

Pathophysiology of obesity. Impact on laparoscopy

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Obesity is a pandemic disease affecting a large group of the population and activating other diseases like diabetes, hypertension and even cancer. An obese patient is an challenge for anesthesia due to its different physiology. A better understanding of the pathophysiology is important for anesthesia as 1 on 4 of our patients today are suffering from obesity. This number is increasing every year even with the explosive demand for bariatric surgery.

The simplest method to measure obesity is the body mass index (BMI = total body weight in kg divided by the quadrate of length in cm). A BMI between 25 and 30 means overweight, between 30 and 40 obese, between 40 and 50 morbid obese, between 50 and 60 super obese and above 60 super obese.

Physiologic changes are due to the weight effect like knee arthrosis, due to the volume effect, like the increased intra abdominal resting pressure, due to the increased organ size like the rise in metabolic activity, due to the increased cardiovascular perfusion needs like the higher cardiac output, due to the hormonal changes like the higher incidence of diabetes or due to the adaptation of organ functions like ventricular hypertrophy.

Adipose tissue increases peripheral everywhere in the body or only central in the abdomen. The peripheral distribution is more frequent in woman (gynoid shape) while central abdominal fat is found more in man (android shape). The waist-to-hip ratio (1). measures this peripheral versus central fat distribution.

The co-occurrence of any three of the following abnormalities, dyslipidemia, elevated blood pressure, impaired glucose tolerance, and central (android) obesity is identified now as metabolic syndrome, also called syndrome X, insulin resistance syndrome or Reaven's syndrome.

A report from the National Cholesterol Education Program – Adult Treatment Panel (NCEP–ATP III) identified metabolic syndrome as an independent risk factor for cardiovascular disease and considered it an indication for intensive treatment. Soon, metabolic syndrome will overtake

cigarette smoking as the number one risk factor for heart disease (2).

The metabolic syndrome is associated with a proinflammatory/prothrombotic state that may include elevated levels of C-reactive protein, endothelial dysfunction, hyperfibrinogenemia, increased platelet aggregation, increased levels of plasminogen activator inhibitor 1.

The etiology of the metabolic syndrome has not been established definitively.

One hypothesis presumes that the primary cause is insulin resistance and this correlates with visceral fat. The link between insulin resistance and cardiovascular disease probably is mediated by oxidative stress, which produces endothelial cell dysfunction, promoting vascular damage and atheroma formation.

The second hypothesis blames hormonal changes for the development of abdominal (android) obesity, insulin resistance, and lipid abnormalities, linking psychosocial problems with acute myocardial infarction.

The primary goal for the management of metabolic syndrome is to reduce the risk of cardiovascular disease and diabetes (3). Bariatric surgery today is the most successful treatment for metabolic syndrome. The mortality and morbidity is now very low in experienced centers (4) and therefore the name of bariatric surgery has changed to metabolic surgery in treating the metabolic syndrome.

DISORDERS IN THE ENDOCRINE SYSTEM

White adipose tissue (WAT) is considered as a mayor endocrine and secretory organ, secreting

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several key hormones, like leptin. These hormones secreted by the adipocytes, are termed adipokines, many of which are linked to immunity and the inflammatory response.

The major expansion in adipose tissue mass, is associated with a state of chronic mild inflammation, as discussed below. As result circulating levels of inflammatory markers such as C-reactive protein, IL-6, IL-18, haptoglobin, MIF and PAI-1, TNF are increased. An exception is adiponectin, with its anti-inflammatory and insulin-sensitising actions, the production and release of which fall in the obese. This state of inflammation is viewed as central to the development of the metabolic syndrome.

TNF- α is expressed by adipocytes, and influences insulin signalling through serine phosphorylation of the insulin receptor substrate-1, so inhibiting insulin action at the adipocyte. IL-6 shares with TNF- α effects on insulin signalling and glucose transport, which might also result in insulin resistance at myocyte, adipocyte and hepatocyte levels.

IL-6 may also play a direct role in atherogenesis (5).

Several studies (6) show that hypoxia is the mechanism inducing extensive changes in human adipocytes in the expression and release of inflammation-related adipokines. Hypoxia may underlie the development of the inflammatory response in adipocytes, leading to obesity-associated diseases. Indeed, the increase in leptin and reduction in adiponectin in obesity may be partly a direct result of hypoxia within WAT. Hypoxia also may stimulate angiogenic factors and neovascularisation within WAT.

