Associated Co-morbid Conditions of Clinically Severe Obesity

2

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A thorough knowledge of the associated co-morbid conditions of clinically severe obesity is warranted for every health care professional interested in bariatric therapy.

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2.1 Introduction

Obesity has become an important public health problem. Its prevalence has progressively increased worldwide [1] to an extent that it is now a significant problem not only in affluent societies but also in developing countries [2–5].

Accurate assessment of total body fat requires sophisticated technology which is not readily available on a large scale [6, 7]. Consequently, the World Health Organisation (WHO) adopted body mass index (BMI), which is calculated by dividing the body weight in kilograms (kg) by the square of the height in metres (m), as a surrogate measure of total body fat [3]. BMI correlates fairly well with the percentage of body fat in the young and middle-aged people among whom obesity is most prevalent [6, 7]. According to this index, obesity is defined in the case of BMI value equal to or greater than 30 kg/m^2 in the western population and 27.5 kg m^2 in the Asian population.

Several large studies have demonstrated increased mortality above this threshold of BMI. In the Framingham study, a prospective cohort study, male and female

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non-smokers aged 40 years who suffered from obesity lived 5.8 and 7.1 years less than their non-obese counterparts [8]. Another study by Fontaine et al. which used data from the National Health and Nutrition Examination Survey (NHANES I and II) and the NHANES III Mortality Study found a marked reduction in life expectancy in young adults with obesity compared to non-obese adults.

However, apart from total body fat, the pattern of fat distribution has great relevance. Excess visceral fat, also referred to as central obesity, has a stronger association with cardiovascular disease than subcutaneous fat which is deposited mainly around the hips and buttocks [9]. Central obesity produces a characteristic body shape that resembles an apple and thus is also referred to as "apple-shaped" obesity as opposed to "pear-shaped" obesity in which fat is deposited on the hips and buttocks. This distribution is also reflected in the waist circumference and Waist: Hip Ratio (WHR) [10].

The INTERHEART study, similarly to other studies, showed that hip fat distribution assessed by hip circumference had a negative predictive effect on myocardial infarction (MI) whereas waist fat distribution assessed by waist circumference was associated with high rates of MI [9].

Body fat distribution, assessed using magnetic resonance imaging in leading research institutions, and its effects on mortality and morbidity is currently a topic of scientific research.

The reason for the increased mortality in obesity is related to the great burden of its associated co-morbidities [11]. It has been demonstrated that obesity treatment and especially bariatric surgery can heal or improve most of the associated diseases and, as a consequence, can increase life expectancy. As a consequence, co-morbidities in combination with BMI have been placed at the basis of the indication for bariatric surgery. In 1991 the Consensus Statement of the NIH Consensus Development Conference codified the first universally accepted guidelines for surgery for obesity and weight-related disease [12]. They asserted that a candidate for surgery for obesity and weight-related diseases is a patient suffering from obesity with:

1. BMI >40 kg/m^2
2. BMI >35 kg/m^2 in the presence of specific co-morbidities:
   - Hypertension
   - Ischemic heart diseases
   - Type 2 diabetes (T2DM)
   - Obstructive sleep apnea syndrome
   - Obesity syndrome/hypoventilation (Pickwickian syndrome)
   - Non-alcoholic fatty liver disease and steatohepatitis
   - Dyslipidemia
   - Gastroesophageal reflux diseases
   - Venous stasis diseases
   - Severe urinary incontinence

These inclusion criteria for bariatric surgery have been adopted by multiple other national guidelines as well [13].

This chapter aims to elucidate the main co-morbid conditions of clinically severe obesity.

2.2 Impaired Glucose Tolerance and Diabetes Mellitus

There is currently no controversy that obesity is associated with impaired glucose tolerance or type 2 diabetes mellitus. Insulin resistance is advocated as the underlying mechanism.

