Impact of Obesity on Gynecological Diseases

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Abstract

Obesity is a chronic illness affecting more than one-third of adults in the United States. In addition to being associated with some of the leading causes of death such as diabetes, heart disease, and stroke, obesity also profoundly affects women's gynecologic health by altering the reproductive cycle thus affecting menstruation, procreation, and contraception, among others. The rate of certain malignancies is also increased. This chapter reviews the impact of obesity on gynecologic aspect of women's health.

Keywords

Obesity • Puberty • Contraception • Infertility • Anovulation • Surgery • Gynecology

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1 Introduction

Obesity is an epidemic affecting more than one-third of all adults in the United States. The Centers for Disease Control and Prevention (CDC) reports that 17 million children and 78.6 million adults are affected in the United States, with an estimated annual medical cost for obesity in the United States of $147 billion in 2008.

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Obesity is the most prevalent among middle-aged adults, with different groups being affected differently; non-Hispanic Blacks have the highest age-adjusted rates (47.8%), followed by Hispanics (42.5%), non-Hispanic Whites (32.6%), and non-Hispanic Asians (10.8%) (Centers for Disease Control and Prevention 2015).

The body mass index (BMI) is a measurement obtained by dividing the person's weight (in kilograms) by the square of the person's height (in meters squared). The parameters for the definition of overweight and obesity vary by race. In some populations, health risks are seen at a much lower BMI (South Asians) and in others at a higher BMI (Blacks) when compared with Caucasians. The classifications for BMI adopted by the National Institute of Health (NIH) and World Health Organization (WHO) for Caucasian, Hispanic, and Black individuals are summarized in Table 1; a normal BMI is between 18.5 and 24.9 kg/m^2, overweight is BMI $\geq$25 kg/m^2, and obese is a BMI $\geq$30 kg/m^2. These cutoffs would underestimate the health risk in the Asian and South Asian population. Thus, in the WHO and NIH guidelines for Asians, overweight corresponds to a BMI between 23 and 24.9 kg/m^2 and obesity a BMI >25 kg/m^2.

In addition to BMI, measurement of waist circumference is vital in recognizing adults at greater health risk, particularly in the individuals whose BMI ranges from 25 to 35 kg/m^2. A waist circumference of $\geq$88 cm in women and $\geq$102 cm in men is considered elevated and suggestive of increased cardiovascular risk. In Asian men and women, a waist circumference >90 cm and >80 cm, respectively, is considered abnormal. In patients with a BMI >35 kg/m^2, measuring waist circumference is unnecessary since these individuals are already at high risk.

Table 1 BMI classification in Western countries

Underweight – BMI <18.5 kg/m^2
Normal weight – BMI $\geq$18.5–24.9 kg/m^2
Overweight – BMI $\geq$25.0–29.9 kg/m^2
Obesity – BMI $\geq$30 kg/m^2
Obesity class I – BMI of 30.0–34.9 kg/m^2
Obesity class II – BMI of 35.0–39.9 kg/m^2
Obesity class III – BMI $\geq$40 kg/m^2

Obese individuals are at increased risk of all-cause mortality, in addition to many serious illnesses including hypertension, dyslipidemia, type 2 diabetes, coronary artery disease, stroke, some types of cancer, sleep apnea, osteoarthritis, and mental disorders such as depression and anxiety.

Obese women have a separate set of complications from men resulting from their elevated BMI. The effect of obesity on women's gynecologic health is reviewed in this chapter.

2 Obesity and the Menstrual Cycle

2.1 Puberty

Increases in weight and body fat are associated with a higher likelihood of early menarche. The decreasing age of puberty in the United States is thought to be due to, at least in part, the increasing prevalence of childhood obesity. According to the CDC, data collected over the past 30 years suggest that obesity rates have doubled in children and quadrupled in adolescents. Meanwhile, the overall age of puberty has decreased from approximately 12.75 years in the 1960s to approximately 12.5 years in the 1990s.

