CLINICAL INSIGHT

OUR SERIES OF TECHNICAL REPORTS WRITTEN BY OUR TEAM OF GLOBAL CENTRAL LAB EXPERTS ON ISSUES AFFECTING CLINICAL TESTING TODAY

PLAYING A CENTRAL ROLE IN TREATING METABOLIC SYNDROME

An Excerpt From the May 2014 Issue of International Clinical Trials
Authored by Dr. Tatiana Souslova, Principal Scientist

Metabolic syndrome is a serious health condition which is defined as a cluster of metabolic risk factors that can increase the risk of developing cardiovascular diseases and diabetes. It impacts everyone to different degrees: children and adults of all genders, races and ethnicities. The prevalence of metabolic syndrome is rising dramatically – according to the American Heart Association (AHA), it now affects about one-in-three US adults.

As with many conditions, awareness, early diagnosis and early treatment can be critical – and clinical laboratories are well-equipped to aid with diagnosis by providing quality lab testing. The potential for successful management of metabolic syndrome is very good as treatments are simple, and can improve and save lives.

DIAGNOSTIC CRITERIA

As early as 250 years ago, long before the syndrome was defined, the Italian physician and anatomist Morgagni identified the link between abdominal obesity, atherosclerosis and hypertension – known today as the key risk factors of metabolic syndrome. Since then, the terminology and the definitions have evolved.

Metabolic syndrome was once known as plurimetabolic syndrome, syndrome X, deadly quartet, insulin resistance syndrome and dysmetabolic syndrome (1). The first official definition was provided by the World Health Organization (WHO) in 1989, followed by the European Group for the Study of Insulin Resistance (EGIR), the American Association of Clinical Endocrinologists (AACE), the US National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) and, most recently, the International Diabetes Federation (IDF) (2-7).

These five official definitions agree on the point that people with multiple metabolic conditions are at higher risk of developing cardiovascular disease and diabetes. However, they disagree on the type and number of metabolic risk factors needed in order to be classified as metabolic syndrome. While each of the five official diagnostic criteria has its merits, it also has its weaknesses – ensuring ongoing debate around metabolic syndrome (see Table 1).

LABORATORY TESTING

Methodologies and instrumentation available in clinical laboratories have evolved enormously in the past couple of years. Today, labs are well-equipped with state-of-the-art instrumentation that can provide rapid and most accurate results, enabling metabolic syndrome to be quickly and easily detected (see Table 2).

Most clinical labs will provide glucose and lipid measurements. Their cut-off points have been established and standardised. Instead of giving triglycerides and HDL cholesterol measurements only, labs will usually provide lipid panel measurements that will help doctors with the overall cardiovascular and diabetes risk assessments and diagnosis.

AVAILABLE TREATMENTS

Metabolic syndrome is becoming increasingly common, but fortunately the treatments are simple. The ATP III, AHA, National Institutes of Health (NIH) and the Endocrine Society recommend treating the underlying causes – for example, obesity and physical inactivity. The cardiovascular risk factors also need special attention. If the lifestyle modifications such as diet, physical exercise and stopping smoking do not change the metabolic risk factors, then cardiovascular risk factors have to be treated. They can be reduced by treating hypertension, glycemic control in patients with diabetes, and lowering of cholesterol (5,14-17).

Metabolic syndrome is a serious condition that can lead to fatal outcomes if not detected and treated. Clinical laboratories are playing a central role in detecting it, and current technologies allow these labs to provide healthcare providers and/or clinical trial sponsors with rapid and accurate results to aid prevention and treatment.

To access the full article, click here.