The association of obesity with diabetes has been demonstrated in several studies. In one of the biggest cohort studies, in which 84,941 female patients were followed up for 16 years, there were 3300 new cases of diabetes mellitus. Importantly, the study revealed that overweight or obesity were the main predictors of type 2 diabetes mellitus [14]. In men, there were similar findings from the Health Professional follow-up study. A 60.9% age-adjusted relative risk of developing diabetes was found in those with a BMI $\geq$ 35 kg/m^2 in comparison to those with BMI <23 kg/m^2 [15].

There is strong and consistent evidence that obesity management can delay the progression from pre-diabetes to type 2 diabetes [16, 17] and may be beneficial in the treatment of type 2 diabetes [18, 19]. In overweight and obese patients with type 2 diabetes, mild and sustained weight loss has been shown to improve glycaemic control and to reduce the need for glucose-lowering medications [18–20]. Small studies have demonstrated that in patients with obesity and type 2 diabetes more extreme dietary energy restriction with very-low-calorie diets can reduce HbA1c to <6.5% (48 mmol/mol) and fasting glucose to <126 mg/dL (7.0 mmol/L) in the absence of pharmacological therapy or ongoing procedures [21]. Weight loss-induced improvements in glycaemia are most likely to occur early in the natural history of type 2 diabetes when a still reversible β-cell dysfunction exists but insulin secretory capacity remains relatively preserved [22].

A substantial body of evidence has now accumulated, including data from several randomised controlled clinical trials, demonstrating that bariatric surgery achieves superior glycaemic control and reduction of cardiovascular risk factors in patients suffering from obesity with type 2 diabetes as compared with other lifestyle/medical interventions [23]. It is obvious that for surgery, to be effective, it should be coupled with optimal medical treatment and lifestyle adjustment [24].

The superiority of bariatric surgery in the treatment of diabetes holds from the economic point of view as well. Indeed, according to the analysis conducted by the International Federation of the Surgery of Obesity and Metabolic Disorders (IFSO), bariatric surgery is cost-effective and, in some instances, a cost-saving approach for the management of patients suffering from obesity and T2DM [24]. With a mild degree of evidence (level 2), a different efficacy of each bariatric procedure in

improving glycaemic control has emerged. Diabetic obese patients undergoing biliopancreatic diversion/duodenal switch (BPD/DS) achieve the greatest rate of T2DM resolution when compared to other surgical procedures. Gastric Bypass (GBP) and Sleeve Gastrectomy (SG) have a similar short- to mid-term effectiveness on the improvement of glycaemic control, while the anti-diabetic effects of Laparoscopic Adjustable Gastric Banding (LAGB) are lower [24].

Based on this accrued evidence, several organisations and government agencies have expanded the indications for metabolic surgery to include patients with inadequately controlled type 2 diabetes and BMI as low as 30 kg/m^2 (27.5 kg/m^2 for Asians) [24, 25]. Even IFSO stated that there was a level 1 of evidence that surgery for obesity and weight-related diseases had an excellent short and mid-term risk/benefit ratio in patients with class I obesity (BMI 30–35 kg/m^2) suffering from T2DM and/or other co-morbidities.

The benefits of surgery can also be encountered in patients with T1DM and morbid obesity. Even if no recovery of the ß-cell function itself is expected, patients with obesity and T1DM are likely to experience a reduction in the daily insulin requirements as a result of the decrease in insulin resistance that is seen after weight loss. Positive effects on other weight-related diseases are a reasonable expectation as well [24].

2.3 Hypertension

The data available so far shows a strong association between obesity and hypertension. In one large cohort study of 82,473 participants, BMI was positively associated with hypertension at age 18 and midlife. There was also a marked increase in the risk of developing hypertension with weight gain [26]. In the Framingham study, the relative risk of hypertension in overweight men and women were 1.46 and 1.75, respectively, even after age adjustment [27]. In the same study, weight reduction in women with obesity aged 18 or older, reduced the risk of hypertension.

Recently, waist circumference (WC) has been considered as a reliable marker in assessing obesity and the risk of hypertension. When WC and BMI were compared as continuous variables in the same regression model, WC was found to be a better predictor of obesity-related hypertension, than BMI [28]. Moreover, WC is comparatively easier and faster to apply than BMI, which requires a weighing scale and subsequent calculation of the index.

