

# Overview of Diagnosis and Management Strategies of Metabolic Syndrome

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**Abstract:** Metabolic syndrome (MetS) consists of the constellation of numerous metabolic abnormalities that have actually been associated with cardiovascular disease, stroke, and all-cause death in the general population. The aim of this review was to address the different approaches to diagnosis of metabolic syndrome and the treatment of MetS its complications and through summarizing the most evidence based that were discussed in previous studies. A literature review was conducted using PubMed, Science Direct, and Google Scholar to search for diagnosis and management of metabolic syndrome. searched included 'metabolic syndrome', 'impaired glucose tolerance', 'type 2 diabetes', 'obesity', 'blood pressure' and 'lipids'. The reference lists from original and review articles were also reviewed to identify other relevant studies. Metabolic syndrome is a condition with hereditary and obtained etiologies that leads to CVD problems in populations throughout the world, however specifically in the West Virginian population offered the rates of diabetes, high blood pressure, and weight problems. Developing a panel of biomarkers with a foreseeable and recognized association with metabolic syndrome can offer a method to spot those at risk and step in as required.

**Keywords:** Metabolic syndrome (MetS), PubMed, Science Direct, and Google Scholar.

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## 1. INTRODUCTION

Metabolic syndrome (MetS) consists of the constellation of numerous metabolic abnormalities that have actually been associated with cardiovascular disease, stroke, and all-cause death in the general population <sup>(1)</sup>. The components of MetS include main weight problems, dyslipidemia (high triglycerides and low HDL cholesterol), raised BP, and impaired fasting glucose <sup>(2)</sup>.

The metabolic syndrome is a constellation of interrelated danger elements of metabolic origin-- metabolic threat elements that appear to straight promote the advancement of atherosclerotic cardiovascular disease (ASCVD) <sup>(3)</sup>. Patients with the metabolic syndrome also are at increased danger for developing type 2 diabetes mellitus. Another set of conditions, the underlying danger elements, generate the metabolic risk factors. In the past couple of years, several specialist groups have attempted to state simple diagnostic criteria to be used in scientific practice to determine patients who manifest the multiple components of the metabolic syndrome. These criteria have varied rather in particular elements, but in general they include a mix of both underlying and metabolic threat elements <sup>(4)</sup>.

The most widely acknowledged of the metabolic threat elements are atherogenic dyslipidemia, raised high blood pressure, and raised plasma glucose. People with these attributes commonly manifest a prothrombotic state and a pro-inflammatory state as well <sup>(5)</sup>. Atherogenic dyslipidemia consists of an aggregation of lipoprotein abnormalities including elevated serum triglyceride and apolipoprotein B (apoB), increased small LDL particles, and a reduced level of HDL cholesterol (HDL-C). If it were a discrete entity with a single cause, the metabolic syndrome is often referred to as. Offered information suggest that it really is a syndrome, ie, a grouping of ASCVD risk aspects, but one that most likely has more than one cause. Regardless of cause, the syndrome determines people at a raised threat for ASCVD. The magnitude of the increased danger can differ according to which components of the syndrome exist plus the other., non-metabolic syndrome risk factors in a particular person <sup>(5,6)</sup>.

The aim of this review was to address the different approaches to diagnosis of metabolic syndrome and the treatment of MetS its complications and through summarizing the most evidence based that were discussed in previous studies.

## 2. METHODOLOGY

A literature review was conducted using PubMed, Science Direct, and Google Scholar to search for diagnosis and management of metabolic syndrome. searched included ‘metabolic syndrome’, ‘impaired glucose tolerance’, ‘type 2 diabetes’, ‘obesity’, ‘blood pressure’ and ‘lipids’. The reference lists from original and review articles were also reviewed to identify other relevant studies.

