DERLEME / *REVIEW*

What is Metabolic Surgery? To Whom and When Should It Be Applied?

Metabolik Cerrahi Nedir? Kime ve Ne Zaman Yapılmalıdır?

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ABSTRACT

Metabolic syndrome is a cluster of cardiometabolic risk factors that cause some complications. Each component of the syndrome needs to be treated. For this purpose, anti-hypertensive, anti-diabetic, and anti-lipidemic agents are used, but weight control plays a key role in treatment. Exercise, reduction of daily calories with diet and increasing physical activity play a role in the control of body weight. Various medical treatments have been tried, but they have not been very effective. The most effective way is still surgery. Although there is no definite accepted definition of metabolic surgery, it can be defined as surgical interventions to treat metabolic syndrome.

The general perception in bariatric surgery is that type 2 diabetes enters remission due to patients' weight loss. After the operation in these patients, blood sugar control has been shown to be achieved while patients are still in the hospital. It has been understood that the gastrointestinal system plays an essential role in glucose homeostasis, and its mechanisms have been tried to be revealed. The foregut hypothesis and the hindgut hypothesis have been suggested.

A hindgut surgery like a duodenal switch has been shown to improve insulin sensitivity and glucose homeostasis without causing a hyperinsulinemic response compared to a foregut surgery like a gastric bypass. Surgeries that modulate the hindgut have more potential to disrupt the absorption of vitamins and minerals than foregut surgeries.

To prevent this, the transit bipartition technique has been developed in recent years. As a result, various methods have been used in metabolic surgery. The choice of a surgical technique should be specific to the patient.

Key words: *metabolic surgery; timing; type 2 diabetes mellitus*

ÖZET

Metabolik sendrom bazı komplikasyonlara neden olan kardiyometabolik risk faktörleri demetidir. Sendromu oluşturan her bileşen tedavi edilmelidir. Bunun için antilipidemik, antidiyabetik, antihipertansif, ilaçlar kullanılır fakat tedavideki kilit rolde kilo kontrolü oynar. Vücut ağırlığının kontrolünde egzersiz, diyetle günlük alınan kalorinin azaltılması ve fiziksel faaliyetlerin artırılması rol oynar. Değişik tıbbi tedavilerlede deneme yapılmış olup çok başarılı olunamamıştır. Hala en etkin yol cerrahi seçenektir. Kesin kabul edilen tanımı olmamakla beraber metabolik cerrahi, metabolik sendromu tedavi etmek için yapılan cerrahi müdahaleler olarak tarif edilebilir.

Genel algı bariatrik cerrahi geçiren hasta kişilerin kilo vermeyle ilişkili tip 2 diyabet hastalığının remisyona girmesidir. Ameliyat sonrası bu hastalar hastanede yatarken kan şeker değerlerinin düzelmeye başladığı görülmüştür. Kan glukozu dengelenmesinde gastrointestinal sistemin önemli rol aldığı anlaşılınca, mekanizmasının ortaya çıkması için çalışmalar yapılmıştır. Ön ve arka barsak hipotezleri ortaya atılmıştır.

Arka barsak ameliyatı olan Duodenalswitch'in ön barsak ameliyatı olan gastrik by-pass'a göre hiperinsülinemik cevaba neden olmadan glukoz dengesini ve insülin duyarlılığında iyileşme sağladığı ortaya konmuştur. Arka barsak modulasyonu yapılan ameliyatlar, ön barsak modülasyonu yapılan ameliyatlara göre mineral-vitamin dengesini daha çok bozma eğilimindedir. Son zamanlarda bunu önlemek için transit bipartisyon ameliyatı geliştirilmiştir. Sonuçta metabolik cerrahi ameliyatlarında değişik teknikler tercih edilmektedir. Yapılacak ameliyat yönteminin kişiye özel olması gerektir.

Anahtar kelimeler: *metabolik cerrahi; zamanlama; tip 2 diyabet*

The adipose tissue accumulated in the body due to irregular and uncontrolled nutrition causes various diseases. These can include hepatosteatosis, hypertension (HT), cardiovascular diseases, osteoarthrosis, type 2 diabetes mellitus (T2DM), alveolar ventilation deficiency, cerebrovascular diseases,, hypertriglyceridemia, and varicose veins. Some of the risk factors that occur mainly due to insulin resistance play a role in the development of cardiovascular diseases. This association, which was first emphasized in 1988 and previously called. Syndrome X, is called metabolic syndrome nowadays. Among them, there are abdominal obesity, increased blood pressure, T2DM, and lipid disorders. Insulin resistance results in

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decreased glucose uptake into cells in various tissues, primarily skeletal muscle, increased lipolysis in adipose tissue, and decreased gluconeogenesis in the liver. Obesity, sedentary lifestyle, smoking, low birth weight, and perinatal malnutrition have also been associated with the development of insulin resistance. Adipose tissue and hormones secreted from this tissue, hypothalamus-pituitary-adrenal axis disorders, advancing age, genetic and environmental causes also contribute to the development of insulin resistance[1]. The frequency of metabolic syndrome increases with increasing age and body weight of the studied population and shows social variability. According to the results of the Turkish Metabolic Syndrome Research conducted in 2004 in our country, the frequency of metabolic syndrome in adults aged 20 years and older was found to be 35%[2].

