antiplatelets used in the management of Coronary Artery Disease are summarized in Table-1.

The Anti coagulants are also used in treatment ,an anticoagulant is a substance that prevents coagulation; that is, it stops blood from clotting. Anticoagulants available for parenteral use include UFH, various LMWHs, and hirudin, and for oral use, the antivitamin K drugs are available. Heparin exerts its anticoagulant effect by accelerating the action of circulating antithrombin, a proteolytic enzyme that inactivates factor IIa (thrombin), factor IXa, and factor Xa. Distinct advantages of LMWH over UFH include decreased binding to plasma proteins and endothelial cells and dose-independent clearance with a longer half-life that results in more predictable and sustained anticoagulation with once- or twice-a day subcutaneous administration. A major advantage of LMWHs is that they do not usually require laboratory monitoring of activity. Direct thrombin inhibitors very specifically block thrombin effects without the need for a cofactor such as antithrombin. Hirudin binds directly to the anion binding site and the catalytic sites of thrombin to produce potent and predictable anticoagulation. Coumarin derivative warfarin acts by inactivating Vit K in the hepatic microsomes thereby interfering with the formation of Vit K dependent clotting factors such as prothrombin.¹²

Thrombolytic drugs are used to dissolve blood clots in a procedure termed thrombolysis. They limit the damage caused by the blockage of the blood vessel. Acute myocardial infarction is the chief indication for thrombolytic therapy, and it should be instituted within 12 hrs of symptoms of onset. Three fibrinolytics Streptokinase, Urokinase and Alteplase (rt-PA) are available in India for clinical use. **Streptokinase** is antigenic, and can cause hypersensitivity reactions and anaphylaxis. It acts by combining with circulating plasminogen to form an activator complex which then causes limited proteolysis of other plasminogen molecules to plasmin.t1/2 is 30-80 min. **Urokinase** activates plasminogen directly and has a plasma t 1/2 of 10-15 min. It is non antigenic, but fever occurs during treatment. **Alteplase** is produced by recombinant DNA technology from human tissue culture; it specifically activates gel phase plasminogen already bound to fibrin, and has little action on circulating plasminogen. It is rapidly cleared by liver and has a plasma t1/2 of 4-8 min. It is non antigenic, but nausea, mild hypotension and fever may occur. In table 1 Antiplatelet drugs are listed.

Table 1: Antiplatelet Drugs

Drug class	Mechanism of Action	Dose	Contra-Indications	Adverse effects
Cyclooxygenase Inhibitors Aspirin	Inhibits cyclooxygenase-1 in platelets and megakaryocytes, and thereby blocks the formation of thromboxane A ₂ (a potent vasoconstrictor and Platelet aggregant).	LD>160mg MD: 70-150mg OD	NSAID hypersensitivity Active peptic ulcer Severe hepatic or renal disease	GI bleed Intracranial bleed GI toxicity Hypersensitivity Alopecia
Thienopyridines Clopidogrel Ticlopidine	Metabolized in the liver to active compounds which covalently bind to the adenosine phosphate (ADP) receptor on platelets and dramatically reduce platelet activation.	LD:300mg MD:75mg OD PO 250 mg twice Daily PO	Severe hepatic disease Pregnancy Lactation	Diarrhea Skin rash Thrombocytopenia Neutropenia Liver dysfunction
Phosphodiesterase inhibitors Dipyridamole	Inhibits phosphodiesterase, which inactivates cyclic AMP. Also stimulates prostacyclin release, and inhibits Thromboxane A ₂ formation.	200mg twice Daily PO	Severe CAD Subvalvular aortic Stenosis Haemodynamic Instability	Head ache GI upset Dizziness
Glycoprotein IIb/IIIa antagonists Abciximab Tirofiban	Prevent clumping of platelets by inhibiting a different receptor on the surface of platelets, the receptor for glycoprotein IIb/IIIa	Bolus: 250mcg /kg Infusion: 0.125mcg/kg/min Bolus: 0.4-0.6mcg/kg Infusion: 0.10-0.15mcg/kg/	Active bleeding Concurrent warfarin History of Intracranial bleed Previous thrombocytopenia Within 30 days of bleeding Major surgery Or severe trauma	Thrombocytopenia Bleeding Nausea Fever Headache Rash