Frisch and Revelle (1971) proposed a "critical fat hypothesis", suggesting that puberty is initiated after a threshold level of fat is established (Frisch and McArthur 1974). The link between puberty and fat appears to be a protein hormone named leptin (Ahima et al. 1996). Leptin is produced in adipose tissue, circulates to the brain, and plays a crucial role in controlling hunger. Levels of leptin increase with increasing adiposity. Although a threshold level is necessary for the onset of puberty in females, evidence supports that leptin plays a permissive role. Leptin stimulates Kiss 1 neurons causing the Kiss 1 neurons to transmit metabolic information to GnRH neurons. Some studies have indicated that leptin also has direct gonadal effects that may contribute to the accelerated puberty in obese adolescents (Sanchez-Garrido and Tena-Sempere 2013).

- Leptin-deficient mice fail to develop puberty, and injection of leptin in prepubertal mice triggers puberty.
- Data derived from observation of children with untreated leptin deficiency or leptin receptor deficiency has demonstrated hypogonadotropic hypogonadism and failure to initiate puberty. Hence, leptin may be the link that determines a critical level of fat and allows/triggers the onset of puberty by communicating with higher centers that control the hypothalamic pulses that trigger puberty.
- It has been reported that girls with an early onset of puberty have an increased risk of PCOS and cardiovascular events later in life.

2.2 PCOS and Insulin Resistance

Notoriously associated with insulin resistance, polycystic ovary syndrome (PCOS) is a complex functional endocrine disorder with clinical features of chronic anovulation, hyperandrogenism, and a derangement in follicular development resulting in polycystic-appearing ovaries. Women with PCOS have a unique disorder of insulin action resulting in a significant insulin resistance that is independent of obesity (Dunaif et al. 1989). The combination of PCOS and obesity has synergistic adverse effects glucose tolerance (Dunaif et al. 1989).

Obesity is characterized by insulin resistance. With increasing weight, the levels of circulating insulin increase, causing a downregulation and decrease in the number of insulin receptors coupled with a concomitant increase in insulin resistance. In insulin resistance, fat, muscle, and liver cells are unable to respond normally to circulating insulin, and thus, higher levels of insulin are needed to help glucose enter the cells. The metabolism of proteins, carbohydrates, and fat and the catabolism of triglycerides are affected by high levels of glucose, leading to an increase in the levels of circulating free fatty acids and LDL cholesterol. The hyperinsulinemia associated with obesity is reversible with weight loss.

Obesity contributes to chronic anovulation in several ways. First, the previously described hyperinsulinemia stimulates androgen production in the ovarian stroma, impairing follicular development. Also, with increasing adipose tissue, peripheral aromatization of androgens results in increased levels of estrogen that exert a negative feedback on the hypothalamo-pituitary-ovarian axis. Furthermore, levels of sex hormone-binding globulin (SHBG), a protein carrier produced in the liver that transports the principal sex steroids, are inversely related to body weight. In obese women, low levels of hepatic SHBG lead to further increases in unbound levels of testosterone and estradiol in the circulation.

The chronic anovulation associated with obesity results in a state of unopposed estrogen that drives the proliferation of endometrial tissue and the resultant frequent, irregular bleeding. Studies have suggested that more than a third of overweight and obese women have irregular menses and that menstrual irregularity correlates with increasing BMI (Hedley et al. 2004). The effect of unopposed estrogen on the endometrium can also result in endometrial hyperplasia and cancer (discussed below, Sect. 7).

Weight loss alone can restore ovulation in patients with PCOS. A moderate decrease in body weight of 5–10% has been shown to be associated with a return of ovulatory function in the majority of obese anovulatory women with PCOS (Crosignani et al. 2003).

The state of hyperestrogenism associated with obesity has also been implicated in the pathogenesis of endometrial polyps. A study by Onalan et al. (2009) demonstrated that obesity was an independent factor in the development of endometrial polyps and positively correlated with their size and number, which could be another factor manifesting with abnormal uterine bleeding in obese women.

3 Infertility and ART

While many obese patients are not infertile, obesity was found to be associated with decreased fertility, diminished response to infertility treatments, and increased risk of miscarriage.