## 3. RESULTS AND DISCUSSION

The pathogenesis of the MetS is progressive and multifactorial. The danger elements of the MetS are of metabolic origin and include abdominal fat accumulation, atherogenic dyslipidaemia, elevated plasma glucose, elevated blood pressure and a prothrombotic and proinflammatory state. The major threat factors are weight problems and insulin resistance (IR) accompanied by increased risk for CVD and T2D. Additionally, aging, physical inactivity and endocrine, and hereditary elements worsen the MetS<sup>(1,4)</sup>.

### ➤ Diagnosis of MetS:

We identified several studies<sup>(7,8,9,10,11,12)</sup> that addressed and stated, compared with those without metabolic syndrome, those with it are at an increased danger of death from CVD, coronary cardiovascular disease, stroke, vascular dysfunction, and all-cause death<sup>(7)</sup>. While the pathogenesis of metabolic syndrome and its elements is not well understood, central obesity and insulin resistance are recognized as causative elements. A number of various organizations have actually described diagnostic requirements for metabolic syndrome, which designates values for obesity (waist circumference or BMI), triglyceride levels, HDL (High Density Lipoprotein) levels, high blood pressure, hyperglycemia, and often urine albumin or albumin: creatinine ratio (**Table1**). Based upon AHA requirements, almost 35% of US grownups, and 50% of those older than 60 years of ages, have metabolic syndrome<sup>(8)</sup>. No matter which criteria are utilized, the main issue is early detection of potential CVD problems and early intervention<sup>(9,10)</sup>.

The NCEP ATP III report and WHO have actually both recognized CVD as the main medical outcome of metabolic syndrome, a lot of individuals with metabolic syndrome will have insulin resistance, which results in increased risk for type 2 diabetes (**Figure 1**). CVD danger rises greatly when diabetes ends up being medically evident. In addition to CVD and type 2 diabetes, people with metabolic syndrome are seemingly more prone to other conditions, including polycystic ovary syndrome, fatty liver, cholesterol gallstones, asthma, sleep disruptions, and some forms of cancer, such as breast, pancreatic, colorectal, and prostate<sup>(11,12)</sup>.

