Diagnosis and Management of Metabolic Syndrome

Essay

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Intensive Care Medicine

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رسالة

توطئة للحصول على درجة الماجستير فى الرعاية المركزة

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Summary

The metabolic syndrome consists of a constellation of factors that raise the risk for CVD and type 2diabetes. Because of the increasing prevalence of obesity, the metabolic syndrome has increased in frequency. ATP III introduced the metabolic syndrome into its clinical guidelines in the effort to achieve CVD risk reduction beyond LDL lowering therapy. Other clinical guidelines likewise have emphasized the need for more clinical attention to the metabolic syndrome. Although not all obese, sedentary persons acquire the metabolic syndrome, a significant subgroup of the population is susceptible to worsening of important contributors to the metabolic syndrome in the presence of energy imbalance. Several factors appear to contribute to this susceptibility, especially genetic predisposition and aging. Certain ethnic groups are particularly susceptible to the syndrome. Insulin resistance is a common feature of many of the components of the metabolic syndrome, and some investigators believe that it plays a key pathogenic role. Although genetic susceptibility is essential, the metabolic syndrome is relatively uncommon in the absence of obesity and physical inactivity. For this reason, lifestyle modification leading to weight reduction and increased physical activity represents first-line clinical therapy of the metabolic syndrome. Smoking cessation, of course, is paramount. A realistic goal for overweight/ obese persons is to reduce body weight by 7% to 10% over a period of 6 to 12 months. Weight reduction should be combined with a daily minimum of 30 minutes of moderate

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Abbrev.	
AHA/NHLBI	American Heart Association/National Heart Lung and blood institute
ASCVD	Atherosclerotic cardiovascular disease
BMI	Body mass index
CAMs	Cell adhesion molecules
CAPN10	Calpain-10
CD36	Cluster of Differentiation 36
CRP	C-reactive protein
CVD	Coronary vascular disease
DECODE	Diabetes Epidemiology Collaboration Analysis of Diagnosis Criteria European
DZ	Dizygotic
EGIR	European Group for the Study of Insulin Resistance
HDL	High density lipoprotein
HDL-c	High density lipoprotein cholesterol
HOMA	Homeostatic model assessment
HOMA-IR	Homeostatic model assessment-insulin resistance
IDF	International federation of diabetes
IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance
IL-1	Interleukin-1
IL-6	Interleukin-6
IR	Insulin resistance
IRS	Insulin receptor substrate

List of Abbreviations (Cont.)

IRS1 .....Insulin receptor substrate 1

IRS2 .....Insulin receptor substrate 2

LAR .....Leptin: adeponectin ratio

LDL .....Low density lipoprotein

LDL-p .....Low density lipoprotein particle

Lp-pLA$_2$ .....Lipoprotein-associated phospholipase-A$_2$

Lyso-pe .....Lysophotidylcholine

mRNA.....Messenger RNA

MS.....Metabolic syndrome

MZ.....Monozygotic

NAFLD.....Non alcoholic fatty liver disease

NCEP-ATPIII.....National cholesterol education programme. Adult treatment panel III

OGTT.....Oral glucose tolerance test

OX-NEFA.....Oxidized none-stratified fatty acid

PAI-1 .....Plasminogen activator inhibitor-1

PPAR-γ.....Peroxisome proliferators activated receptor-γ

SNP ..... Single-nucleotide polymorphism

T2DM .....Type 2 diabetes mellitus

TNF-α .....Tumor necrotic factor-α

US .....United States

WHO.....World Health Organization

β3 AR .....β3-adrenergic receptor

11β-HSD1.....11β-hydroxysteroid dehydrogenase type 1

3P25.....Chromosome 3, short arm, band 25

Introduction

The prevalence of metabolic syndrome (MS) has increased significantly over the past decade among both adults and adolescents. Older age, postmenopausal state, higher body mass index (especially, visceral fat), high carbohydrate intake, and physical inactivity are associated with an increased risk of developing the metabolic syndrome with concomitant increase in diabetes and coronary heart diseases ***(Kolovo et al., 2007)***.

The metabolic syndrome, a concurrence of abdominal fat, disturbed glucose and insulin metabolism, dyslipidemia, and hypertension has been strongly associated not only with subsequent development of type 2 diabetes but also with atherothrombosis. The pathophysiology of this association is complex. The metabolic syndrome affects the thrombogenicity of circulating blood. Apart from its effect on platelets, a procoagulant and hypofibrinolytic state has been identified; mainly the result of the inflammatory state, dyslipidemia, and liver fat accumulation that accompany the metabolic syndrome ***(Alessi et al., 2008).***

Insulin resistance and ectopic fat accumulation are fundamental to diagnose metabolic syndrome and associated clinical conditions. Clinical examination and simple biochemistry tests are sufficient to diagnose this syndrome in the majority of patients. The measurement of insulin sensitivity is desirable, but impractical for routine use ***(Olufadi and Byrne, 2008)***.