REFERENCES

1. Cripaldi G and Maggi S, The metabolic syndrome: a historical context, Diabetes Voice 51, 2006
2. Definition, diagnosis and classification of diabetes mellitus and its complications, Report of a WHO consultation, 1999
3. Balkau B and Charles MA, EGIR Comment on the provisional report from the WHO consultation, Diabet Med 16, pp442-443,1999
4. Executive summary of the third report of the NCEP expert panel on detection, evaluation and treatment of high blood cholesterol in adults (ATP III), JAMA 285, pp2,486-2,497, 2001
5. Grundy SM et al, National Heart, Lung and Blood Institute Diagnosis and management of the metabolic syndrome, Circulation 112(17): p2,735, 2005
6. American College of Endocrinology: Insulin resistance syndrome (position statement), Endocr Pract 9 (supplement 2): pp9-21, 2003
7. The IDF consensus worldwide definition of the metabolic syndrome, IDF, 2006
14. Grundy SM et al, Report of the AHA/National Heart, Lung and Blood Institute/American Diabetes Association conference on scientific issues related to management, Circulation 109(4): p551, 2004
15. Rosenzweig JL et al, Primary prevention of cardiovascular disease and type 2 diabetes in patients at metabolic risk: an Endocrine Society clinical practice guideline, J Clin Endocrinol Metab 93(10): p3,671, 2008
16. Pearson TA et al, AHA Guidelines for primary prevention of cardiovascular disease and stroke: 2002 update. Consensus panel guide to comprehensive risk reduction for adult patients without coronary or other atherosclerotic vascular diseases, Circulation 106(3): p388, 2002
17. Eberly LE et al, Metabolic syndrome: risk factor distribution and 18-year mortality in the multiple risk factor intervention trial, Multiple Risk Factor Intervention Trial Research Group, Diabetes Care 29(1): p123, 2006

Table 1: Definition of Metabolic Syndrome

Criteria for diagnosis	WHO 1998	EGIR 1999	AACE 2003	NCEP-ATP III 2005	IDF 2006
Main risk factors required					
Key risk factors	Insulin resistance in top 25%; glucose ≥ 110mg/dl (6.1mmol/L); 2-hour glucose ≥ 140mg/dl (7.8mmol/L)	Insulin resistance or fasting hyperinsulinemia in top 25%	High risk of insulin resistance or body mass index (BMI) ≥ 25kg/m2 or waist ≥ 102cm (men) or ≥ 88cm (women)	N/A	Waist ≥ 94cm (men) or ≥ 80cm (women)
Plus additional number of key risk factors are required for diagnosis					
Number of key risk factors	≥ 2 of:	≥ 2 of:	≥ 2 of:	≥ 3 of:	≥ 2 of:
Additional risk factors required for diagnosis					
Triglycerides	≥ 150mg/dl (1.7mmol/L)	≥ 180mg/dl (2.0mmol/L) or drug treatment for dyslipidemia	≥ 150mg/dl (1.7mmol/L)	≥ 150mg/dl (1.7mmol/L) or drug treatment for elevated triglycerides f	≥ 150mg/dl (1.7mmol/L) or drug treatment or high triglycerides
HDL Cholesterol	< 35mg/dl (0.9mmol/L) (men) < 40mg/dl (women) (1.0mmol/L)	< 40mg/dl (1.0mmol/L)	< 40mg/dl (1.0mmol/L) (men) < 50mg/dl (1.3mmol/L) (women)	< 40mg/dl (1.0mmol/L) (men) < 50mg/dl (1.3mmol/L) (women) or drug treatment for low HDL cholesterol	< 40mg/dl (1.0mmol/L) (men) < 50mg/dl (1.3mmol/L) (women) or drug treatment for low HDL cholesterol
Glucose	N/A	110-125mg/dl (6.1-6.9mmol/L)	≥ 110mg/dl; (6.1mmol/L) ≥ 2-hour glucose 140mg/dl (7.8mmol/L)	≥ 100mg/dl (5.6mmol/L) or drug treatment for elevated blood glucose	≥ 100mg/dl (5.6mmol/L) or diagnosed diabetes
Obesity	Waist/hip ratio > 0.9 (men) or > 0.85 (women) or BMI ≥ 30kg/m2	waist ≥ 94cm (men) or ≥ 80cm (women)	N/A	Waist ≥ 102cm (men) or ≥ 88cm (women)	N/A
Hypertension	≥ 140/90mmHg	≥ 140/90mmHg or drug treatment for hypertension	≥ 130/85mmHg	≥ 130/85mmHg or drug treatment for hypertension	≥ 130/85mmHg or drug treatment for hypertension
Helpful additional factors	Microalbuminemia	N/A	N/A	CRP, Fibrinogen	Leptin, adiponectin, ApoB, HOMA, OGTT, microalbumin, CRP, TNF-alpha, IL-6, Fibrinogen, pituitaryadrenal axis evaluation, etc (7)
Comments	BMI is not a reliable measure of obesity, insulin insensitivity is difficult to measure, microalbuminemia is rarely found in non-diabetics. First official definition of metabolic syndrome	Insulin resistance is difficult to measure	BMI is not a reliable measure of obesity, insulin insensitivity is difficult to measure	Cut-off values represent consensus of experts. Most commonly agreed upon criteria	Ethnicity-specific cut-off points