The Anti anginals includes nitrates ,the **nitro dilators** are drugs that mimic the actions of endogenous Nitric Oxide (NO) by releasing NO or forming NO within tissues. These drugs act directly on the vascular smooth muscle to cause relaxation and therefore serve as endothelial-independent vasodilators. NTG reduces myocardial oxygen demand while enhancing myocardial oxygen delivery. NTG an endothelium independent vasodilator has both peripheral and coronary vascular effects .NTG dilates normal and atherosclerotic epicardial coronary arteries as well as smaller arteries that constrict with certain stressors (eg:cold ,mental or physical exercise).Topical or oral nitrates are acceptable alternatives for patients without ongoing refractory symptoms. Tolerance to the hemodynamic effects of nitrates is dose and duration dependent and typically becomes important after 24hrs of continuous therapy with any formulation. The **Beta blockers** competitively block the effects of catecholamines on cell membrane beta receptors. Beta 1 adrenergic receptors are located primarily in the myocardium; inhibition of catecholamine action at these sites reduces myocardial contractility, sinus node rate, and AV node conduction velocity. Through this action they blunt the heart rate and contractility responses to chest pain , exertion, and other stimuli. They also decrease systolic blood pressure. All these effects decrease myocardial oxygen demand.Beta blockers should be started early in the absence of contraindications. These agents should be administered intravenously followed by oral administration in high risk patients with ACS as well as in patients with ongoing rest pain or orally for intermediate and low risk patients.There is no evidence that any member of this class of agents is more effective than other, except that

beta-blockers without intrinsic sympathomimetic activity are preferable. The initial choice of agents includes metoprolol, Propranolol, or atenolol. The **Calcium Channel Blockers** are agents reduce cell transmembrane inward calcium flux, which inhibits both myocardial and vascular smooth muscle contraction; some also slow AV conduction and depress sinus node impulse formation. Nifedipine and Amlodipine have the most peripheral arterial dilatory effects but little or no AV or sinus node effects, whereas verpamil and diltiazem have prominent AV and sinus node effects and some peripheral arterial dilatory effects as well. The **ACE Inhibitors** act by producing vasodilation by inhibiting the formation of angiotensin II. This vasoconstrictor is formed by the proteolytic action of renin (released by the kidneys) acting on circulating angiotensinogen to form angiotensin I. Angiotensin I is then converted to angiotensin II by angiotensin converting enzyme. ACE also breaks down bradykinin (a vasodilator substance). Therefore, ACE inhibitors, by blocking the breakdown of bradykinin, increase bradykinin levels, which can contribute to the vasodilator action of ACE inhibitors. ACE inhibitors have shown to reduce mortality rates in patients with AMI or who recently had an MI and have LV systolic dysfunction, in diabetic patients with LV dysfunction, and in a broad spectrum of patients with high risk chronic CAD, including patients with normal LV function. Accordingly ACE inhibitors should be used in such patients as well as in those with hypertension that is not controlled with beta blockers and nitrates.

Lipid lowering drugs :The lipid lowering drugs commonly used are summarized in Table 2.

Table 2: Lipid Lowering Drugs

Drug class	with Doses	Lipid/Lipoprotein Effects	Side effects	Contraindications
HMG CoA reductase inhibitors (statins)	rosin (20-80 mg) atorvastatin (20-40 mg) rosin (20-80 mg) rosin (20-80 mg) rosin (10-80 mg) rosin (0.4-0.8 mg)	LDL $\sim$ 18-55% HDL $\sim$ 5-15% TG $\sim$ 7-30%	Myopathy Increased liver enzymes	Absolute Active or chronic liver disease Relative Concomitant use of certain drugs
Bile acid sequestrants	colestyramine (4-16 g) colestipol (5-20 g) cholestyramine (2.6-3.8 g)	LDL $\sim$ 15-30% HDL $\sim$ 3-5% TG No change or increase	Gastrointestinal distress Constipation Decreased absorption of other drugs	Absolute TG >400 mg/dL Relative: TG >200 mg/dL
Nicotinic acid	niacin release (line) nicotinic acid (1.5-3 gm)	LDL $\sim$ 5-25% HDL $\sim$ 15-35% TG $\sim$ 20-50%	Flushing, Hyperglycemia Hyperuricemia (or gout) Upper GI distress Hepatotoxicity	Absolute Chronic liver disease, Severe gout Relative: Diabetes, Hyperuricemia, Peptic ulcer disease
Fibric acids	fenofibrate (200 mg BID) rosin (1000 mg BID)	LDL $\sim$ 5-20% (may be increased in patients with high TG), HDL $\sim$ 10-20%, TG $\sim$ 20-50%	Dyspepsia Gallstones Myopathy	Absolute Severe renal disease Severe hepatic disease

