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Feature Article

Diabesity, Fatabetes, or Metabolic Syndrome: Different Names … Same Condition?

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This article has been approved for 2 CPE units. The online CPEU quiz and certificate of completion can be accessed in the Members Only section of the RPG web site via the My CPEU link. This CPE offering is available to current RPG members only and the expiration date is August 20, 2010.

Members without internet access can request a copy of the quiz and certificate of completion from Megan Sliwa, RD, LDN, Address: 425 North Front Street, Apartment 424, Columbus, OH 43215. Please provide your name, ADA number, and phone number.

Despite advances in detection and treatment of cardiovascular disease (CVD) and diabetes, these conditions continue to result in serious health complications, disability, and premature death. In addition, the incidence rates of CVD, diabetes, and related complications are expected to increase as the United States (U.S.) population ages and the prevalence of obesity continues to rise. At present, approximately 24 million people in the U.S. are diagnosed with diabetes, but another 54 million are considered prediabetic. Since 1990, the prevalence of diabetes has increased by 61%. During 1999-2002, more than half (54.8%) of people with diabetes were obese (BMI > 30) and 85.2% were overweight (BMI of 25-29.9) (1,2). The state of health risk for these metabolic conditions is spelled out in Table 1 (3).

Table 1
The State of Health Risk

- Two out of three Americans are overweight or obese
- More than 70 million (nearly one in four) Americans have varying degrees of insulin resistance
- An estimated 54 million (more than one in six) Americans have prediabetes
- Nearly one in four U.S. adults have high cholesterol
- One in three American adults have high blood pressure

The state of prediabetes is often preceded by a condition which has been labeled by many names (Table 2) and defined by several different professional, national, and international organizations (Table 3). The criteria established by these organizations for the diagnosis of what has been called "Metabolic Syndrome" vary from one to another, with some overlap (Table 4). All organizations seem to agree on certain core components of Metabolic Syndrome: obesity, dyslipidemia, hypertension (HTN), and insulin resistance (IR), with classification of IR established using different laboratory diagnostics. However, these organizations

Table 2
Metabolic Syndrome, AKA...

Metabolic Syndrome	Several specific definitions using a composite of medical parameters to establish as a disease entity
Insulin Resistance	Pathological condition associated with many disease states; a state in which a given level of insulin produces a less than expected biological effect; associated with abnormalities in both glucose and lipid metabolism
Diabesity	Associates obesity as a strong underlying factor in the development of diabetes
Fatabetes	Like "diabesity"
Prediabetes	Condition preceding frank diagnosis of diabetes which has specific diagnostic criteria established based on blood glucose levels; impaired fasting glucose and impaired glucose tolerance are the two manifestations
Reaven's Syndrome	Named after Gerald Reaven, one of the first to examine this cluster of metabolic risk factors in both CVD and diabetes
Deadly Quartet	Obesity, HTN, hyperglycemia, and hypertriglyceridemia
Hypertriglyceridemic Waist	
Dysmetabolic Syndrome	
Syndrome "X"	

Table 3
Organizations Establishing Definitions of Metabolic Syndrome

WHO	World Health Organization (1999)
EGIR	European Group for the Study of Insulin Resistance
NCEP-ATPIII	National Cholesterol Education Program – Adult Treatment Panel III (2001)
AACE	American Association of Clinical Endocrinologists – AACE Position Statement on the Insulin Resistance Syndrome (2003/2006)
IDF	"The International Diabetes Federation Consensus Worldwide Definition of the Metabolic Syndrome" (1999; revised 2006 based on ATPIII)
AHA/NHLBI	American Heart Association and National Heart, Lung and Blood Institute of NIH "Scientific Statement: Diagnosis and Management of the Metabolic Syndrome" (2005)

apply the criteria differently to identify the cluster of metabolic derangements (4-7).

Of specific note to renal healthcare specialists, microalbuminuria is listed as a criterion in a couple of the organizational definitions of Metabolic Syndrome, i.e. WHO and AACE (8). Recent large-scale clinical trials exploring the value of diet and exercise as modifiable factors for management of diabetes and development of CVD, such as the Look AHEAD (Action for Health in Diabetes) Study, further established this link (9). Look AHEAD analyses have described that increased BMI and abdominal obesity are associated with albuminuria in overweight and obese adults with type 2 diabetes. This same bidirectional association has also been implicated in the development of nephropathy in type 1 diabetes, as assessed by the FinnDiane Study (10). Using the WHO, NCEP, and IDF definitions of Metabolic Syndrome, this study concluded that Metabolic Syndrome is a risk factor beyond albuminuria for cardiovascular morbidity and diabetes-related mortality in type 1 diabetes.