3.1 Fertility

A cohort study of 53,910 couples enrolled in the Danish National Birth Cohort found a dose-response relationship between increasing BMI and decreased fecundity (Ramlau-Hansen et al. 2007). As described above (Sect. 2.2), obesity is associated with an endocrinopathy that manifests by hyperinsulinemia and insulin resistance, coupled with hyperandrogenemia, leptin deficiency, increased LH, abnormal FSH-LH ratio, decreased sex hormone-binding globulin, increased estrogen, and decreased progesterone levels. This hormonal profile affects neuroregulation of the hypothalamic-pituitary-gonadal axis resulting in anovulation and decreased fertility. Weight loss is capable of correcting the anovulation associated with obesity and PCOS. Insulin-sensitizing drugs, predominantly metformin, have also been shown to restore ovulation in some women with PCOS.

Beyond anovulation, obesity itself appears to be associated with a lower fecundity (Gesink Law et al. 2007). In a cohort study by Zaadstra et al. (1993), an increased waist to-hip ratio was found to be associated with delay in time to conception, even after adjustment for patient weight and cycle length or regularity. A Dutch study found that the probability of natural conception declined by 4% per kg/m^2 in women with a BMI >29 kg/m^2 (van der Steeg et al. 2008). The mechanisms related to this decrease in fertility in obese ovulatory women are not completely understood.

3.2 Miscarriage

There is evidence that obesity increases the rate of spontaneous abortions by almost threefold compared to women of normal weight. In a retrospective study of 712 egg donation cycles (Bellver et al. 2007), showed the rate of miscarriages to be 13.3% in normal-weight women, 15.5% in overweight women, and 38.1% in obese women. Various theories have been proposed to explain this increased rate. Obesity and the associated endocrine alterations may affect corpus luteum function (Sherman and Korenman 1974; Fedorcsák et al. 2000), early embryo development (Kawamura et al. 2002; Fedorcsák and Storeng 2003), or endometrial receptivity (Alfer et al. 2000; Gonzalez et al. 2000) hence affecting embryo implantation and early development.

3.3 Assisted Reproductive Technology (ART)

In addition to affecting the chances of spontaneous pregnancy, obesity also diminishes success rates with ART. With increasing BMI, there is evidence for an increase in in-vitro fertilization (IVF) cycle cancelation states, increasing gonadotropin requirements, a decrease in the number of oocytes collected, and an overall decrease in the rate of live births. An increase in body habitus also makes the procedure of oocyte retrieval technically challenging with increased rate of complications. At this point in time, many fertility practices will counsel their morbidly obese patients about weight loss prior to initiating ART aiming at a threshold BMI of less than 40 to qualify for IVF.

4 Contraception

4.1 Combination Oral, Transdermal, and Vaginal Contraceptives

Obesity may impair the efficacy of combined contraceptives. There is evidence of a higher risk of oral contraceptive (OC) failure in obese women when compared to normal-weight women. In a study by Holt et al. (2005), it was shown that women with a BMI >27.3 had a 60% higher risk of OC failure and those with a BMI >32.2 had a 70% higher risk. Similar results were seen in clinical trials of the combination transdermal patch, showing increased failure in women weighing above 90 kg (Zieman et al. 2002).

Also, combination OC (COC) and obesity are both independent risk factors for venous thromboembolism (VTE). A case-control study found that in women using oral contraceptives with a BMI greater than 25, the rate of VTE is tenfold

higher than in lean women not using oral contraceptives (Abdollahi et al. 2003).

While the American Congress of Obstetricians and Gynecologists (ACOG) (American College of Obstetrics and Gynecology 2006) does not label obesity an absolute contraindication for combined contraceptives, it states OCs should be used with caution in obese women above the age of 35. The CDC Medical Eligibility Criteria [USMEC] rate obesity with BMI $\geq$30 kg/m^2 at category 2 [benefits generally outweigh the risks]; they also say the obese women who use COCs are more likely than obese women who do not use the pill to develop a VTE.

- USMEC puts malabsorptive bariatric surgery into category 3 (risks generally outweigh benefits) although restrictive bariatric procedures [sleeves or bands] are category 2.
- Obese women with hypertension or previous DVT/PE would fall into category 3/4 based on these factors.

