Update in The Management of Obesity

Ketut Suastika

ABSTRACT

Significant increase of obesity prevalence in almost all countries in the world recently has had obesity as a global health problem, and WHO in 1998 defined it as “the global epidemic”. Simply, obesity is defined as an excessive fat accumulation in fat tissue due to imbalance of energy intake and expenditure. Body mass index is a simple method for defining the degree of overweight and obesity, however, waist circumference is the preferred measure of abdominal obesity because it has greater relationship with the risk of metabolic and cardiovascular diseases.

Body fatness reflects the interactions of development, environment and genetic factors. The role of genetic factors has already existed, nevertheless, environment factors are likely more important in developing obesity. Increased mortality among the obese is evident for several life-threatening diseases including type 2 diabetes, cardiovascular disease, gallbladder disease, and hormone-sensitive and gastrointestinal cancers. Risks are also higher for some non-fatal conditions such as back pain, arthritis, infertility and, in many westernized countries, poor psychosocial functioning. Obesity is not only threatening health, also impacts on high economic and social cost.

Effective prevention of obesity should be focused to high risk individuals or groups. Individuals who have some existing weight-related problems and those with a high risk of developing obesity co-morbidity such as cardiovascular disease and type 2 diabetes should be a key priority in this prevention strategy.

Although weight loss in obese persons of any age can improve obesity-related medical complications, physical function, and quality of life, the primary purpose for weight-loss therapy may differ across age group. The current therapeutic tools available for weight management are: (1) lifestyle intervention involving diet, physical activity, and behavior modification; (2) pharmacotherapy; and (3) surgery. Moderate weight loss (5-10% of initial weight) by any programs is a realistic target in management of obesity associated with improvement of risk factors of metabolic and cardiovascular diseases.

Key words: obesity, consequences, management, benefit of weight loss.

INTRODUCTION

Obesity is an important health problem because it has tight relationship with metabolic and cardiovascular diseases. Significant increase in prevalence of obesity in a almost all countries in the world recently has led obesity to be a global health problem, and WHO in 1998 defined as “the global epidemic”.1 Obesity affects one-third of industrial countries, and chronic diseases have made obesity to be a major killer.2 The latest reports in United States (NHANES 2003-2004) found that 17.1% of US children and adolescents were overweight and 32.2% of adults were obese. Comparing NHANES 1999-2000, 2001-2002, and 2003-2004, the prevalence of overweight among children and adolescents and obesity among men increased significantly during 6-year period from 1999 to 2004; among women, no significant increase in obesity was observed.3

Our study in three villages in Bali involving 1070 people found that the prevalence of obesity by waist circumference (WC, abdominal obesity) were 12.8% at Pedawa village, 17.7% at Ceningan village, 20.6% at Sangsit village, and totally 17.7 %. By body mass index (BMI), the prevalence of overweight at risk and obesity were 14.6% and 13.5% at Pedawa village, 13.1% and 12.8% at Ceningan village, 16.7% and 26.4% at Sangsit village, and totally 15.2% and 19.1%, respectively.4,5

Obesity, actually, affects people not only in developed countries, but also in developing countries. Prevention and control of noncommunicable diseases is a high priority for WHO and obesity management as an important part of the strategy.

DEFINITION AND CLASSIFICATION OF OBESITY

Simply, obesity is defined as an excessive fat accumulation in fat tissue, which is generally caused by imbalance of energy intake and expenditure. Body mass index (BMI) is a simple method for defining the degree of overweight and obesity and it is closely related with the measurement of body fatness by hydrostatic method. Even though it is related to health consequences, distribution of body fat is more important. Fat accumulation at
abdomen (central or abdominal obesity) is more associated with cardiovascular diseases than with peripheral distribution. While this can be measured with serial magnetic resonance imaging (MRI), computed tomography (CT), or by dual-energy x-ray absorptiometry (DEXA), it is usually assessed with a single CT or MRI scan performed at L3/L4 level and the visceral fat area calculated. The ratio waist to hip circumference (WHR) is also used as a measure of abdominal obesity; however, waist circumference (WC) is the preferred measure of abdominal obesity compared to the WHR.1,6,7

