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The Role of Bariatric Surgery in Improving Reproductive Health

Scientific Impact Paper No. 17
October 2015

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1. Background

Obesity is a common problem among women of reproductive age. Twenty-six percent of women in the UK have a body mass index (BMI) of more than 30 kg/m^2. Women are three times as likely to be admitted to hospital with a primary diagnosis of obesity as men.[1] Female patients outnumber male patients seeking bariatric surgery by a ratio of around 3:1[2] and approximately 70% of these women are of childbearing age.[3] In one study,[4] 25% (29/115) of women presenting for bariatric surgery suffered from infertility.

Obesity has a negative impact on natural conception, pregnancy and the long-term health of mother and child due to an increased rate of congenital anomalies, pregnancy complications and the possibility of metabolic disease in later life; and the likelihood of miscarriage in obese women who do conceive is raised.[5]

Women who are obese respond less well to drugs used for ovarian stimulation for the treatment of anovulation and assisted conception, although this does not always equate with reduced ongoing pregnancy rates.[6,7] Obesity per se may affect the technical feasibility of clinical procedures such as visualising the ovaries on ultrasound scan or oocyte retrieval.[8,9] Obesity affects oocyte and embryo health and may also affect endometrial receptivity. Whereas autologous in vitro fertilisation (IVF) in obese women results in fewer live births, donor egg pregnancies in obese women have been shown in one meta-analysis of six studies[10] to result in safe births, suggesting that it is the quality of the oocyte, and not necessarily the reproductive environment that is affected by obesity. On the other hand, some authors have shown that obesity may influence the receptivity of the uterus.[11,12]

Pregnancy in obese women can precipitate metabolic illness and is associated with obstetric risks. In the largest study of its kind of 16000 women,[13] a maternal BMI of greater than 30 kg/m^2 was associated with an increased risk of gestational diabetes, gestational hypertension, pre-eclampsia and fetal macrosomia compared with women with a BMI of less than 30 kg/m^2. Induced labour and caesarean delivery, anaesthetic complications, perioperative morbidity and longer hospital stays are more prevalent in obese women.[14–18]

The effective ways to induce long-term weight reduction in women with severe obesity are either significant sustained lifestyle changes, which are not achieved by most very obese people in the long term,[3,19] or bariatric surgery. National Institute for Health and Care Excellence (NICE) guidelines[20] recommend that bariatric surgery be considered when the BMI is 40 kg/m^2 or more, or for those with a BMI between 35 and 40 kg/m^2 in the presence of other comorbidities and where other nonsurgical methods have proven unsuccessful.

This paper reviews the most recent evidence on the safety and efficacy of bariatric surgery as an intervention to improve female fertility and reproductive outcomes in obese women.

2. Bariatric surgery procedures

Bariatric surgery may be restrictive, aiming to reduce calorie intake by reducing gastric capacity, and/or malabsorptive. Restrictive procedures include laparoscopic adjustable gastric banding (LAGB), silastic ring gastroplasty (SRG), vertical banded gastroplasty (VBG) and sleeve gastrectomy (SG). An example of a malabsorptive bariatric procedure is biliopancreatic diversion (BPD); Roux-en-Y gastric bypass (RYGB) is both a restrictive and malabsorptive procedure.

Bariatric surgery results in a loss of up to 15–25% of body weight that is sustained in the long term, as well as significant reductions in healthcare costs and comorbidities associated with obesity, such as diabetes, hypertension and certain cancers.[3] Serious complication rates associated with laparoscopic

bariatric surgery are comparable to routine elective procedures such as laparoscopic cholecystectomy when performed in large centres.[21]

In LAGB, an adjustable silicone band is placed around the upper part of the stomach to create a small upper-stomach pouch that limits hunger and food intake while promoting an early feeling of satiety after meals. The complication rate is around 13% and the reoperation rate is 12%.[22] The most common complications of LAGB include proximal gastric pouch enlargement (10%) or the port site becoming infected (2.6%).[23]

In RYGB, a small stomach pouch is isolated from the rest of the stomach and empties directly into the lower portion of the jejunum, thereby delaying mixing of food with bile and pancreatic juices. The result is an early sense of satiety that reduces the desire to continue to eat.[24] Complications include bleeding, anastomotic leak with peritonitis, deep vein thrombosis and internal hernias.