There are some distinct advantages to using the terminology Metabolic Syndrome, despite the differential definitions. It serves as an operational definition for risk factors predisposing one to various metabolic risks. Most clinicians do not measure global risk

Table 4
Different Organizational Definitions and Characterizations for Diagnosis of Metabolic Syndrome

AHA/NHLBI (2005)	**IDF** (2006)
Any three or more of the following criteria: 1. Elevated waist circumference >102 cm (40 in.) in men and >88 cm (35 in.) in women 2. Elevated triglycerides (TG) ≥150 mg/dL (1.7 mmol/L) or drug treatment for elevated TG 3. Elevated blood pressure (BP) ≥130 mmHg systolic BP or ≥85 mmHg diastolic BP or drug treatment for HTN 4. High density lipoprotein cholesterol (HDL-C) <40 mg/dL in men and <50 mg/dL in women or drug treatment for reduced HDL-C 5. Elevated fasting glucose ≥100 mg/dL or drug treatment for elevated glucose	Central obesity (defined as waist circumference with ethnicity-specific values) plus any two of the following factors: 1. Raised TG ≥150 mg/dL (1.7 mmol/L) or specific treatment for this lipid abnormality 2. Reduced HDL-C <40 mg/dL in males and <50 mg/dL in females or specific treatment for this lipid abnormality 3. Raised BP ≥130/85 mmHg or treatment of previously diagnosed HTN 4. Raised fasting plasma glucose ≥100 mg/dL or previously diagnosed type 2 diabetes
NCEP (2001)	**WHO** (1999)
1. Abdominal obesity defined by waist circumference >102 cm (40 in.) in men and >88 cm (35 in.) in women 2. TG ≥150 mg/dL 3. HDL-C <40 mg/dL in men and <50 mg/dL in women 4. BP ≥130/85 mmHg 5. Fasting plasma blood glucose ≥110 mg/dL	Diabetes, impaired fasting glucose, impaired glucose tolerance, or IR (assessed by clamp studies) and at least two of the following criteria: 1. Waist-to-hip ratio >0.90 in men and >0.85 in women 2. Serum TG ≥1.7 mmol/L or HDL-C <0.9 mmol/L in men and <1.0 mmol/L in women 3. BP ≥140/90 mmHg 4. Urinary albumin excretion rate >20 µg/min or albumin-to-creatinine ratio ≥30 mg/g

Table 5
Risk Factors of Cardiometabolic Risk (CMR)

Modifiable CMR Factors	Non-Modifiable CMR Factors
Overweight/obesity	Age
High blood glucose	Race/ethnicity
High LDL cholesterol	Gender
Low HDL cholesterol	Family history
High triglycerides	
Hypertension	
Hypercoagulation	
Inflammation	
Smoking	
Physical inactivity	
Unhealthy eating	
Psychosocial issues	
Health disparities	

or use multivariate predictive equations as "metabolic syndrome" is easier. Classification as an entity encourages clinicians to look for other abnormal factors, as Metabolic Syndrome is usually defined by at least three, and as many as five, factors. Finally, it has been established by the San Antonio Heart Study that Metabolic Syndrome is a better predictor of diabetes than of CVD (11).

If one were to characterize Metabolic Syndrome, it could be described by a cluster of factors which are all strongly correlated with Cardio-Metabolic Risk (CMR): IR, visceral distribution of body fat (aka. central or abdominal adiposity), dyslipidemia, HTN, and prothrombotic state. CMR is a clustering of risk factors or markers that predispose people to CVD and/or Type 2 diabetes. Intra-abdominal fat is high-risk fat linked to IR, dyslipidemia, HTN, and vascular inflammation. This factor also appears to be a common thread in all of the organizational definitions of Metabolic Syndrome. Table 5 lists both the modifiable and non-modifiable risk factors that are hallmarks of cardiometabolic risk (CMR) (3).

Assessing CMR offers several important and distinct advantages (3):

1. Provides clinicians with a comprehensive view of a patient's health and potential risk for future disease and complications
2. Recognizes that not all risk factors are created equal, given their differential effects on future CVD or diabetes risk
3. Refocuses clinical attention on the value of systematic evaluation, education, lifestyle behavior changes, disease prevention, and treatment
4. Supports an integrated approach to health care

This interpretation of CMR is further complicated, or perhaps more aptly justified, by the identification of another condition, known as Metabolically Obese, Normal Weight (MONW). MONW was first described in an article in the *American Journal of Clinical Nutrition* in 1981 as, "A great many disorders, including maturity-onset (Type 2) diabetes, hypertension, and hypertriglyceridemia, are frequently associated with adult-onset obesity and improve with caloric restriction. It is the premise of this brief review that there are patients with these disorders who are not obese according to standard weight tables or other readily-available criteria, but who would also respond favorably to caloric restriction. It is proposed that such individuals might be characterized by hyperinsulinism and possibly an increase in fat cell size compared to patients of similar age, height and weight and/or to themselves at an earlier time. The possibility is also discussed that inactivity is a contributing factor in some of these individuals and that for them, the appropriate therapy might be exercise"(12). MONW refers to individuals who have many of the predisposing risk factors characterizing CMR, but who are of normal weight, yet still may display the characteristic profile of large abdominal girth, or the "apple" shape.

