Introduction

Obesity has recently gained the attention of many physicians over the world as the numerous morbidities associated with a high body mass index (BMI) have become evident ***(Bauer et al., 2014).***

Health hazards linked to obesity include diabetes mellitus type 2 (T2DM), insulin resistance, heart disease, dyslipidemia, hypertension, stroke, venous thrombus formation, osteoarthritis and psychosocial effects ***(Bray, 2013)***.

Furthermore mortality and cardiovascular disease related mortality are particularly increased in the overweight populace ***(Sjöström et al., 2004).***

Bariatric surgery is defined as gastrointestinal surgery that helps morbidly obese patients to lose weight. It offers the only realistic chance of long-term weight reduction and resolution or improvement of co-morbidity for the majority of these patients ***(Sato et al., 2009).***

Bariatric surgical procedures affect weight loss through two fundamental mechanisms: malabsorption and restriction. Some procedures have both a restrictive and malabsorptive component ***(Ganesh et al., 2006).***

Sleeve Gastrectomy is an operation that restricts food intake. Most of the stomach is removed during this surgery, which may decrease ghrelin, a hormone that prompts appetite. Lower amounts of ghrelin may reduce hunger more than other purely restrictive surgeries, such as gastric band ***(Barazzoni et al., 2007).***

Bariatric surgery is formally considered a component of the early management of T2DM to slow rate the progression of the disease and, thereby reduce mortality, morbidity and cost of treatment, thereby improving the quality of life ***(Dixon et al., 2011).***

The exact influential mechanism of bariatric surgery on glucose metabolism is uncertain; however, it is thought to be secondary to the effects of hormones, principally: ghrelin, peptide YY (PYY) and glucagon like peptide-1 (GLP1) ***(Nocca et al., 2011).***

Bariatric therapy for weight reduction and treatment of comorbidities has been proven in numerous studies ***(Sundbom, 2014).*** But it is yet still unclear which bariatric procedure should be chosen for diabetic patients in order to achieve the best results in diabetes remission ***(Li et al., 2016).***

Aim of the Work

The aim of this study is to focus on the role of Laparoscopic Sleeve Gastrectomy (LSG) as a method of bariatric treatment in patients with type 2 Diabetes or abnormalities in glucose homeostasis, and glycemic control status [blood glucose, hemoglobin A1c (HbA1c) and hypoglycemic treatment.

Chapter (1)

Pathophysiology of Obesity

Regulations of food intake and energy expenditure are important to maintain normal weight. Ghrelin produced by the stomach modulates short-term appetitive control, and leptin is produced by adipose tissue to signal fat storage reserves in the body and mediates long-term appetitive controls. For several reasons, homeostasis of energy balance can be broken, of which underlying mechanisms are remain incompletely understood. When calorie intake exceeds energy expenditure, the extra energy is stored in various organs. The main characteristic of obesity is long-term imbalance between calorie intake and energy expenditure, resulting in over accumulation of fat in body ***(Flier, 2004).***

The main causes of obesity are excessive food intake, decreased physical activity and genetic susceptibility. In some cases, endocrine disorders, medications, psychiatric illness or other factors are involved. Most of dietary fat is in the form of triglycerides (TAG), cholesterol and phospholipids. Among them, TAG is most important in obesity. Dietary TAG, which cannot be absorbed by the intestine, are digested into free fatty acids and monoglycerides. Once across the intestinal barrier,

they are reformed into triglycerides and packaged into chylomicrons or liposomes, which are released into the blood. Finally they are mainly captured by hepatocytes, adipocytes or muscle fibers. TAG is the main source of energy and important components of body. However, excess TAG is accumulated in many organs ***(Scherer, 2006)***.

In the postprandial state of energy excess, surplus carbohydrates are catabolized to form acetyl- CoA, which is a feedstock for the fatty acid synthesis pathway (lipogenesis) (Fig. 1). Taken together, excess food is stored as TAG in various organs. Adipose is a dynamic tissue which interacts with other organs and has important endocrine functions. The major form of adipose tissue is white adipose tissue ***(Rosen and Spiegelman, 2006).***