In SG, a partial gastrectomy is performed to reduce stomach volume while maintaining the normal anatomy of the rest of the gastrointestinal tract. Originally performed to aid initial weight loss prior to a duodenal switch, it has gained popularity as a stand-alone operation. The metabolic effects and weight loss appear similar in the first few years to RYGB surgery,[25–28] but RYGB appears superior after 3 years.[29]

Calorie malabsorption does not appear to be a symptom of LAGB, SG and RYGB, whereas BPD and biliopancreatic diversion with duodenal switch (DS) are malabsorptive procedures which reduce nutrient absorption by bypassing a large portion of the small intestine,[30] this can lead to iron, calcium, folate, thiamine, B12 and fat-soluble vitamin deficiencies. Other complications of BPD and DS include steatorrhoea, protein malnutrition, anastomotic leak, deep vein thrombosis and internal hernia.

The cardiometabolic consequences of central obesity (prediabetes or diabetes, raised triglycerides and high blood pressure resulting in higher risk of stroke and heart attack[31]) are increasingly being recognised as the primary target for bariatric surgery interventions. The adverse effects of obesity on fertility, obstetric and perinatal outcomes primarily result from the metabolic effects of obesity. For instance, insulin resistance, seen in metabolic syndrome and polycystic ovary syndrome (PCOS), is associated with poor oocyte quality and endometrial receptivity, and lower fertilisation and implantation after IVF.[32] Several prospective and randomised controlled studies[29,33] have shown that short-term remission of diabetes can be achieved in 40% of patients after bariatric surgery. Many of these patients may relapse in the long term, but still retain much better long-term glycaemic control.[34]

3. Conception after bariatric surgery

The effect of weight loss through bariatric surgery on fertility has been the subject of much interest and numerous publications.[35–44] While in many of these studies the numbers are small and appropriate control groups have not always been included, together they do suggest that bariatric surgery improves the markers of PCOS which influence fertility, including anovulation, hirsutism, hormonal changes, insulin resistance, sexual activity and libido.

Several studies[39–41,45] have found improvements in sex hormone profiles and the resolution of PCOS following bariatric surgery. For instance, a cross-sectional study of 16 obese women who underwent bariatric surgery (6 LAGB, 10 RYGB)[42] demonstrated improvement in luteal function, although not to the same level as the 14 normal weight subjects to which they were compared. Legro et al.[43] measured changes in ovulatory function following bariatric surgery over a longer time frame (24 months), although only 30% completed the full 24 months. In completers, a 4 kg ($P < 0.001$) reduction in android fat occurred, but luteal phase length and reproductive hormones, aside from circulating estradiol, were unaltered. A shortening of the follicular phase length, which has been proposed to represent a normalising of menstrual regularity, was reported after bariatric surgery, as was improvement in female sexual function as measured by the Female Sexual Function Index. A small study of 20 patients with PCOS followed up over an average of

9 years[44] found improvement in PCOS symptoms (menstrual cycle improved in 82%, hirsutism in 29% and type II diabetes in 78%) and successful conception in those attempting pregnancy (six patients).

In a study of 110 young Italian women who were previously unsuccessful at becoming pregnant,[46] 60 conceived after postoperative weight loss. The type of surgery was not related to changes in fertility, as only the amount of weight lost (a weight loss of greater than 5 kg/m^2, OR 20.2, P = 0.01) and the BMI achieved at time of conception (P = 0.01) were predictive of becoming pregnant. As with much of the research in this area, studies that document improvements in fertility after bariatric surgery are hampered by a lack of power to determine statistical significance.[47–50] Stratification of risk according to type of surgery is often not possible,[51,52] although preliminary results seem to indicate that weight loss, and not the type of surgery, is the mediator for improved fertility.[46]

4. Fertility treatment and bariatric surgery

With regard to assisted conception, in one case series,[53] four out of five IVF treatments following bariatric surgery resulted in live term births, but the authors highlighted a possible increased risk of ovarian hyperstimulation syndrome, which can lead to ascites and significant morbidity. Furthermore, laxity of skin with depleted adipose tissue can limit the bioavailability of subcutaneous administration of the gonadotrophin hormones required for the treatment.[54]

Other factors limiting IVF accessibility, such as maternal age, need to be borne in mind when considering appropriate treatment for obesity, especially in the light of recommendations that women wait for at least a year after surgery before attempting to become pregnant.[55] In women over the age of 30 years, early referral for bariatric surgery should be considered in order to increase the safety of subsequent IVF treatments.

