Original Article

# Laparoscopic Tubal Re-anastomosis or In Vitro Fertilisation in Previously Ligated Patients: A Comparison of Fertility Outcomes and Survey of Patient Attitudes

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# Abstract

Introduction: We aim to compare live birth rates, cost analysis and a survey of patient attitudes between laparosopic tubal re-anastomosis and IVF. Materials and Methods: Retrospective study: A retrospective study was done in a single reproductive medicine and IVF unit in Singapore, from January 2011 to December 2016. Previously ligated patients underwent either laparoscopic tubal re-anastomosis or IVF. The primary outcome was first live birth after treatment. Interval to first pregnancy, miscarriage and ectopic pregnancies were also reported. Survey: Patients attending the subfertility clinic completed a questionnaire on IVF and tubal re-anastomosis, on preferred choice of treatment, before and after reading an information sheet. Results: Retrospective study: 12 patients underwent tubal re-anastomosis while 31 patients underwent IVF treatment. Pregnancy (75.0% vs 35.5%) and live birth (58.3% vs 25.8%) were significantly higher in the tubal surgery group (P<0.05%) after transferring all available embryos in one stimulated IVF cycle. Cost per live birth was lower in the tubal surgery group (SGD27,109 vs SGD52,438). Survey: One hundred patients participated in the survey. A majority of patients preferred tubal surgery to IVF (68.2% vs 31.8%) before given information on the procedures, but indicated a preference for IVF (54.6%) to surgery (45.4%) after receiving information on the procedures. Conclusion: For women less than 40 years of age, desiring fertility after tubal ligation, laparoscopic tubal re-anastomosis offers better live birth rates and cost-effectiveness. Patients in Singapore are equivocal as to their preference after education regarding the choices. Thus laparoscopic tubal re-anastomosis remains a viable alternative to IVF treatment.

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Key words: Artificial reproductive technology, Laparoscopic tubal reversal, Previous tubal ligation

# Introduction

Tubal ligation remains a common method of contraception, despite the availability of multiple other reversible methods.<sup>1</sup> A sizeable proportion (up to 30%) of women who undergo sterilisation seek fertility after the procedure, for reasons such as a new marriage, regret, or loss of a child.<sup>2,3</sup> For these women, the options are either tubal reversal surgery or IVF.

Conventionally, microsurgical tubal reversal was performed via a laparotomy. However, in the past few decades, surgeons have increasingly used laparoscopy to perform this procedure, with equivalent outcomes.<sup>4</sup> With the relative ease of access to In Vitro Fertilisation (IVF) technologies and the high technical skills required for tubal re-anastomosis, there has been an increase in the use of (IVF) techniques and a consequent decline in surgical tubal reversal. However, a recent ASRM committee opinion paper posited that surgical tubal re-anastomosis is a feasible alternative to IVF for previously ligated patients.<sup>5</sup> With the advancement in IVF techniques and success rates, the role of tubal reversal in the management of this group of women needs to be re-evaluated.

We have previously published on the outcome of tubal reversal surgery, and showed similar fertility outcomes in women undergoing laparotomy and laparoscopic tubal

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reversal surgery (Tan and Loh).<sup>6</sup> Here we aim to compare the outcomes between laparoscopic tubal anastomosis and IVF in women with previous tubal ligation in a single Reproductive Medicine and IVF unit. In addition, we wanted to gain a better understanding of the attitudes and perceptions of patients with regards to the 2 treatment options.

# **Materials and Methods**

## Retrospective Study

We conducted a retrospective review of all cases with previous tubal ligation, who underwent subsequent fertility treatment from January 2011 to December 2016, in a single Reproductive Medicine and IVF unit in Singapore.

All couples underwent standard fertility assessment, namely history, pelvic examination, semen analysis, ultrasound scans of the pelvis and determination of ovarian reserve. A non-directive counseling of the option of laparoscopic tubal reversal or IVF were offered when there are no contraindications to either treatment modalities.

