The Metabolic Syndrome:
Controversy and value of using a medical home model in chronic disease prevention

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The metabolic syndrome (MetSyn) remains a controversy in clinical practice. The syndrome, which has been described by different names over the past four decades, continues to surface in the literature, as proponents and opponents discuss its utility in daily practice. The definition of the syndrome has changed over time, which has affected its prevalence and association with adverse outcomes.

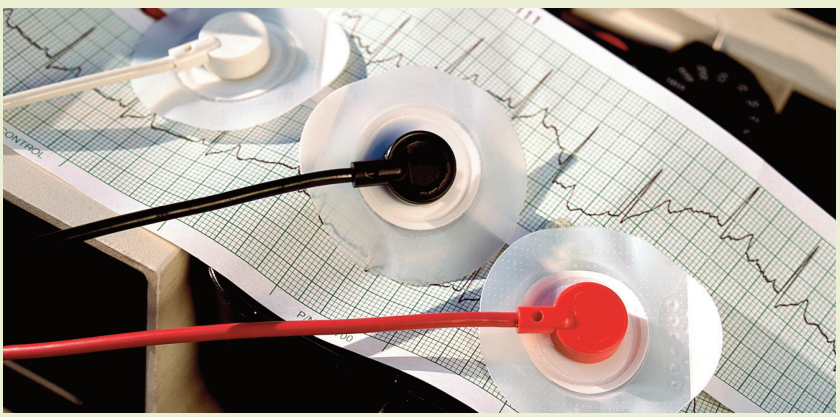
The syndrome may be most important in clinical practice by stratifying patients at higher risk for progression to type 2 diabetes mellitus and cardiovascular (CV) events and those at higher need for more intensive pharmacologic and nonpharmacologic interventions, which could be part of a patient-centered medical home (PCMH) model of practice.

Underlying associations

The underlying association between upper body obesity, diabetes, atherosclerosis and cardiovascular disease has been known since the 1940s. The terms metabolic syndrome, syndrome X, cardiometabolic syndrome and insulin resistance syndrome have all been used in past decades to describe associated factors in individuals who have an increased risk of diabetes and CV events.

Although definitions of MetSyn have changed over time, they have all included some measure of impaired glucose metabolism, elevated blood pressure, central obesity and dyslipidemia as defined by elevated triglycerides and decreased high-density lipoprotein cholesterol (HDL-C). Several groups, including the National Cholesterol Education Program (NCEP), American Heart Association and International Diabetes Federation, have recently defined MetSyn. The differences between these definitions are outlined in Table 1 and are seen in the aspects of central obesity measurement and cutoff for fasting glucose.[1]

Metabolic syndrome in children and adolescents has been more challenging to define because the specific parameters at any age are generally based on distributions within that age group in the 95th percentile rather than linked to specific measures.[2] The increase of childhood obesity and its sequel of insulin resistance in the pediatric population heighten the need to identify individuals at high risk for premature progression to overt diabetes or subsequent cardiovascular disease.



Although terms for the syndrome have been in existence since the 1950s, controversy over its value in clinical medicine continues.[3] Naming the syndrome acknowledges the constellation of risk factors associated with increased cardiovascular risk in a large segment of the population, an estimate using representative national data from 2003 to 2006 suggested that 36% of the adult population had the criteria for metabolic syndrome.[4] Although MetSyn has been associated with increased risk of both diabetes and cardiovascular disease, recommended responses to its presence does not extend beyond the evidenced-based treatment of its components.

Recommendations regarding pharmacologic treatment of some of the components of metabolic syndrome exist although others do not. For example, current recommendations regarding treatment of impaired fasting glucose including lifestyle modifications and, potentially metformin.

Treatment of an isolated depressed HDL in the face of no other lipid abnormalities has little guidance. Abnormalities in other risk factors included in the syndrome may modify how aggressively lifestyle and pharmacologic agents are used or advanced for any risk factor. Current trends in the prevalence of obesity and type 2 diabetes warrant a fresh evaluation of the value of the term metabolic syndrome in clinical practice.

In light of the long-perceived association between the risk factors in the

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definition of MetSyn and cardiovascular events, several studies have attempted to determine whether the constellation of risk factors as a syndrome confers a greater risk for individuals than that of the risk factors themselves. Does the diagnosis of MetSyn increase a patient's risk for CV events to a greater extent than the sum of having all the independent risk factors? The literature has been mixed in decisively defining increased risk, although it has defined a correlation among the independent risk factors.