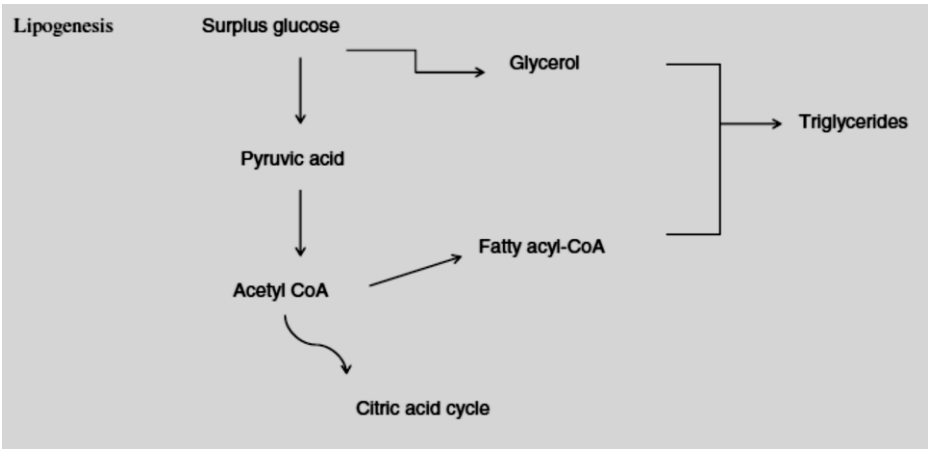

Figure (1): Lipogenesis pathway ***(Rosen and Spiegelman, 2006)***

We can get energy from white adipose cells during fasting because it store and release energy in the form of lipids. Also, white adipose cells have the ability to secrete hormones and cytokines ***(Friedman, 2009)***. Brown adipose cells (or brown adipocytes), which are darkly pigmented due to the high density of mitochondria in cytochromes, store also triglycerides and produce heat by burning fatty acids to maintain body temperature ***(Cannon and Nedergaard, 2004).***

Brown and white adipocytes are located together in the subcutaneous tissue or in the visceral peritoneum, forming a multi-depot adipose organ ***(Cinti, 2005)***. The main components of white adipose tissue (WAT) are white adipocytes, whereas brown adipose tissue (BAT) is mainly composed of brown adipocytes. Also, intermediate forms of adipocytes between white and brown adipocytes are present in all depots of the adipose organ ***(Vitali et al., 2012).***

Under the influence of insulin, the adipocyte takes up free fatty acids (FFAs) from the blood and then stores them in the form of intracellular lipid droplets and fat mobilization is suppressed. In adipose tissue, fatty acids may be released into circulation for delivery to other tissues. In a surplus caloric state, adipocytes become hypertrophic, which induce cellular

signaling for the recruitment, proliferation and differentiation of new fat cells. Failure of new adipogenesis may cause existing fat cells to undergo excessive hypertrophy, causing adipocyte dysfunction, which results in pathogenic adipocytes and adipose tissue endocrine and immune responses ***(Capurso, 2012).***

Dysfunction of adipogenesis results in ectopic fat storage, i.e., intra-abdominal, perimuscular, perivascular, pericardial, and periosteal fat accumulation ***(Pasarica et al., 2009)***.

Ectopic fat storage such as pericardial and perivascular space may have direct pathogenic effects on the myocardium, coronary arteries and peripheral vessels, via dysregulated local secretion of vasoactive and inflammatory factors ***(Gray and Vidal-Puig, 2007).***

Skeletal muscle constitutes 40 % of body weight in normal persons and uses 35–40 % of total oxygen consumption in the resting state. During exercise, consumption of oxygen and metabolic fuels increases markedly to provide the adenosine triphosphate (ATP) necessary for the contractile process. Glycogen, glucose, and free fatty acids are main fuels for energy metabolism in muscle ***(Felig and Wahren, 1975).***

The skeletal muscle can be categorized into type I, type IIa and type IIb. Type I and type IIa fibers appear red due to the presence of myoglobin, and type IIb fibers are white due to the absence of myoglobin. Type I fibers, also called slow twitch or slow oxidative fibers, contain large amounts of myoglobin, many mitochondria, and many blood capillaries , and have an ability to split ATP at a slow rate, have a slow contraction velocity, very resistant to fatigue, and have a high capacity to generate ATP by oxidative metabolic processes using mainly triglycerides. Type IIa fibers, also called fast twitch or fast oxidative fibers, contain very large amounts of myoglobin, many mitochondria and many blood capillaries , and have a very high capacity for generating ATP by oxidative metabolic processes, split ATP at a very rapid rate, have a fast contraction velocity and are resistant to fatigue, and are found less in humans. Type IIb fibers, also called fast twitch or fast glycolytic fibers contain a low content of myoglobin, relatively few mitochondria, relatively few blood capillaries, and large amounts of glycogen. Type IIb fibers generate ATP by anaerobic metabolic processes, not able to supply skeletal muscle fibers continuously with sufficient ATP, fatigue easily, split ATP at a fast rate, and have a fast contraction velocity ***(Forbes and Welle, 1983).***