Table 1. Proposed Classification of Weight by BMI in Adult Asians

<table>
<thead>
<tr>
<th>Classification</th>
<th>BMI (kg/m²)</th>
<th>Risk of co-morbidity</th>
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<tbody>
<tr>
<td>Underweight</td>
<td>&lt; 18.5</td>
<td>Low (but increased risk of other clinical problems)</td>
</tr>
<tr>
<td>Normal range</td>
<td>18.5-22.9</td>
<td>Average</td>
</tr>
<tr>
<td>Overweight</td>
<td>&gt; 23</td>
<td></td>
</tr>
<tr>
<td>At risk</td>
<td>23-24.9</td>
<td>Increased</td>
</tr>
<tr>
<td>Obese I</td>
<td>25-29.9</td>
<td>Moderate</td>
</tr>
<tr>
<td>Obese II</td>
<td>&gt; 30</td>
<td>Severe</td>
</tr>
</tbody>
</table>

The Asia-Pacific Perspective: Redefining Obesity and Its Treatment, 2000

Different from Europeans, Asia-Pacific populations have different body fat distribution, a more centralised distribution of fat. Morbidity and mortality are occurring in people with lower BMIs and smaller WC. Thus they tend to accumulate intra-abdominal fat without developing generalised obesity. Therefore, classification of obesity by BMI for Asian population is recommended different ranges based on risk factors and morbidities (Tabel 1). Abdominal obesity is defined for Asian people as WC > 90 cm for men and WC > 80 cm for women. The measurement of overweight and obesity in children and adolescents poses particular problems due to different rates of maturation and growth. The BMI-for-age chart is recommended. Those greater than the 95<sup>th</sup> percentile are considered obese, whilst those greater than 85<sup>th</sup> percentile of BMI for age are “at risk”.8

ETIOLOGY OF OBESITY

Body fatness, in general, reflects the interactions of development, environment and genetic factors. The role of genetic factor is proven by increase twice to three times the prevalence of obesity at individuals with family history of obesity. Numerous genetic models of obesity in rodents have been identified.9 Genes, when mutated in particular ways, confer marked obesity in rodents; and it has been reviewed by Allison et al.10 Based on epidemiological studies in Europe, environment factors that influence the prevalence of obesity are: (1) demography factors: (a) age (increasing with age at least until 55 years in men and 70 years in women), (b) gender (woman usually has higher prevalence after 50 years), (c) ethnics; (2) sociocultural factors: (a) levels of education (the prevalence of obesity is higher in those with lower education), (b) income/professional (the prevalence of obesity is higher among lower incomes), (c) marriage status (usually increases after married); (3) biological factor: parity (BMI increases with number of parities); (4) behavior factors: (a) nutrition (fat contained in food), (b) smoking (smoking induces weight loss and smoking cessation increases body weight), (c) alcohol consumption (moderate alcohol consumption associated with higher BMI), (d) physical activity (inactive people are heavier than those physically active).7 The health experts and common people themselves are aware that food intake changing recently is the most important environment factor that causes obesity. Turning traditional food to fastfood containing higher calories, higher fat, and lower fibers induces obesity in most countries in the world, including Indonesia.

CONSEQUENCES OF OBESITY

A large-scale prospective study involving 750,000 individuals proved that obesity increase risk of all-cause mortality, with elevated risk of 1.9 being reported both men and women who are more than 40% of the average weight. Increased mortality among the obese is evident for several life-threatening diseases including type 2 diabetes, cardiovascular disease, gallbladder disease, and hormone-sensitive and gastrointestinal cancers. Risks are also higher for some non-fatal conditions such as back pain, arthritis, infertility and, in many westernized countries, poor psychosocial functioning. Approximately relative risks among the obese for several health problems have recently been reported by WHO. (Table 2)

ECONOMIC AND SOCIAL COSTS

The costs of obesity to community and individuals may be divided into the direct costs to the health system and the indirect or social costs to the individual and community (eg sick days, individual expenditure on weight loss). Economic costs directly depends on major diseases associating obesity such as type 2 diabetes, coronary heart disease, hypertension, endometrial cancer, arthritis and colorectal cancer.

