Frailty of the Obese Patient and the Obesity Paradox After Surgical Stress

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1.1 Introduction

Obesity is a metabolic disease characterized by abnormal or excessive adipose tissue accumulation and body weight increase. It is recognized on the basis of a number of anthropometric characteristics and can be classified according to the body mass index (BMI = weight [kg]/height [m^2]) into three different classes [1]:

- *class I*: BMI 30–34.9
- *class II*: BMI 35–39.9
- *class III*: BMI ≥40

Obesity reduces life expectancy, especially when BMI > 35 [2, 3], since it is generally related to concomitant chronic metabolic complications (hypertension, insulin resistance, cholesterol and glucose increase), which are prognostic factors for cancer [4], cardiovascular diseases (CVD) and stroke [2, 5].

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1.2 The Obesity Paradox

The obesity paradox has been observed in many cases in the literature; clinically healthy obese patients have an increased overall survival in cases of heart failure, even though their condition reduces life expectancy. Furthermore, under acute stress, such as surgical stress, obesity "protects" against mortality [6–27]. This evidence-based conclusion is supported by the literature, even though a few citations do not confirm these findings [18–22].

In 2003, Dindo et al. [7] studied postoperative complications in 6336 patients undergoing elective general surgery. Patients were classified according to BMI: non-obese (BMI < 30), mildly obese (BMI 30–35) and severely obese (BMI > 35). The incidence of complications was the same in all three groups (16.3% vs. 16% vs. 15.1%) and an additional multivariate regression analysis showed that obesity was not a risk factor. Mortality was not investigated. In a prospective, multi-centric clinical study, Mullen et al. [8] found that in 118,707 patients undergoing non-bariatric surgery, the mortality risk related to BMI showed a reverse J-shaped relationship; highest rates were found in underweight and morbidly obese patients. Overweight and moderately obese patients had the lowest risk of mortality. A prospective analysis of a single center clinical study investigating postoperative complications [9] studied 4293 patients, of whom 743 were obese. Obese patients more frequently reported diabetes (18.1% vs. 4.7%), hypertension (30.3% vs. 14.2%), cardiac (21.3% vs. 16.7%) or pulmonary (18.6% vs. 14.4%) diseases. They used medications more frequently than normal-weight patients, yet they were less frequently smokers (26.9% vs. 35.4%). Obesity resulted in a significantly longer intervention time, higher intraoperative blood loss and rate of surgical site infections (SSI) but not mortality, considered at 30 days. Furthermore, mildly obese or overweight patients had longer overall survival. The above observations were confirmed by several studies. Vargo et al. [10] studied 6,240,995 patients who underwent cardiovascular surgery, of whom about 10% were obese. These patients had lower in-hospital mortality (2% vs. 4.2%, $p < 0.0001$), postoperative stroke (1.3% vs. 2.3%) and incidence of pneumonia (3.6% vs. 5.1%), the most common complication, but a higher incidence of acute renal failure (8.7% vs. 8.2%) and need for blood transfusions (20.9% vs. 19.3%). The risk of wound infection was also higher (1.1% vs. 0.8%). In the vascular surgery setting [11, 12], obese patients had lower cardiac and respiratory morbidity as well as lower mortality in comparison to normal-weight patients. However, a higher rate of wound complications was observed. Obese patients who underwent esophageal [13], gastric [14] and colon surgery [15–17] had prolonged intraoperative intervention time and increased complication rate and SSI but had no difference in perioperative mortality and reoperation rate. Similar results were observed in patients who underwent surgery for Crohn's disease [18]; BMI did not influence cardiac, pulmonary and renal complications or mortality but patients with a BMI > 40 had a higher prevalence of SSI.

In addition, obese patients affected by various organ cancers experienced less serious morbidity and lower risk-adjusted odds of mortality, despite a higher frequency of deep venous thrombosis, renal complications and ventilator dependency (considered as >48 h) [19]. Benjamin et al. [20] retrospectively reviewed the ACS-NSQJP database and extrapolated 101,078 patients who underwent emergency abdominal surgery between 2005 and 2010; approximately 30% were obese, 32% overweight, 3.5% underweight and the remaining normal weight. A history of diabetes and hypertension was more frequent in the obese group; a higher complication rate was evident in the underweight and morbidly obese patients. Crude mortality was increased in the underweight group alone.