5. Miscarriage rates after bariatric surgery

There is a paucity of evidence on miscarriage rates following bariatric surgery; studies or case series to date are insufficiently powered. Given that prepregnancy obesity and excessive gestational weight gain increase miscarriage rates,[56,57] it is likely that bariatric surgery should result in a reduced risk of miscarriage.

6. Maternal and fetal outcomes

Most studies have demonstrated improved maternal and fetal outcomes in women who have had bariatric surgery compared with untreated obese women[58–60] or previous pregnancies in the same women.[61] However, comparison with the latter group raises obvious limitations in interpretation since factors such as maternal age, parity and smoking are not controlled for. However, two large, population-based matched cohort studies[62,63] have lent substantial weight to the emerging themes of an increased incidence of reduced intrauterine growth and an increased rate of preterm births after bariatric surgery.

In the first study,[62] 339 women with a singleton delivery after bariatric surgery (84.4% gastric bypass) were matched to 1277 unexposed women (after adjusting for BMI, parity, age, date of delivery and smoking). Infants in the first group had a shorter mean gestational age (274 versus 278 days), a higher risk of being small for gestational age (SGA; adjusted OR [aOR] 2.29, 95% CI 1.32–3.96) and a lower mean birthweight (3312 g versus 3585 g), but had a lower risk of being large for gestational age (aOR 0.31, 95% CI 0.15–0.65). When analysing data from women with gastric bypass (n = 286) alone, the risk of SGA was even higher (aOR 2.78). With respect to other outcomes, in contrast to smaller studies, no statistically significant differences were found between the groups regarding the risk of gestational diabetes mellitus, pre-eclampsia, labour induction, caesarean section, postpartum haemorrhage, Apgar score less than 7, admission to neonatal intensive care unit or perinatal death. The discrepancy between gestational diabetes and pre-eclampsia risk in this study compared with other smaller studies can be explained by the correction made for BMI, thereby eliminating the effect of weight loss.

In the second study,[63] a large Swedish nationwide cohort of 2562 obese women who had undergone bariatric surgery was compared with 12 379 controls matched for maternal age, parity, early pregnancy BMI, early pregnancy smoking status, educational level and year of delivery. This study also found that post-surgery births carried an increased risk of an SGA birth (5.2% versus 3.0%; OR 2.0, CI 1.5–2.5; $P < 0.001$) and a lower risk of a large-for-gestational-age birth than in matched controls. There was also a higher incidence of preterm births (both indicated and spontaneous preterm delivery were increased) in the post-bariatric surgery cohort (9.7% versus 6.1%; OR 1.7, 95% CI 1.4–2.0; $P < 0.001$). Interestingly, maternal BMI modified the risk of preterm birth. An increased risk for preterm birth was only observed in women with a BMI less than 35 kg/m^2 (BMI less than 30 kg/m^2: 10.4% versus 5.3%; OR 2.0; BMI 30–34.9 kg/m^2: 9.3% versus 6.2%; OR 1.8; BMI greater than 35 kg/m^2: 7.8% versus 7.2%; OR –0.9; $P = 0.01$ for interaction). No differences were detected for stillbirth or neonatal death. The increased risks for preterm and SGA birth, as well as the decreased risk for large-for-gestational-age birth, remained when post-surgery births were compared with births of women eligible for bariatric surgery.

Other smaller studies[48,58,64–67] have demonstrated increased SGA in infants born after bariatric surgery compared with untreated obese women, as well as fetal growth restriction or lower birthweight in pregnancies after bariatric surgery when compared with the same women's pregnancies before bariatric surgery, or in BMI-matched controls.[68] However, most studies also show improvement in all other maternal and fetal outcomes, including rates of gestational diabetes, pregnancy-induced hypertension, macrosomia and congenital abnormalities.[60,69]

The evidence for an increase in caesarean rates after bariatric surgery is equivocal, with some studies suggesting higher rates and some lower rates compared to very obese women, with wide variation in practice, and further studies are therefore needed for clarity.[69] A large population study of 159 210 deliveries[70] found that the 298 deliveries to women who had previously undergone bariatric procedures exhibited similar rates of most perinatal and obstetric complications compared to the rest of the population, except for rates of caesarean delivery (OR 1.4), premature rupture of membranes (OR 1.9), labour induction (OR 2.1) and fetal macrosomia (birthweight greater than 4 kg; OR 2.1). However, the correlation between previous bariatric surgery and caesarean delivery was the only variable that remained significant when controlled for possible confounders (such as previous caesarean delivery, obesity, fertility treatments, premature rupture of membranes, labour induction, diabetes mellitus, hypertensive disorders and fetal macrosomia).[70,71]