Cardiovascular risk

The cross-sectional Telde Study showed that the prevalence of all cardiovascular risk factors increased in patients having successively higher levels of evidence of impaired glucose regulation. The prevalence of hypertension increased from 30.1% to 34.5%, 39.6% and 55.4% among individuals with normal glucose tolerance (NGT) to isolated IFG (impaired fasting glucose), isolated IGT (impaired glucose tolerance) and IFG/IGT, respectively.[5] Likewise, mean triglyceride levels increased from 97.9 mg/dL to 109.47 mg/dL, 125.49 mg/dL and 132.61 mg/dL, respectively, and HDL-C decreased from 55.77 mg/dL to 55.38 mg/dL, 53.43 mg/dL and 51.98 mg/dL, respectively, across the four groups. Finally, using the 2005 International Diabetes Federation definition, the rate of MetSyn increased from 13.2% to 57.2%, 64.4% and 75.6%, respectively, across the four groups.[5]

This correlation has been demonstrated in pediatric populations as well. An evaluation of the National Health and Nutrition Examination Survey (NHANES) from 2005 to 2006 using fasting blood glucose and two-hour postprandial glucose among participants aged 12 to 17 years of age found a high prevalence of prediabetes, defined as having IFG (fasting plasma glucose $>$ 100 mg/dL and $<$ 126 mg/dL), IGT (2-hour postprandial $>$ 140 mg/dL and $<$ 200 mg/dL). In this age group, the prevalence of IFG, IGT, and IFG or IGT (prediabetes) was 13.1%, 3.4% and 16.1%, respectively.[5] The estimated prevalence of IFG was 87.1% higher than the 7% estimated from NHANES data from 1999 to 2000; a rapid increase in the prevalence of central obesity in adolescents was considered a potential factor in this rise.

There was a strong association between the prevalence of prediabetes and adolescents who were overweight ($>$ 95th percentile of BMI), with the frequency of prediabetes 2.6 times higher in the overweight group. In addition, there was a strong association between prediabetes and cardiometabolic risk factors, including high blood pressure, hypertriglyceridemia and central obesity, as well as hyperinsulinemia in this group. Adolescents with two of these four risk factors had a significantly higher prevalence of prediabetes, suggesting that clustering of metabolic risk factors should be used to target adolescents at higher risk for progression to type 2 diabetes mellitus and CV events.[6]

However, evaluating the additive risk that the thresholds of MetSyn provide to individuals over the independent risk factors shows lower yield. A study using NHANES data evaluated the association between the risk factors for MetSyn and cardiovascular disease, based on the World Health Organization (WHO) and NCEP definitions of the syndrome.[7]

The study used modeling to calculate long-term CVD outcomes based on each patient's risk factors. By calculating each patient's risk, the authors were able to evaluate how well the constructs of MetSyn predicted CV events. The study concluded that the use of the syndrome as a definition did not provide any more discrimination than the

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Table 1: Comparison of Definitions of Metabolic Syndrome			
Risk Factor	**NCEP ATP III (2001)**	**NHLBI/AHA 2005**	**IDF (2006)**
	Three or more of the following	Three or more of the following	Central Obesity defined using waist circumference and any two of the following
Waist circumference (males)	> 102 cm	> 102 cm	
Waist circumference (females)	> 88 cm	> 88 cm	
Hypertension	BP ⩾130/85 mm Hg or medication	BP ⩾130/85 mm Hg or medication	BP >130/85 mm Hg or medication
Triglycerides	⩾150 mg/dL or medication	⩾150 mg/dL or medication	> 150 mg/dL or medication
HDL- cholesterol (men)	< 40 mg/dL or medication	< 40 mg/dL or medication	< 40 mg/dL or medication
HDL- cholesterol (women)	< 50 mg/dL or medication	< 50 mg/dL or medication	< 50 mg/dL or medication
Fasting Blood Glucose	⩾110 mg/dL or medication	⩾100 mg/dL or medication	⩾100 mg/dL or medication

NCEP ATP III—National Cholesterol Education Program, Adult treatment.
Panel III. **NHLBI/ AHA**—National Heart, Lung, Blood Institute/American Heart Association. **IDF**—International Diabetes Federation.

use of the independent risk factor evaluation. The authors found that using MetSyn added little to assessing each patient's risk of future CV events.[6]