Different results were obtained in obese patients admitted to the intensive care unit (ICU) for blunt trauma [21]. Obese patients had fewer head injuries but more chest and lower-extremity traumas. Nevertheless, they had more complications, longer time of mechanical ventilation and ICU stay. In the above study, obesity was an independent risk factor for mortality. In a prospective study on 1167 patients admitted to the ICU after trauma, Bochicchio et al. [22] examined the outcome of 62 obese (BMI > 30) patients (5.3% of the total). More than a two-fold increase in risk of infection was observed and seven-times higher likelihood of in-hospital death. Ditillo et al. [23] accessed the USA National Trauma Data Base and identified 32,780 morbidly obese patients who had blunt trauma injury. These patients had higher in-hospital complication rate, longer ICU- and in-hospital stay and higher mortality in morbidly obese patients compared with the non-obese population. Furthermore, Diaz et al. [24, 62] measured fasting glucose plasma levels in 1334 blunt trauma patients and found that mortality was related more to hyperglycemia than to morbid obesity (BMI > 40). Observations on adult patients in ICUs, including medical patients, produced contradictory results [25, 26]. Overall an inversely proportional relationship between overweight-mild obesity and mortality was observed, but these patients had an increased risk of infection, multiple organ failure with longer overall stay in the ICU. Most of the studies were heterogeneous and the interpretation of the results should be considered with caution since obesity was defined only on the basis of BMI, an imperfect measure.

1.3 The Obesity Paradox Revised

Several factors must be considered, since it is quite difficult to explain why after surgical stress, overweight and mildly obese patients seem to show a better prognosis in comparison to the normal-weight patients.

- ***BMI*** The definition of obesity using the BMI alone is misleading and incomplete [1]. It does not distinguish if the increase of the fat is peripheral or central, visceral or subcutaneous. We know that adipose tissue is not only an energetic reserve useful during periods of food deprivation, but it forms the diffuse endocrine system. Visceral and subcutaneous adipose tissue possesses different patterns of hormone secretion and regulates specific metabolic pathways. The increase of visceral fat has a higher pathogenic potential than the subcutaneous adipose tissue. Prognosis of obese patients with heart failure had a good linear relationship with overall survival and waist circumference (considered an index of central adiposity) but not BMI [27, 28]. The same observation was true for surgical patients [29].
- ***Inflammatory pattern of obesity*** Obesity is not only a metabolic but also an attenuated inflammatory disease [30]. Adipose tissue secretes TNFα and other

cytokines, which mediate inflammatory cell activation causing endothelial cell dysfunction. The inflammatory pathways elicited by obesity are the same as induced by surgical stress and it may be possible that obese patients have an adaptive immune-protection exerted by an attenuated inflammation against an acute stress. Mullen et al. [8] considered that the nutritional reserve and more efficient metabolic state of obese patients would be able to elicit a more appropriate inflammatory (and immune) response to surgical stress.

- ***Patient selection*** The main results reported in observational studies in the literature [8, 10, 11, 13, 20] showed that obese patients (especially morbidly obese) were younger than the control population. We suspect that obese patients were selected for intervention only when they were young and at low risk of mortality.
- ***Heterogeneity of the obese population*** Obese patients are a heterogeneous population and up to 30% are metabolically healthy (MHO) with normal insulin sensitivity, low visceral fat storage and absence of significant angiopathy [31]. Intra- and postoperative risks are similar to those of normal-weight patients. MHO patients have normal mean arterial blood pressure, C-reactive protein, HDL cholesterol, triglycerides and plasma glucose. The risk of developing type 2 diabetes mellitus (T2DM) and CVD is 1.24 times higher than in the normal-weight population [32], since these patients easily progress to metabolically unhealthy obesity (MUO), in particular metabolic syndrome; gender (female), low HDL-cholesterol levels, greater insulin resistance and more visceral (and abdominal) fat are the prognostic predictors [33]. It is noteworthy that 30-day morbidity following colon resection in colorectal cancer patients can be predicted by visceral fat not BMI [29]. Furthermore, the presence of the metabolic syndrome, including central obesity, entails a higher risk of respiratory events (OR 2.6) and SSI (OR 3.47) following surgery [34]. In the above mentioned study, mortality was not analyzed, and conclusions cannot be made on the influence of central adiposity on the obesity paradox.
- ***Presence of comorbidities*** Table 1.1 illustrates potential risk factors for complications and death after surgery and trauma in obese patients.