Several pathophysiological mechanisms are believed to be at the basis of the association between obesity and hypertension. The most convincing one is the increase of the circulating plasmatic volume as a consequence of the reduced clearance of the Atrial Natriuretic Peptide (ANP); indeed, the physiologic inactivation of this hormone by fat tissue seems to be impaired by hyperinsulinemia and insulin resistance. Moreover, hyperinsulinemia is responsible for hyperplasia of the muscular layer of arterioles with a consequent increase of peripheral vascular resistance. Another possible explanation of hypertension is that hyperinsulinemia and insulin resistance impair endothelial function and the production of nitric oxide (NO). This, in turn, results in peripheral vasoconstriction.

2.4 Heart Disease

There is unequivocal evidence that there is an increased risk of coronary artery disease (CAD) in obesity. In the Asian Pacific Cohort Collaboration study in which more than 300,000 participants were followed up, there was a 9% increased incidence of ischaemic heart disease for every unit change in BMI. Increased risk of CAD was also found in the Framingham and Nurses Health Studies [27–29]. Indeed, obesity and in particular "central obesity" is associated with hypertriglyceridemia, decreased HDL and increased LDL levels; atherogenesis and consequent coronaropathy are also triggered by hypertension and impaired glucose tolerance.

Obesity can be associated with congestive heart failure (CHF). When the risk of heart failure (HF) was evaluated in the Framingham study, it was twofold higher in the group with obesity than in the non-obese group [30]. The increase of the body mass requires a bigger left ventricular ejection volume. This leads to an eccentric left ventricular hypertrophy which progressively becomes insufficient and decompensated, and CHF becomes clinically overt at this point.

Paradoxically, the analysis of the data retrieved from the Framingham study shows that a higher BMI is associated with longer survival in patients with congestive heart failure (CHF). In a retrospective analysis of 7767 patients with CHF who were categorised into 4 BMI ranges including obesity (BMI > 30 kg/m^2), there was reduced overall mortality within higher BMI groups in an almost linear trend. After further analysis, overweight and obese patients had a hazard ratio of 0.88 compared to healthy weight patients (taken as the reference group) whereas underweight patients with stable CHF had a 1.21 risk of death when they were compared to the same reference group [31]. The reason for this so-called "obesity paradox" is not clear. Probably other concomitant cardiovascular diseases linked to obesity may have led to the diagnosis of HF in its earlier stages, thus reducing the risk of death from CHF. On the other hand, the results of cardiopulmonary testing in overweight and healthy weight patients suffering from CHF were found to be similar [32, 33]. Therefore, the explanation of the paradox remains still unclear.

Considering the well-known noxious effects of obesity and the incomplete understanding of the mechanism of this "paradox", treatment of obesity is still recommended to reduce CHF associated mortality. Elucidating the mechanism of this paradox is still an area of scientific research.

On this aforementioned basis, it's simple to understand why weight loss induced by surgery is associated with a reduction in the incidence of major cardiovascular events, including myocardial infarction and stroke. As stated by the IFSO commission in 2016, cardiovascular event reductions after weight loss are more relevant in patients with a high cardiovascular risk [24]. There is also evidence that the resolution of obesity is associated with improvement of functional status and symptoms in patients with pre-existing ischemic heart disease or heart failure; however, the effects on long-term prognosis are not known [24].

Weight loss after bariatric surgery is associated with regression or improvement of early structural markers of atherosclerosis (carotid intima-media thickness, brachial flow-mediated dilation, and coronary artery calcium score) [24]. A lower

degree of evidence exists about the issue of heart transplantation in the population with obesity. Preliminary results regarding this issue suggest that, in patients with severe obesity and end-stage heart failure, bariatric surgery may be useful as a bridge to successful heart transplantation [24].

