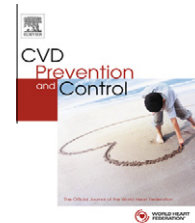




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REVIEW

Metabolic obesity: A new therapeutic target for cardio-metabolic risk reduction

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Available online 12 June 2010

KEYWORDS

Metabolic obesity;
Cardio-metabolic risk;
Waist circumference;
Body mass index;
Metabolic surgery

Summary

During the last couple of years, the focus of attention has drifted from coronary risk to cardio-metabolic risk because of the growing epidemic of cardio-metabolic disorders such as obesity, metabolic syndrome, diabetes, and cardiovascular disease (CVD). Physical inactivity and consumption of high-energy foods are the root causes of this epidemic.

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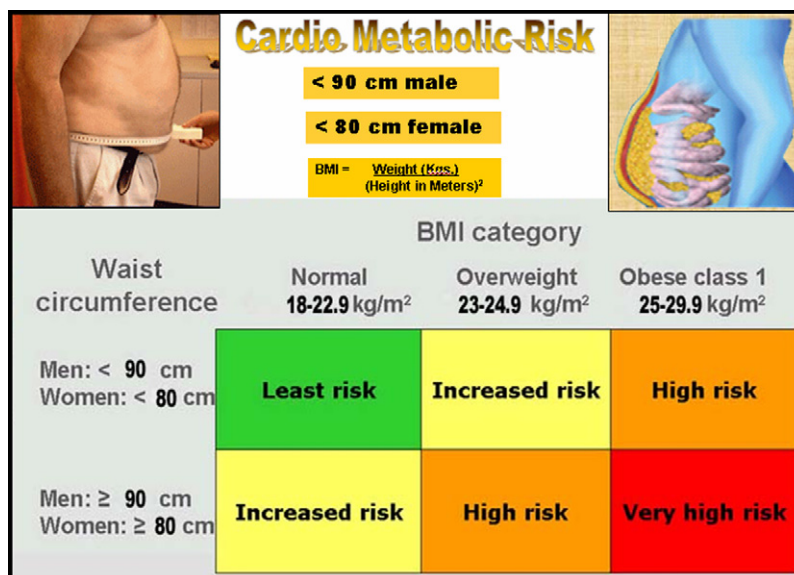


Figure 1 Assessment of cardio-metabolic risk in Asian Indians.

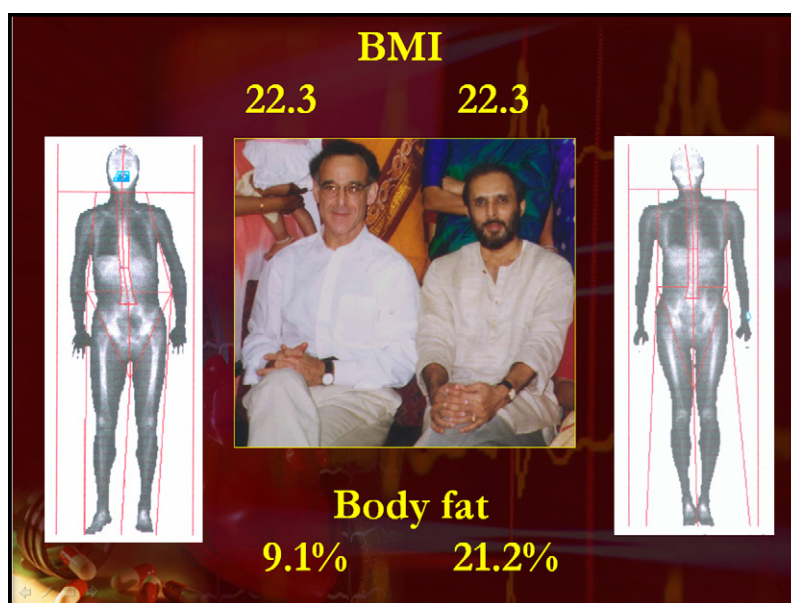


Figure 2 Abnormal body fat composition in Indians.

Assessment of cardio-metabolic risk

The assessment of cardio-metabolic risk is of crucial importance to check the growing menace of cardio-metabolic diseases. This risk can be simply assessed by measuring the waist circumference (WC) and body mass index (BMI) as shown in Fig. 1. The normal body mass index for Asian Indians is 18–22.9 kg/m² and normal waist circumference is <90 cm for men and <80 cm for women [1].

If the WC is normal and the BMI is also normal, the cardio-metabolic risk is lowest. However if the waistline is above normal then even in the presence of a normal BMI, the cardio-metabolic risk is increased. With a further

increase in BMI coupled with increased WC, the cardio-metabolic risk increases progressively.

