Cardiovascular risk factors: lipids and lifestyle changes

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A b s t r a c t

Most of the modifiable risk factors of cardiovascular diseases can be treated by lifestyle changes. Nevertheless, treatment strategies concentrate almost solely on pharmaceutical interventions, neglecting the beneficial effects of heart healthy diets and exercise training programmes. The above also holds true for metabolic syndrome (MS), which is a cluster of multiple risk factors that include diabetes mellitus type 2 (T2DM), high blood pressure, central obesity, decreased HDL cholesterol, elevated LDL cholesterol and triglycerides. Whereas the pathophysiology of the metabolic syndrome is extremely complex, the first line interventions are lifestyle changes in conjunction with pharmacological management of dyslipidaemia, hypertension and hyperglycaemia. High serum cholesterol has been increasingly recognized as a major risk factor for coronary heart disease (CHD) and current research focuses on the concept that LDL is the predominant atherogenic lipoprotein. Regular exercise training and healthier eating in combination with pharmacological intervention, if needed, reduce waistline and body mass index, lower blood pressure and improve lipid profile to a great extent.

Key words: coronary artery disease, diabetes mellitus, metabolic syndrome, exercise training, statins.

Introduction

According to the American Heart Association, the metabolic syndrome is characterized by a group of metabolic risk factors including abdominal obesity; atherogenic dyslipidaemia; elevated blood pressure; insulin resistance or glucose intolerance; prothrombotic state; and proinflammatory state.

Patients with MS are at increased risk of coronary heart disease (CHD) and other diseases related to plaque build-ups in arterial walls (e.g. stroke and peripheral vascular disease) and type 2 diabetes. Other conditions associated with the syndrome include physical inactivity, hormonal imbalance and genetic predisposition.

There are no well-accepted criteria for diagnosing the metabolic syndrome. The criteria proposed by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) [1], with minor modifications, are currently recommended and widely used. The American Heart Association, the Adult Treatment Panel III (ATP III) [1], The International Diabetes Foundation Federation (IDF) [2] and the National Heart, Lung, and Blood Institute recommend that the metabolic syndrome be identified as the presence of three or more of the following components (Table I).

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Table I. Criteria of metabolic syndrome

	Men	Women
Waist circumference	≥40 inches (102 cm)	≥35 inches (88 cm)
Triglycerides	≥150 mg/dL	≥150 mg/dL
HDL cholesterol	≤40 mg/dL	≤50 mg/dL
Blood pressure	≥130/85 mmHg	≥130/85 mmHg
Fasting glucose	≥100 mg/dL	≥100 mg/dL

Table II. Modifiable risk factors for CHD

physical inactivity
smoking
hypercholesterolaemia
hypertriglyceridaemia
low HDL cholesterol
arterial hypertension
hyperglycaemia

The primary goal of the clinical management of MS is to reduce the risk for cardiovascular disease and type 2 diabetes. Then, the first-line therapy is to concentrate on the major modifiable risk factors for cardiovascular disease (Table II).

For managing both long- and short-term risk, lifestyle changes are the first-line interventions to reduce the metabolic risk factors.

Lifestyle interventions

Risk factors involved in the metabolic syndrome can be altered by lifestyle changes such as diet, physical activity, and smoking. The risk of developing MS is substantially lower in individuals who are physically active, non-smoking, have a relatively low carbohydrate intake and moderate alcohol consumption, and who maintain a BMI in the non-obese range [3]. Treatment of obesity, encouragement of physical activity and healthier diet through lifestyle modification characterize the basic foundation for the treatment of MS. Cholesterol has a significant positive linear relationship with weight change. Weight loss in obese patients has long-term beneficial effects especially on LDL and cholesterol and glucose tolerance, blood pressure and insulin sensitivity [4-6].

In 2006, evidence-based nutritional recommendations for the treatment and prevention of type 2 diabetes and the metabolic syndrome were published [7].

According to these recommendations:
- protein should contribute up to 10-20% of total daily energy;
- saturated fatty acids and trans-unsaturated fatty acids should be no more than 10% of total energy and further lowered to less than 8% if the serum LDL-C level is increased;
- cholesterol intake should be 300 mg or less per day;
- carbohydrate intake should range between 45 and 60% of total energy.

To recapitulate, in management of both long- and short-term risk, lifestyle therapies are the first-line interventions to reduce the metabolic risk factors.