2.5 Dyslipidemia

Dyslipidemia, consisting of reduced high-density lipoprotein (HDL) and increased triglycerides, is associated with obesity [34]. The underlying mechanism is largely due to insulin resistance. Very low-density lipoprotein (VLDL) clearance in plasma is dependent on the rate of hepatic synthesis and catabolism by the lipoprotein lipase, an enzyme that is also involved in the synthesis of HDL [34, 35]. In obesity, insulin resistance is associated with the increased hepatic synthesis of VLDL and impaired lipoprotein lipase function [36].

There is evidence that dyslipidemia, in obesity, can occur even in the absence of insulin resistance. In 1998, Gary et al. showed a significant association between obesity, particularly central obesity, and dyslipidemia after adjustment for insulin resistance.

2.6 Cerebrovascular Disease

Currently, available evidence shows that the risk of haemorrhagic and ischaemic stroke is increased in men with obesity. In women this association holds as far as ischaemic stroke is concerned; haemorrhagic stroke, on the other hand, lacks correlation with obesity. In the Korean prospective study involving 234,863 men who were followed up for 9 years, a significant positive association was found between BMI and the risk of ischemic stroke; in the case of haemorrhagic stroke, a "J-shaped" association was found, showing that its risk increased more than that of ischaemic stroke at the upper and lower extremes of BMI [37].

In a prospective study of 39,053 participants (all women) who were followed up for an average of 10 years, 432 strokes occurred. 307 were ischaemic, 81 haemorrhagic and 4 undefined. In obese subjects (BMI > 30 kg/m^2), the hazard ratios (95% CI) for total stroke, ischaemic stroke and haemorrhagic stroke were 1.5 (1.16–1.94), 1.72 (1.30–2.28) and 0.82 (0.43–1.58), respectively.

The reason for the different risk of haemorrhagic stroke between men and women with obesity is not fully understood and is under the scrutiny of the scientific community.

It is noteworthy that, central obesity (where fat is preferentially distributed around the trunk) is important in predicting mortality after stroke. In the Israel heart disease study, stroke mortality was predicted by central obesity alone, independently of BMI, hypertension, diabetes and socioeconomic status [38].

2.7 Metabolic Syndrome

According to the National Cholesterol Education Program's Adult Treatment Panel III (NCEP: ATP III), the metabolic syndrome is defined when at least 3 of the following 5 features are present: (1) waist circumference above 40 inches for men and above 35 inches for women, (2) triglycerides above 150 mg/dL, (3) HDL cholesterol below 40 mg/dL for men and 50 mg/dL for women, (4) blood pressure above 130/85 mmHg, (5) fasting glucose above 100 mg/dL.

Insulin resistance, which leads to an abnormal lipid and glucose metabolism, appears to be at the basis of metabolic syndrome [39]. This syndrome was initially believed to be an independent risk factor of cardiovascular disease; however, this has recently been challenged as the sum of the combined risk factors at the basis of the metabolic syndrome does not outnumber the sum of individual factors [40].

A moderate (level 2) level of evidence exists that bariatric surgery can achieve greater improvement in each component of the Metabolic Syndrome compared with non-surgical weight loss therapies [24].

2.8 Pulmonary Diseases

Several studies have linked obesity and obstructive sleep apnea (OSA). In the Wisconsin Sleep Cohort study, obesity showed a strong association with OSA [41]. In another study, increased neck circumference, which correlates with obesity, had a strong connection with obstructive sleep apnea [42]. The mechanism responsible for OSA in obesity is the external compression by the fat tissue on the airways with consequent narrowing of their lumen [43].

Asthma is another condition that is likely to occur in obesity. There is evidence that obesity increases the risk of asthma. In one prospective multicentre study, the prevalence of asthma was observed to increase in patients with obesity. Indeed, in recent clinical research, 75% of the patients who sought medical care for asthmatic respiratory distress were reported to be either obese or overweight [44]. The mechanism linking obesity and asthma is chronic systemic inflammation driven by increased inflammatory cytokines and chemokines, and other adipocytes-derived factors [45]. In turn, the chronic inflammation increases airway hyper-responsiveness which is typical of asthma.