Distressing enough, Indians have abnormal body fat composition so that for the same BMI they have a larger proportion of visceral fat. This is exhibited in Fig. 2.

The body mass index of the past president of ADA (left) and Dr. C. Yagnik (right), a Diabetologist from India, is the same (22.3 kg/m²) but there is a tremendous difference in the body fat (9.1% and 21.2%, respectively). This phenomenon has led to the term ‘thin fat Indians’. Thus Indians are more prone to develop the metabolic syndrome.

A CT scan is usually not required for the evaluation of the presence of metabolic obesity. But, in case of doubt, the

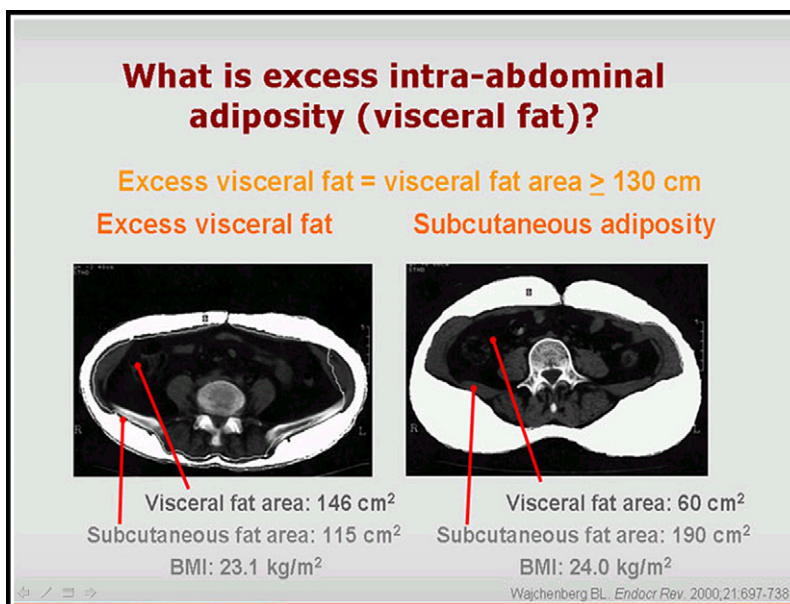


Figure 3 CT scan of patients with excess visceral fat (left) and subcutaneous adiposity (right).

quantitation of subcutaneous and visceral fats can be made by CT or MRI (Fig. 3).

Obesity in childhood and adolescence

Obesity in childhood and adolescence is reaching alarming and epidemic proportions and in the Indian context, this is about 15–20%. As a consequence of this, a new epidemic of childhood diabetes is emerging and it is speculated that if the same trend continues, type 2 diabetic children may be in catheterization laboratory as early as third decade of their life for evaluation of coronary artery disease and this is indeed very distressing.

Cardio-metabolic consequences of metabolic obesity

The adipocyte present in the visceral fat secretes a panoply of diabetogenic and atherogenic hormones (Fig. 4) which results in a clustering of cardio-metabolic risk factors, resulting in the development of type 2 diabetes mellitus

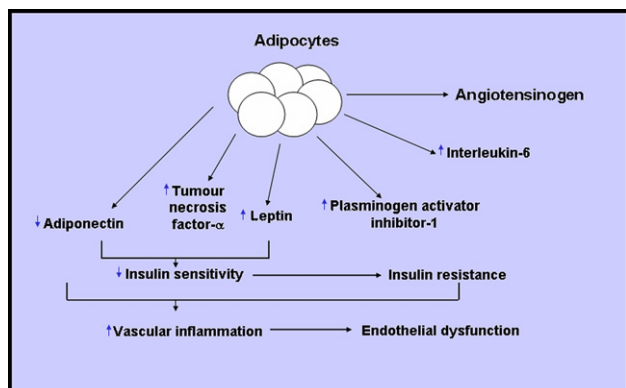


Figure 4 Role of adipocyte in metabolic obesity.

(T2DM) on the one hand and on the other hand causing cardiovascular disease. The presence of T2DM further adds to the development of cardiovascular disease (Fig. 5).

Is metabolic syndrome associated with increased cardiovascular mortality?

Lakka et al. [2] in his paper of 12 years follow-up has demonstrated that metabolic syndrome is associated with increased coronary heart disease mortality, cardiovascular heart disease mortality, and all-cause mortality (Fig. 6).

Treatment

The treatment of metabolic obesity has three components:

- (a) Lifestyle modification.
- (b) Drugs.
- (c) Metabolic surgery.

