Female sterilization reversal in the era of in-vitro fertilization

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Purpose of review
Regret after female sterilization is not uncommon in the United States. Prior to the development of assisted reproductive technology (ART), surgical reversal of sterilization was the only option for patients interested in fertility. First performed in 1972, this procedure has since been refined over the years by gynaecologic surgeons. With in-vitro fertilization (IVF) gaining popularity, interest in sterilization reversal has waned. However, sterilization reversal should remain an important option in patients seeking pregnancy after tubal ligation.

Recent findings
A direct comparison between IVF and sterilization reversal is challenging due to inherent differences in reporting fertility outcomes. However, sterilization reversal may optimize fertility in younger women, whereas IVF may be more effective in older women. The surgical approach to sterilization reversal can be laparotomic, laparoscopic or robotic. Clinical decision making should include consideration of the risk of ectopic pregnancy, interval from sterilization to reversal, type of sterilization procedure, planned anastomotic site and projected remaining tubal length.

Summary
In the era of IVF, sterilization reversal still has a place in the management in restoring fertility. Creating awareness of the role of sterilization reversal is the first step in improving access to adequate training in this procedure for the next generation of reproductive surgeons.

Keywords
in-vitro fertilization, sterilization reversal, tubal ligation, tubal surgery

INTRODUCTION

Female sterilization is one of the world's most common methods of contraception. In the U.S., nearly 21.6% of women ages 30–39 years and nearly 39.4% of women ages 40–49 years use some form of permanent sterilization [1]. Globally, the prevalence of permanent sterilization in 2019 was 24% in women ages 15–49 years [2]. The risk of regret after permanent sterilization is significant, particularly in high-risk populations such as those with ages less than 30 years, low socioeconomic status, sterilization in the postpartum period, low parity, or in a new relationship [3▪,4]. In the U.S., up to 30% of women regret their decision for permanent sterilization, and 1–2% will seek out sterilization reversal [4,5]. For patients interested in fertility after sterilization, the two options are either in-vitro fertilization (IVF) or surgical reversal of sterilization.

HISTORY OF STERILIZATION REVERSAL PROCEDURES

Tubal reanastomosis was first performed in 1972 via laparotomy by Garcia [6]. This technique involved an abdominal incision, excision of the occluded ends of the fallopian tubes and end-to-end anastomosis. A splint was often placed in the tube for several weeks to prevent reocclusion [7–9]. In the late 1970s, the microscopic camera was introduced to allow for higher precision in open surgery. The procedure was thus further refined with a two-layer technique, wherein the anastomosis consisted of suturing the tubal muscularis and tubal serosa separately [8].

In 1989, it was performed laparoscopically for the first time by Sedbon *et al*. [10]. The procedure has continued to improve with advancing technology and improved optic resolution. The two-layer technique is commonly employed, and the procedure

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Curr Opin Obstet Gynecol 2022, 34:244–249

DOI:10.1097/GCO.0000000000000802

KEY POINTS

- Sterilization reversal and IVF each have advantages and disadvantages that must be considered on an individual patient basis.
- Sterilization reversal procedures have more favourable outcomes over IVF in younger patients, while the opposite may be true in older patients.
- The risk of ectopic pregnancies after surgical tubal reanastomosis has been shown to be significantly increased compared with IVF.
- Studies have found similar success rates between microsurgical laparotomy, laparoscopy and robotic approaches to sterilization reversal.
- A number of prognostic factors have been identified in attempts to predict the ideal candidate for sterilization reversal vs. in-vitro fertilization; however, much of these data are inconclusive.

involves microsuturing with fine suture (e.g. 6-0 to 10-0) [11]. Other techniques include single-layer, four-quadrant sutures or the use of microstaplers or biologic glue for seromuscular fixation [12–14]. Tubal patency is commonly confirmed intraoperatively. In 1995, Dubuisson and Swolin [15] described a laparoscopic single suture technique placed at 12 o'clock once the tubal ends were prepared and the mesosalpinx approximated. In 1998, Falcone *et al.* [16] performed the procedure robotically. Robotic surgery conquered some of the technical drawbacks of laparoscopy, including tremor filtration, 3D imaging and improved dexterity. These features enhanced the precision of this microsurgical procedure.

IN-VITRO FERTILIZATION VS. STERILIZATION REVERSAL

Interest in tubal surgery has waned over the last two decades, largely due to the large strides made in assisted reproductive technology (ART). IVF involves administering gonadotropins to stimulate the ovaries, retrieving eggs and either freezing them or creating embryos for transfer. This method bypasses the tubal occlusion from sterilization procedures that prevent pregnancy.