The association of Obstructive Sleep Apnea Syndrome (OSAS) and asthma with obesity requires an accurate assessment of the respiratory function before surgery; instrumental investigations such as chest X-ray, pulmonary function tests, arterial blood gas are mandatory [24]. If the diagnosis of sleep apnea syndrome is suspected nocturnal oximetry or polysomnographic examination is suggested to assess whether a respiratory therapy device such as C-PAP (Continuous Positive Airways Pressure), should be used peri-operatively [24].

In 2016, IFSO implemented in its Position Statements the results of several studies demonstrating that bariatric surgery for obesity may result in resolution or improvement of (OSAS) and significant improvement of asthma management, defined as symptoms, level of lung function, and use of medication in asthmatic patients.

2.9 Gastrointestinal Diseases

A great part of the epidemiological studies to date have found an association between obesity and increased risk of Gastroesophageal Reflux Disease (GERD). In one large cross-sectional population study, which was part of a randomised trial, involving 10,537 subjects, the adjusted odds ratios for heartburn and acid regurgitation in obese patients were 2.91 (95% CI 2.07–4.08) and 2.23 (95% 1.44–1.99) respectively, compared with those with normal BMI. Recent evidence from a meta-analysis involving data from studies between 1966 and 2004 has demonstrated that obesity is significantly associated with GERD, oesophageal cancer and erosive esophagitis and that the severity of these disorders increases with increasing weight [46].

Another gastrointestinal disease that has been linked to obesity is cholelithiasis. Data from the literature shows that females with a BMI of more than 45 kg/m^2 had a sevenfold increase in the risk of gallstone disease compared to those with a BMI of less than 24 kg/m^2 [47].

Consequently IFSO, in 2016, issued the grade B recommendation to perform cholecystectomy during bariatric surgery for patients with biliary symptoms or patients with gallstones documented during pre-operative ultrasonography [24].

Liver disease is a common feature in the obese population, in the form of the so-called Non-Alcoholic Fatty Liver Disease (NAFLD). NAFLD consists of a spectrum of disease manifestations that have in common the absence of excessive alcohol consumption. On one end of the spectrum, there is simple steatosis, also referred to as non-alcoholic fatty liver (NAFL) disease. Patients with simple steatosis or NAFL just have steatosis without histologic evidence of hepatocellular injury. At the other end of the spectrum, there is Non-Alcoholic Fatty Liver Steato-Hepatitis (NASH) which combines steatosis and hepatocellular injury and which may be associated with hepatic fibrosis also. Prognosis changes dramatically whether patients have NASH or non-NASH disease. It is generally accepted that patients with simple steatosis progress very slowly, if at all. On the other hand, patients with NASH are more likely than the non-NASH group to have progressive liver disease and can experience complications such as cirrhosis and HCC. There is probably a wide range of factors that predispose patients to progress from simple steatosis to NASH; however, the exact rate of progression is unknown. Lebovics and Rubin, in their recent review of NAFLD, report a 20% rate of conversion from simple steatosis to NASH over a 15-year follow-up [48, 49]. Some genomics studies to date, have implicated genetic factors associated with the progression of NAFLD, although these factors lack clinical application at the moment. It is also interesting to note

that while hepatic injury induced by NASH is similar to that seen in patients with alcoholic liver disease, NASH does appear to progress more slowly and is less severe on histology than steatohepatitis caused by alcohol [50, 51]. Indeed, over a relatively short period of follow-up, only 2% of NASH patients on average progressed to decompensated liver disease and cirrhosis [52, 53]. Once cirrhosis develops in NASH patients, their overall prognosis appears to be dismal. The clinical course of patients who had NASH-related cirrhosis was found by Ratziu et al. to be similar to those with cirrhosis from hepatitis C [54].

It is accepted by most experts that while patients with steatosis alone are not at risk for HCC, patients with cirrhosis from NASH are at risk for HCC. So far, the exact pathogenesis of NASH-related HCC remains unclear although experts do agree that age and advanced fibrosis are established risk factors for HCC in NASH. Even if there are variations from study to study on the overall incidence of NASH-related HCC, there is consistent evidence that the risk of HCC is lower than hepatitis C-related cirrhosis. For example, Yatsuji et al. calculated an incidence of HCC of 11.3% in 5 years for patients with cirrhosis secondary to NASH; which is lower than the incidence of HCC in patients with hepatitis C-related cirrhosis [55].