The primary outcome measure is the time to first live birth after tubal reversal surgery, or the transfer of all available embryos generated through 1 stimulated cycle of IVF accordingly. Patients are censored after a live-birth, with further frozen embryo transfers and pregnancies after the first live birth excluded. Ectopic pregnancies, miscarriages, duration of surgery and hospitalisation were also reported. A cost-benefit analysis was performed. Exclusion criteria were: other sub-fertility factors such that natural fertility was unlikely (fibroids distorting endometrium, endometriosis, severe adenomyosis, oligo- or asthenozoospermia, female partner aged 40 years and above) patients with unilateral anastomosis, and anti-mullerian hormone levels (AMH) <1. All laparoscopies were performed by the same surgeon. IVF patients were under the management of a team of doctors, and were followed up until transfer of all embryos (up to 10 months) and first resulting live birth, up to 24 months. Tubal reversal patients were followed up for 24 months post-surgery. Institutional IRB approval was granted for this study.

## **IVF Protocol**

All patients on the IVF arm underwent controlled ovarian stimulation (COS) on day 2 of their menses, after an ultrasound scan to exclude the presence of a dominant follicle (>9mm diameter). This was achieved using recombinant FSH and/or human menopausal gonadotrophin at doses of 150 to 450 units, for 8 to 14 days. Gonadotrophin-releasing hormone (GnRH) antagonist was started after 5 days of COS. When two or more leading follicles have reached 17mm in diameter, Ovidrel 250mc was used to trigger final follicular maturation, with oocyte retrieval performed 34 to 36 hours later. Embryos generated were transferred in the fresh cycle if there were no contraindications, with supernumerary embryos transferred in subsequent frozen cycles. Up to 2 cleavage stage embryos or blastocysts were transferred, at the attending physician's discretion, with luteal phase support achieved with vaginal progesterone for 4 weeks post embryo transfer (Crinone 8% gel twice daily). A Clinical Pregnancy was registered where a intrauterine gestation sac with a fetal pole was seen at 4 weeks post ET. Live birth data was gathered from the ART registry at the hospital.

# **Surgical Technique**

The surgery was carried out via 4-port laparoscopy in a typical configuration: 5mm ports at umbilicus bilateral iliac fossa, and suprapubic area. Both fallopian tubes were surveyed and the point of ligation, be it through the Pomeroy method or application of Filshie clips, was excised. Instillation of a vasoconstrictor (Pitressin diluted in normal saline) was performed through a 26G spinal needle into the meso-salpinx around the ligated region. This served to hydro-dissect the peritoneal layers from the muscular layer of the fallopian tubes, and maintained a blood-free operating field. A uterine manipulator was then inserted to allow for hydrotubation. The scarred segment of the tubes were first identified and resected until healthy ends of the tube could be identified, with good patency as evidenced by the free flow of methylene blue dye from the proximal resection point upon hydrotubation. For the distal tubal segment, the lumen was identified, cannulated proximally and injected with methylene blue with a hollow probe, to ensure free flow of dye through the fimbrial end. The mesosalpinx was approximated with 30 polyglactin suture if the tubal segments were too far apart to aid in the anastomosis. A single-layer, two-stitch technique was utilised for re-anastomosis with 6-0 PDS sutures placed at the 12 and 6 o'clock positions of the tube. The suture was passed through the muscularis and mucosa in a single plane. Successful re-anastomosis is evidenced by free flow of methylene blue through the fimbrial end at hydrotubation. Leakage of dye through the anastomotic site is commonly seen and does not indicate failed re-anastomosis, as long as dye flows through the fimbrial end.

## **Statistical Analysis**

Statistical analysis between groups was performed using chi-squared tests and Fisher's exact test for non-parametric parameters. A value of P < 0.05 is considered statistically significant.

## Survey

A survey of patient preferences between the 2 treatment methods was conducted. Patients attending the sub-fertility clinic in the same tertiary institution in Singapore, were approached for participation. Survey forms were given out in the waiting area and collected before the patient left the clinic. A total of 100 patients were surveyed. The questionnaire can be divided into 3 main components: demographics, information on both IVF and laparoscopic tubal re-anastomosis (including treatment overview, success rates, costs and complications), and the choice of treatment before and after reading the information.

# Results

#### *Retrospective Study*

There were 31 patients in the IVF group and 12 patients in the tubal reversal surgery group. The baseline characteristics of the 2 groups were largely similar (Table 1). Transfer of all fresh and frozen embryos derived from one IVF stimulation cycle was completed within 4.5 months (range 3.0–10.0 months).