2. Interventional procedures

Interventional procedures are **non-surgical** procedures used to treat blocked coronary arteries and increase blood flow to the heart. Interventional procedures are performed in the cardiac catheterization laboratory. A sheath (thin, plastic tube) is inserted into an artery in the groin or sometimes the arm. A long, slender tube called a catheter is inserted through the sheath and guided through the blood vessel to the arteries surrounding the heart.¹³

A diagnostic procedure called **coronary angiography** is performed, before the interventional procedures, to assess whether the coronary arteries are narrowed and/or whether the heart valves are working correctly. During angiography, a small amount of contrast material is injected through the catheter and is photographed as it moves through the heart's chambers, valves and major vessels.¹⁴

Balloon angioplasty (Percutaneous Transluminal Coronary Angioplasty or PTCA): A small balloon at the tip of a specially designed catheter is inflated to compress the fatty matter into the artery wall and stretch the artery open to increase blood flow to the heart.¹³

Stent : A stent is a small stainless steel tube that can be placed in a coronary artery at the point where it's blocked during an angioplasty. It helps to keep the artery open so that blood may flow freely. A stent remains in the artery permanently, holding it open, improving blood flow to the heart muscle and relieving symptoms such as chest pain. Over a several-week period, the artery heals around the stent. A drug-eluting stent represents a revolutionary breakthrough that helps to ensure the sustained benefit of angioplasty in patients with coronary artery obstructions. The key ingredient is a drug called rapamycin, which is slowly released into the vessel lining, to prevent scar tissue growth through the openings in the stent mesh, which frequently leads to reblockage. **d. Atherectomy** : Atherectomy is a procedure to open coronary arteries by removing plaque (cholesterol and other fatty substances) from the arteries. Directional coronary atherectomy (DCA) is a surgical technique that uses a catheter with an inflatable balloon to push a cutting device against the blockage. The **Rotablation** (Percutaneous Transluminal Rotational Atherectomy or PCRA) is a special

catheter, with an acorn-shaped, diamond-coated tip, is guided to the point of narrowing in the coronary artery. The tip spins around at a high speed and grinds away the plaque on your artery walls. This process is repeated as needed to improve blood flow. The microscopic particles are washed safely away in the blood stream and filtered out by the liver and spleen. The **cutting balloon** catheter has a special balloon tip with small blades. When the balloon is inflated, the blades are activated. The small blades score the plaque, then, the balloon compresses the fatty matter into the artery wall.¹³⁻¹⁴

3. Cardiovascular surgery

Coronary Artery Bypass Graft Surgery (CABG) is performed to create a detour for the blood to bypass a blocked coronary artery. Usually two or more of the major arteries to the heart must have severe blockage before physicians recommend surgery. The heart surgeon takes a piece of blood vessel from another part of the body, usually a leg vein or an artery from the chest and grafts it to bypass the blockage.¹⁵

4. Life style modification

Patients with documented coronary artery disease should actively pursue lifestyle modifications that reduce the risk of future cardiovascular events.¹⁶

Smoking cessation: Tobacco use is one of the most important contributors to recurrent cardiovascular events. Tobacco use induces endothelial dysfunction, reduces coronary vasoreactivity, increases circulating carbon monoxide levels, impairs functional status, and raises blood pressure. Smoking cessation is imperative, and it is more likely to be successful for those patients who are counseled by a physician or who enroll in a formal smoking cessation program that can be multifaceted to include addictive therapy, behavioral therapy, hypnosis, and acupuncture. Nicotine replacement therapy and bupropion are the pharmacologic agents of choice.

