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Review

Polycystic ovary syndrome and endometrial hyperplasia: an overview of the role of bariatric surgery in female fertility

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ABSTRACT

One of the most effective methods to tackle obesity and its related comorbidities is bariatric surgery. Polycystic ovary syndrome (PCOS) and endometrial hyperplasia (EH), which are associated with increased risk of endometrial carcinoma, have been identified as potentially new indications for bariatric surgery.

PCOS is the most common endocrine disorder in women in the reproductive age and is associated with several components of the metabolic syndrome such as obesity, insulin resistance and hypertension. EH is a pre-cancerous condition which arises in the presence of chronic exposure to estrogen unopposed by progesterone such as both in PCOS and obesity.

The main bariatric procedures are Roux-en-Y gastric bypass, laparoscopic sleeve gastrectomy and laparoscopic adjustable gastric banding. These procedures are well established and when correctly selected and performed by experienced bariatric surgeons, they can achieve significant weight loss and remission of obesity related co-morbidities.

Studies have shown that bariatric surgery can play an important role in the management of patients with PCOS and improve fertility. Similarly, bariatric surgery has a positive effect on endometrial hyperplasia, making surgically induced weight loss a potentially attractive option for endometrial cancer prevention and treatment.

Obesity has an adverse impact on spontaneous pregnancy, assisted reproduction methods and feto-maternal outcomes. After bariatric surgery obese women with subfertility can achieve spontaneous pregnancy. However, while bariatric surgery reduces the risk of pre-eclampsia and gestational diabetes, there is an increased risk of small for gestational age and possible increased risk of stillborn or neonatal death.

In this article we will review the evidence regarding the use of bariatric surgery as a treatment modality in patients with PCOS and EH. We also provide an overview of the common bariatric procedures.

Contents

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Introduction

Obesity is a global epidemic with over 2.1 billion people worldwide now regarded as overweight or obese [1], which is likely to increase despite various steps that have been taken to address this problem such as public education, instituting sugar tax schemes or reducing the calorific content in foods [2–4]. One of the more recent methods to treat obesity is bariatric surgery and current evidence support that it is an effective treatment that results in sustainable reductions in weight and in the risks associated with morbid obesity and the related co-morbidities [5]. In 2013 the registered bariatric procedures worldwide have reached a historic high number of 470,000 [6]. With improvement in all outcomes, the eligibility criteria for bariatric surgery continue to expand [7–9]. Moreover, new potential indications are emerging such as idiopathic intracranial hypertension, non-alcoholic fatty liver disease, chronic kidney disease, polycystic ovary syndrome (PCOS) and endometrial hyperplasia (EH) [10–12,13,14].

PCOS is the most common endocrinopathy of women of reproductive age that is associated with insulin resistance, hyperandrogenism, adverse cardiovascular risk factors and subfertility. Identification and management of PCOS constitute a major burden for the healthcare system [15]. Endometrial hyperplasia is a relatively common condition that affects women of all age groups. It relates to excessive cellular proliferation leading to increased volume of the endometrial tissue [16]. EH is diagnosed three times more commonly than endometrial cancer, and can progress to cancer if left untreated. Without intervention, the risk of progression to carcinoma (EC) is less than 1% for women with simple hyperplasia, 3% for complex nonatypical hyperplasia, and up to 29% for women with atypical complex hyperplasia [17]. World Health Organisation guidelines in 2014 have re-classified EH by categorizing it as hyperplasia without atypia and hyperplasia with atypia [18].

A recent systematic review showed that the risk of EC was three times higher in women with PCOS compared to women without the disease. The risk is even higher, up to three folds in obese women, and obesity is a predominant feature in PCOS. Management strategies to reduce the risk of EC in women with PCOS are therefore vital [16].

Polycystic ovary syndrome

PCOS can affect up to 10% in women of reproductive age [19]. PCOS is a heterogeneous disorder in which the principal features are androgen excess (clinically or biochemically), ovulatory dysfunction, and polycystic ovaries [13,15].

The pathogenesis of PCOS remains uncertain and likely to be multifactorial including interactions between genetic and environmental factors such as fetal exposure to androgens, obesity and sedentary lifestyle. These can lead to increased GnRH pulsatile secretion and hyperinsulinaemia/insulin resistance, both of which result in increased adrenal and ovarian androgen secretion. The overall effect is an increased level of free androgens (worsened by reducing SHBG) resulting in the clinical features of hirsutism, anovulation and infertility (by arresting follicular development) [15].

Anovulation results in subfertility and decreased progesterone release result in unopposed oestrogen effects causing breakthrough bleeds and increased risk of endometrial hyperplasia, which can progress to endometrial cancer (2.7-fold risk increase) [21].

PCOS in both lean and obese individuals is independently associated with impaired glucose tolerance, insulin resistance, metabolic syndrome, Type 2 diabetes mellitus, hypertension, increased risk of cardiovascular disease, deranged lipid profile, sleep apnoea and obesity [7,13,20,22,23]. Obesity and PCOS additively contribute to the evolution of metabolic syndrome. The similarity in the background and mechanism has led to the opinion that PCOS constitutes a female type of metabolic syndrome (syndrome XX) [24]. Obesity is very common in PCOS with almost 60% of affected women being obese [25]. This obesity is predominantly central, contributing further to the establishment of metabolic syndrome even in very young individuals [22]. Hyperinsulinaemia plays a cardinal role in the pathophysiology of both PCOS and metabolic syndrome with hyperandrogenaemia. Both lean and obese women with PCOS have increased circulating insulin levels relative to those of serum glucose compared with healthy lean and obese women [26]. Such a finding strongly suggests a certain degree of hepatic insulin resistance irrespective of obesity. Of note is that lean PCOS females present only hepatic insulin resistance while obese affected individuals present global insulin resistance [15]. Hence, there is a significant metabolic heterogeneity in women with PCOS strongly influenced by obesity. Forty percent of such women will develop diabetes by the age of 50. This is not always dependent on BMI. The development of diabetes is not only attributed to peripheral insulin resistance but also to insufficient β-cell response to meals [27].

The relationship between PCOS and obesity is multifactorial and bi-directional. PCOS can exacerbate obesity and obesity can exacerbate PCOS in a vicious cycle pattern [20]. Additionally, PCOS negatively affects the main components of the metabolic syndrome which constitute the established indications for bariatric surgery (such as Type 2 diabetes, hypertension or

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