Accordingly, consideration should be given to a progestin-only contraceptive or to intrauterine devices. The levonorgestrel intrauterine device is a particularly attractive option for obese women given its non-contraceptive benefits of endometrial cancer risk reduction and decreased menstrual bleeding.

4.2 Progestin-Only Contraceptives

Progestin-only pills (POPs) are not as widely used as COC. They are particularly a good option for postpartum women, where the risk of thrombosis is elevated, since they do not increase the risk of VTE and do not negatively affect breast milk. Despite their increased safety profile, POPs used in the United States are associated with undesirable side effects such as irregular bleeding, and they have a very stringent daily timing (within 3 hours). POPs do not reliably suppress ovulation; however, their effectiveness relies on the changes they exert on the cervical mucus and the endometrium. For obese women, and women with other contraindications to COCs, the POPs offer the advantage that they do not increase the risk of venous thromboembolism while they maintain a success rate similar to that of OC.

Injectable progestins have mechanisms of action similar to POPs that include increased cervical mucus viscosity, creation of an endometrium unfavorable for implantation, and unpredictable ovulation suppression. Their use is very popular in the United States. Depot medroxyprogesterone acetate (DMPA) has a contraceptive efficacy equivalent or better than that of COC but has a much better safety profile. In obese women, DMPA is safe. There are studies showing possible weight gain with the use of DMPA; however, not all studies have shown this effect.

4.3 Intrauterine Devices (IUD)

IUDs are one of the most effective methods of contraception. There are currently five different IUDs available in the United States, and they include one copper containing IUD and four different levonorgestrel-releasing IUDs. The effectiveness of IUDs is not affected by BMI as the mechanism of action does not rely on systemic hormone levels. In the Contraceptive CHOICE project, the overall failure rates of IUDs were less than one per hundred woman-years with no differences between various BMIs (Xu et al. 2012).

The levonorgestrel-releasing IUD is a particularly attractive option for obese women. It exerts its contraceptive function by rendering the endometrium atrophic and stimulating thick cervical mucus, but its non-contraceptive uses are equally attractive. Since obese women have high rates of dysfunctional uterine bleeding and endometrial hyperplasia (Sect. 2.2), the levonorgestrel-releasing IUD is often used in obese women to minimize vaginal bleeding and decrease the risk of premalignant endometrial lesions.

5 Surgical Risk

Obese women are at higher risk of experiencing surgical and anesthetic complications. In a paradox referred to as the “obesity paradox” (Mullen

et al. 2009), otherwise healthy obese patients undergoing non-bariatric surgery were found to have lower mortality and morbidity than normal-weight patients. However, obese patients commonly have comorbid conditions such as hypertension, obstructive sleep apnea, coronary artery disease, or a difficult airway, and these patients have an increased rate of surgical mortality and morbidity compared to the normal-weight patients.

5.1 Surgery in the Obese Patient

Physical exam and particularly the bimanual exam may be difficult in the clinic setting to decide on the preferred route of surgery. In this case, further imaging such as MRI is recommended for guidance. As in all patients, the least invasive route should be considered for better outcomes.

Abdominal surgery in obese women takes longer and has a higher blood loss and higher rate of wound complications and surgical site infections, increased risk of VTE, and increased hospital stay. As the BMI rises, so do the risk of surgical site infection (Olsen et al. 2009) and wound complications (Nugent et al. 2011). Some intraoperative considerations have been suggested for surgery in obese patients. First, placement of the skin incision needs to be tailored to each patient, as anatomy of the abdominal wall may be distorted. In cases where an abdominal fat pad covers the lower abdomen, one must be aware that an incision under the fat pad is subjected to an intense maceration. Also, surgical instruments must be adapted to the situation, using wide retractors to maintain the thick abdominal wall. Mass closure, subcutaneous drains, and prophylactic antibiotics can be considered in order to minimize wound disruption.

The implications for laparoscopic surgery are also present. The position of the umbilicus relative to the aortic bifurcation and the rest of the abdomen vary and may make abdomen penetration with a Veress needle challenging. Open laparoscopic entry has been found to be safer in obese subjects (Byron et al. 1989). Also of concern is that operating in the pelvis requires the patient to be in the Trendelenburg position. This positioning is known to increase intrathoracic pressure and particularly for obese patient may be associated with impaired oxygenation and difficulty in ventilation. The use of longer trocars and instruments needs to be anticipated. Laparoscopic surgery in obese patients may be more complicated and the risk of conversion to laparotomy is elevated, but these obstacles can be partly overcome with surgical experience (Wattiez et al. 2002).