Exercise : Functional capacity is a strong predictor of major adverse cardiac events. Functional capacity can be improved by following an exercise program that entails at least 30 minutes of exercise 3 or 4 days per week; a daily regimen is optimal. This is especially important for those patients who

have either suffered a myocardial infarction or underwent a coronary artery revascularization procedure.

Weight Control: The best weight management strategy is diet and exercise. Ideal benchmarks are a body mass index between 19 kg/m² and 25 kg/m² and a waist circumference of not more than 40 inches for men and 35 inches for women. Weight loss has a favorable metabolic syndrome impact on many cardiac risk factors, including hypertension, a high LDL level, a low HDL level, and glucose intolerance.¹⁷

Vegetarian Diet : Vegetarians have been shown to have a 24% reduced risk of dying of heart disease. Despite the strong benefits of a vegetarian diet, it is likely that with a few changes to the typical vegetarian diet, the risks of heart disease could be reduced even further. Vegetarian diets are sometimes low in Vitamin B12, which can lead to increased homocysteine levels—a risk factor for heart disease. Since vegetarians do not eat fish, some vegetarians do not have high intakes of Omega-3 fatty acids. There is strong evidence that higher intakes of Omega-3 fatty acids reduce the risk of heart disease. Both of these shortcomings can be easily overcome by taking a vitamin B12 supplement and increasing intake of omega-3 fatty acids via ground flax seeds or flax oil, walnuts, and canola oil.

Effects on different population

Hypertension is highly prevalent among populations of African descent in Europe and North America and deserves a special detailed outline in these populations. The increased prevalence of hypertension among these populations in Europe appears to be a major contributor to the observed elevated stroke risk.¹⁸ Over the past decades there seems to be a trend towards a decrease in cardiovascular mortality in North America and Western Europe.²¹ The profile of CVD, however, varies among the developing countries. Countries in the earliest phases of epidemiological transition have a large burden of rheumatic heart disease, as well as infectious and nutritional cardiomyopathies.²⁵ The Mediterranean populations—Greeks and Italians in particular—have been reported to have among the highest life expectancies and the lowest incidence rates of all-cause mortality.³⁰ According to the World Health Organization, the standardized cardiovascular mortality rates vary considerably between northern and southern European populations. Moreover, results from the 25-year follow-up of the Seven Countries Study indicate that the prevalence of cardiovascular disease varied from 2%–10% in southern European countries and from 10%–18% in northern European countries. The investigators attributed the differences in mortality rates between the 16 cohorts to the nutritional habits of the participants and, in particular, to the intake of saturated fatty acids and flavonoids.³⁰

Genetic and Gender influence on CAD

The genetic variable underlying sex differences in cardiovascular disease is the complement of sex chromosomes (XX or XY). Genes on the X chromosome affect development of cardiovascular diseases through modulation of mitochondrial function, adiposity, response to hypoxia, apoptosis, and response to androgens.²⁶ Despite these shortcomings, many treatment modalities identified

from major clinical studies may apply to women, but with some exceptions.²⁷

Traditionally, coronary heart disease (CAD) has been considered as a disease predominantly affecting men and for a long time women were not included in cardiovascular research programs. Although the life-time risk of CHD is one in three for women¹⁹, they are still not fully aware of their risk of CHD and perceive the chance of dying of breast cancer as far more likely than of CHD.²⁰ Unique to women is the influence of their hormonal status on CHD.²² In comparison with men of a similar age and postmenopausal women, the incidence of CHD is significantly lower in premenopausal women suggesting that endogenous estrogens have a protective effect on the development of CHD.^{23,24} Observational and epidemiologic studies provide convincing evidence that administration of estrogen-based therapy reduces both all-cause and cardiovascular mortality associated with these conditions in women.^{27,28,29}

Recommendations

Firstly establish CVD and its risk factors as an urgent public health priority,

Increase funding and resources to combat CAD and to improve monitoring and evaluation. We can emphasize prevention as key and use public policy to make healthful choices easier. Form comprehensive and innovative collaborations involving public, private and nonprofit sectors. Policies that support comprehensive tobacco control programs—those which combine school-based, community-based and media interventions—are extremely effective at curbing smoking and reducing the incidence of cancer and heart disease. We have to promote wellness programs and media campaigns—the importance of health screenings in primary care settings are proven to help reduce rates of chronic disease. We have to promote physical activity among kids and adults this can reduce rates of obesity and help prevent other chronic diseases.