Table 1: Metabolic Syndrome Testing

Test	Common methods	Clinically signifi cant levels	Recommended use
Lipid Panel (4)			
Total cholesterol	Enzymatic	Desirable: < 200mg/dl (5.2mmol/L) Borderline: 200-239mg/dl (5.2-6.2mmol/L) High: ≥ 240mg/dl (6.2mmol/L)	Cardiovascular risk assessment Metabolic syndrome diagnosis
LDL cholesterol	Calculation if triglycerides < 400mg/dl, or enzymatic	Desirable: < 130mg/dl (3.4mmol/L) Borderline: 130-159mg/dl (3.4-4.1mmol/L) High: ≥ 190mg/dl (4.9mmol/L)	
HDL cholesterol	Enzymatic	Low: < 40mg/dl (1.0mmol/L) High: ≥ 60mg/dl (1.6mmol/L)	
Triglycerides E	nzymatic	Desirable: < 150mg/dl (1.7mmol/L) Borderline: 150-199mg/dl (1.7-2.2mmol/L) High: 200-499mg/dl (2.3-5.6mmol/L) Very High: ≥ 500mg/dl (5.6mmol/L)	
Glucose (17)			
Fasting glucose (plasma or serum)	Enzymatic	≥ 126mg/dl (7.0mmol/L)	Diabetic risk assessment or/and diagnosis
Oral Glucose Tolerance Test	Enzymatic	≥ 200mg/dl (11.1mmol/L)	Metabolic syndrome diagnosis
Insulin Resistance*			
Insulin	Immunoassay	N/A	Identifi cation of patients with metabolic syndrome risk, cardiovascular and diabetic risks, monitoring of medication
C-peptide	Immunoassay	N/A	Evaluation of pancreatic beta-cells function and verifi cation of the insulin source
HOMA1-IR	Calculation from insulin and fasting plasma glucose	N/A	Clinical trials for the estimation of insulin resistance
HOMA1-%B	Calculation from insulin and fasting plasma glucose	N/A	Clinical trials for the estimation of pancreatic beta-cells function
Haemoglobin A1C (18)			
HbA1C	High-performance liquid chromatography	≥ 6.5%	Diagnosis and monitoring of diabetes
Estimated average glucose	Calculation from HbA1C	N/A	Monitoring of diabetes
Microalbumin (19)			
Random urine albumin (microalbumin)	Turbidimetry or nephelometry	Normal: < 30mg/g creatinine Moderate increase: 30-300mg/g creatinine Severe increase: > 300mg/g creatinine	Kidney disease and/or management of diabetic complications

* There are no established cut-off values; clinically signifi cant ranges will vary depending on methodologies used

If you've missed any of our Clinical Insight Technical Reports please visit our website for a free download at www.acmgloballab.com/Clinical-Insight