As with all patients, efforts to choose the least invasive surgery should be exerted. If appropriate, the vaginal route for hysterectomy is preferred to reduce postoperative pain and morbidity. This technique can also be challenging because of the size of the obese patient's legs and buttocks, as well as the presence of redundant vaginal sidewalls, all of which can make visualization and surgery more difficult.

According to the American College of Chest Physicians, obese woman who undergo gynecologic surgery for longer than 45 min fall in the category of moderate risk of VTE and should receive some form of prophylaxis unless at high risk of major bleeding. VTE prophylaxis can either be low molecular weight heparin, low-dose unfractionated heparin, or mechanical prophylaxis with intermittent pneumatic compression.

Appropriately positioning the obese patient is of paramount importance and can prove to be challenging. The operating table can usually accommodate a patient weighing up to 205 kg, and some tables can accommodate up to 455 kg. Positioning of the patient should take into account surgeon ergonomics and provide protection to the patient from nerve injury and pressure sores. If the patient is to be placed in the lithotomy position, the boot-type stirrups are preferred for better lower extremity alignment and decreased pressure on the knees and hips as compared to the candy cane stirrups.

5.2 Anesthesia in the Obese Patient

Risks of anesthesia are higher in obese women with most issues related to technical problems such as constructing an airway, gaining venous

access, or providing effective ventilation. Before undertaking gynecologic surgery, a preoperative consultation with an anesthesiologist should be considered. The obese patient has an increase in cardiac output and a relatively lesser increase in blood volume, resulting in a relative hypovolemia with poor tolerance to fluid overloading and hemorrhage. Respiratory function is altered as well. There is a decrease in functional residual capacity and reserve expiratory volume, associated with an increase in the closure capacity and alveolar dead space. This results in a mismatch of ventilation and perfusion that can lead to hypoxia. The oral airway in the obese patient is suboptimal due to decreased neck mobility and narrowing of the pharyngeal space soft tissue effect. In addition, there is an increased risk of aspiration of gastric contents due to the higher intra-abdominal pressure. All of these concerns must be addressed at the preoperative consultation.

6 Urinary Incontinence

Urinary incontinence, a loss of bladder control, affects more than 13 million women in the United States. The four main types of urinary incontinency include stress urinary incontinence (SUI), urge incontinence, overflow incontinence and functional incontinence. Patients often present with mixed symptoms.

Obesity is an independent risk factor for the development of both stress and urge incontinence, with obese women having up to a 4.2-fold greater risk of than women of normal weight (Alling Moller et al. 2000). The severity of incontinence appears to be influenced by the duration and extent of obesity; which could be explained by the raised intra-abdominal pressure caused by central obesity conveying additional pressure on the pelvis and bladder. This association is further corroborated by studies showing that weight loss among obese women leads to a reduction in episodes of urinary incontinence (Subak et al. 2009).

The mid-urethral sling procedure for the management of SUI has been found to be safe and effective in both obese and nonobese women, regardless of BMI (Weltz et al. 2015).

7 Endometrial Cancer and Other Malignancies

Obesity is directly associated with a number of malignancies including colon cancer, kidney cancer, esophageal cancer, as well as endometrial cancer and postmenopausal breast cancer (Bianchini et al. 2002). The normal balance between cell proliferation and apoptosis in vulnerable tissues may be distorted by the endocrinopathies of obesity that includes fat cell alterations in the metabolism of sex steroids, insulin, and growth factors.

Obese women are at a two-fourfold higher chance of developing endometrial cancer than women of normal weight. In obese women presenting for bariatric surgery, the rate of endometrial hyperplasia was found to be 10% (Modesitt et al. 2015).