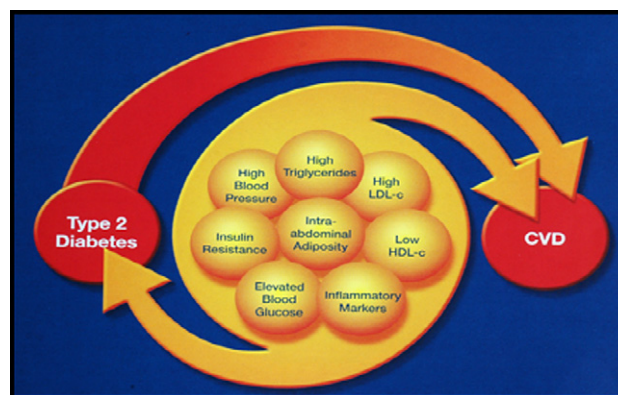


Figure 5 Clustering of cardio-metabolic risk factors in metabolic obesity.

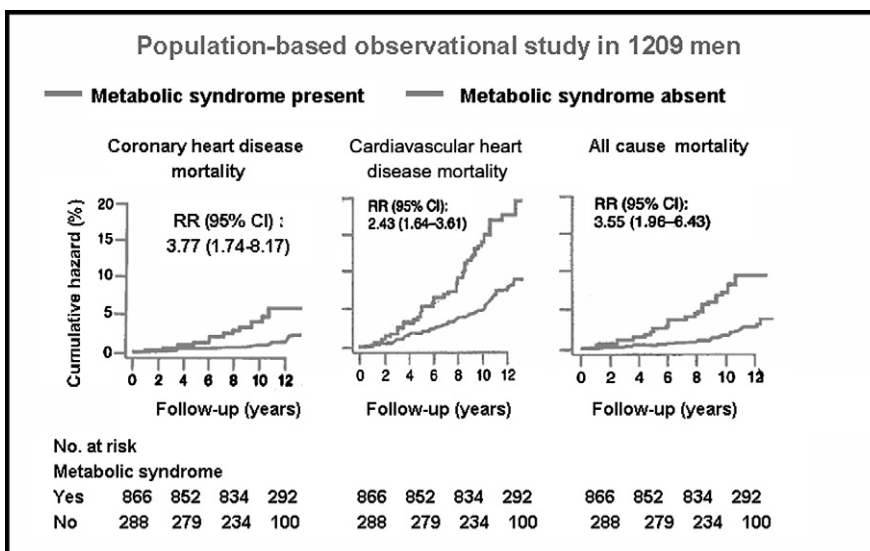


Figure 6 Adverse prognostic implication of cardiovascular metabolic syndrome.

Lifestyle modification

Modern society is engulfed in a lifestyle of physical inactivity (Fig. 7) and consumption of high-energy foods due to a booming economy and TV Cola and computer culture (Fig. 8). There is also tendency to upsize food items when we need to minimize and not maximize (Fig. 9). The ‘‘M’’ of McDonald’s in reality stands for metabolic obesity.

Drugs

The two drugs which are used in the treatment of obesity are Sibutramine and Orlistat [3]. Rimonabant came with a bang to target cardio-metabolic obesity but despite its efficacy it has been withdrawn from the market due to its psychiatric side effects. Sibutramine is used at a dose of 10–15 mg once a day for individuals with lack of satiety and frequent snacking. However, it should not be used in individuals with CVD as shown in the SCOUT trial. Orlistat is used in doses of 60–120 mg three times a day in individuals at risk of developing type 2 diabetes, high LDL-choles-



Figure 8 TV Cola culture.



Figure 7 Physical inactivity.



Figure 9 Upsizing food.

terol, and CVD. The most commonly reported adverse effects of orlistat include steatorrhea, bloating, oily spotting, fecal urgency, and fecal incontinence. Usually drug therapy is associated with weight loss of 5–10% in the first

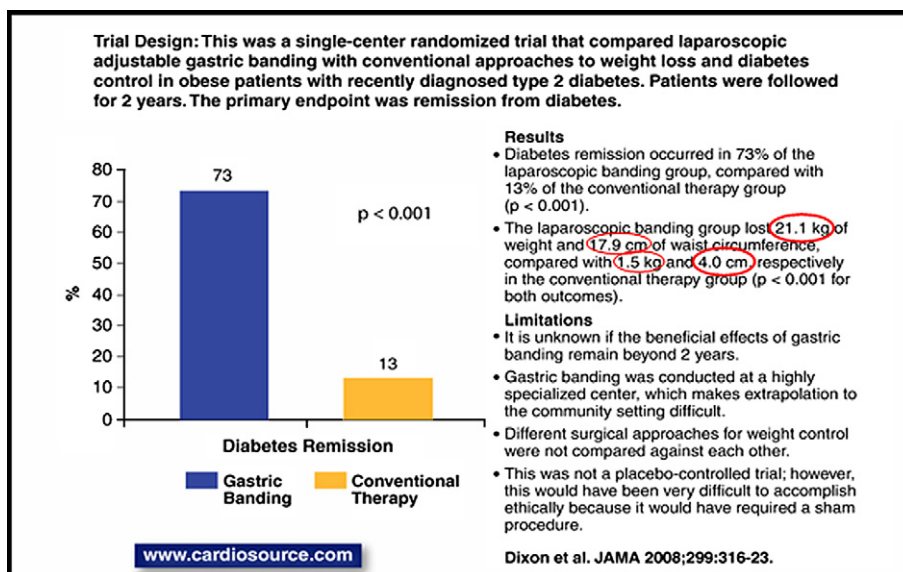


Figure 10 Adjustable gastric banding & conventional therapy for type 2 diabetes.