Current and potential therapies for metabolic syndrome target obesity, insulin resistance, dyslipidemia, hypertension, inflammation, pro-thrombotic state, and the environmental conditions that promote obesity. Given the diverse pathological mechanisms leading to the syndrome, a broad approach targeting multiple etiologic factors is reasonable ***(Phillippa, 2005)*.**

Bariatric surgery for the treatment of adolescent obesity is an extremely invasive procedure and it can only be indicated in extremely restricted circumstances in this age group. The American Paediatric Surgical Association Clinical Task Force on Bariatric Surgery recommends that adolescents may be candidates for the procedure if they have a body mass index greater than 50, or greater than 40 and associated with co-morbidities (sleep apnea, diabetes mellitus) ***(Lottenberg, 2007)*.**

Aim of the Work

- To review new concepts of the metabolic syndrome.
- To highlight the emerging therapeutic options for the metabolic syndrome and how this may alter the prospect of cardiovascular patients.

Metabolic Syndrome

Introduction

The metabolic syndrome is a clustering of factors that increasing CVD risk including hyperinsulinemia, obesity, dyslipidemia (small dense low-density lipoprotein, hyper-triglyceridemia, and decreased high-density lipoprotein cholesterol), and hypertension. The pathogenesis of the syndrome has multiple origins. However, obesity and sedentary lifestyle coupled with diet and still largely unknown genetic factors clearly interact to produce the syndrome (Figure 1) ***(Steinberger et al., 2009).***

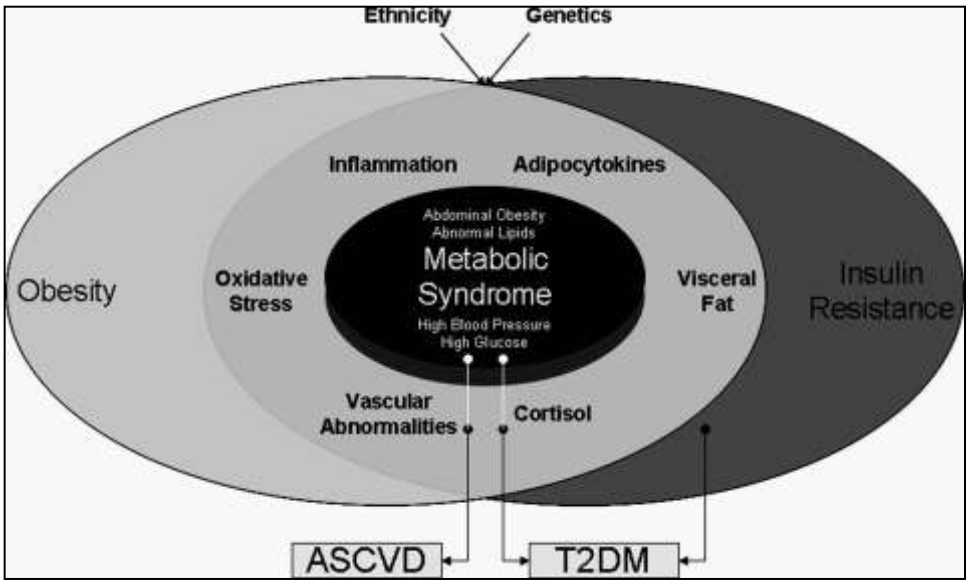

Figure (1): Schematic of components of the MS ***(Steinberger et al., 2009).***

There is currently substantial confusion between the conceptual definition of the metabolic syndrome and the clinical screening parameters and cut-off values proposed by various organizations (NCEP-ATP III, IDF, WHO, etc) to identify individuals with the metabolic syndrome ***(Després et al., 2008).***

In 1988, Reaven noted that dyslipidemia, hypertension, and hyperglycemia commonly cluster together and called this clustering Syndrome X, which was recognized as a multiplex risk factor for CVD . The metabolic syndrome has been associated with various names since being originally described by ***Reaven (1988).***

These names include:

1. Diabesity
2. Syndrome X
3. Deadly quartet
4. Deadly pentad disease
5. Dysmetabolic syndrome
6. Polymetabolic syndrome
7. Coronary risk syndrome
8. Insulin resistance syndrome
9. Atherothrombogenic syndrome