There are two types of endometrial cancer. Type I endometrioid adenocarcinomas are the most common, comprising 75% of all cases. They are estrogen-dependent and low-grade and are preceded by endometrial hyperplasia. On the other hand, type II endometrial cancers have a serous or clear cell histology and no precursor lesion and are generally more aggressive. Type I is the endometrial cancer that is more common in obese women; since obesity is often associated with hyperestrogenism due to peripheral aromatization of androgens to estrogen in the adipose tissue. More importantly, the chronic anovulatory status, which is frequently seen in obese women, results in the endometrium being exposed to unopposed estrogen. In the absence of progesterone-induced endometrial shedding, endometrial hyperplasia can frequently develop.

While at this time performing an endometrial biopsy for all women with a BMI >30 is not recommended, ACOG recommends sampling the endometrium of all obese women with symptoms of heavy or irregular uterine bleeding regardless of age (ACOG 2012).

Almost half of women with endometrial cancer or hyperplasia don't know that obesity affects their cancer risk (Beavis et al. 2015), so it is the role of providers to identify these patients at high risk and provide them with the appropriate counseling and education.

8 Pelvic Imaging in the Obese Patient

8.1 Ultrasound

Ultrasound is often the imaging modality of choice in gynecology. However, transabdominal ultrasound is the radiologic modality that is the most affected by obesity because of the attenuation of the ultrasound beam by the layers of adipose tissue. Nonetheless, the availability of transvaginal imaging provides easier accessibility to the reproductive organs by bypassing the abdominal pannus. An often-used solution to the decreased penetration of the transvaginal ultrasound is by placing a hand on the pelvic organs to push them closer to the probe, which in some cases may afford better visualization.

Abdominal scanning in the obese patient is often more challenging. The abdominal pannus limits visualization by both increasing the depth of insonation required and by attenuating the strength of the ultrasound beam. The abdominal pannus also increases the ergonomic challenge for the sonographer. Since the pannus is usually at its thickest between the pubis symphysis and the umbilicus, the patient or an assistant can be enlisted for help by lifting the fat pad upwards toward the patient's head, thus providing a flatter and thinner abdominal wall and closer distance to the pelvic organs.

The use of technology such as harmonic imaging, a nonlinear propagation of ultrasound through body tissues, can improve the quality of the image because fat will act to increase the harmonic waves created. Also, when available, the use of the preset "penetration" mode may result in higher quality image.

When ultrasound imaging fails to provide adequate visualization of the pelvic organs, the imaging modality of choice is MRI when a gynecologic condition is suspected. CT scan is preferred in urologic and gastrointestinal conditions.

8.2 Computed Tomography (CT)

CT imaging of the pelvis is generally adequate in obese patients. The main limiting factors for CT imaging in obesity are size of the patient relative to the machine, positioning, artifacts, and radiation exposure. In fact, CT scan manufacturers set a weight limit for the table beyond which the table can be damaged and the warranty is void. Also, the aperture through which the patient should go is set at a diameter of 70 cm, with newer enhanced models fitting up to an 80–90 cm diameter. The best practice in the case of patients with severe obesity is to obtain an exact weight and abdominal girth immediately prior to the procedure. In cases where the abdominal girth may be over the limit, there are abdominal binders that can be used for this purpose, also serving the additional benefit of preventing the pannus from hanging asymmetrically to the side causing artifacts. Another consideration in the use of CT scan is the quantity of contrast material used. The dose is typically obtained by considering the patient's weight, and this may expose obese patients to a higher-than-necessary dose of contrast. A solution to this problem may be to use the lean body weight as opposed to the actual weight.

8.3 Magnetic Resonance Imaging (MRI)

Compared with ionizing radiation or sound waves, the radiofrequency used by MRI penetrates large amount of fat. Hence, MRI is the modality least affected by obesity. Challenges for MRI, like for CT scan, are mostly related to the size of the patient and the problems with positioning and length of the procedure. The tight fit of the patient in the aperture can cause claustrophobia and even motion artifacts. Also, there is a risk of skin burn if the patient is tightly fitting in the gantry. This can be minimized by placing cloth protections at the areas of friction (Glanc et al. 2012).

9 Weight Loss

More than two-thirds of adults in the United States are either attempting to lose weight or preserve their weight. For patients who are overweight or

obese and at risk for obesity-associated disorders, a number of weight loss interventions are available, including lifestyle, diet, exercise, pharmacotherapy, and surgery. Even moderate weight loss of 5–10% is associated with a reduction in obesity-associated morbidity.