Table 6
Summary of Concerns Regarding Metabolic Syndrome (13)

- Criteria are ambiguous or incomplete. Rationales for thresholds are ill-defined.
- Value of including diabetes in the definition is questionable.
- Insulin resistance as the unifying etiology is questionable.
- No clear basis for including/excluding other CVD risk factors.
- CVD risk value is variable and dependent on the specific risk factors present.
- The CVD risk associated with the syndrome appears to be no greater than the sum of its parts.
- Treatment of the syndrome is no different than the treatment for each of its components.
- The medical value of diagnosing the syndrome is unclear.

The inconsistencies inherent in this disorder have led to a controversial debate, questioning the existence of Metabolic Syndrome and favoring a default to CMR. "Metabolic Syndrome: Time for a Critical Appraisal" was a joint statement prepared by both the American Diabetes Association and the European Association for the Study of Diabetes in 2005. This statement puts forth arguments questioning the clarity of the existing definition(s) of Metabolic Syndrome. A summary of the expressed concerns is listed in Table 6 (13,14).

Despite the variability in definition and controversy questioning the existence of Metabolic Syndrome as an established disease state, there is one thing that is agreed upon. Whether a healthcare professional believes they are treating a "disease" or whether they diagnose even one of the CMR risk factors, treatment is essential. Recognition of even one factor should prompt the clinician to look for others as they cluster together. CVD varies tremendously depending on how many components of CMR are present and the extent above the normal range the patient's laboratory or anthropometric values fall (3).

CMR factor assessment integrates a broader approach to health management by giving clinicians the tools to assess patient's risk for both diabetes and CVD. As discussed, CMR is influenced by an array of risk factors, including traditional and emerging ones. This type of assessment looks beyond clinically evident problems or abnormalities to assess and manage underlying or subclinical processes. Focusing on evaluation, education, disease prevention, lifestyle, behavior change, and treatment of all related risk factors can optimize health outcomes for patients at risk. Two clinical trials that demonstrate the health benefits of diet and physical activity in both the prevention and improved management of diabetes include the Diabetes Prevention Program and the Look AHEAD studies, respectively (9,15). In the Diabetes Prevention Program, dietary intervention coupled with thirty minutes per day of physical activity resulted in a 58% reduction of progression from prediabetes to type 2 diabetes (15).

The goals for clinical management of CMR include weight control, treating the patient for both diabetes and CVD risks, prevention of type 2 diabetes, and prevention of cardiovascular events. The methods for achieving these goals are therapeutic lifestyle changes, for example the Mediterranean diet and physical activity, along with pharmacologic therapy. Medication goals are summarized in Table 7.

Currently, several new therapeutic drug classes based on naturally occurring gut hormones are being explored and studied

Table 7
CMR Clinical Management: Pharmacologic

- Overall Optimization of the Lipid Profile
  - ♦ Treat elevated TG
  - ♦ Improve low HDL-C
  - ♦ Reduction of LDL (lowers CVD risk, but does not impact metabolic syndrome)
- Achieve Blood Pressure Goals
- Achieve Blood Glucose Goals (Mediterranean Diet)
- Minimize Prothrombotic State (aspirin)
- Correct Insulin Resistance
  - ♦ Weight reduction
  - ♦ Increased physical activity
  - ♦ Drugs that decrease IR have not been proven to reduce coronary artery disease risk and no consensus exists on whether these insulin sensitizers should be used in non-diabetic individuals with Metabolic Syndrome

for the treatment of prediabetes and Metabolic Syndrome/CMR. These drug classes include the incretin mimetics, dipeptidyl peptidase-4 inhibitors, and other glucagon-like peptide-1 analogs. These classes seem to hold promise for potentially altering disease progression through various proposed mechanisms of β-cell preservation and reduction of inflammatory processes, at least in animal models.

A recurrent theme for treatment is that initial therapy for CMR/Metabolic Syndrome should consist of caloric restriction and increased physical activity. The role of the Registered Dietitian is clearly stamped on the management of these risks.

To quote Vicki K. Sullivan, PhD, RD, "It is important to continue aggressively emphasizing the management of those things that are under our control, such as diet, exercise and behavioral changes. Likewise it is important to take into account the individual differences in genetics and energy balance that are sometimes beyond our control"(16). This sounds like a prescription for job security … and it's guaranteed, when you circle back to the state of risk at the beginning of this article. ◆

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