Obesity, metabolic syndrome and bariatric surgery: A narrative review

Obesity and insulin resistance are at the center of most cases of metabolic syndrome (MetS), which might increase the risk of cardiovascular disease by approximately twofold and type 2 diabetes mellitus by approximately fivefold. Aside from lifestyle intervention and drug therapy, bariatric surgery (BS) is considered a definitive treatment for this disease.

PREDICTORS AND MARKERS OF OBESITY AND METS IN ASIA

The worldwide prevalence of obesity has risen steadily, but the challenge of identifying high-risk individuals remains. Previous estimations of obesity used a simple anthropometric index, such as waist circumference, waist-to-hip ratio, waist-to-height ratio or body mass index[1]. A recently developed anthropometric parameter (the new hip index) found a U-shaped relationship between mortality and hip circumference, height, and weight in the USA. However, the hip index was not an independent risk factor for diabetes mellitus in China[2].

Several recent studies have been published on the predictors of MetS. Serum gamma-glutamyl transferase was positively associated with MetS and its components in Korean children and adolescents, and could be a useful measure for identifying young people with MetS[3]. Another study found that lipid accumulation product, visceral adiposity index, and the products of triglycerides and glucose were reliable novel surrogate markers for identifying MetS in middle-aged and elderly Chinese individuals[4]. Elevated circulating member B levels of the family with sequence similarity 3 might be a predictor of MetS

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onset and progression[5]. Plasma xanthine oxidase activity was correlated with indices of insulin resistance and liver dysfunction in Japanese patients with type 2 diabetes and MetS[6]. Table 1 shows the summary results for predictors and markers of obesity and MetS.

MECHANISM OF OBESITY AND METS

The leading mechanisms of obesity include environmental and genetic factors, as well as energy balance dysregulation; the main treatment strategies include therapeutic lifestyle changes, adjunctive pharmacotherapy and BS[7].

Adipose tissue is a metabolic and endocrine tissue known to secrete adipocytokines or adipokines, which are bioactive molecules, such as fatty acids, adiponectin, leptin and interleukin-6. Recently, obesity-induced tissue remodeling was induced by various stromal cells; insufficient lipolysis in adipose tissue, and the amount of stored and removed triglycerides in adipocytes were found to be related to obesity[8,9]. Furthermore, endurance exercise training is reported to increase catecholamine-stimulated adipocyte lipolysis[9].

The impact of adipose tissue insulin resistance on whole-body glucose metabolism might be mediated by adipose tissue inflammation, and clinical trials with anti-inflammatory drugs, such as salicylate in type 2 diabetes and monoclonal antibody against interleukin-1β in cardiovascular diseases are now under study[10]. However, hedonic hunger was negatively associated with good glycemic control in obese and type 2 diabetes patients[11]. Methods that could inhibit appetite and increase leptin might improve glycemic control and quality of life in obese type 2 diabetes patients[12].

BS, also known as metabolic surgery, is the most effective means of obtaining major and sustainable weight loss, reducing cardiovascular deaths, and lowering the incidence of cardiovascular events in obese individuals[13]. The specific mechanisms of these beneficial effects have remained largely unknown. Except for the mechanical explanations of restriction and malabsorption, it is well accepted that the mechanisms of action are largely determined by visceral signals and weight-independent factors, such as hormones, bile acids, gut microbiota, microbiota-bile acid interactions, the nervous system and other potential underlying mechanisms[14].

There are several studies on basic mechanistic research of BS. In diabetic rats, the restoration of myocardial glucose uptake alleviates diabetic cardiomyopathy after duodenal-jejunal bypass surgery through facilitating myocardial glucose transporter (GLUT; GLUT1 and GLUT4) translocation[15]. Although BS can treat morbid obesity, until the mechanism can be clarified, we imagine that the beneficial effects of surgical treatment could also be achieved through non-surgical devices.