In obesity structural and metabolic changes in skeletal muscle occur. In general obese populations have a larger lean body mass than non-obese subjects. In some obese people, muscle mass can be much lower than expected (sarcopenic obesity). It is characterized by fewer type I and/or more type IIb muscle fibers in obese individuals than in lean individuals ***(Forbes and Welle, 1983).***

The predominance of type II fibers in severe obesity might result in low capacity of lipid oxidation and an increase in fat storage within skeletal muscle. Glucose transport in muscles was stimulated approximately 2.5-fold by insulin from lean persons, but there was little or no stimulation of glucose transport in muscles from severely obese patients either with or without type 2 diabetes. In muscle, fatty acids are a substrate for oxidation. Fatty acid oxidation did not differ between the muscles of lean and obese individuals but was significantly reduced in severely obese individuals. In contrast, glycolytic metabolism is increased. Muscle fatty acid metabolism is more sensitive to physical activity, during which fatty acid utilization from extracellular and intracellular sources may increase enormously. Adipose tissue fat mobilization increases to meet the demands of skeletal muscle during exercise ***(Hulver et al., 2003).***

Insulin resistance (IR) is defined as a reduced efficiency of circulating insulin in target tissues such as skeletal muscle, liver and adipose tissue. The main cause of insulin resistance and DM is the fat accumulation in the body. Insulin resistance manifests with decrease of insulin stimulated glucose uptake and utilization in the skeletal muscle, impaired insulin-mediated inhibition of hepatic glucose production in the liver, and a reduced ability of insulin to inhibit lipolysis in the adipose tissue (Fig. 2). Subsequent high glucose level results in compensatory hyperinsulinemia. Other important conditions associated with IR include hyperuricemia, gallstones, thrombophilia, endothelial dysfunction and polycystic ovary syndrome ***(Fujioka et al., 1987).***

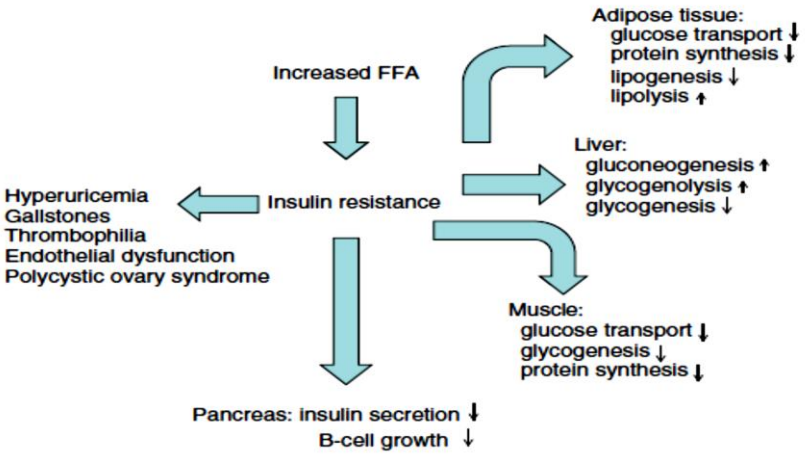

Figure (2): Insulin resistance ***(Fujioka et al., 1987).***

Obstructive sleep apnea (OSA) is a common disorder with obesity and involves cessation or significant decrease in airflow in the presence of breathing effort. It is caused by obstruction of the upper airway. These episodes are associated with recurrent oxyhemoglobin desaturations and arousals from sleep. The patients may become conditioned to the daytime sleepiness and fatigue associated with significant levels of sleep disturbance. Weight loss reduces upper airway collapsibility during sleep ***(Schwartz et al., 2008)***.