Table 1. Comparison of baseline characteristics between IVF and tubal reversal (patient age <40 years old)

	IVF (n = 31), mean (SD)	Tubal Reversal (n = 12), mean (SD)	P Value
Age	35 (4)	34 (4)	0.546
BMI	23.0 (4.8)	23.4 (3.2)	0.790
Parity	2.8 (1.1)	2.6 (0.8)	0.468
AMH	4.2 (3.2)	5.7 (1.4)	0.148

AMH: Anti-mullerian hormone level; BMI: Body Mass Index; IVF: In vitro fertilisation; SD: Standard deviation

Table 2 shows the outcome for all patients. The pregnancy rate (PR) was higher in the tubal-reversal group, up to 1 year after surgery, than the IVF group, 75% (9/12) vs 35.5% (11/31) (P = 0.039). The live birth rate (LB) was also higher after tubal-reversal surgery compared with the IVF group 58.3% (7/12) vs 25.8% (8/31) (P = 0.045). The miscarriage rates were similar, with 1 ectopic pregnancy in the surgery group (11.1%) and none in the IVF group. In the IVF group, there was a single case of twins (9.1%) and 2 cases of clinically important ovarian hyperstimulation syndrome (OHSS) (6.5%); neither of these events occurred in the tubal-reversal group. The mean number of embryos transferred was 1.9 and 1.3 for cleavage stage and blastocyst stage respectively (Table 3).

In the surgical arm, 9 patients were ligated by Filshie clips (75.0%), 2 patients by the Pomeroy method (16.7%), and one by Falope Rings (8.3%). All the patients who underwent tubal reversal surgery were discharged the next day, except for one patient who was discharged on the same day. The mean (standard deviation [SD]) duration of surgery was 156 (SD 20) minutes. The mean (SD) interval from surgery to conception was 3.9 (SD 4.8) months (Fig. 1).

## Cost Analysis

The estimated costs of IVF in our centre are as f ollows: fresh cycle SGD12,500, frozen embryo transfer SGD4000. A total of 31 fresh and 8 thaw cycles were performed, with 8 live births resulting in the IVF

Table 2. Comparison of outcome measures between IVF and tubal reversal (patient age  ${<}40$  years old)

	IVF (n = 31)	Tubal reversal (n = 12)	P value
Pregnancy rate	35.5% (11/31)	75.0% (9/12)	0.039
Miscarriage rate	27.3% (3/11)	11.1% (1/9)	1.0
Ectopic rate	0% (0/11)	11.1% (1/9)	0.279
Live birth rate	25.8% (8/31)	58.3% (7/12)	0.045
Multiple rate	9.1% (1/11)	0% (0/11)	1.0
OHSS rate	6.5% (2/31)	0% (0/12)	

IVF: In vitro fertilisation; OHSS: Ovarian hyperstimulation syndrome

Table 3. Number of embryos transferred (mean)

	Mean number of embryos transferred	
Cleavage stage	1.9	
Blastocyst	1.3	



Figure 1. Interval to pregnancy post-treatment (months)

group. The average bill for a tubal reversal procedure with one day hospitalisation is SGD15,132. As ectopic pregnancy is the main complication of this surgery, the cost of treatment (SGD8180) is included in this analysis. 12 patients underwent tubal reversal and one patient underwent treatment for ectopic pregnancy, with a resultant 7 live births. This puts the cost of a live birth at SGD52,438 for the IVF group, which is approximately double that of the surgery group (SGD27,109). We have omitted to include the additional costs of OHSS treatment for 2 patients, complications for multiple pregnancies, loss of days from work, as these complications can be largely mitigated with the use of agonist triggering and freeze-all strategies in high risk patients, and the transfer of single blastocysts. These findings are in agreement with many other studies, which show that tubal surgery is more cost-effective in patients below 37 to 40 years of age.6,7,8

## Survey

A total of 100 patients participated in the survey. 12 forms were incompletely filled and excluded from analysis. The mean age of the patients was 35.1 (SD 3.6) years. More than half (64.8%) of the patients were nulliparous, 28.4% had one child, and 6.8% had 2 or more children. Majority of the respondents (77%) attended university and stayed in government housing (71%) (Table 4).