**Table 1: Diagnostic Criteria for Metabolic Syndrome**

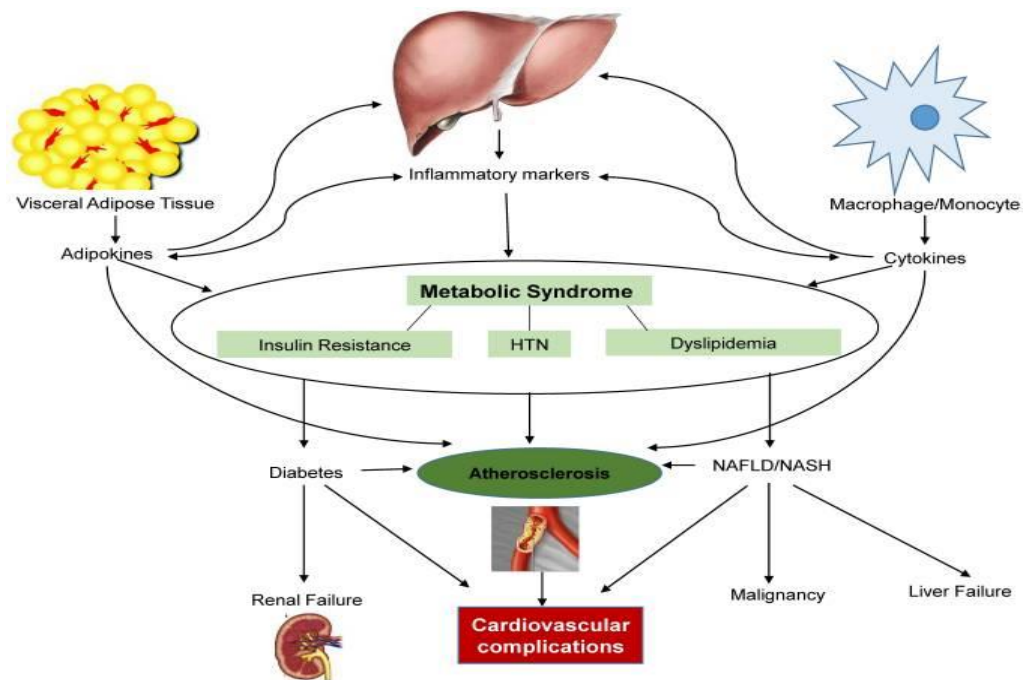
	IDF (Obesity + $\geq 2$ )	AHA ( $\geq 3$ )	NCEP ATP III ( $\geq 3$ )	WHO (Insulin resistance/Diabetes + $\geq 2$ )	EGIR (hyperinsulinemia + $\geq 2$ )
Obesity	BMI $>30\text{kg/m}^2$ or specific gender and ethnicity waist circumference cutoffs	Waist circumference for males $>40\text{in}$ , females $>35\text{in}$	Waist circumference for males $>40\text{in}$ , females $>35\text{in}$	Waist/hip ratio $>0.9$ in males and $>0.85$ in females or BMI $>30\text{kg/m}^2$	Waist circumference for males $\geq 94\text{cm}$ , females $\geq 80\text{cm}$
Elevated Triglycerides	TG $\geq 150\text{mg/dL}$ or treatment of this lipid abnormality	Fasting TG $\geq 150\text{mg/dL}$ or treatment of this lipid abnormality	TG $\geq 150\text{mg/dL}$ or treatment of this lipid abnormality	TG $\geq 150\text{mg/dL}$	TG $\geq 177\text{mg/dL}$
Decreased HDL	HDL $<40\text{mg/dL}$ in males and $<50\text{mg/dL}$ in females or specific treatment for this lipid abnormality	HDL $<40\text{mg/dL}$ in males and $<50\text{mg/dL}$ in females or treatment for this lipid abnormality	HDL $<40\text{mg/dL}$ in males and $<50\text{mg/dL}$ in females or treatment for this lipid abnormality	HDL $<35\text{mg/dL}$ in males and $<39\text{mg/dL}$ in females	HDL $< 39\text{ mg/dL}$
Hypertension	SBP $\geq 130$ or DBP $\geq 85\text{ mm Hg}$ or treatment of previously diagnosed	BP $>130/85\text{mm Hg}$ or taking medication for hypertension	SBP $\geq 130$ or DBP $\geq 85\text{ mm Hg}$ or taking medication for hypertension	$\geq 140/90\text{mm Hg}$	$\geq 140/90\text{mm Hg}$ or taking medication for hypertension

	IDF (Obesity + $\geq 2$ )	AHA ( $\geq 3$ )	NCEP ATP III ( $\geq 3$ )	WHO (Insulin resistance/Diabetes + $\geq 2$ )	EGIR (hyperinsulinemia + $\geq 2$ )
	hypertension				
Hyperglycemia	Fasting plasma glucose $>100\text{mg/dL}$ or previously diagnosed type 2 diabetes	Fasting glucose $>100\text{mg/dL}$ or taking medicine for high glucose	Fasting glucose $>100\text{mg/dL}$ or taking medicine for high glucose	Insulin resistance required	Insulin resistance required (plasma insulin $>75^{\text{th}}$ percentile)
Other				Urine albumin $\geq 20\mu\text{g/min}$ or Albumin: creatinine ratio $\geq 30\text{mg/g}$	

**IDF- International Diabetes Federation, AHA- American Heart Association, NCEP ATP III- National Cholesterol Education Program-Adult Treatment Panel III, WHO- World Health Organization, EGIR- European Group for the Study of Insulin Resistance, BMI- Body Mass Index, SBP - Systolic Blood pressure, DBP- Diastolic Blood Pressure, BP - Blood Pressure, TG- Triglycerides, HDL-High Density Lipoprotein**

Other studies <sup>(13,14)</sup> shows that adipocytes produce bioactive substances, referred to as adipokines or adipocytokines. Accumulation of adipocytes results in the dysregulated production of adipokines, which contributes to the advancement of metabolic syndrome <sup>(13)</sup>. The list of these dysregulated adipokines and cytokines is continuously growing and is a reflection of the heterogeneity of fat due to the number of resident cell types (14).