Surgery	Strengths	Weaknesses
Roux-en-Y gastric bypass	Most common form of bariatric surgery in the United States Less malabsorptive than duodenal switch Improvement in hypertension, hyperlipidemia, and diabetes	More invasive than gastric banding Malabsorption may lead to vitamin deficiencies Higher risk of complications than gastric banding.
Duodenal switch	Highest rate of weight loss Improvement in hypertension, hyperlipidemia, and diabetes	Greatest risk of vitamin deficiencies Greatest risk complications
Gastric banding	Smallest risk of complications Least invasive procedure	Least improvement in hyperlipidemia, hypertension, and diabetes

Parameter	International guideline (kg/m ²)	Consensus for Asian Indians (kg/m ²)
BMI without co-morbidity	40	37.5
BMI with co-morbidity	35	32.5

3–6 months. As per international guidelines, drug therapy is utilized in individuals with BMI above 27.5 with co-morbidities/BMI above 30. However, for Asian Indians the consensus is BMI above 25 with co-morbidities/BMI above 27.

Metabolic surgery

This has emerged as a very exciting option for metabolic obesity. It offers several benefits:

(a) *Mortality benefit:* This is the only modality that has shown a mortality benefit. An American study [4]

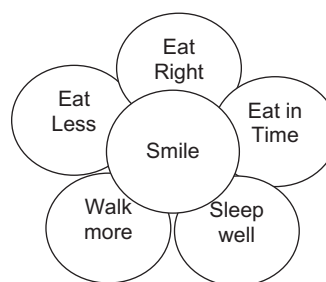


Figure 11 The simple mool mantra for preventing metabolic obesity.

has shown a 40% reduction in all-cause mortality during a mean follow-up of 7.1 years and a Swedish study [5] has shown a 29% reduction in mortality over a mean follow-up of 10.9 years.

(b) *Dramatic remission of diabetes:* In a study [6] comparing adjustable gastric banding and conventional therapy for type 2 diabetes, remission of diabetes occurred in 73% of the laparoscopic banding group,

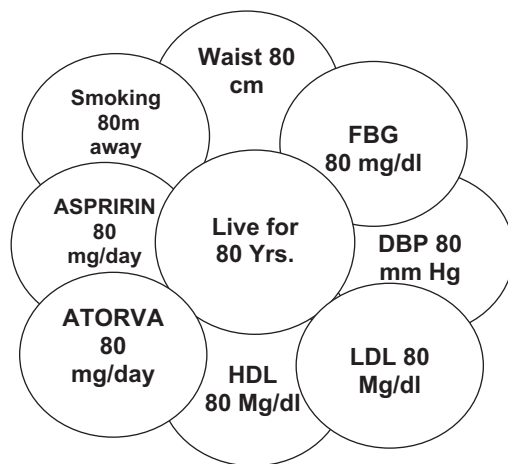


Figure 12 The rule of 80s for preventing CVD.

compared with 13% of the conventional therapy group ($p < 0.001$) (Fig. 10).

- (c) *Marked loss of weight and decrease in WC:* The same study [6] showed that the laparoscopic banding group lost 21 kg of weight and 17.9 cm of waist circumference, compared with 1.5 kg and 4.0 cm, respectively, in the conventional therapy group ($p < 0.001$ for both outcomes) .

However how long these effects will persist is still not clear.

Types of bariatric surgery

The different types of bariatric surgery are shown in Table 1. Gastric banding is the most popular surgery with least complications but it is not the most effective one.

Interestingly, transoral methods for reducing gastric volume or bypassing the stomach altogether as a treatment for

obesity are gaining steam and this may prove to be a boon for these patients in the future.

Indications for bariatric surgery

The indications of bariatric surgery are a little different for Asian Indians compared to those for the western population (Table 2).

Conclusion

Thus metabolic obesity is associated with increased cardio-metabolic risk and development of type 2 diabetes and cardiovascular disease. Prevention is the best solution and this can be achieved using a simple mool mantra (Fig. 11). To prevent CVD and increase longevity, one has to follow the rule of 80 (Fig. 12).

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