Social and economic impacts of obesity among teenagers, which are greater than many chronic disease problems, have been shown by Gortmaker et al.11 In the
study, it was found that compared to individuals without overweight, women with overweight finished school-year little bit longer, willingness to be married, lower income, higher poverty rate; in men there was also willingness to be married. A study in Sweden showed that obesity caused bad impact to health-related quality of life, especially in women aged 35-64 years.¹² Loss of weight will improve quality of life, such as physical function, dignity, and sexual life.¹³

PREVENTION OF OBESITY

Effective prevention of obesity should be focused on: (1) environment factors including social, culture, politic and structural elements which influence population at large scale; (2) program should be addressed to high risk individuals or groups; and (3) treatment protocol for obese individuals. There are three levels of prevention, they are: universal prevention, selected prevention, and targeted prevention.¹ Universal prevention should be aimed to the whole population to stabilize the level of obesity and eventually lower the incidence and hence the prevalence of obesity. A reduction in weight-related disease by lifestyle modification including improved diet and physical activity levels are objectives, as well as a reduction in smoking and alcohol consumption. Selected prevention aims to educate sub-groups of the population with a high-risk of obesity. Such strategies can be initiated in appropriate settings which allow access to these high-risk group, including schools, community centres and primary care venues. Targeted prevention aims to prevent weight gain and reduce the number of people with weight-related disorders in those individuals that are already overweight or those with biological markers associated with excess adiposity, who are not yet obese. Individuals who have some existing weight-related problems and those with a high risk of developing obesity co-morbidity such as cardiovascular disease and type 2 diabetes should be a key priority in this prevention strategy.¹,⁸

TREATMENT OF OBESITY

Although weight loss in obese persons of any age can improve obesity-related medical complications, physical function, and quality of life, the primary purpose for weight-loss therapy may differ across age group. The current therapeutic tools available for weight management are: (1) lifestyle intervention involving diet, physical activity, and behavior modification; (2) pharmacotherapy; and (3) surgery.

Lifestyle Intervention

Behavior approaches are designed to help participants learn new behaviors related to energy balance. Simply put, this involves teaching participants to reduce caloric intake and to increase energy expenditure.¹⁴ Principles of dietary measures in Asian-Pacific people are: food selection should be guided by available foods which vary from country to country; distribution of food intake should be as even as possible throughout the day and meals should not be ‘skipped’ as a weight control method; meal should be adequately sized so that snacks are not needed between meals; 20-30% or less of the total dietary energy should be from fats and oils; carbohydrates should account for 55-65% of total energy; protein should not exceed 15% of total energy; fresh fruits, vegetables and wholegrain foods should be encouraged; and alcohol intake should be restricted.⁸ A low-calorie diet that reduces energy intake by 500-1000 kcal/d results in a weight loss of ≈ 0.4-0.9 kg/week and a weight loss of ≈ 8-10% by 6 months.¹⁵ Very low calorie diet (VLCD), a diet of 400 to 800 kcal per day, is

<table>
<thead>
<tr>
<th>Greatly increased (RR&gt;3)</th>
<th>Moderately increased (RR 2-3)</th>
<th>Mildly increased (RR 1-2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2 Diabetes</td>
<td>Coronary heart disease</td>
<td>Cancer (breast cancer in postmenopausal women, endometrial cancer, colon cancer)</td>
</tr>
<tr>
<td>Gallbladder disease</td>
<td>Hypertension</td>
<td>Reproductive hormone abnormalities</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>Osteoarthritis (knees and hips)</td>
<td>Polycystic ovary syndrome</td>
</tr>
<tr>
<td>Metabolic Syndrome</td>
<td>Hyperuricemia and gout</td>
<td>Impaired fertility</td>
</tr>
<tr>
<td>Breathlessness</td>
<td></td>
<td>Low back pain</td>
</tr>
<tr>
<td>Sleep apnoea</td>
<td></td>
<td>Increased anaesthetic risk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Foetal defects associated with maternal obesity</td>
</tr>
</tbody>
</table>
VLCDs have been shown to produce excellent initial weight loss, which averages 20 kg in 12 weeks. As for physical activity, another important factor in weight management, advise should be tailored for age and cultural climate and emphasise increased daily activity such as walking and climbing stairs. It is not necessary for the obese patient to participate in strenuous activity; low to medium intensity is sufficient.

Pharmacotherapy

On the basis of their mechanisms of action, drugs used for weight loss can be divided into two categories—appetite suppressants (act on the central nervous system) and lipase inhibitors (act on gastrointestinal system). The mechanism of action, their side effects and their Drug Enforcement Administration status are seen in Table 3. Rimonabant, a novel selective cannabinoid-1 receptor blocker, has been shown to reduce body weight and improve cardiovascular risk factors in obese patients. Specific groups in which antiobesity drugs are not recommended i.e. children, patients who have previously suffered adverse effects from drugs in this category, pregnant and lactating women, and patients who are concurrently taking other selective serotonin re-uptake inhibitors.