The system by which adipose build-up elucidates dysregulation is not entirely clear at this time, but some suggest that it is at least partly due to systemic oxidative tension induced by weight problems <sup>(15)</sup>. One proposed system by which weight problems produces oxidative tension is mitochondrial and peroxisomal oxidation of fats, which can create reactive oxygen species (ROS) in oxidation responses. Malondialdehyde (MDA), a lipid peroxidation end product, is increased in conditions marked by obesity and insulin resistance. It is able to improve expression of pro-inflammatory cytokines, resulting in systemic stress <sup>(16)</sup>. In addition to MDA, F-2 isoprostanes (F2-IsoPs) are likewise a product of polyunsaturated fatty acid peroxidation. A study has revealed that BMI is substantially associated with the F2-IsoP concentration. Another marker of oxidative tension is urinary 8-iso prostaglandin F<sub>2</sub> $\alpha$  (8-iso PGF $\alpha$ ). It has been shown to be positively correlated with obesity and insulin resistance <sup>(17)</sup>.



**Figure1: Interaction of adipokines, cytokines, and inflammatory markers that contribute to the development of metabolic syndrome and its complications. HTN-Hypertension, NAFLD/NASH- Nonalcoholic fatty liver disease/nonalcoholic steatohepatitis**

Many investigations confirm that numerous cardiovascular threat elements of endogenous origin frequently aggregate in one person. This aggregation was initially observed numerous years earlier,<sup>(18,19)</sup> more just recently, a number of terms have actually been proposed to explain this clustering: metabolic syndrome,<sup>(20)</sup> syndrome X,<sup>(21)</sup> the "lethal quartet,"<sup>(22)</sup> insulin-resistance syndrome,<sup>(23,24)</sup> and hypertriglyceridemic waist<sup>(25)</sup>. The term metabolic syndrome is most typically utilized in the cardiovascular field. The metabolic syndrome is typically referred to as a discrete entity, it is crucial to acknowledge, as kept in mind previously, that it is a syndrome and not a specified uniform entity. No single pathogenesis has actually been clarified, nor might one exist. Hence, the syndrome might vary from a cluster of unassociated threat elements to a constellation of danger aspects connected through a typical underlying system. From a medical perspective, existence of the metabolic syndrome recognizes an individual at increased danger for ASCVD and/or type 2 diabetes mellitus. Ultimately, a much better understanding of the particular cause(s) of the syndrome might offer an enhanced quote of danger of establishing ASCVD or type 2 diabetes mellitus for people. In the meantime, nevertheless, the existence of the syndrome is a more basic sign of greater danger for these conditions. Because of a recorded high relative threat for ASCVD occasions and type 2 diabetes mellitus, the metabolic syndrome certainly brings a fairly high life time threat for these conditions even when shorter-term (10-year) threat remains in the low-to-moderate variety<sup>(26,27,28)</sup>.

#### ➤ Proper treatment and management of MetS:

##### *Management through controlling Diets:*

Beyond weight control and decrease of overall calories, the diet plan needs to be low in hydrogenated fats, trans fats, cholesterol, salt, and basic sugars<sup>(29)</sup>. In addition, a number of other research studies specified that<sup>(29,30)</sup>, there ought to be sufficient consumptions of fruits, veggies, and entire grains; fish consumption need to be motivated with acknowledgment of issues about the mercury material of some fish. Extremely high carb consumption can worsen the dyslipidemia of the metabolic syndrome<sup>(29,30)</sup>. ATP III recommended that for people going into cholesterol management the diet plan must include 25% to 35% of calories as overall fat. It is hard to sustain the low consumption of saturated fat needed to keep a low LDL-C if the fat material goes beyond 35%. On the other hand, if the fat material falls listed below 25%, triglycerides can increase and HDL-C levels can decrease<sup>(31)</sup>; therefore, very-low-fat diet plans might worsen atherogenic dyslipidemia. To prevent any worsening of atherogenic dyslipidemia in patients with the metabolic syndrome, some detectives prefer fat consumptions in the variety of 30% to 35%; others, nevertheless, are worried about possible weight gain arising from long-lasting consumption of greater fat consumption and therefore choose consumptions in the variety of 25% to 30%<sup>(31)</sup>.