Recent reports indicate that weight loss induced by surgery could be beneficial for NASH although the lack of randomised clinical trials precludes a precise assessment of this benefit. As a consequence of this mild level of evidence (level 2), IFSO issued a grade B recommendation that weight loss after bariatric surgery could provide improvement or resolution of non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) [24].

2.10 Reproductive Disease

Obesity has a detrimental effect on female fertility [56]. In women over the age of 18 whose BMI is higher than 32 kg/m^2, the relative risk of anovulatory cycles and consequent infertility is 2.7 times higher [57]. For women having ovulatory cycles, the chance of conceiving a child is decreased by 5% for every BMI-unit increase [58].

The reasons for the decreased fertility are multiple and include higher leptin and lower adiponectin levels. Additionally, the production of steroids in the ovaries is compromised and in association with the elevated insulin levels, this leads to an inhibition of the sex hormone-binding globulin synthesis by the liver and hyperandrogenemia [59]. Reduced fertility is also due to the higher incidence of polycystic ovary syndrome (characterised by anovulation, hyperandrogenism and a polycystic ovary) in women with obesity [60]. Weight loss in women with polycystic ovary syndrome, obtained by lifestyle therapy, pharmacological therapy and surgery for obesity, improves spontaneous ovulation and pregnancy rates [61]. Since weight loss improves the chances of conception, it has to be considered the first-line therapy for women with this condition [62]. This grade B recommendation was issued by IFSO in the context of 2016 Position Statements with a level 2 of evidence; in particular, IFSO members pointed out that weight loss as a treatment for infertility should be considered in the first line regardless of the presence or absence of

polycystic ovary syndrome and that weight loss could be achieved by lifestyle therapy, pharmacologic therapy or surgery.

There are other reproductive complications of obesity that can occur during pregnancy and labour. These include gestational diabetes, macrosomia, dystocia and increased rates of caesarean sections [63].

In addition to the effects on female reproductive physiology, obesity also has an impact on male reproduction [64]. MOSH or Male Obesity Secondary Hypogonadism is a well-known entity. The detailed effects of obesity on reproductive physiology are discussed in another chapter.

2.11 Psychosocial and Psychiatric Problems

Obesity in the affluent society has been associated with several untoward outcomes in terms of psychosocial or socioeconomic well-being. Women with obesity, for example, were found to be more likely to drop out from school, had a 20% lower chance of getting married, earned lower salaries in comparison to females who were not overweight [65]. However, the cause–effect relationship can be either way since socioeconomic status can be responsible for obesity and viceversa [66].

Overt psychiatric disorders have been linked to obesity. These disorders include schizophrenia and schizoaffective disorders, psychosis, bipolar disorder, substance abuse disorders, eating disorders (Bulimia, BED, and NES), neurocognitive disorders and personality disorders. Treatment with certain psychotropic medications, including antipsychotics and mood stabilisers, previous psychiatric hospitalisations, as well as a history of suicide attempts or other self-injurious behaviours also are widely considered risk factors for poor post-operative outcomes. Some of these conditions, in particular severe, uncontrolled psychosis, bipolar disorder, and substance abuse are widely considered contraindications to surgery [67–69].

Minor mental health problems such as mood and anxiety disorders are very common; they are considered negative predictors for the outcome of surgery for obesity, but not a contraindication for treatment, provided the patient is receiving appropriate mental health treatment [24].

2.12 Osteoarthritis

Osteoarthritis (OA) is strongly associated with obesity. In the Framingham cohort study, data from 1420 participants indicated that obesity was an important independent risk factor for OA after adjustment for age, physical activity and levels of uric acid [70].