Age		Number of participants (n=88)	Chose IVF <b>BEFORE</b> reading information (n=28)	Chose surgery <b>BEFORE</b> reading information (n=60)	
•	<35	38 (43%)	18 (47%)	20 (53%)	
•	35 and above	50 (57%)	10 (20%)	40 (80%)	
Parit	Parity				
•	0	55 (62%)	21 (38%)	33 (62%)	
•	1 and above	33 (38%)	7 (21%)	27 (79%)	
Hou	sing				
•	Public housing	62 (71%)	22 (35%)	40 (65%)	
•	Private property	26 (29%)	6 (23%)	20 (77%)	
Educ	Education level				
•	Did not attend university	20 (23%)	8 (40%)	14 (60%)	
•	Degree or higher	68 (77%)	20 (29%)	46 (71%)	

Before reading the information sheet, 28 (31.8%) patients preferred IVF and 60 (68.2%) preferred surgery (Table 5). After having read the information, more patients indicated a preference for IVF (54.6%) to surgery (45.4%). We found that younger patients under 35 years of age are just as likely to choose surgery as IVF, while older women had a preference for tubal surgery, particularly after information was given. Parity, housing type and educational level had less of an impact on patient choice. There was no significant difference in baseline characteristics between participants who chose the same option and those who chose a different treatment option after reading the information.

Table 5. Treatment choices before and after reading information

	n (%)		
Treatment choice <b>BEFORE</b> reading information			
• IVF	28 (31.8%)		
Tubal surgery	60 (68.2%)		
Treatment choice AFTER reading information			
• IVF	48 (54.6%)		
Tubal surgery	40 (45.4%)		

## Conclusion

In this paper, we sought to determine the relevance of tubal reversal surgery a decade after our initial publication<sup>6</sup>. This is of rising importance as more women seek fertility treatment post-sterilisation. The changing dynamics of the financing model for IVF treatment in Singapore, and the rising incidence of re-marriages (22.7% of all marriages in 2017) also contribute to this trend. We found that the cumulative pregnancy rates were largely similar at 75% by 18 months (58% live births), compared with 68% by 48 months in the previous cohort where both open and laparoscopic approaches were utilised. These datasets compare favourably to other published data (pooled PR 65%).<sup>9</sup>

Our results show that both pregnancy and live birth rates in the surgery group were roughly double that of the IVF group after the completion of one stimulated IVF cycle. Since there was no significant difference in the mean age between the 2 groups, the miscarriage rates were similar as expected. The main complication of tubal reversal is ectopic pregnancy (1 case in the surgery group vs none in the IVF group). The risk of ectopic pregnancies after surgical reversal has been shown to be raised by up to 3-fold (pooled data 5.6%).<sup>6,9,10,11</sup> In our study, the ectopic occurred in a patient at very

high risk because of narrowed tubal lumen as seen at surgery. However, this is offset by the risk of multiple pregnancies and OHSS in the IVF group. Another advantage of surgery over IVF is that patients can try to conceive in every cycle without further treatment, with the possibility of more than one pregnancy being achieved. In fact, 2 of the patients in the surgery group went on to have more than one child.

This is a good prognosis cohort with proven fertility, with tubal ligation as their only infertility diagnosis. The pregnancy (35.5%) and live birth (25.8%) rates in the IVF group are largely similar to the 27% LBR according to the HFEA database for patients of the same age group, encompassing all diagnoses.<sup>12</sup>

# Prognostic Factors for Tubal Reversal

A number of prognostic factors have been studied, including method of sterilisation, BMI, interval between sterilisation to reversal and age.<sup>13–19</sup> Only age has been consistently found to affect success rates. Women 40 years and older should undergo proper counselling so that they can have realistic expectations of their fertility, whichever method they choose.

Although no difference has been found in reversal success among the different sterilisation methods, the numbers studied are small. It is intuitive that techniques like the Filshie clip, which destroy the smallest portion of the tube, will be more amenable to reversal. It is possible that with the more destructive surgical approaches, there is not enough healthy tube left to reconstruct, and surgery may not be attempted at all.