There are inherent challenges in comparing success rates of sterilization reversal surgery to IVF. Outcomes after tubal surgery are generally reported on a per-patient basis over time, highlighting the cumulative success rate over months and years. In contrast, IVF success rates are typically reported on a per-cycle basis. An additional element that complicates the interpretation of success rates is age. For example, the age at which a frozen embryo was conceived may be different than the age of the patient at the time of IVF, and therefore may create higher success rates compared to a patient of the same age undergoing sterilization reversal. Another major confounding factor is cost and insurance coverage. Many states do not mandate IVF coverage or guarantee coverage for sterilization reversal. Some insurances may only cover one procedure and not the other, therefore directing clinical decision-making [17].

It behooves the provider to obtain the following items prior to counselling a patient: a measure of ovarian reserve (e.g. AMH, AFC, ovarian volume), tubal ligation surgical report and pathology report (if excision was performed), hysterosalpingogram to evaluate the proximal stump and a semen analysis to ensure the absence of a severe male factor.

When counselling patients regarding sterilization reversal vs. IVF, there are additional factors that need to be considered. Patient age, desired family size, prior history of infertility and cost/insurance coverage are some of the most important factors.

The main advantage of sterilization reversal surgery is that it is a one-time outpatient procedure. Patients can have the opportunity to conceive every month afterwards resulting in a desirable cumulative pregnancy rate and may conceive more than once without incurring additional costs. The disadvantages include the low risk of surgical complications, difficulty finding a skilled and recently experienced surgeon, the increased risk of an ectopic pregnancy and the risk of failure of the procedure [17].

The main advantages of IVF are excellent success rates per-cycle and the fact that it is less surgically invasive. IVF also has the inherent advantage of screening for aneuploidy and/or monogenic/single gene defects. In addition, frozen embryos can reduce the risk of birth defects and genetic abnormalities associated with age if subsequent pregnancies are desired. The main disadvantages are costs associated with stimulation, monitoring, retrieval, embryo transfer, storage, time lost from work for daily monitoring and discomfort of injections, and the risks of multiple gestation and ovarian hyperstimulation syndrome [17].

Comparing success rates

A 2017 systematic review by van Seeters *et al.* [18] evaluated four studies comparing fertility outcomes with surgical reversal of sterilization vs. IVF. Overall, this review suggests that sterilization reversal procedures have more favourable outcomes over IVF in

younger patients, while the opposite may be true in older patients.

The first study was a retrospective cohort comparing pregnancy outcomes on a per-patient basis [19]. The choice for IVF or surgical reversal was patient preference and both treatments were covered by insurance. Surgical reversal was performed by laparotomy using a microsurgical approach, and patients were followed for a minimum of 14 months. In women less than 37 years of age, delivery rates were higher with sterilization reversal (72.2%) than with IVF (52.4%) ($P = 0.012$). However, in women ages 37 years and older, delivery rates with IVF (51.4%) were higher than those after sterilization reversal (36.6%) (NS). Therefore, age seemed to play an important role in the outcomes of each procedure. Of note, the time from treatment to delivery was 21 months in the sterilization reversal group compared with 14 months in the IVF group. This longer time to pregnancy may discourage some patients from pursuing sterilization reversal.

The second retrospective cohort in this review only included women younger than 40 years of age [12]. The cohorts were highly uneven in their size, with only nine patients in the sterilization reversal group and 327 patients in the IVF group. Still, they reported significantly higher rates of both pregnancy (77.8 vs. 46.8%) and live births (66.7 vs. 34.6%) in the surgery group compared with the IVF group.

The third study was a cost-analysis that included standard costs of physicians, medications, surgery, laboratories, costs of IVF cycles, diagnostic imaging, management of miscarriages, ectopic pregnancies and ovarian hyperstimulation syndrome [20]. Their work suggested that in women younger than 40 years of age, tubal reanastomosis was more cost-effective than IVF ($23 914 vs. $45 839, respectively). In women aged 40 years and older, IVF was more cost-effective than surgery ($111 445 vs. $218 742, respectively).

The fourth study compared fertility outcomes after laparotomic microsurgical sterilization reversal vs. IVF [21]. In this study, it should be noted that sterilization reversal was paid for by health insurance, whereas IVF after previous sterilization was not. Nonetheless, they reported a live birth rate after surgical reversal of 51%, whereas the live birth rates per IVF cycle were 21–39% depending on age.