**Surgical Treatment**

Surgery can be an effective therapy to treat those with BMI > 40 kg/m². Gastric bypass procedures result in more weight loss than gastroplasty. Bariatric procedures in current use (gastric bypass, laparoscopic adjustable gastric band, vertical banded gastroplasty, and biliopancreatic diversion and switch) have been performed with an overall mortality rate of less than 1%. Adverse events occur in about 20% of cases. A laparoscopic approach results in fewer wound complications than an open approach.

Pharmacologic and surgical management of obesity in primary care has proposed by American College of Physicians (APC). The guideline is based on the evidence report and accompanying background papers developed by the Southern California Evidence-Based Practice Center. The college recommends as follows:

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Table 3. Medications Used for Weight Loss

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of Action</th>
<th>Side Effects</th>
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</thead>
<tbody>
<tr>
<td>Sibutramine†</td>
<td>Appetite suppressant: Combined Norepinephrine and serotonin reuptake Inhibitor</td>
<td>Modest increases in heart rate and blood pressure, nervousness, insomnia</td>
</tr>
<tr>
<td>Phentermine†</td>
<td>Appetite suppressant: Sympathomimetic amine</td>
<td>Cardiovascular, gastrointestinal</td>
</tr>
<tr>
<td>Diethylpropion†</td>
<td>Appetite suppressant: Sympathomimetic amine</td>
<td>Palpitations, tachycardia, insomnia, gastrointestinal</td>
</tr>
<tr>
<td>Orlistat*</td>
<td>Lipase inhibitor: Decreased Absorption of fat</td>
<td>Diarrhea, flatulence, bloating, abdominal pain, dyspepsia</td>
</tr>
<tr>
<td>Bupropion</td>
<td>Appetite suppressant: Mechanism Unknown</td>
<td>Paresthesia, insomnia, central nervous system effects</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Appetite suppressant: Selective serotonin Reuptake inhibitor</td>
<td>Agitation, nervousness, gastrointestinal</td>
</tr>
<tr>
<td>Sertraline</td>
<td>Appetite suppressant: Selective serotonin Reuptake inhibitor</td>
<td>Agitation, nervousness, gastrointestinal</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Mechanism unknown</td>
<td>Paresthesia, changes in taste</td>
</tr>
<tr>
<td>Zonisamide</td>
<td>Mechanism unknown</td>
<td>Somnolence, dizziness, Nausea</td>
</tr>
<tr>
<td>Rimonabant</td>
<td>Cannabinoid-1 receptor Blocker</td>
<td>Nausea, dizziness, influenza, anxiety, diarrhea, insomnia</td>
</tr>
</tbody>
</table>

* Approved by the U.S. Food and Drug Administration for weight loss.
† Drug Enforcement Administration schedule IV.
**Recommendation 1**: clinicians should counsel all obese patients (defined as those with a BMI > 30 kg/m²) on lifestyle and behavioral modifications such as appropriate diet and exercise, and the patient’s goals for weight loss should be individually determined (these goals may encompass not only weight loss but also other parameters, such as decreasing blood pressure or fasting blood glucose levels); **Recommendation 2**: pharmacologic therapy can be offered to obese patients who have failed to achieve their weight loss goals through diet and exercise alone. However, there needs to be a doctor–patient discussion of the drugs’ side effects, the lack of long-term safety data, and the temporary nature of the weight loss achieved with medications before initiating therapy; **Recommendation 3**: for obese patients who choose to use adjunctive drug therapy, options include sibutramine, orlistat, phentermine, diethylpropion, fluoxetine, and bupropion. The choice of agent will depend on the side effects profile of each drug and the patient’s tolerance of those side effects; **Recommendation 4**: surgery should be considered as a treatment option for patients with a BMI of 40 kg/m² or greater who instituted but failed an adequate exercise and diet program (with or without adjunctive drug therapy) and who present with obesity-related comorbid conditions, such as hypertension, impaired glucose tolerance, diabetes mellitus, hyperlipidemia, and obstructive sleep apnea. A doctor–patient discussion of surgical options should include the long-term side effects, such as possible need for reoperation, gall bladder disease, and malabsorption; and **Recommendation 5**: patients should be referred to high volume centers with surgeons experienced in bariatric surgery.