The role of the physician is to identify patients who would benefit from losing weight, determining an ideal body weight, and educating the patient about available options. The initial management is a combination of diet, exercise, and lifestyle modifications with a goal to create an energy deficit by either decreasing intake or increasing expenditure or ideally both. Pharmacological agents can be a useful adjunct to diet and exercise, with bariatric surgery increasingly used as a final option.

9.1 Diet

In a normal adult, approximately 22 calories are required to maintain a kilogram of body weight. Once a patient's daily energy expenditure is calculated, one can calculate their daily caloric intake that generates a daily deficit. This is also used to estimate the resulting weekly weight loss. Diets providing less than 800 calories per day are not generally recommended.

Balanced low calorie/portion-controlled diets are the most commonly recommended diets. They encourage the intake of foods with adequate nutrients, in addition to proteins, minimal carbohydrates, and essential fatty acids, while eliminating alcohol, sugar-containing beverages, and other sources of food that are high in carbs/calories but poor in nutrients.

- Low and very low carbohydrate diets have been popular for many years. Low carbohydrate diets contain 60–130 g of carbohydrates and very low carbohydrate diets contain up to 59 g of diets. They are based on the fact that restriction of carbohydrates leads to glycogen mobilization and rapid weight loss primarily due to glycogen breakdown. Hence, they are more effective for short-term weight loss than low-fat diets.
- Low-fat diets are another commonly used strategy for weight loss, recommending a reduction in the daily intake of fat to less than 30% of total dietary intake. Considering a diet of approximately 1500 calories, this would mean about 45 g or less of fat, which can be counted using the nutrition information labels on food packages.
- The Mediterranean diet is inspired from the traditional diets of Greece, Spain, and the south of Italy. It includes primarily plant-based foods, such as vegetables, fruits, whole grains, legumes, and nuts. It replaces butter with monounsaturated fats such as olive oil and contains a moderate amount of dairy products and low amount of meat. A meta-analysis of eight cohort studies demonstrated that patients that adhered to a Mediterranean diet had a significantly improved health status, with a reduction in overall mortality, mortality from cardiovascular diseases, incidence and decreased mortality from cancer, and incidence of Parkinson's disease and Alzheimer disease (Sofi et al. 2008).

9.2 Exercise

Exercise alone, without dietary changes, results in only modest reductions or no loss in weight.

Adding exercise to diet has only slight additional benefits than diet alone. In a systematic review of 17 randomized trials, it was found that there was only a slight increase in weight loss in the diet and exercise group compared to the diet alone group and that this difference was statistically significant in only two of the studies (Catenacci and Wyatt 2007). However, adding exercise to diet has other important benefits independent of weight loss, such as attenuating the diet-induced loss of muscle mass.

9.3 Pharmacotherapy

In addition to diet, exercise, and lifestyle modification, drug therapy can be a helpful adjunct to weight loss in overweight patients with

comorbidities and obese patients. The role of medications for weight loss has been questioned because of concerns about efficacy and safety; hence, the decision to initiate medications should only be made after a thorough evaluation of risks and benefits.

There are five drugs currently approved for long-term use: orlistat, lorcaserin, phentermine-topiramate, bupropion-naltrexone, and liraglutide. Phentermine, benzphetamine, phendimetrazine, and diethylpropion have only been approved for short-term use.