There has actually long been an interest in the concern of whether altering the macronutrient material of the diet plan can promote weight decrease. For several years, a low-fat diet plan was promoted since the high calorie density of fat might increase the possibility of weight problems. More just recently, interest has actually grown in the possibility that high-protein, low-carbohydrate diet plans will boost weight decrease<sup>(32)</sup>. The reasoning appears to be that fat and protein use satiety that is missing with carbs. That this result of fat and protein on satiety makes the

diet plan more efficient for producing weight reduction is a disputable hypothesis. Research study recording that high-fat/high-protein/low-calorie diet plans can attain long-lasting upkeep of a lower body weight is doing not have. After 1 year of usage of low-carbohydrate diet plans, badly overweight patients reveal no more weight decrease than those consuming a standard weight-loss diet plan<sup>(33)</sup>. High-fat diet plans not just have the tendency to be greater in hydrogenated fat however they typically lack fruits, veggies, and entire grains all which are very important parts in presently suggested diet plans. High-protein diet plans of any sort are not well endured by people with persistent kidney disease who have actually significantly lowered glomerular filtering rate; excess protein boosts phosphorus load, which can trigger acidosis and intensify insulin resistance<sup>(34,35)</sup>.

##### **Medical Management of the Metabolic Syndrome:**

Lots of research studies<sup>(4,5,6)</sup> observed and revealed that the main objective of medical management in people with the metabolic syndrome is to minimize threat for medical atherosclerotic disease. Even in individuals with the metabolic syndrome, first-line treatment is directed towards the significant threat aspects: LDL-C above diabetes, high blood pressure, and objective. When it is not present in an individual with the metabolic syndrome, Prevention of type 2 diabetes mellitus is another essential objective. For people with recognized diabetes, danger aspect management should be magnified to lessen their greater threat for ASCVD. The prime focus in management of the metabolic syndrome per se is to reduce the flexible, underlying threat aspects (weight problems, physical lack of exercise, and atherogenic diet plan) through way of life modifications. Efficient way of life modification will lower all the metabolic threat elements. If

outright threat is high enough, factor to consider can be offered to including drug treatment to the program. The top priority of drug treatment is elevations of LDL-C, high blood pressure, and glucose; existing standards for their management need to be followed. Efforts need to be made to bring about smoking cessation in any cigarette smokers (4,5,6).

A series of research studies (26,27,28) have actually discovered that numerous middle-aged individuals with the metabolic syndrome are at increased outright threat for ASCVD in the future (eg, 10-year danger). As mentioned formerly, due to the fact that of the high relative danger for ASCVD, long-lasting (life time) threat for ASCVD is increased even when 10-year threat is not thought about to be high, eg, in young grownups who establish the syndrome. An intensifying aspect raising life time danger for ASCVD is an increased possibility for establishing early type 2 diabetes mellitus.

ATP III recommended that for people getting in cholesterol management the diet plan must consist of 25% to 35% of calories as overall fat. If the fat material surpasses 35%, it is tough to sustain the low consumption of saturated fat needed to preserve a low LDL-C. On the other hand, if the fat material falls listed below 25%, triglycerides can increase and HDL-C levels can decrease (31); therefore, very-low-fat diet plans might intensify atherogenic dyslipidemia. To prevent any worsening of atherogenic dyslipidemia in patients with the metabolic syndrome, some detectives prefer fat consumptions in the variety of 30% to 35%; others, nevertheless, are worried about possible weight gain resulting from long-lasting intake of greater fat consumption and hence choose consumptions in the variety of 25% to 30% (31).