PREDICTION AND RECURRENCE OF OBESITY AFTER BS

The role of BS in treating obesity and obesity-related complications has been repeatedly shown, but the recurrence of obesity and diabetes after BS is another serious concern. In the USA, the remission rates of type 2 diabetes at 2, 6 and 12 years of follow up were 75, 62 and 51% after Roux-en-Y gastric bypass, respectively[16]. The main preoperative predictive factors of type 2 diabetes remission through BS include a younger age, shorter diabetes duration, lower glycosylated hemoglobin level, appropriate fasting C-peptide, no insulin use and visceral fat area[17,18]. Recently, Li *et al.*[19]

Table 1 | Summary of predictors and markers of obesity and MetS in Asia

Authors	Design/sample	Title	Findings
Park et al. (2017)[3]	Cross-sectional study; Korean children and adolescents (867 boys and 751 girls)	Serum gamma-glutamyltransferase level and metabolic syndrome in children and adolescents: Korean National Health and Nutrition Examination Survey	Serum gamma-glutamyl transferase was positively associated with MetS and its components in Korean children and adolescents, and could be a useful measure for identifying young people with MetS
Li et al. (2018)[4]	Cross-sectional study; Middle-aged and elderly Chinese population (476 men and 516 women)	Clinical surrogate markers for predicting metabolic syndrome in middle-aged and elderly Chinese	Lipid accumulation product, visceral adiposity index, and the products of triglycerides and glucose have reliable predictive accuracy for diagnosis of MetS in both the ATPIII and IDF criteria. LAP might perform better than VAI and TyG for predicting MetS
Wang et al. (2018)[5]	Prospective study of a community-based cohort; Chinese participants without MetS (88 men and 122 women, aged between 40 and 65 years), followed up for 5 years	Effects of circulating member B of family with sequence similarity 3 on the risk of developing metabolic syndrome and its components: A 5-year prospective study	Elevated circulating member B levels of the FAM3B may be a predictor of MetS onset and progression. The number of MetS components also showed an increasing trend as the circulating FAM3B levels raised. ROC analysis showed that the optimal cut-off of FAM3B for predicting MetS was 23.98 ng/mL
Sunagawa et al. (2019)[6]	A pilot exploratory study; 50 Japanese patients with type 2 diabetes mellitus and MetS (26 men and 24 women)	Activity of XO in plasma correlates with indices of insulin resistance and liver dysfunction in patients with type 2 diabetes mellitus and metabolic syndrome: A pilot exploratory study	Plasma XO activity was correlated with indices of insulin resistance and liver dysfunction in Japanese patients with type 2 diabetes and MetS. Importantly, the value of plasma XO activity was not correlated with the serum UA level. The multiple regression analyses further suggested that the value of plasma XO activity would be influenced by liver dysfunction (ALT) and hepatic insulin resistance (HOMA-IR)

ALT, alanine transaminase; ATPIII, Adult Treatment Panel III; FAM3B, member B of family with sequence similarity 3; HOMA-IR, homeostatic model assessment of insulin resistance; IDF, International Diabetes Federation; LAP, lipid accumulation product; MetS, metabolic syndrome; ROC, receiver operating characteristic; TyG, triglycerides and glucose; UA, uric acid; VAI, visceral adiposity index; XO, xanthine oxidase.

found that mutation carriers related to the feeding center had less weight loss over both short-term and long-term periods after BS. A shorter duration of diabetes is more closely related to the long-term remission of diabetes, and with stronger prevention of diabetes-related microvascular and macrovascular complications for up to 25 years[18].

Less is known about the factors leading to recurrence. Further studies are warranted on the predictors of gastrointestinal hormones and metabolic profiles of long-term remission and relapse of type 2 diabetes after BS in obese patients[19,20].

Meanwhile, weight loss surgeons are constantly exploring new types of BS to increase and maintain effectiveness, and reduce complications and nutritional deficiencies. There are currently several new surgical approaches, such as stomach intestinal pylorus-sparing surgery and single anastomosis duodenal-ileal bypass with sleeve gastrectomy.

SUMMARY

In summary, because of the high prevalence of obesity and its close relationship with MetS, patients with MetS who undergo BS benefit tremendously. These benefits can also be achieved through non-surgical measures, including medication, diet and exercise. When non-surgical measures have failed, BS is a good solution in most cases. There are several clinical studies that give preliminary results on predicting the long-term efficacy of BS in patients with obesity or MetS. However, long-term and large samples in randomized controlled studies are urgently required to understand more fully the relationship between obesity, MetS and BS.

DISCLOSURE

The author declares no conflict of interest.

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