Why exists hypoxia in adipose tissue? It is widely suggested that WAT is poorly oxygenated in the obese. There are several arguments in favour: the proportion of the cardiac output and blood flow that goes to WAT is not increased in the obese, despite the expansion of the tissue mass (7); obese subjects do not exhibit the postprandial increase in blood flow to adipose tissue that occurs in the lean; hypertrophied adipocytes are larger than the normal increasing the diffusion distance of O₂ within tissues (8). With respect to the last point, large adipocytes may be up to 150 (or even 200) μ m in diameter (9) with the normal diffusion distance of O₂ being 100-200 μ m. Indeed, in some situations and in some tissues, a partial pressure of O₂ of close to zero has been reported at only 100 μ m from the vasculature.

As we mentioned before leptin is primarily synthesized and secreted by adipocytes. One of the major functions of this hormone is the control of

energy balance. By binding to receptors in the hypothalamus, it reduces food intake and promotes elevation in temperature and energy expenditure.

Human obese subjects have high plasma leptin concentrations that do not induce the expected responses (i.e., a reduction in food intake and an increase in energy expenditure). This suggests that obese humans are resistant to the effects of endogenous leptin.

Leptin resistance is demonstrated in obese patients by the lack of effect of exogenous leptin administration to induce weight loss. The mechanisms that may account for leptin resistance in human obesity include a limitation of the blood-brain-barrier leptin transport system, there is a threshold plasma leptin concentration (about 25 ng/mL) above which the transport of leptin into the cerebrospinal fluid does not increase anymore in spite of high values of plasma leptin concentration. Hence, in patients with severe obesity, the large increase in leptin plasma levels may not be adequately translated in regulatory signals to the hypothalamus to control the excessive weight gain. Other mechanisms for leptine resistance could be a mutated leptin receptor in the hypothalamus or an inhibition of the leptin signaling mechanisms in leptin-responsive neurons of the hypothalamus (10).

Leptin appears to be a blood pressure and blood volume-regulating factor in normal situations. However, in conditions of chronic hyperleptinemia, such as obesity, leptin may function pathophysiologically for the development of hypertension as well as cardiac and renal disease.

Leptin resistance may have arisen during evolution to facilitate energy storage in times of plenty in order to avoid the consequences of starvation when food availability was limited. Whereas leptin secretion in humans is not acutely modulated by single meal ingestion, a more chronic stimulus of food intake, such as a decrease or an increase over several days, does affect leptin secretion.

Hence, a sharp decline in leptin plasma levels plays a major role in the body's short-term adaptation to starvation. In humans, leptin is considered more as a hormone involved in the survival of people exposed to situations of famine rather than a hormone that can limit the excessive weight gain of people exposed to an environment of plenty.

Hormonal regulation of metabolism is therefore effective in periods of food shortage. No efficient mechanism is created by evolution theory to regulate continuous oversupply.

Leptin is the humoral component of a negative feedback loop between adipose tissue and brain.

Leptin is secreted from fat in proportion to the degree of adiposity, is transported across the blood-brain barrier (BBB), and acts in the brain to decrease appetite and increase thermogenesis, actions that ultimately decrease adiposity. However, leptin fails as an adipostat because leptin resistance arises in obesity.

DISORDERS IN THE RESPIRATORY SYSTEM

Due to the fat excess metabolism obese patients have a greater absolute oxygen consumption and a greater carbon dioxide production.

Fat accumulation at intercostals muscle, diaphragm and intra abdominal is associated with decreased chest wall compliance and is a known cause of impaired lung expansion with permanent hypoventilation and atelectasis.

Therefore, all lung volumes are reduced, namely forced vital capacity (FVC), forced expiratory volume in 1 second, residual volume (RV), expiratory reserve volume, functional residual capacity (FRC) and total lung capacity and can cause marked dyspnea (11). It explains the need for CPAP, PEEP and recruitment maneuvers peri operative.

Lung compliance is also decreased due to an increase in pulmonary blood flow.

This all increases the work of breathing, increases oxygen consumption and limits the needed post operative extra capacity (reserve capacity).

Morbid obesity impairs gas exchange at rest compared with non obese persons. PaO₂ is lower and mean AaDO₂ is 4 times higher than predicted due to ventilation perfusion mismatch in the lower portions of the lung.

Morbidly obese women have better gas exchange at rest compared with morbidly obese men which is likely again due to lower waist-to-hip ratios in women. The increased intra abdominal fat volume displaces the diaphragm upwards and reduces the ventilation in the lower lung lobes. The waist to hip ratio and not the weight or BMI is the best indication of gas exchange. Weight loss improves pulmonary gas exchange. Every 5 kg reduction in weight increases the PaO₂ and decreases the AaDO₂ by 1 mmHg respectively (11).

Some obese patients develop obstructive sleep apnoea (OSA) and in some of those patients it progresses to obesity hypoventilation syndrome (OHS).