High-fat diet plans not just tend to be greater in saturated fat however they typically are lacking in fruits, veggies, and entire grains all of which are crucial elements in presently suggested diet plans. (26,27,28).

#### 4. CONCLUSION

Metabolic syndrome is a condition with hereditary and obtained etiologies that leads to CVD problems in populations throughout the world, however specifically in the West Virginian population offered the rates of diabetes, high blood pressure, and weight problems. Developing a panel of biomarkers with a foreseeable and recognized association with metabolic syndrome can offer a method to spot those at risk and step in as required. Beyond way of life treatments directed towards underlying danger elements, attention needs to be offered to the metabolic threat elements. If ASCVD or diabetes exists, or if the 10-year danger as figured out by Framingham danger aspects is reasonably high, then drug treatments for threat aspects might be needed as specified by present standards. Recommended concepts of management for each of the metabolic threat elements are likewise should be thought about.

#### REFERENCES

- [1] Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, Fruchart JC, James WP, Loria CM, Smith SC., Jr: Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 120: 1640–1645, 2009.
- [2] Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of 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). *JAMA* 285: 2486–2497, 2001.
- [3] The International Diabetes Federation consensus worldwide definition of the metabolic syndrome.
- [4] National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). 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) final report. *Circulation*. 2002; 106: 3143–3421.
- [5] Park YW, Zhu S, Palaniappan L, Heshka S, Carnethon MR, Heymsfield SB. The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988–1994. *Arch Intern Med*. 2003; 163: 427–436.
- [6] Ferrannini E, Haffner SM, Mitchell BD, Stern MP. Hyperinsulinemia: the key feature of a cardiovascular and metabolic syndrome. *Diabetologia*. 1991; 34: 416–422.

- [7] Ford ES. The metabolic syndrome and mortality from cardiovascular disease and all-causes: findings from the National Health and Nutrition Examination Survey II Mortality Study. *Atherosclerosis*. 2004;173:309–14.
- [8] Aguilar M, Bhuket T, Torres S, Liu B, Wong RJ. Prevalence of the metabolic syndrome in the United States, 2003–2012. *Jama*. 2015;313:1973–4.
- [9] Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA. et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. *Current opinion in cardiology*. 2006;21:1–6. [
- [10] Alberti KG, Zimmet P, Shaw J. Metabolic syndrome—a new world-wide definition. A Consensus Statement from the International Diabetes Federation. *Diabetic medicine: a journal of the British Diabetic Association*. 2006;23:469–80.
- [11] Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C, American Heart A. et al. Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. *Circulation*. 2004;109:433–8.
- [12] Bhandari R, Kelley GA, Hartley TA, Rockett IR. Metabolic syndrome is associated with increased breast cancer risk: a systematic review with meta-analysis. *International journal of breast cancer*. 2014; 2014:189384.
- [13] Ryo M, Nakamura T, Kihara S, Kumada M, Shibazaki S, Takahashi M. et al. Adiponectin as a biomarker of the metabolic syndrome. *Circulation journal: official journal of the Japanese Circulation Society*. 2004; 68:975–81.
- [14] Deng Y, Scherer PE. Adipokines as novel biomarkers and regulators of the metabolic syndrome. *Annals of the New York Academy of Sciences*. 2010;1212:E1–E19.
- [15] Furukawa S, Fujita T, Shimabukuro M, Iwaki M, Yamada Y, Nakajima Y. et al. Increased oxidative stress in obesity and its impact on metabolic syndrome. *The Journal of clinical investigation*. 2004; 114:1752–61.
- [16] Raghavan S, Subramaniyam G, Shanmugam N. Proinflammatory effects of malondialdehyde in lymphocytes. *Journal of leukocyte biology*. 2012; 92:1055–67.
- [17] Fernandez-Sanchez A, Madrigal-Santillan E, Bautista M, Esquivel-Soto J, Morales-Gonzalez A, Esquivel-Chirino C. et al. Inflammation, oxidative stress, and obesity. *International journal of molecular sciences*. 2011; 12:3117–32.
- [18] Kylin E. Studien über das Hypertonie-Hyperglykämie-Hyperurikämie-Syndrom. *Zentralbl Innere Med*. 1923; 44: 105–127.
- [19] Vague P. La différenciation sexuelle, facteur déterminant des formes de l'obésité. *Presse Med*. 1947;30: 339–140.
- [20] Bjorntorp P. Abdominal obesity and the metabolic syndrome. *Ann Med*. 1992; 24: 465–468.
- [21] Reaven GM. Role of insulin resistance in human disease (syndrome X): an expanded definition. *Annu Rev Med*. 1993; 44: 121–131.
- [22] Kaplan NM. The deadly quartet. Upper-body obesity, glucose intolerance, hypertriglyceridemia, and hypertension. *Arch Intern Med*. 1989; 149: 1514–1520.
- [23] DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diabetes Care*. 1991; 14:173–194.
- [24] Stern MP. The insulin resistance syndrome: the controversy is dead, long live the controversy! *Diabetologia*. 1994; 37: 956–958.
- [25] Lemieux I, Pascot A, Couillard C, Lamarche B, Tchernof A, Almeras N, Bergeron J, Gaudet D, Tremblay G, Prud'homme D, Nadeau A, Despres JP. Hypertriglyceridemic waist: a marker of the atherogenic metabolic triad (hyperinsulinemia; hyperapoprotein B; small, dense LDL) in men? *Circulation*. 2000; 102: 179–184.
- [26] Somaa B, Almgren P, Tuomi T, Forsen B, Lahti K, Nissen M, Taskinen MR, Groop L. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care*. 2001; 24: 683–689.
- [27] Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, Salonen JT. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA*. 2002;288: 2709–2716.