These lifestyle interventions include:
- weight loss to achieve a desirable body weight (BMI less than 25 kg/m^2);
- increased physical activity, with a goal of at least 30 min of moderate-intensity activity on most days of the week;
- healthy eating habits that include reduced intake of saturated fat, trans fat and cholesterol.

Management of obesity

Obesity is becoming a global epidemic [8] and in the past 10 years in the Western world, dramatic increases in obesity have occurred in both children and adults. Recently, the AHA has addressed and reviewed a variety of weight loss approaches for the management and treatment of obesity.

Modest weight loss can improve diastolic function and affect the entire cluster of coronary heart disease risk factors simultaneously. This statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism reviews the relationship between obesity and the cardiovascular system, evaluates the effect of weight loss on coronary heart disease risk factors and coronary heart disease, and provides practical weight management treatment guidelines for cardiovascular healthcare professionals. The data demonstrate that weight loss and physical activity can prevent and treat obesity-related coronary heart disease risk factors and should be considered a primary therapy for obese patients with cardiovascular disease [9]. Particular emphasis has been placed on visceral obesity, as the visceral adipose tissue appears to be particularly reactive in response to tissue growth. Recent studies have pointed out a strong association between intra-abdominal fat and metabolic syndrome [10].

Weight loss in obese patients has long-term beneficial effects especially on LDL and cholesterol and glucose tolerance, blood pressure and insulin sensitivity [4, 6].

Even moderate weight loss can be associated with major effects on all components of the metabolic syndrome and related risk factors [1, 10-12]. As diet and physical exercise may be difficult to put into practice and maintain over time, pharmacological interventions may then become necessary to contribute to weight loss and maintenance.

Management of atherogenic dyslipidaemia

Atherogenic dyslipidaemia is an important component of MS and is characterized by increased levels of triglycerides and apolipoprotein (apo) B, small and dense low-density lipoprotein cholesterol (LDL-C) particles, and low levels of high-density lipoprotein cholesterol (HDL-C) [13-15].

Elevated LDL-C is a major cause of coronary heart disease (CHD). The relationship between LDL-C and CHD risk is continuous over a broad range of LDL-C levels: the higher the LDL-C level, the greater the CHD risk.

Although national guidelines for cholesterol management have existed since 1988 [16], many individuals who are treated for elevated cholesterol have not achieved their targeted cholesterol levels. Studies [17, 18] show that 17 to 73% of treated patients actually meet their target levels, whereas people at greatest risk fail to do so. The Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults known as Adult Treatment Panel III (ATP III) [16-18] called for more aggressive treatment of hypercholesterolaemia. These guidelines have substantially increased the number of people who should receive lifestyle and drug treatment. To help patients achieve the target cholesterol and triglyceride (TG) levels necessary to reduce cardiovascular risk, a multidisciplinary, collaborative approach to patient care is essential.

Lipid management often requires extensive lifestyle counselling in addition to prescribed drug therapies. Because of physicians' time limitations and the expertise of other healthcare providers, patients' needs are best met by a collaboration of physicians, nurses, dieticians, and exercise specialists, among others. Several studies have shown improved outcomes with a collaborative approach to CHD prevention [13].

Nutritional management of lipids

Effective nutrition education and support can improve blood lipids and body mass; improve physical activity levels; reduce insulin resistance; improve the health of people with type 2 diabetes mellitus who control their glucose; and decrease the development of type 2 diabetes.

The inclusion of nutrition is key to a collaborative approach. There is evidence from dietary studies that a marked reduction in LDL-C decreases the risk

of CHD [19-22]. The principal dietary strategy for lowering LDL-C levels is to replace cholesterol-raising fatty acids (i.e. saturated and trans fatty acids) with dietary carbohydrate and/or unsaturated fatty acids. By that standard, risk is reduced most effectively when trans fatty acids and saturated fatty acids are replaced with cis unsaturated fatty acids. The effects of carbohydrates and of lauric acid-rich fats on CAD risk remain uncertain [23]. The increasing interest in accounting for genetic components of cardiovascular disease may help further understanding of inter-individual variations in response to dietary interventions and offer personalized medicine for both preventative and therapeutic management of CHD.

Physical activity

The importance of physical activity, like nutrition, cannot be overestimated. First of all exercise training studies observe lower plasma triglyceride concentrations [24, 25]. Exercise training studies do not support an exercise-induced change in total cholesterol, although exercise training longer than 12 weeks with good adherence is more likely to increase plasma HDL-C [13, 26-31] in a dose-dependent manner.

