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The metabolic syndrome

Background

The metabolic syndrome (MetSy) is increasingly common in Australia. It is associated with the rise in obesity and lifestyle risk behaviours. It is also controversial – its value in predicting cardiovascular disease and diabetes risk and in guiding therapy has been challenged.

Objective

This article aims to provide advice on the diagnosis of the MetSy and the principles for its prevention and management in the context of primary care, taking into consideration aetiological factors and the complexity of managing its constituent risk factors.

Discussion

Diagnosis of the MetSy is useful in focusing attention on central adiposity and insulin resistance as risk factors both for the syndrome, and cardiovascular and diabetes morbidity and mortality. Its assessment requires measurement of waist circumference – a simple but seldom performed procedure in general practice. The most essential components for the prevention and management of the MetSy are measures to change diet and physical activity in order to achieve and sustain weight loss.

Keywords

metabolic syndrome; prediabetic state, diabetes mellitus; lipid metabolism disorders; hypertension; preventive medicine

CPD

The metabolic syndrome (MetSy) is increasingly common, both in Australia and overseas. The Australian Diabetes, Obesity and Lifestyle study (AusDiab) in 2000, found that 19% of Australians aged 25 years and over met the criteria for a diagnosis of the MetSy.[1] The follow up study in 2004–05, found the annual incidence of the MetSy to be 3%. The prevalence in general practice appears to be similar. A 2006 Bettering the Evaluation and Care of Health (BEACH) study found that while 43.7% of patients had central obesity, 15.6% had the MetSy.[2]

What is the MetSy and why is it important?

The MetSy is a cluster of risk factors comprising:

- excess abdominal weight
- lipid abnormalities
- hypertension
- elevated glucose levels.

It is not only an epidemiological clustering of risk factors, but also has a common underlying pathophysiological cause: insulin resistance associated with central adiposity. These are in turn related to underlying genetic and early life influences and a range of lifestyle risk factors, including sleep deprivation and physical inactivity.

Until recently, there has been a multiplicity of definitions. This has been resolved in 2009 by the publication of a joint statement and a single definition agreed to by a number of relevant national and international bodies.[3] The presence of any three of the five risk factors described in *Table 1* is diagnostic of the MetSy. This definition does not require the measurement of insulin resistance or a glucose tolerance test. It does, however, require ethnic and nation specific thresholds for waist circumference to be assessed. For European populations, the cut-off for waist circumference is ≥102 cm in males and ≥88 cm in females, whereas in Asian populations it is ≥90 cm in males and ≥80 cm in females (*Table 2*).[4]

The MetSy is important because it identifies patients at increased risk of cardiovascular disease (CVD), diabetes and chronic kidney disease (CKD). The risk of having CVD, diabetes and CKD among people with the MetSy is 2–3 times that of people without the condition.[5] It also increases the risk of complications in those with CVD and diabetes. Overall meta-analysis of studies suggests that there is a 1.6–fold increase in mortality in patients with the MetSy compared to those without it.[6]

Table 1. Criteria for clinical diagnosis of the MetSy[3]

Measure	Categorical cut point
Elevated waist circumference	Population specific (see *Table 2*)
Elevated triglyceride levels (or drug treatment for elevated triglycerides)	≥1.7 mmol/L
Reduced HDL-C (or drug treatment for reduced HDL-C)	<1.0 mmol/L in men, <1.3 mmol/L in women
Elevated blood pressure (or drug treatment for hypertension)	≥130 systolic or ≥85 diastolic
Elevated fasting glucose (or drug treatment for elevated glucose)	>5.5 mmol/L

Table 2. Waist circumference thresholds for abdominal obesity[4]

	Recommended threshold in waist circumference for abdominal obesity (high risk)	
Population	**Men**	**Women**
European/North American	≥102 cm	≥88 cm
Asian	≥90 cm	≥80 cm
Central and South American	≥90 cm	≥80 cm
Middle Eastern/Mediterranean	≥94 cm	≥80 cm
Sub-Saharan African	≥94 cm	≥80 cm

There have been questions raised about how much extra value the MetSy provides in predicting CVD and diabetes risk over and above its constituent risk factors.[7] For example, fasting glucose was found to be a better predictor of diabetes risk than the MetSy in the AusDiab study.[8] Nor does the MetSy provide a quantifiable assessment of absolute CVD risk, as it does not take into consideration other key determinants of risk such as smoking, age and gender. Therefore it can only provide an estimate of relative risk, ie. twice the risk of a CVD event compared with similar patients who do not have the MetSy. The main advantage of the detection of the MetSy is its focus on central obesity and preventive interventions to address this as well as hyper-insulinaemia.

What are the barriers to diagnosis?

Although the data required is readily available, the MetSy is infrequently diagnosed in Australian general practice. Our own research suggests that waist circumference is the least frequently recorded measure in middle aged patients in general practice (recorded in less than 1 in 5 patients).[9] It is unclear why this is so, given the emphasis on waist circumference in the recommendations of a number of guidelines including The Royal Australian College of General Practitioners *Guidelines for preventive activities in general practice*.[10,11] The low rate of assessment appears to be due to reluctance on the part of clinicians and patients. One simple strategy found to be successful in The Netherlands was to mail a tape measure to patients inviting them to have their risk of the MetSy assessed if they had a waist circumference above a cut-off.[12] This may be particularly useful in men who may be less likely to seek preventive care opportunistically when presenting for other conditions. However, it is important to remember that the cut-off for waist circumference differs for various ethnic groups (*Table 2*).