In 2020, Chua *et al.* [22] reported outcomes of their retrospective study of sterilized patients between 2011 and 2016 in Singapore who underwent either IVF ($n = 31$; transfer of all available embryos generated through one stimulated IVF cycle) or laparoscopic tubal reanastomosis ($n = 12$; after Pomeroy ligation, Filshie clips or Falope Rings). After 24 months, they similarly found higher pregnancy rates (75 vs. 35.5%) and live birth rates (58.3 vs. 25.8%) in the tubal surgery group ($P < 0.05$). All of the patients included in this study were less than 40 years of age. In the surgery group, the mean interval from surgery to conception was 3.9 months. In terms of complications, the surgical group had one case of an ectopic pregnancy. The IVF group had one case of twins and two cases of clinically significant ovarian hyperstimulation syndrome.

Comparing rates of ectopic pregnancies

The risk of ectopic pregnancies after surgical tubal reanastomosis is thought to be increased by approximately three-fold [9,12,22]. Schippert *et al.* [23] reported an ectopic rate of 6.7% with surgery vs. 5.6% with ART. However, the study did not describe the types of anastomoses or fallopian tubal length. Boeckxstaens *et al.* [19] reported a rate of 3.6% after surgery vs. 0% after IVF. Tan and Loh [12] reported a more dramatic difference in ectopic pregnancy rates (33% after surgery vs. 1.8% after IVF).

Comparing surgical approaches to tubal reanastomosis

When it comes to sterilization reversal, surgical approach is a key differentiating factor. Some surgeons perform tubal reanastomosis via microsurgical laparotomy, a refined version of the technique first described in the 1970 s. Others perform the procedure using laparoscopic or robotic approaches, taking advantage of advances in endoscopic technology. Each approach has its own advantages and disadvantages relating to cost, operative time, recovery time and learning curve. However, when it comes to the bottom line of pregnancy rates, studies have found similar success rates between approaches.

Van Seeters *et al.* [18] reviewed four studies from the early 2000 s that compared the laparotomic microsurgical method with the laparoscopic method [12,14,18,24,25]. The pooled pregnancy rates from all studies were 68% for laparotomic and 66% for laparoscopic [relative risk (RR) 1.08, 95% confidence interval (95% CI) 0.90–1.30]. Time to pregnancy was only evaluated in one of the studies, which found no significant difference between the laparotomic and laparoscopic approaches (3.6 vs. 5.0 months). None of the studies reported a significant difference in the rates of ectopic pregnancies.

Two studies compared the robotic approach to the laparotomic microsurgical approach and neither detected any difference in pregnancy rates (61 and

61% for robotic cohorts vs. 70 and 79% for laparotomic cohorts) [26,27]. One of the studies did detect a significant difference in ectopic pregnancy rate between robotic and laparotomic approaches (22 vs. 10%, respectively) [27].

One study compared the robotic approach to the laparoscopic approach and found a nonsignificant difference in pregnancy rate between the robotic group ($n = 10$) and the laparoscopic group ($n = 15$) (50 vs. 40%, respectively) [28].

Elci *et al.* [29▪▪] performed a retrospective analysis of their patients who underwent tubal reanastomosis via robotic, laparoscopic and laparotomic approaches with otherwise similar surgical technique for the anastomosis. Pregnancy rates after laparotomy ($n = 41$), laparoscopy ($n = 37$) and robotics ($n = 63$) were statistically similar (52.6 vs. 67.3 vs. 61.2%, respectively).

As surgical innovation continues and the tubal anastomosis procedure is further refined, novel surgical approaches are being evaluated. Guan *et al.* [30] described an approach using the single-site robotic platform for tubal reanastomosis, and verified tubal patency at 2 months postoperatively. This approach could have potential benefits in regard to cosmesis. Another surgical approach gaining popularity in gynaecologic surgery is transvaginal natural orifice transluminal endoscopic surgery (vNOTES). Liu *et al.* [31] performed a tubal reanastomosis using this approach via a posterior colpotomy, demonstrating its feasibility.

Prognostic factors in sterilization reversal

A number of prognostic factors have been studied in attempts to predict the ideal candidate for sterilization reversal vs. IVF. Method of sterilization, time interval between sterilization and reversal, age, tubal length, and anastomosis site have all been implicated in success rates after tubal reanastomosis [13,24,32–37].