Obesity leads to an increase in body mass by augmenting adipose tissue and ectopic fat accumulation in the liver, muscles and other organs. This modification causes morphological, metabolic and functional changes in a unique pattern for each obese patient.

The most frequent complications of postoperative and traumatic stress are repercussions on the cardiovascular and pulmonary system: cardiac failure, pulmonary

Table 1.1 Comorbidities of obesity relevant for surgical risk definition

Blood hypertension
Cardiovascular disease
Restrictive pneumopathy
Obstructive sleep apnea syndrome
Obesity hypoventilation syndrome
Type 2 diabetes mellitus
Nonalcoholic fatty liver disease
Chronic kidney disease
Malnutrition
Sarcopenia

insufficiency, deep venous thrombosis and pulmonary embolism. They are the most frequent causes of death after bariatric surgery [35].

Arterial hypertension, CVD and obesity hypoventilation syndrome should be considered in the assessment of the surgical risk [36–38]. Obstructive apnea syndrome contributes to worsening of cardiovascular and pulmonary function [39]. The use of the STOP-bang questionnaire is a useful prognostic tool to evaluate the risk of ventilation-related complications [40]. T2DM increases the risk of complications after surgery [41, 42]. Obesity and T2DM independently increase the risk of SSI [43–45], but perioperative correction of hyperglycemia is an effective preventive measure [46, 47]. Malnutrition (detected by hypoalbuminemia) and sarcopenia (detected on the basis of functional and morphological changes in muscle mass) also indicate a higher risk of complications after surgery [48–50].

1.4 Risk Prediction in Emergency Surgery of Obese Patients

Elective bariatric surgery is associated with a low risk of complications (2–5%) and mortality (0.18%) [51]. After elective general surgery, the rate of complications in obese patients ranges from 10.8 to 13.8% with a mortality rate of about 1.2%. Following trauma, they are 9.3% and 3%, respectively. Emergency abdominal surgery is characterized by a substantial increase of the complications (17.2–27.7%) and mortality (3.8–4.9%), depending on the obesity class. The excellent results of bariatric surgery depend on a careful selection of the patients, preventive measures for enhanced recovery after surgery and intensive treatment of complications. ASA physical status is the most used system for predicting the risk of surgical patients [52]. Obese patients are classified as class 2 or 3 with substantial underevaluation of the emergency surgery cases. In bariatric surgery, obese patient prognostic factors include male gender, age >45, BMI > 50, hypertension and risk factors for pulmonary embolism [53]. DeMaria elaborated the Obese Surgery Risk Mortality Score (OSRMS) [53] following bariatric surgery by evaluating the prognostic factors stated above scored 1 each. He considered 3 classes: A (score 0–1), 39–65% of the cases, B (2–3), 35–52% of the cases and C (4–5), 2–11% of the cases [52–55], which correlate with progressive mortality rates of 0.31%, 1.90% and 7.56% [52]. The most frequent causes of death were pulmonary failure, pulmonary embolism and cardiac events (60.6%). The OSRMS was validated for mortality in several studies but failed to predict the risk of complications [53–56] and was not validated for general elective or emergency surgery.

A further predictive factor was identified in a multi-centric prospective cohort study by the StarSurg group [57], which found a significant relationship between BMI and major complications in patients affected by gastrointestinal malignancies. All obese patients affected by these cancers are at a high risk of complications and mortality, especially when associated sarcopenia is present.

Finally, we have to consider the role of emergency surgery. In their revision of the ACS-NSQIP, Hyder et al. [58] examined 56,942 emergency and 136,311 elective interventions and found that the mortality rate was 3.97% in the first group and 0.4% in the latter. In a separate paper, Bohen et al. [59] confirmed that major morbidity and mortality were higher following emergency surgery (16.75% vs. 9.73% and 3.74% vs. 1%, $p < 0.001$). Bohen et al. [59] and Nandan et al. [60] identified 22 risk factors for adverse events after emergency surgery and elaborated the Emergency Surgery Acuity Score. The mortality rate was 22.8% for score 10, 59.1% for score 15 and 100% for score 22. The risk factors were demographic (age > 60 years), clinical or determined by laboratory tests. Most of them are frequently associated with obesity (hypertension, dyspnea, ventilator requirement, congestive heart failure, infection and sepsis), with longer stay in hospital, higher rate of complications, reoperation and death [61]. Under these conditions, optimal resuscitation and perioperative care strategies (see Chaps. 2–5) are essential to achieve the best results we can.

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