Current data support a favourable impact of exercise training on lipid and lipoprotein profiles. Furthermore, the incidence of diabetes mellitus correlates inversely with the degree of physical activity [32]. Regular aerobic exercise of 30 min/day at a moderate intensity can cut the risk for impaired glucose tolerance by half and the diabetes risk by up to three quarters [33, 34].

Although there is no direct proof that endothelial dysfunction leads to atherosclerosis, it has been shown that endothelial dysfunction is associated with increased cardiovascular mortality [33, 35]. Endothelial dysfunction is found when the endothelium has been damaged. This occurs as a result of smoking, hyperglycaemia, hyperlipidaemia, and hypertension. It can be improved by intensive physical exercise not only in normoglycaemic patients but also in patients with diabetes mellitus and coronary artery disease [36]. In diabetics, however, this effect is not yet found after 4 weeks but rather after a prolonged training period of 6 months, which may be due to the diffuse rather than focal atherosclerotic process throughout the coronary tree with little normally functioning endothelium left to release nitric oxide (NO) and to react with a vasodilatory stimulus like acetylcholine.

A meta-analysis could show that normoglycaemic patients with coronary artery disease [37] benefited from endurance training as part of a rehabilitation with a reduction of mortality of 31%. To obtain these benefits, energy consumption due to physical exercise training should ideally be between 1000

and 2000 kcal/week, which corresponds to 3-5 hours of sub-maximal endurance training per week [38].

Activity should thus be undertaken at moderate to high intensity, 3 to 7 days/week, for at least 30 min/day and for 60 min/day by people who need to achieve weight loss [39].

Pharmacological interventions and lipids

Lifestyle modifications, although very powerful, are difficult to implement and maintain and sometimes not sufficient in treating the metabolic syndrome; therefore, supportive pharmacotherapy often remains necessary. Medical therapies for dyslipidaemia are key for people at high risk for the disease and for people with known atherosclerosis.

Based on the recommendations by the National Cholesterol Education Program (NCEP) [1], statins stand up as first-line therapy for aggressive LDL-C-lowering intervention [40]. These agents work by competitively inhibiting the rate-limiting step of cholesterol synthesis and upregulating LDL receptors in the liver. In order of potency, they are rosuvastatin, atorvastatin, simvastatin, and then, listed alphabetically, fluvastatin, lovastatin, and pravastatin.

A recent retrospective analysis involving all patients actively taking simvastatin 80 mg at the Veterans Affairs Medical Center showed that high-dose simvastatin was required to reduce events in the very high risk cohort with MS [41, 42]. In addition, the post hoc analysis of the Treating to New Target (TNT) study shows that patients with CHD and MS gain benefit from high dose atorvastatin therapy [43]. A subgroup analysis of the Measuring Effective Reductions in Cholesterol Using Rosuvastatin therapy (MERCURY) I study [44] demonstrated that 10 mg rosuvastatin was more beneficial across the lipid profile, compared with commonly used doses of other statins. Results of the COmparative study with rosuvastatin in subjects with METabolic Syndrome (COMETS) also point out the lipid-modifying effects of rosuvastatin in patients with MS [45]. Moreover, rosuvastatin had a significantly greater effect than atorvastatin on lowering LDL-C and improving HDL- and non-HDL-C levels.

Once LDL-C goals are reached, then non-HDL-C becomes a logical target for treatment. The goal levels for non-HDL-C are 30 mg/dL greater than the LDL-C goal [39]. Statin therapy can be intensified in patients with elevated non-HDL-C. Low HDL-C (<40 mg/dL) is considered a tertiary goal in patients with coronary disease who have reached their LDL-C and non-HDL-C goals [40, 42]. For all patients, lifestyle changes including weight loss, regular exercise and low carbohydrate intake have a positive impact on HDL-C levels. HDL-C is a key component of the metabolic syndrome. Reversal of an inactive lifestyle and weight loss is likely to improve both HDL-C and the other parameters of this syndrome.

In conclusions primary and secondary prevention of cardiovascular diseases needs to focus on all modifiable risk factors and implement pharmaceutical therapy wherever appropriate.

Although exercise training should be part of every treatment regimen in patients with diabetes according to national and international guidelines, it is only integrated into the daily routine by a minority of patients. This ought to change, since only a multifactorial risk intervention which includes exercise training has the potential to treat the underlying causes of both diabetes and coronary artery disease. Neither we as physicians nor our patients can afford to continue to neglect this potent therapeutic option which deserves to be included in all of our daily lives.

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