Patient health literacy and attitudes can be further barriers to the assessment and management of the MetSy. In one study in Finland, patients with the MetSy were more likely to have blame-shifting attitudes and to be socially alienated than those without the syndrome.[13]

There are many ways in which the risk of diabetes and CVD can be assessed in clinical practice: diagnosis of the MetSy, assessment of absolute CVD risk, completion of the Australian Diabetes Risk Assessment (AUSDRISK) questionnaire and score for diabetes risk and a range of single risk measures. The diagnosis of the MetSy needs to be explained in the context of broader assessments of CVD or diabetes risk and can provide additional information, which may help in targeting particular risk factors such as central obesity or loss of muscle tone or muscle mass.

Can it be prevented?

The MetSy can be prevented by interventions that modify diet and physical activity and control weight. Physical activity is especially important. The risk of MetSy is reduced by increased leisure time physical activity, especially higher intensity activities such as fast walking or jogging.[14] It is increased by sedentary behaviour such as watching television, especially in older patients.[15] Interventions in childhood and adolescence, including reduction in screen time and increased participation in sporting activities, may decrease the likelihood of the MetSy developing later in life. Measures to prevent MetSy should be integrated with broader preventive health measures to control the global rise of chronic diseases such as CVD and diabetes. The diabetes prevention trials have demonstrated that it is possible to prevent diabetes in high risk populations and preventive strategies targeting the MetSy should naturally be linked to these.[16–18]

How is it managed?

Ideally, management of the MetSy should focus on its underlying cause. The mainstays of treatment are lifestyle interventions to address central obesity and insulin resistance.[19] Weight loss interventions based on caloric restriction, increased physical activity and behaviour modification have been recommended by the National

Health and Medical Research Council new obesity management guidelines.[11] These may include general advice such as reducing portion size and high energy foods, as well as a dietary program to create a 2 500 kilojoule energy deficit – usually designed by a dietician. The goal is to achieve a 5–10% reduction in weight.

Although weight loss depends more on dietary restrictions than physical activity, physical fitness has independent effects on glucose metabolism and diabetes and CVD risk.[20,21] In the presence of the MetSy, increased emphasis should be placed on at least 30 minutes of aerobic activity and resistance training, especially in the elderly and in those who have comorbid depression.[22]

The next step is to consider medications and other conditions that may contribute to the risk of central obesity and insulin resistance. Foremost among the medications are psychotropic medications, notably the newer antipsychotic agents. Long term use of antidepressants, including selective serotonin reuptake inhibitors has also been associated with increased risk of the MetSy. Other medications that may contribute to weight gain include some anticonvulsants and beta-blockers (notably propranolol).[11] Polycystic ovary syndrome (PCOS) and sleep apnoea require appropriate management if these are present.

There are unfortunately no medications currently licensed for use in Australia to specifically reduce insulin resistance in patients with the MetSy. Metformin and the thiazolidinediones (or 'glitazones') may reduce glucose and triglyceride levels. However, their role in treating the MetSy is still controversial and neither is approved for this purpose in Australia (except in the treatment of PCOS). Furthermore, metformin was found to be inferior to lifestyle interventions in the United States Diabetes Prevention Program Outcome trial and its long term follow up.[18,23] Thus, drug therapy needs to currently focus on medications to address each of the physiological factors separately – blood pressure, lipids and glycaemia. Careful monitoring is required, however, as there is a risk that use of statins may reduce physical activity (through reduced exercise tolerance and muscle pain) and contribute to weight gain and insulin resistance.[24]

Bariatric surgery may need to be considered to achieve sufficient weight loss, especially in patients with a body mass index greater than 35. Gastric surgery has been demonstrated to reverse the MetSy in obese patients and prevent diabetes.[25,26] Improving access to affordable surgical interventions remains a challenge to our health systems.

Conclusion

In the absence of specific therapeutic regimens, the MetSy remains a controversial diagnosis. Its value is as an additional clinical indicator which underscores the importance of addressing central adiposity and associated insulin resistance as risk factors for CVD and diabetes. It is important for the focus of treatment of the MetSy to be on lifestyle changes, especially increased physical activity and weight reduction.

Key points

- Diagnosis of the MetSy is based on meeting three of five criteria (central adiposity, elevated plasma triglyceride, reduced high density lipoprotein cholesterol, hypertension and elevated fasting glucose).
- Measurement of waist circumference is a key part of the assessment.
- The MetSy conveys 2–3 times the risk of diabetes and CVD and 1.6 times the overall mortality.
- Prevention and treatment should focus firstly on increasing physical activity and reducing weight.
- Associated conditions such as PCOS and sleep apnoea need to be identified and managed, and the use of medications associated with weight gain modified where possible.
- There is no specific pharmacotherapy. Treatment should focus on management of individual risk factors such as lipids, blood pressure and glucose. However, care needs to be taken not to accelerate weight gain and reduce capacity for physical activity.

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