Obstructive hypoventilation syndrome (OHS) or Pickwickian syndrome is defined as the presence of awake hypercapnia (PaCO2 >45 mmHg) in the obese patient (BMI >30 kg/m2) after other causes that could account for awake hypoventilation, such as lung or neuromuscular disease, have been excluded ***(Piper and Grunstein, 2011).***

It is distinguished from the "overlap syndrome," which is the term used to describe the association of COPD and OSA. Malignant obesity hypoventilation syndrome (MOHS) is a subset of patients with severe OHS and characterized by systemic hypertension, diabetes and the metabolic syndrome, left ventricular (LV) hypertrophy with diastolic dysfunction,

pulmonary hypertension and renal and hepatic dysfunction ***(Marik , 2012).***

Venous thromboembolism such as deep vein thrombosis or pulmonary embolism is a rare disease but can result in death, and most of those who survive suffer from serious sequel. Obesity is a proinflammatory and prothrombotic state and increases the rate of venous thromboembolism ***(Cushman, 2007).*** Also the obesity induces the raised intra- abdominal pressure and decreased blood flow in the legs ***(Darvall et al., 2007).*** And it is postulated that obesity results in increased activity of the coagulation cascade and decreased fibrinolysis ***(Stein et al., 2005).***

Definition of Obesity

Obesity is often defined simply as a condition of abnormal or excessive fat accumulation in adipose tissue, to the extent that health may be impaired. However, obese individuals differ not only according to the degree of excess fat, which they store, but also in the regional distribution of the fat within the body. Indeed, excess abdominal fat is as great a risk factor for disease as is excess body fat ***(Jackson et al., 2011).***

Body Mass Index

One of the most commonly used indices of relative weight is the Body Mass Index (BMI), which is defined as body weight in kilogram divided by height, in meters squared. It was not originally intended as an index of obesity but is now commonly employed as such in epidemiological studies, to predict obesity-related morbidity and mortality in adults. A BMI of 30 kg/m2 is considered the threshold of obesity. BMI however, does not distinguish between weight associated with muscle and weight associated with fat. BMI can be considered to provide the most useful, albeit crude, population-level measure of obesity. The classification of overweight and obesity in adults as proposed by WHO (1998) is shown in Table 1. ***(Deurenberg et al., 1999).***

Table (1): Classification of weight status in adults according to Body Mass Index (BMI) ***(Deurenberg et al., 1999).***

Classification	BMI (kg/m2)	Risk of co-morbidities
Underweight	< 18.5	Low (but risk of other clinical problems increased)
Normal range	18.5 – 24.9	Average
Overweight:	≥ 25	
Pre-obese	25 – 29.9	Increased
Obese class I	30.0 – 34.9	Moderate
Obese class II	35.0 – 39.9	Severe
Obese class III	≥40.0	Very severe

Chapter (2)

Management of Morbid Obesity

Reducing body weight in overweight and obese patients not only helps reduce the risk of these comorbidities from developing but also helps in their management. Weight management techniques need to take into account the needs of individual patients so they should be culturally sensitive and incorporate the patient's perspectives and characteristics. Effective weight control involves multiple techniques and strategies including dietary, physical, behavioural therapies, also pharmacotherapy and surgery as well as combinations of these strategies ***(Butrum et al., 1988).***

Medical therapy for severe obesity has limited short-term success and almost nonexistent long-term success. Once severely obese, the likelihood that a person will lose enough weight by dietary means alone and remain at a BMI below 35 kg/m2 is estimated at 3% or less. The NIH consensus conference recognized that for this patient population, medical therapy has been uniformly unsuccessful in treating the problem and had an extremely small impact on BMI ***(Summerbell et al., 2005).***

Despite massive efforts health care providers to influence weight through diet, physical activity and lifestyle changes, the only effective long-term method for weight loss has been shown to be bariatric surgery ***(O'Brien et al., 2010).***

A) Non-surgical management of morbid obesity

1. Dietary Therapy

Reducing overall consumption of calories by initiating treatment with a diet producing a calorie deficit of 500 to 1000 kcal/d from the patient's habitual diet, with the goal of losing approximately 1 to 2 lb/wk, This often translates into a diet of 1000 to 1200 kcal/d for most women, and a diet between 1200 and 1600 kcal/d for men and heavier women ***(Nordmann et al., 2006).***

a) Macronutrient composition:

A diet rich in whole grains, fruits, vegetables and dietary fiber; consuming two servings of fish high in omega-3 fatty acids per week; decreasing sodium to less than 2300 mg/d; consuming three cups of milk per day; limiting cholesterol to less than 300 mg/d; and keeping 45%- 65% of calories from carbohydrates, total fat between 20% -35% of daily calories