The definition of metabolic syndromerefers to the coexistence of at least three of the following medical conditions: abdominal obesity, high blood pressure, high blood sugar, high serum triglyceride level, and low high-density lipoprotein level. However, different study groups can use different definitions (Table 1). The data obtained in the metabolic syndrome research study is based on the evaluations made by accepting the waist circumference as 102 cm in men and 88 cm in women. A higher frequency of metabolic syndrome could be detected if the 94–88 cm accepted today is considered a limit.

Metabolic syndrome, of course, leads to life-threatening complications. Therefore, each component of the syndrome needs to be treated. For this purpose, anti-hypertensive, anti-diabetic, and anti-lipidemic agents are used, but weight control plays a key role in treatment because the production of substances such as TNF-alpha, adiponectin, resistin, and PAI-1 induced by increased visceral fat, and the complex and not yet fully illuminated inflammatory processes caused by them underlie the metabolic syndrome. Although the ideal way to control weight is to reduce the daily calorie intake and increase physical activity with diets and exercises, unfortunately, there is not much success in today's society.

For this purpose, various medical treatments have been tried, but very effective results have not been achieved. Nowadays, the most effective way to treat obesity is still bariatric surgery. The definition of bariatric surgery is derived from the Greek words *baros* (weight) and *iatricos* (treatment). The concept has evolved into metabolic surgery over time due to the positive effects of bariatric surgery on weight control as well as diabetes, hypertension, and blood lipid profile. Although there is no precise definition of metabolic surgery, it can generally be defined as surgical interventions to treat metabolic syndrome.

The studies that started in the field of bariatric surgery in the 1950 s enabled the introduction of the frequently used surgical methods when the 80s were reached and the spread of these methods with the introduction of laparoscopy in gastrointestinal surgery in the 90s. The general perception during this period was that type 2 diabetes entered remission due to patients' weight loss. However, in a study conducted in 1995[3], the whole perception began to change when they published studies showing that patients with type 2 diabetes who underwent a gastric bypass had blood glucose control achieved while the patients were still in the hospital, that is, before losing significant weight. Since then, it has been understood that the gastrointestinal tract plays a vital role in glucose homeostasis, and its mechanisms have been tried to be revealed. Gastric bypass surgery has been shown to divert food from the duodenum, reducing glucagon release with anti-insulin activity. Beyond that, the early access of foods to the lower parts of the small intestine stimulates the release of incretins, and it is known that glucagon-like peptide-1 (GLP-1) and gastric inhibitory polypeptide (GIP) with typical incretin activity have trophic effects on pancreatic beta cells and increase insulin secretion.

At this point, two different views emerged. According to the first view: "disabling the duodenum improves type 2 diabetes (the foregut hypothesis), which occurs as a result of disruption of the balance between incretins and peptides with anti-incretin activity in the body"[4]. The second view is that the increase in the production of GLP-1 released from the L cells with the early arrival of the food in the terminal ileum plays a major role in the control of diabetes (the hindgut hypothesis)[5]. Although the place of surgery remains controversial for the treatment of T2DM, which has been tried to be treated with insulin despite the hyperinsulinemic condition for decades, at the point we have reached today, even the American Diabetes Association recommends metabolic surgery with a high level of evidence (category A) in candidates eligible for surgery even for the treatment of T2DM regardless of the level of glycemic control if the body mass index (BMI) is 40 kg/m^2 or more, and in patients with a BMI of 35–39.9 kg/m^2 when hyperglycemia cannot be adequately controlled despite the lifestyle changes and optimal medical treatment[6]. Even in the same guideline, it was emphasized that metabolic surgery could be considered in cases