## Benefits of Laparoscopic Surgery

Laparoscopic tubal reversal surgery is a technically challenging operation, requiring advanced endoscopic training and experience.<sup>14</sup> However, it confers clear benefits over laparotomy, in terms of faster patient recovery and shortened hospitalisation stay of 1 day (in our series) versus 3 to 6 days where laparotomy had been employed.<sup>4,6</sup> Laparoscopic tubal reversal was also initially thought to have inferior pregnancy rates compared to laparotomy.<sup>20,21</sup> This has been refuted in numerous studies.<sup>4,6,9,21</sup> Another commonly cited advantage of laparotomy over laparoscopy is shorter operating times.<sup>4,6,22</sup> In our study, the mean operating time is 156 minutes. Compared to time taken for laparotomy (range 128–160 minutes),<sup>4,6</sup> the difference is not large. There is a well-documented learning curve for this surgery, of approximately 10-15 cases, whereby the operating time is shortened considerably.<sup>4,6,21,23</sup> In a previous study consisting of 9 cases, the mean operating time was 195

minutes; this has shortened to an average of 156 minutes in the our 12 cases.

Surgical complications have been shown to be rare. There were no instances of complications in our study. In a large cohort of 202 laparoscopic tubal reversal patients, there was only one report of venous thrombosis in the lower leg, reported as likely secondary to patient positioning.<sup>14</sup> Another unintended outcome is conversion to laparotomy, which has been quoted at 5.3% in another study.<sup>14</sup> There were no cases of laparotomy conversion in our study.

In the hands of an experienced surgeon, laparoscopic tubal reversal is a safe operation, with acceptable operating times, good success rates and rapid patient recovery times.

# Interval to Live Birth

This is a vital consideration for patients pursuing fertility, as oocyte number and quality decrease with advancing maternal age. A couple who fails to get pregnant after tubal re-anastomosis can be offered IVF; the question is how soon after surgery do we start to consider IVF. A large cohort study has found cumulative live birth rates of 21% by 1 year, 40% by 2 years and 50% by 5 years after tubal re-anastomosis.<sup>24</sup> Similarly, our study found an average interval of 3.9 months (range 1–18 months) from surgery to pregnancy, with a cumulative live birth rate of 58.3% by 18 months. Thus, a couple can reasonably try naturally for pregnancy for 12–18 months, before moving on to IVF if unsuccessful.

Due to the much longer follow up period (80 months) in the surgery group compared to the IVF group (19 months), there is a question of bias in favour of the surgery group. In our study, this is less of a concern, as almost all the patients in the surgery group conceived within 6 months.

# Survey

This survey is done on a population of sub-fertile patients. It would have been more relevant to survey patients who have been ligated and now seek fertility treatment, but will take a long time to accrue a number of such patients.

This survey highlights the initial reluctance of patients to undergo IVF. This may be due to the general public's poor understanding or misconceptions about IVF. They may feel that IVF is an unnatural process, excessively costly or raises the rates of congenital defects. Surgery on the other hand, restores normal anatomy and function, and may be more acceptable to the patients. However, after reading the information, a large proportion of patients eventually choose IVF, showing that attitudes and perceptions can be changed when non-directive information has been given.

In our survey, patients who chooses surgery initially tend to be older than 35 years of age, have at least one child, and live in private housing. Multiparous women are likely to be more confident of their own natural fertility, and thus will lean towards surgery. Being older, they may be more wary of new technology. Conversely, respondents younger than 35 are more likely to choose IVF initially. They may be more willing to try new methods and embrace new technology.

The results of this and other studies clearly show that tubal reversal is significantly more successful than IVF in patients aged <40 years. This is stated in the information given to patients. In spite of the lower success rates, a large proportion of patients still choose to undergo IVF after reading the information provided. This illustrates the importance of patient autonomy and counselling to enable them to make well-informed choices. Success rate may be the most foremost consideration for the clinician, but it may not be the most important for the patient.

## Limitations

The retrospective nature and small sample sizes limit the generalisation of this study. However, our results are largely in keeping with other published reports of cost-effectiveness of tubal reversal over IVF in young patients, and the success rates of laparoscopic tubal reversal.

## Conclusion

For a woman below 40 years old, desiring fertility after tubal ligation and with no other sub-fertility factors, laparoscopic tubal reversal may offer better pregnancy and live birth rates, and may be more costeffective compared to IVF. Patients in Singapore have a preference for tubal reversal particularly if they are older and have received non-directive counselling of both approaches.

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