- Orlistat alters fat digestion by inhibiting pancreatic lipases, resulting in incomplete hydrolysis of fat and increased fat excretion in feces. The efficacy of orlistat has been demonstrated in many clinical trials demonstrating that initial weight loss is greater and that weight regain is slowed as compared with lifestyle/placebo. In addition, orlistat showed other beneficial effects such a reduction in HbA1c, improvement in blood pressure, and an improvement in lipid values more than what can be explained by weight loss alone. The predominant side effects are gastrointestinal, mainly cramps, flatus, fecal incontinence, and oily spotting. These side effects are high initially and then subside as patients learn to avoid them by avoiding high-fat diets. Absorption of fat-soluble vitamins (A, D, E, K) is lowered by orlistat therapy.
- Lorcaserin is a selective agonist of the serotonin 2C receptor; it reduces appetite and therefore body weight. It appears to have similar efficacy as and fewer side effects than orlistat. In addition to weight loss, lorcaserin has other beneficial effects including decreases in blood pressure, lipid levels, fasting glucose, and insulin levels. Side effects are generally mild, and they include headache, upper respiratory infections, dizziness, and nausea.
- Liraglutide is a long-acting glucagon-like peptide-1 analog that is available for use in the United States for treatment of type 2 diabetes. It is also approved for use at higher doses in the treatment of obese patients or patients with a BMI $\geq$27 kg/m^2 with at least one weight-related comorbidity. Liraglutide has been associated with a significant reduction in weight when compared to placebo in diabetes and non-diabetes trials. At the higher doses used for obesity treatment, liraglutide has higher rates of nausea and vomiting, side effects that may be partly responsible for the weight loss effect of the drug. Other side effects include diarrhea, hypoglycemia, and anorexia.
- A preparation of combined phentermine and extended-release topiramate has been approved for obese adults or adults with BMI $\geq$27 kg/m^2 with at least one weight-related comorbidity. This combination has been shown to increase weight loss in the first year of use. The most common side effect is dry mouth, constipation, and paresthesia.
- The combination preparation of bupropion-naltrexone is not recommended as first-line therapy, but can be used for the obese smoker who desires therapy for smoking cessation and weight loss. Naltrexone is an opioid receptor antagonist used to treat alcohol and opioid dependence, and bupropion is used for depression and the prevention of weight gain during smoking cessation. The combination reduces weight by 4–5% compared to placebo. Side effects include nausea, headache, and constipation.
- The sympathomimetic drugs phentermine, diethylpropion, benzphetamine, and phendimetrazine are only approved for short-term treatment, up to 12 weeks. They reduce food intake by causing early satiety. Phentermine is the most widely prescribed weight loss drug; however, because of the potential side effects, potential for abuse, and limited duration of use, they are usually not recommended. They are contraindicated in patients with coronary artery disease, hypertension, and hyperthyroidism or in patients who have a history of drug abuse.

9.4 Bariatric Surgery

Candidates for bariatric surgery include obese patients with a BMI $\geq$40 kg/m^2 or patients with

a BMI $\geq$35 kg/m^2 with at least one serious comorbidity, such as type 2 diabetes or hypertension. Adults with BMI between 30 and 34.9 Kg/m^2 can also be candidates if they suffer from uncontrolled type 2 diabetes or metabolic syndrome.

Bariatric surgical procedures cause weight loss through two main mechanisms: malabsorption and restriction. Some procedures have both components. Malabsorptive procedures shorten the length of the functional small intestine and decrease the absorption of nutrients. Restrictive procedures work by limiting the caloric intake by reducing the stomach's capacity.

- The Roux-en-Y gastric bypass (RYGB) is the most commonly performed bariatric procedure. It involves the creation of a small gastric pouch that is divided and separated from the distal stomach and anastomosed to a limb of small bowel. While it is mainly a restrictive procedure, it also has a malabsorptive component that participates in weight loss.
- The laparoscopic adjustable gastric banding is a restrictive procedure where an adjustable silicone ring is placed around the entrance of the stomach. Saline can be injected through an infusion port into the band to reduce its diameter, to increase the amount of restriction.
- Another restrictive procedure, the sleeve gastrectomy is a partial resection of the greater curvature of the stomach, which creates a tubular stomach. This procedure is easier to perform than the RYGB. The created tubular stomach is small and resistant to stretching due the absence of the fundus.

10 Conclusion

The impact of obesity on women's reproductive health is significant with harmful effects noted on the menstrual cycle, fertility, contraception, urinary incontinence, surgical risk, imaging studies, and certain malignancies. Weight loss is a difficult but an achievable solution to many of these consequences. Weight loss can be achieved best in a multidisciplinary approach.

11 Cross-References

- ▶ Conservative Management of Endometrial Cancer
- ▶ Workup and Management of Polycystic Ovary Syndrome

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