Age has consistently been shown to be the most important prognostic factor for a successful surgery. Age has an inverse correlation with pregnancy rates after sterilization reversal [17]. Berger *et al.* [36] reported that women less than 30 years old had a pregnancy rate of 88%, and showed pregnancy and live-birth rates decreasing significantly with increasing age. A multicentre study in the Netherlands reported a 45% pregnancy rate in women ages 40–45 years [38].

In the study by Elci *et al.* [29▪▪] of 141 patients under 40 years of age who underwent tubal reanastomosis, several prognostic features were identified. There was a statistically significant difference in pregnancy rates between those who underwent sterilization less than 5 years prior [odds ratio (OR) 3.048, CI 1.669–5.586] and those who underwent sterilization at least 10 years prior (OR 0.378, CI 0.188 –0.759). However, this study did not address the relationship between age and duration of sterilization. An older study by Hanafi [34] similarly reported a pregnancy rate of 91% if the reversal procedure was performed 1–5 years after sterilization, vs. 72% if the procedure was performed 11–15 years after sterilization ($P = 0.0006$). This analysis reported a moderate correlation between age and number of years sterilized ($r = 0.567$), yet still identified duration of sterilization as a statistically significant factor on pregnancy rate after controlling for age [34]. Three other studies did not find a significant relationship between the sterilization interval and pregnancy rates [13,19,32].

Elci *et al.* [29▪▪] also saw a dramatic difference in pregnancy rates based on type of sterilization. Patients who had a laparoscopic tubal ligation (LTL) with a seal-and-cut device were 18 times more likely to get pregnant after sterilization reversal compared with those who had a Pomeroy tubal ligation (PTL). However, the number of LTL patients was significantly lower ($n = 23$) than the number of PTL patients ($n = 118$). Several other studies have investigated pregnancy rates after reversals of Falope rings, Filshie clips, Pomeroy method and coagulation [18]. Hirth *et al.* [39] reported a higher percentage of pregnancies after reversal of Filshie clip sterilization (82%) compared with other methods (Pomeroy 49%, Falope rings 38% and coagulation 28.5%, $P = 0.02$). Berger *et al.* [36] similarly reported a pregnancy rate of 76% after reversals of Filshie clips and Falope rings, compared with 68 and 67% after sterilization by resection or coagulation ($P < 0.001$). However, other studies comparing sterilization methods have found no significant difference in postreversal pregnancy rates [13,32–35].

The location of tubal anastomosis may also have prognostic value. Elci *et al.* [29▪▪] found that those who had an ampullar-ampullar anastomosis were four times more likely to get pregnant compared with those who had an isthmic-ampullar or isthmic-isthmic anastomosis. This is in contrast to other hypotheses of isthmic-isthmic anastomoses having greater success [17]. Reproducible data supporting either hypothesis are lacking, and studies have shown no significant association between anastomosis location and fertility [13,32,33,35].

Another hypothesized prognostic factor is postoperative tubal length. Experts suggest considering deferring surgical intervention if final tubal length is predicted to be less than 4 cm [17]. However, data supporting this recommendation are conflicting, as many studies have found no significant difference

in pregnancy rates between shorter or longer tubal lengths [13,32,33,35,40].

CONCLUSION

This review highlights the most recent available data regarding sterilization reversal procedures in the era of IVF. Success rates of sterilization reversal depend largely on age and may be more successful and efficient than IVF in patients less than 40 years old. These success rates should be interpreted in the setting of the known increased risk of ectopic pregnancy after tubal surgery. Surgical approach does not appear to have a consistent association with pregnancy rates, though more research is needed to compare not only laparotomic, laparoscopic and robotic approaches, but also novel approaches such as single-site and natural orifice surgery. Other factors such as type of sterilization, time interval from sterilization to reversal, tubal length and anastomosis site have been postulated to have prognostic relevance, though the data to date are collectively inconclusive.

Many of the recent reports of tubal surgery outcomes are from expert surgeons trained specifically in tubal reversal surgery. However, the number of surgeons experienced in this procedure are decreasing at an alarming rate, and there is a lack of adequate training in microsurgical techniques in current gynaecologic surgery training programmes. Despite the data supporting tubal reversal surgery, patients may realistically only have access to IVF or may have to travel great distances to access a tubal surgeon. To best care for this population, the next generation of reproductive surgeons must have opportunities to learn tubal surgery techniques.

Acknowledgements

None.

Financial support and sponsorship

None.

Conflicts of interest

There are no conflicts of interest.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

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