Policies that give kids healthier food choices at school can help curb rising rates of youth obesity. Ensuring that every neighborhood has access to healthy foods will improve the nutritional status of our country.

CONCLUSION

The high burdens of CAD in the developing countries are attributable to the increasing incidence of atherosclerotic diseases, perhaps due to urbanization and higher risk factor levels (such as obesity, diabetes, dyslipidemia, hypertension, etc), the relatively early age at which they manifest, the large sizes of the population, and the high proportion of individuals who are young adults or middle-aged in these countries.

We should establish CVD and its risk factors as an urgent public health priority. We should spread awareness, most of us are not aware of the connection of the risk factors for heart disease and their personal risk of falling victim to this disease.

REFERENCES

1. Ravi Rasalingam, Thomas A. Pearson. An Integrated approach to risk factor modification. Eric J Topol, Robert M. Califf, Jeffrey M. Isner, Eric N. Prystowsky, Judith L Swain, James D Thomas et al. Text Book of Cardiovascular Medicine, 2nd Edition, Lippincott Williams & Wilkins 2002: 247-261.
2. Dzau VJ, Antman EM, Black HR, Hayes DL, Manson JE, Plutzky J, Popma JJ, Stevenson W. The cardiovascular disease continuum validated: clinical evidence of improved patient outcomes: part I:

- pathophysiology and clinical trial evidence (risk factors through stable coronary artery disease). *Circulation* 2006;114:2850–2870.
3. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, McQueen M, Budaj A, Pais P, Varigos J, Lisheng L, for the INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;364:937–952.
 4. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet* 2005;365:217–223.
 5. JM Gaziano. Global Burden of Cardiovascular disease. Zipper, Libby, Bonow, E Braunwald. Braunwald's Heart Disease-A Textbook of cardiovascular medicine, 7th Edition, 2005:1-19.
 6. Desmond G Julian, Diseases of the Coronary Arteries- Causes, Pathology and Prevention. Desmond G Julian, J C Cowan, J M Mclenachan. Cardiology 8th Edition Elsevier; 2005: 78-88.
 7. Karen Okrainec, Devi K.Banerjee, Mark Jeisenberg. Coronary artery disease in the developing world. *American Heart Journal* 2004; 148: 7-15.
 8. Coronary Artery Disease [Cited on 20/4/2012] ; Available from URL: <http://www.texheart surgeons.com/cad.htm>
 9. Richard E. Klabunde. Cardiovascular Pharmacology Concepts. [Cited on 6/01/2012] ; Available from URL <http://cvpharmacology.com/clinical%20topics/angina-2.htm>
 10. Bertram G Katzung, Kanu Chatterjee. Vasodilators and the treatment of Angina Pectoris. Bertam G. Katzung. Basic & Clinical Pharmacology, 9th Edition, Mc Graw Hill Publications, New York, 2004: 184-199.
 11. K.D Tripathi. Drugs Affecting Coagulation Bleeding and Thrombosis. K D Tripathi. Essentials of Medical Pharmacology, 5th Edition, Jaypee Brothers medical Publishers, New Delhi; 2003: 557-574.
 12. Lionel H O, Bernard J Gersh. Which Therapy for Which Condition. Lionel H O, Bernard J Gersh. Drugs for the Heart. 6th Edition, 349-358.
 13. Coronary Artery Disease Treatment - Coronary Interventions Angioplasty, Stents And Atherectomy [Cited on 14/1/2012] ; Available from URL: http://www.clevelandclinic.org/heartcenter/pub/guide/disease/cad/treatment_interventional.htm
 14. Options for treating coronary artery disease [Cited on 15/4/2012] ; Available from URL: <http://www.ynhh.org/cardiac/diagnosis/treatment.html>
 15. Cardiac Diseases: Coronary Artery Diseases. [Cited on 29/4/2012] Available from URL: <http://www.columbiasurgery.org/pat/cardiac/chd.html>
 16. Coronary heart disease [Cited on 8/5/2012], Available from URL: http://en.wikipedia.org/wiki/Coronary_heart_disease.
 17. Coronary artery disease [Cited on 19/5/2012], Available from URL: <http://www.clevelandclinicmeded.com/diseasemanagement/cardiology/cad/cad.htm#therapy>
 18. Charles Agyemang, Juliet Addo, Raj Bhopal, Ama de Graft Aikins and a. Karien Stronks Cardiovascular disease, diabetes and established risk factors among populations of sub-Saharan African descent in Europe: a literature review, Published: 11 August 2009, Globalization and Health 2009, 5:7 doi:10.1186/1744-8603-5-7,
 19. Lloyd-Jones DM, Larson MG, Beiser A, Levy D. Lifetime risk of developing coronary heart disease. *Lancet* 1999;353:89–92.
 20. Legato MJ, Padus E, Slaughter E. Women's perceptions of their general health, with special reference to their risk of coronary artery disease: results of a national telephone survey. *J Womens Health* 1997;6:189–198
 21. Rosamond WD, Chambless LE, Folsom AR et al. Trends in the incidence of myocardial infarction and in mortality due to coronary heart disease, 1987–1994. *New Engl J Med* 1998;339:861–867.
 22. Jeanine E. Roeters van Lennep, H. Tineke Westerveld, D. Willem Erkelens, Ernst E. vander Wall, Risk factors for coronary heart disease: implications of gender, The Netherlands, Cardiovascular Research 53 (2002) 538–549, Elsevier, 21 May 2001
 23. van der Schouw YT, van der GY, Steyerberg EW, Eijkemans JC, Banga JD. Age at menopause as a risk factor for cardiovascular mortality. *Lancet* 1996;347:714–718.
 24. Hu FB, Grodstein F, Hennekens CH et al. Age at natural menopause and risk of cardiovascular disease. *Arch Intern Med* 1999;159:1061–1066
 25. K Srinath Reddy, Cardiovascular diseases in the developing countries: dimensions, determinants, dynamics and directions for public health action, All India Institute of Medical Sciences, New Delhi, Public Health Nutrition: 5(1A), 231–237, DOI: 10.1079/PHN2001298
 26. Miller VM. Sex-based differences in vascular function. *Women's (London Engl)*. 2010;6(5):737–752.
 28. Mosca L, Benjamin EJ, Berra K, et al; American Heart Association. Effectiveness-based guidelines for the prevention of cardiovascular disease in women—2011 update: a guideline from the American Heart Association. *Circulation*. 2011;123(11):1243–1262.
 29. Kalantaridou SN, Naka KK, Bechlioulis A, et al. Premature ovarian failure, endothelial dysfunction and estrogen-progestogen replacement. *Trends Endocrinol Metab*. 2006;17(3):101–109.
 30. Shuster LT, Gostout BS, Grossardt BR, Rocca WA. Prophylactic oophorectomy in premenopausal women and long-term health. *Menopause Int*. 2008;14(3):111–116.
 31. Shuster LT, Rhodes DJ, Gostout BS, et al. Premature menopause or early menopause: Long-term health consequences. *Maturitas*. 2010;65(2):161–166.
 32. Anastasios S Dontas, Nicholas S Zerefos, Demosthenes B Panagiotakos, and Dimitrios A Valis, Mediterranean diet and prevention of coronary heart disease in the elderly, *Clin Interv Aging*. 2007 March; 2(1): 109–115. PMID: PMC2684076
 33. Murray CJL, Lopez AD, eds. The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability from Diseases, Injuries, and Risk Factors in 1990 and Projected to 2020. Boston, Mass: Harvard School of Public Health; 1996.

Cite this article as:

Pranay Wal, Ankita Wal, Nikita Saraswat, Shalini Singh, Shikha Bajpai. Role of various risk factors associated with cardiovascular diseases. *Int. Res. J. Pharm.* 2013; 4(5):44-50