In the majority of studies quoted so far in this paper, most patients have undergone gastric bypass surgery. In contrast, the cohort study by Lapolla et al.[72] examined LAGB patients only. In this study there were lower rates of gestational hypertension, pre-eclampsia, caesarean section and SGA compared with non-LAGB obese controls or pregnancies from the same women prior to LAGB. Furthermore, LAGB patients had rates of SGA comparable to those of normal weight controls (1.4% versus 2.3%). Ducarme et al.[73] analysed neonatal outcomes retrospectively in a cohort study of three French centres involving 63 births after LAGB and 31 after RYGB surgery; they reported a significantly lower mean birthweight (2993 g versus 3253 g; $P = 0.02$) after LAGB than after RYGB. However, no significant differences were noticed regarding SGA (32.3% versus 17.1%, $P = 0.06$), umbilical arterial blood pH less than 7.0 (9.7% versus 0%; $P = 0.11$), low Apgar scores, perinatal mortality, and neonatal intensive care unit admission. Neonatal outcomes in relation to the interval from surgery to conception or compared with the BMI at the beginning of the pregnancy were not significantly different. Moreover, Facchiano et al.[74] found no significant difference in outcomes between 20 RYGB and 22 LAGB pregnancies for both obstetric and birth outcomes, including SGA.

Several studies[46,75–78] have reported favourable outcomes after SG and fewer nutritional deficiencies than following RYGB or BPD. Two studies only[4,79] have reported outcomes following BPD, with one study on VBG;[50] all three reported similar outcomes to the cohort studies examining LAGB and gastric bypass outcomes.

7. Management of reproductive health after bariatric surgery

When considering the type of bariatric surgery most beneficial for women of childbearing age, the long-term benefits of RYGB on weight outcomes,[29] diabetes treatment and hence fertility need to be balanced against the more desirable nutritional profile of SG and LAGB during pregnancy. Although few studies have directly compared pregnancy outcomes after different types of surgery, SG has been shown to result in less anaemia, and less vitamin and micronutrient deficiency during pregnancy when compared with RYGB and BPD.[76–78] While RYGB does not lead to malabsorption of macronutrients, the maintenance of adequate nutrition during pregnancy is potentially influenced by the reduction in fat-soluble vitamin uptake. All patients are advised to remain on lifelong vitamin supplementation following bariatric surgery, but poor adherence to optimal intake can be a problem despite increased support and advice.[80,81]

7.1 Contraception

All patients are given contraceptive advice before and after surgery and are advised against becoming pregnant during the initial weight loss phase when in a state of negative energy balance.[55] Despite being given this advice, only 60% of a cohort of 1000 Swedish women after bariatric surgery were aware of the advice and 30% were not using contraception in the first year after surgery.[82] This can be problematic in younger woman, where rates of unplanned pregnancy are high. Consideration should be given to non-oral contraception, given that there may be reduced absorption of oral hormonal preparations.

In some women, delaying pregnancy may significantly alter their age-related conception risk. One case series of women who became pregnant after bariatric surgery[83] found that one-half (ten patients) had conceived within 18 months of surgery, with a high percentage of pregnancies described as unintentional (80%), some of which occurred despite the use of contraception (48%). Outcomes were not compared between early and late conceivers, but there were few complications and all pregnancies resulted in live healthy births. There have been case reports[84] of nutritional deficiencies affecting fetal outcomes in early pregnancy after bariatric surgery, but a study by Sheiner et al.[51] showed no difference in outcome between early and late conception following bariatric surgery and argued that current recommendations to delay conception until 12–18 months after surgery are based on theoretical risk rather than evidence. It calls for a more personalised approach, taking into account maternal age and balancing theoretical nutritional risk against the risk that delaying pregnancy in older women who have undertaken bariatric surgery may further compromise their chance of conceiving a healthy child.

7.2 Antenatal care

Expert opinion recommends that post-operative bariatric patients are treated as a specialist obstetric population with specific needs.[85] They should be given intensive dietetic support, preferably by dieticians with experience of managing the nutritional complications of bariatric surgery, and closely monitored for nutritional deficiencies with supplementation given as required. In all patients regardless of surgery type, monitoring of ferritin, vitamins A, D, B1, B12 and K1, and folate should be carried out.[86,87] In addition, weight should be carefully monitored, and weight gain should be in line with the usual guidelines depending on their BMI at conception.[88] Close observation and regular assessment of fetal growth throughout pregnancy should be carried out, together with monitoring for gestational diabetes.