Algorithm for suggested management of obesity has been recommended by APC. The target audience is all clinicians caring for obese patients, defined as those with a BMI of 30 kg/m² or greater. For the Asia-Pacific region, general procedure in management of obesity is seen in Figure 1.

Management of obesity in children differs from that in adults in that the prevention of weight gain is of important rather than focusing on weight loss. The best and most effective way to treat children with obesity is to treat the family, and not the child alone, by encouraging increased daily activity and healthy eating habit.

**Goal for Obesity Therapy**

The achievement of weight normalization is often unrealistic and does not have to be the ultimate goal of weight-reduction strategy. Moderate weight loss (5-10% of initial body weight) can have substantial health benefits (Figure 2).

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**BENEFIT OF WEIGHT LOSS IN OBESITY**

**Effect on Components of Metabolic Syndrome**

The experts agree that obesity is the most important condition which preceeds metabolic syndrome (MetS). Insulin resistance is proposed to be the main factor connecting between obesity and MetS.®

Weight loss or weight gain influences the prevalence of diabetes in adult population. The US First National Health and Nutrition Examination Survey, Epidemiologic Follow-up Study (NHANES) found of 1929 non-diabetic subjects with overweight after following up for 10 years, each kg weight gain was correlated with increasing of 49% risk for diabetes, and each kg weight loss was associated with 33% reducing risk of diabetes. Decreasing incidence of diabetes (odd ratio 0.16) on following up for 8 year after weight loss by surgery also reported by Swedish Obese Subjects (SOS) study. Ten percent weight loss, reduced fat mass, intraabdominal and subcutaneous fat in 21 older men, were followed by the reduced levels of triglyceride, VLDL-cholesterol, apolipoprotein B, and hepatic lipase activity, increased HDL2-cholesterol level and improved insulin sensitivity. Lipid profile improvement after weight loss among obese subjects was also reported by some researchers. The components of MetS were found in 68% of 185 obese subjects; and weight loss of 6.5% with VLCD intervention for 4 weeks lower the systolic and diastolic blood pressure of 11.1 mmHg and 5.8 mmHg respectively.
reduced levels of plasma glucose of 17 mg/dl, triglyceride of 94 mg/dl, and total cholesterol of 94 mg/dl.\textsuperscript{28}

**Effects on Inflammation**

Fat tissue releases inflammatory cytokines, namely adipocytokines, and fibrinolytic regulators. Some of them, tumor necrosis factor-\(\alpha\) (TNF-\(\alpha\)) and interleukin-6 (IL-6), have an important role in consequences of obesity related to cardiovascular diseases, besides expressed and released by fat tissue, they affect endothelial functions, and induce cytokines and adhesion molecules in endothelial cells which are the center of the initial stage of atherogenesis. Inflammatory cytokines are found higher among obese subjects, especially abdominal obese, than those with non-obese. IL-6 was detected 2-3 fold higher in omental fat tissue than in subcutaneous fat tissue.\textsuperscript{29}

Weight loss with any treatments actually could lower inflammatory cytokines. Higher levels of TNF-\(\alpha\), IL-6, P-selectin, intracellular adhesion molecules-1 (ICAM-1), and vascular adhesion molecules-1 (VCAM-1) in obese women compared to non-obese women were observed and reported by Ziccardi et al.\textsuperscript{30} The levels of all cytokines were reduced after 10\% weight loss following programs (diet, exercise, and behavioral counselling) for 1 year. Similar findings reported that compared to normal women, obese non-diabetics and diabetic women have higher levels of serum leptin, IL-6, TNF-\(\alpha\) and CRP and fat tissue. Reduced body weight decreased levels of serum IL-6, CRP and leptin, but TNF-\(\alpha\).\textsuperscript{31,32} Weight loss also reduced adipocytokines as reported by some researchers.\textsuperscript{33-35}

Weight loss also improves levels of hemostatic factors. Compared to control subjects, weight loss of 9.4 kg among men and 7.4 kg among women decreased significantly the levels of plasminogen activator inhibitor-1 (PAI-1) of 31\%, tissue-plasminogen activator antigen (t-PA) of 24\%, and factor VII of 11\%; but not levels of D-dimer, fibrinogen, and protein C.\textsuperscript{36}

REFERENCES

at 19th World Diabetes Congress (IDF 2006). Cape Town, 3-7 December 2006.