- [28] Sattar N, Gaw A, Scherbakova O, Ford I, O'Reilly DS, Haffner SM, Isles C, Macfarlane PW, Packard CJ, Cobbe SM, Shepherd J. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation*. 2003; 108: 414–419.
- [29] Krauss RM, Eckel RH, Howard B, Appel LJ, Daniels SR, Deckelbaum RJ, Erdman JW Jr, Kris-Etherton P, Goldberg IJ, Kotchen TA, Lichtenstein AH, Mitch WE, Mullis R, Robinson K, Wylie-Rosett J, St. Jeor S, Suttie J, Tribble DL, Bazzarre TL. AHA Dietary Guidelines: revision 2000: a statement for healthcare professionals from the Nutrition Committee of the American Heart Association. *Circulation*. 2000; 102: 2284–2299.
- [30] US Department of Health and Human Services and US Department of Agriculture. Dietary Guidelines for American 2005. 6th ed. Washington, DC: US Government Printing Office; Jan 2005.
- [31] Kris-Etherton PM, Harris WS, Appel LJ; American Heart Association. Nutrition Committee. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation*. 2002; 106: 2747–2757.
- [32] Garg A, Bantle JP, Henry RR, Coulston AM, Griver KA, Raatz SK, Brinkley L, Chen YD, Grundy SM, Huet BA. Effects of varying carbohydrate content of diet in patients with non-insulin-dependent diabetes mellitus. *JAMA*. 1994; 271: 1421–1428.
- [33] Foster GD, Wyatt HR, Hill JO, McGuckin BG, Brill C, Mohammed BS, Szapary PO, Rader DJ, Edman JS, Klein S. A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med*. 2003; 348: 2082–2090.
- [34] Stern L, Iqbal N, Seshadri P, Chicano KL, Daily DA, McGrory J, Williams M, Gracely EJ, Samaha FF. The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. *Ann Intern Med*. 2004; 140: 778–785.
- [35] Mitch WE, Maroni BJ. Nutritional considerations in the treatment of patients with chronic uremia. *Miner Electrolyte Metab*. 1998; 24: 285–289.
- [36] Mitch WE. Beneficial responses to modified diets in treating patients with chronic kidney disease. *Kidney Int Suppl*. 2005; 94: S133–S135.