Although some centres advise deflation of the gastric band during pregnancy in order to ensure sufficient nutrition, a Cochrane review conducted in 2013[89] concluded that there were no randomised controlled studies that compared elective deflation of the gastric band balloon in pregnancy versus intention to maintain optimal band inflation and that further research was needed in this area. Deflation of the band has the distressing consequence of weight regain, renewed risk of gestational diabetes and relapse from diabetes. In addition, delayed gastric emptying potentially disrupts the interpretation of glucose tolerance testing, and diagnosis of gestational diabetes is probably best performed on a diurnal blood glucose profile rather than an attempt at formal glucose tolerance testing.

In pregnant patients, surgical complications can be missed and mistaken for medical complications of pregnancy.[90] Potential causes of abdominal pain in pregnancy in women who have undergone bariatric surgery need to be wider than usual and include, for example, band slippage or erosion, bowel herniation or intussusception.[91–93]

8. Effect on neonates and infants

Although there appears to be some clear benefits for women considering bariatric surgery to aid fertility and reproductive health, it remains debatable whether improved maternal and fetal outcomes following bariatric surgery are seen in all domains. Significant reductions in obesity and metabolic consequences thereof have been seen in offspring born to the same women prior to and after BPD surgery.[94] However, a more recent study of offspring born before and after surgery (predominantly LAGB and SG), which evaluated BMI data compiled from birth to 10 years of age,[95] showed that obesity rates were *increased* in those born after rather than before surgery. This is interesting in the light of evidence that SGA is associated with a high risk of metabolic syndrome in adulthood.[96] SGA is also associated with minor cognitive deficiencies, hyperactivity or attention deficit disorders at 5 years or learning difficulties at 8 years. Whether SGA infants born after bariatric surgery develop any long-term effects has not been investigated.

The potential adverse effects of bariatric surgery need to be balanced against the evident improvement in overall maternal health, the improvement in conception rate, and the potentially reduced risk of obesity and metabolic illness in the offspring. Further work is needed to differentiate between outcomes after different types of surgical interventions.

9. Opinion

The detrimental effects of obesity on fertility and obstetric outcomes are well established.[3] Bariatric surgery can lead to an improvement in several important markers of fertility including hyperinsulinaemia and ovulatory function. Moreover, maternal outcomes and morbidity in pregnancy are better than for similarly obese patients, and comparable to those in the general population, and long-term outcomes for infants born following bariatric procedures also appear improved.[97] When bariatric surgery is considered in women who wish to improve their chance of conceiving naturally or through assisted means, patients, obstetricians and surgeons balance the risks of intervention against the benefits of improved long-term health, longevity and wellbeing. In women of childbearing age, this includes the ability to conceive and carry a healthy pregnancy to term. There is increasing awareness that bariatric surgery is not so much aimed at achieving weight loss but as a treatment for metabolic disturbance. Fertility difficulties fall into this realm and remain one of the key reasons that women consider undergoing surgery, hoping to improve not only their own health, but that of their future family.

Areas for future research include the question of whether improvements in fertility, maternal and fetal outcomes seen after bariatric surgery are dependent on the maintenance of long-term weight loss, or whether specific improvements in cardiometabolic factors independent of weight loss but specific to RYGB are relevant. The extent to which different types of surgery differ in efficacy and adverse effects on pregnancy, or long-term risk of obesity and cardiometabolic disease in the offspring needs further investigation, in light of their different mechanisms of action. Outcomes after SG, which has increased in popularity, are not well studied. However, since this treatment has comparable short-term weight loss and metabolic effects to RYGB, but potentially less malabsorption of nutrients and vitamins, it should become a priority area of research.

The long-term outcomes of offspring of women undergoing bariatric surgery should also be examined. A more personalised approach to the choice of bariatric surgery and the timing of subsequent pregnancies as part of the management of fertility and female reproduction should be implemented. This might be guided by understanding how different surgical approaches impinge on or alter reproductive outcomes.

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This Scientific Impact Paper was produced on behalf of the Royal College of Obstetricians and Gynaecologists by:
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All RCOG guidance developers are asked to declare any conflicts of interest. A statement summarising any conflicts of interest for this Scientific Impact Paper is available from: https://www.rcog.org.uk/en/guidelines-research-services/guidelines/sip17/.

The final version is the responsibility of the Scientific Advisory Committee of the RCOG.

The review process will commence in 2018, unless otherwise indicated.