Table 1. *Metabolic syndrome definitions*

	IDF	NCEP	WHO	AACE
Diagnosis	If the blood glucose level is	If 3 out of the 5 criteria below are present	If the blood glucose level is	
	abnormal and if at least two of the following are present		abnormal and if at least two of the following are present	Shows risk factors
Glycemia	Fasting blood sugar of 100–125 mg/dL or T2DM		Glucose intolerance, T2DM	Fasting blood sugar of 100–125 mg/dL or >140 mg/dL
		Blood sugar of 100-125 mg/dL	or insulin resistance	at the 2nd hour after OGTT
Abdominal obesity	Waist circumference:	Waist circumference:	BMI>30 and	BMI≥25 and
	≥94 cm in men	>102 cm in men	Waist-to-hip ratio:	Waist circumference:
	≥80 cm in women	>88 cm in women	>0.9 in men	>102 cm in men
			>0.85 in women	>88 cm in women
Lipid profile	T G≥150 mg/dL or	T G≥150 mg/dL or	T G≥150 mg/dL or	T G≥150 mg/dL or
	HDL	HDL	HDL	HDL
	<40 in men	<40 in men	<35 in men	<40 in men
	<50 in women	<50 in women	<39 in women	<50 in women
Hypertension	Being treated for systemic arterial HT or Blood Pressure of ≥130/85 mmHg	Blood Pressure of ≥130/85 mmHg	Being treated for systemic arterial HT or Blood Pressure of ≥160/90 mmHg Microalbuminuria ≥20 mcg/dk	Blood Pressure of ≥130/85 mmHg

OGTT, oral glucose tolerance test; T2DM, Type 2 diabetes mellitus; TG, triglyceride; HDL, high (density) lipoprotein; NCEP, US national cholesterol education program; IDF, international diabetes federation; WHO, World Health Organization; AACE, American College of Endocrinology / American Association of Clinical Endocrinologists.

when hyperglycemia could not be controlled despite oral and injectable treatments even in those with a BMI of 30–34.9 kg/m^2 (category B).

However, the incident is not limited to the incretin activity, obese individuals, or T2DM. Important pathophysiological mechanisms that mediate the beneficial effects of metabolic surgery include multi-organ insulin sensitivity (hepatic and skeletal muscle), beta-cell function, changes in the bile acid composition and flow, and increased metabolic activity in brown adipose tissue. Furthermore, the increase in microbial diversity in the intestine and changes in the ratio of some specific bacterial species may contribute to this metabolic activity[5–7]. There are studies reporting that complete remission was achieved in T2DM in up to 85% of patients after metabolic surgery, even in individuals with a BMI of 28–35 kg/m^2, and that the rates of patients using anti-hypertensive and anti-lipidemic agents decreased from 38% to 11% and from 56% to 4%[8]. One of the problems is that the metabolic effect of each type of surgery is different from each other, and individual differences between patients can affect the results. For example, a hindgut surgery like a duodenal switch has been shown to improve insulin sensitivity and glucose homeostasis without causing a hyperinsulinemic response compared to a foregut surgery like a gastric bypass[9]. Of course, surgeries that modulate the hindgut have more potential to disrupt the absorption of vitamins and minerals than foregut surgeries. In order to prevent this, in recent years, methods for ensuring the effectiveness of the posterior intestine are being tried in the form of transit bipartition without preventing contact of the food with any small intestinal tissue. In order to prevent this, in recent years, methods for ensuring the effectiveness of hindgut surgeries, in the form of transit bipartition, without preventing contact of food with any small intestine tissue, have been tried.

The difference between metabolic surgery and traditional bariatric surgery is mainly based on the characteristics of patients. Patients who prefer bariatric surgery are typically young, predominantly female, and patients with a relatively lower T2DM prevalence than patients with a similar BMI. On the contrary, although patients who are

considered eligible for metabolic surgery are often obese, they are older, predominantly male, and have more severe T2DM and cardiovascular diseases[10,11]. It is not surprising that these differences have an impact on surgical outcomes (such as diabetes remission rates and cost-effectiveness) and patient care issues. Traditional bariatric surgery is perceived as an attempt to reduce the risk of future diseases (such as obesity-related metabolic or cardiovascular complications) rather than treating existing diseases. This false perception is observed in many bariatric surgery guidelines nowadays, but it should not be forgotten that T2DM is a progressive disease that causes an increased risk for cardiovascular diseases and microvascular complications. Furthermore, the rate of metabolic recovery after surgery in patients with T2DM is related to the duration of T2DM. The shorter the duration of the disease is, the better the outcomes are[12–14]. This means reduced success and cost-effectiveness if surgical treatment is unnecessarily delayed. The patient acceptance criteria used for bariatric surgery have low significance for metabolic surgery. For example, the BMI cannot be considered as a stand-alone criterion for metabolic surgery because the BMI is neither a standard diagnostic parameter nor a measure that determines the severity of T2DM. For this reason, it was concluded that metabolic surgery should be considered even in Class I obese individuals, in which diabetic control is difficult, at the 2nd Diabetes Surgery Summit, where 75% of the participants consisted of diabetologists or endocrinologists[15–17].

Conclusion

Definitions related to bariatric surgery are shifting towards metabolic surgery due to the positive effects of the method on metabolic status. The bariatric surgery procedures considered as the most effective way of treating obesity are regarded as the most effective methods in the treatment of T2DM nowadays. Due to differences in the effectiveness of these methods, there is a need for patient-specific method choices rather than creating treatment protocols indexed to a non-standard parameter such as BMI.

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