The mechanism of OA has been attributed to direct chronic strain on the joints related to the overweight. However, some authors have raised the hypothesis that non-mechanical aetiologies may contribute to OA in obesity because the same changes of OA present in weight-bearing joints have also been demonstrated in non-weight bearing joints. There is growing evidence that dysregulation of

adipokines (hormones from adipose tissue) such as adiponectin, visfatin and resistin may trigger OA, suggesting that osteoarthritis may be a systemic disease in obesity [71, 72].

2.13 Cancer

There is considerable evidence of an association between obesity and some cancers [73]. These include cancer of the gallbladder, oesophagus (adenocarcinoma), thyroid, kidney, uterus, colon and breast [74, 75]. In the USA, 14% of cancer deaths are attributed to obesity; this percentage reaches 20% in female individuals.

This link has further been strengthened by the observation that a reduced incidence of cancer and reduced mortality from cancer is registered after weight loss [76, 77]. It was estimated that the hypothetical correction of the excess weight in the US population [78] would have been able to prevent about 900,000 cancer deaths.

So far, the underlying mechanism linking these cancers to obesity is not clear. In the case of uterus and breast cancers, it is thought to be the higher oestrogen levels synthesised from adipose tissue [79, 80].

Considering that there are no randomised clinical trials on this topic, IFSO attributed a grade C level to the statement that surgery for obesity can reduce the incidence of some malignancies and the mortality related to them [24].

2.14 Conclusions

Obesity is an epidemic disease not only affecting industrialised societies but also developing countries. It is associated with a reduced life expectancy because of the great burden of associated diseases. These can affect virtually every organ from cardiovascular to the respiratory, reproductive and gastrointestinal system. Metabolism is also negatively affected by obesity as demonstrated by the high prevalence of diabetes, dyslipidemia and endocrine pathologies. Even several psychosocial and psychiatric diseases have been pathogenetically linked to obesity. Moreover, there is growing evidence that obesity increases the likelihood of some cancers; this is far from being a sheer statistical connection because several scientific studies have demonstrated a clear pathogenetic mechanism connecting obesity and cancer.

Most of these pathologies can regress or at least improve with weight loss interventions and especially with bariatric surgery. Thus, these co-morbidities and their resolution represent, along with BMI, a keystone in the indication for bariatric surgery. Moreover, the presence of these diseases can modify the operative risk and, as a consequence, careful pre-operative evaluation is required and, when possible, optimisation of the patient. Last, but not least, post-operative results, weight loss included, can be affected by the pre-existing pathologies; patients operated on for obesity should be followed up on a patient-tailored rather than a standardised schedule.

For all these above-mentioned reasons, it is important for every healthcare professional involved in the therapy for obesity to have a thorough knowledge of these diseases.

Key Points

- *The resolution or improvement of co-morbidities has to be considered as another goal of bariatric surgery and must be given the same importance as weight loss in its outcomes.*
- *Excess visceral fat, also referred to as central obesity, has a stronger association with cardiovascular disease than subcutaneous fat.*
- *Weight loss-induced improvements in glycaemia are most likely to occur early in the natural history of type 2 diabetes when a still reversible ß-cell dysfunction exists and insulin secretory capacity remains relatively preserved.*
- *In the Asian Pacific Cohort Collaboration study in which more than 300,000 participants were followed up, there was a 9% increased incidence of ischaemic heart disease for every unit change in BMI*
- *Available evidence shows that the risk of haemorrhagic and ischaemic stroke is increased in men with obesity.*
- *For women having ovulatory cycles, the chance of conceiving a child is decreased by 5% for every BMI-unit increase*
- *A moderate (level 2) level of evidence exists that bariatric surgery can achieve greater improvement in each component of the Metabolic Syndrome compared with non-surgical weight loss therapies.*
- *Obesity treatment and especially bariatric surgery can heal or improve most of the diseases associated with obesity and as a consequence can increase life expectancy.*
- *According to the analysis conducted by the International Federation of the Surgery of Obesity and Metabolic Disorders (IFSO), bariatric surgery is cost-effective and, in some instances, a cost-saving approach for the management of patients suffering from obesity and T2DM.*

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