5% of morbid obese persons has OSA. It is defined as several (more than 5) apnoea episodes

(of at least 10s) secondary to pharyngeal collapse that occur during sleep. The incidence increase with obesity and increasing age. More than 95% of cases go unrecognized. Hints for undiagnosed sleep apnea: excessive somnolence, daytime somnolence, snoring, awaken from sleep choking, morning headaches. hypoxemia and desaturation exists during the night. Diagnosis is confirmed by sleep studies and treatment is continuous positive airway pressure (CPAP) mask (at least one month before the operation).

OHS is less usual and affects control breathing. Hypoxemia and hypercapnea are found and OSA is present in 85% of cases. If it progresses, Pickwickian syndrome can appear consisting in: obesity, excessive somnolence, hypoventilation with hypoxemia and hypercapnea, polycythemia and right heart failure.

Carbon dioxide sensitivity and respiratory drive are partly under the control of leptin. But the relative leptin insensitivity in obesity is also associated with a reduced ventilatory response to carbon dioxide.

DISORDERS IN THE CARDIOVASCULAR SYSTEM

An overweight person is moving less; nevertheless the demand for adipose tissue perfusion is permanent higher. Cardiac output increases 0,1 L/min for each extra kg of fat mass. Pulmonary and systemic arterial hypertension develops.

This creates a load on the cardiovascular system that adapts with increases in blood volume, in extra vascular fluid, in red blood cell mass, and most frequent with right ventricular dilatation and left ventricular hypertrophy.

The increased fat mass and extra vascular fluid changes the pharmacokinetic profile of hydrophobe and hydrophile drugs. Every drug in anesthesia has a different pharmacologic profile in lean versus obese patients. Next lecture will take the discussion of pharmacology and dosage of anesthetic drugs in the obese.

Morbidly obese individuals have severely reduced cardio respiratory fitness that is similar to those with established systolic dysfunction heart failure. This contractile dysfunction is described by the lipotoxicity hypothesis or simpler by the obesity cardiomyopathy. There is an inverse graded relationship between BMI and cardio respiratory fitness measured by stress tests (12). These data suggest that the impairment in V̇O₂ max in morbidly obese persons is related to BMI. These

findings are consistent with overall higher expected mortality in morbidly obese persons.

DISORDERS IN THE ABDOMINAL SYSTEM

The abdominal pressure volume relation is linear in obese and lean persons creating a constant compliance C (or its reciprocal the abdominal elastance E) and the abdominal pressure at zero volume PV0 (or resting pressure) characterizing each patients abdomen with only two parameters (13).

The variations in abdominal compliance between persons is very large and dependent on gender, age, previous laparoscopy, number of gravidity but not on the BMI (14). The abdominal compliance is smaller in the android versus the gynoid shape. The PV0 rises according with the BMI explaining the smaller abdominal workvolume for the surgeon and the higher ventilator pressures (15).

Most surgeons frequently suspect the anesthesiologist of not giving sufficient relaxants in morbid obese patients and they have to use higher pneumoperitoneum pressures to achieve again a sufficient work volume. Abdominal compliance changes using the beach chair position and after more than one hour pneumoperitoneum at 15 mmHg (16).

Muscle relaxants change only the PV0 and not the abdominal compliance in obese and lean persons. Pre operative weight loss lowers the intra abdominal fat volume and reduces therefore the PV0 (17).

Laparoscopy with CO2 increases the ventilatory load but this is not different from lean patients. Tissue oxygenation and skin perfusion however declines more in the morbid obese patients versus the lean patients explaining the higher rate of wound infections in morbid obese patients (18).

CONCLUSION

All respiratory function tests are reduced increasing the post operative risk for respiratory insufficiency.

The permanent higher cardiac output state induces dilatation of the right and hypertrophy of the left ventricle. Obesity cardiomyopathy and pulmonary hypertension might develop.

Abdominal compliance is not changed but the resting abdominal pressure is increased requiring maximum muscle relaxation and other techniques like the beach chair position to improve the surgical workspace.

BMI is a simple measurement of the severity of obesity, not of the pathophysiologic changes or the risks for anesthesia. Intra abdominal fat accumulation, a determinant of the metabolic syndrome, together with dyslipidemia, elevated blood pressure and impaired glucose tolerance is the most important risk factor for anesthesia. An intensive pre operative weight reduction by diet or intragastric balloon is the best preparation before anesthesia in patients with this android fat distribution.

Metabolic syndrome increases the risk for cardiovascular disease and diabetes substantial. Metabolic surgery is the most successful treatment for metabolic syndrome.

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