Other studies have found a greater association between the presence of MetSyn than independent risk factors. A study using data from the Cardiovascular Health Study, a longitudinal registry of individuals >65 years of age sponsored by the National Heart, Lung, and Blood Institute found that using the ATP III criteria provided increased prognostic information, after adjustment for traditional CV risk factors and those included in the definition of MetSyn. The WHO criteria added more prognostic information than traditional risk factors did.[8]

Value in clinical practice

As the controversy regarding the value of MetSyn continues in the literature, the question of its value in clinical practice remains. Central to this question is the likelihood that clinicians can use the presence of the syndrome to improve the care they provide or the outcomes of the patients they serve. This brings us to the question of evidence for interventions: specifically, are there interventions that can be recommended in this population to reduce risk for future CV events?

There is evidence that lifestyle interventions and, for patients with impaired fasting glucose or glucose intolerance, pharmacologic interventions can reduce the risk of progression to diabetes and CV events. There is no question that the risk factors that comprise MetSyn are correlated with each other and obesity.

A study using NHANES data from 1999 to 2004 to determine associations between hypertension, diabetes, dyslipidemia, and obesity categorized obesity by four classes. Using normal-weight individuals as a referent population, the authors found that individuals with BMI ⩾40 had odds ratios of 4.8 for hypertension, 5.1 for diabetes, 2.2 for dyslipidemia, and 2.0 for MetSyn after adjustment.[9]

Because obesity appears to be highly correlated with the risk factors of MetSyn, an evaluation of studies aimed at reducing obesity should provide us with information regarding potential interventions. A meta-analysis of 17 studies demonstrated that lifestyle changes, primarily aimed at weight reduction, improved diet and exercise, were as effective as pharmacologic interventions, with a 50% reduction in progression to diabetes in patients who had impaired glucose tolerance.[10]

Another study based on data from the Diabetes Prevention Program evaluated the effect of intensive lifestyle and metformin on cardiovascular disease risk factors. After three years of follow-up, individuals in the intensive lifestyle intervention group using medications for hypertension and hyperlipidemia to achieve established goals required 28% and 25% less medication than the metformin or placebo groups, respectively. This was in addition to a 50% reduction in progression to overt diabetes in the intensive lifestyle intervention group and a 37% reduction in the metformin group when compared with placebo.[11]

Evaluating the PCMH approach

In a sense, the diagnosis of MetSyn synthesizes several risk factors in an effort to provide physicians with a more holistic approach of the patient's risk for

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DM or cardiovascular events, an approach consistent with osteopathic practice. This type of approach is also consistent with core competencies that are part of the PCMH.

The PCMH is a new model of primary care that has been endorsed by the American College of Physicians, American Academy of Family Practice and American Osteopathic Association.

A proactive team providing primary and secondary prevention is central to the PCMH. In this environment, MetSyn can be used as a marker for obese patients needing heightened attention to lifestyle and other interventions to reduce risk of adverse events.

The controversy regarding the added predictive ability that a diagnosis of MetSyn gives to individuals does not invalidate the syndrome. By identifying the subset of obese patients who have risk for progression to diabetes or CV events, the syndrome can increase the perceived need for intervention in these patients.

The MetSyn has value in identifying individuals with the constellation of risk factors in a population-management approach. Potential systematic interventions for this group would include group visits, patient engagement in self-management and increased reinforcement of goals by the practice, much like asthma can be managed now.

To make this a reality, reimbursement systems must change to provide the increased time physicians need to focus on prevention and increased resources—including information technology and human resources—to engage patients and reduce likelihood of progression to CV events.

Final notes

The metabolic syndrome has been used as a concept since the middle of the previous century when clinicians identified an association between abdominal obesity and cardiovascular disease. The concept has been refined using hypertension, glucose intolerance and dyslipidemia in the presence of central obesity in at least three different definitions.

The constellation of CV risk factors represented in MetSyn are associated with obesity and have grown in prevalence, along with the obesity rate in the United States. With 66% of the population currently overweight or obese, MetSyn gives us a method of identifying obese patients who are at high risk for progression to diabetes if they have impaired fasting glucose tolerance, and to CV events if they have the full syndrome. By identifying people at risk for future events, we can utilize tools in our practice—electronic medical records, registries, and a team approach to risk factor management—to demonstrate the power of the medical home as an agent of change.

These changes are consistent with the lifelong learning of objectives of practice-based learning and systems-based practice.

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