Review Article

Where Microsurgical Tubal Reanastomosis Stands in the *In vitro* Fertilization Era

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Abstract

Among various options of contraception, bilateral tubal ligation (BTL) remains the most frequently used method for women worldwide even at present. However, up to 30% of those who undergo BTL eventually change their minds and wish to conceive again for a variety of reasons, such as a change in marital status or simply wanting more children. In this case, we can either approach it surgically with tubal re-anastomosis (TA) or by *in vitro* fertilization (IVF)-embryo transfer. Despite the many advantages of TA which lead the American Society of Reproductive Medicine Committee Opinion to recommend it as the primary choice of treatment in posttubal ligation infertility in 2012, IVF is widely being chosen as the first-line treatment nowadays. This study will review the efficacy of TA in various aspects, including pregnancy rate, cost-effectiveness, feasibility, and accessibility, based on review of the literature and our experience. Through this study, we intend to provide a basis for gynecologists to consider TA as the first option in women who wish to conceive again after BTL in this day and age of IVF.

Keywords: Bilateral tubal ligation, effectiveness, *in vitro* fertilization, tubal re-anastomosis

Introduction

Bilateral tubal ligation (BTL) is the most commonly used method of contraception for women worldwide. About 25% of women aged 15–44 years (about 200 million women worldwide) choose BTL for contraceptive purpose.[1] In the United States, approximately 700,000 cases of BTL are performed every year,[2] and according to CDC data from 2013 to 2015, about 22% of women aged 15–44 choose BTL.[3]

However, around 30% of those who undergo BTL regret their decision of sterilization due to a change in marital status, a new partner, loss of a child, or simply wanting more children, and some of them wish to conceive again.[4-6] In this case, we can either consider a surgical approach with tubal re-anastomosis (TA) or *in vitro* fertilization ((IVF)-embryo transfer. The ASRM Committee Opinion continued to recommend microsurgical TA as the technique of choice for tubal ligation reversal in 2021, as they did 10 years ago in 2012.[7,8] However, the reality is that IVF is widely being chosen as the first-line treatment nowadays.

The first investigation of the results of TA was reported by Seppälä in 1985, in which 5.2% of 10,028 initiated TA cycles were born.[9] Thereafter, the birth rate per TA reported by Norfork for 1981–1983 was 11.5%, Gomel's report in Vancouver for 1984–1985 was 10.3%, and the overall results in the USA for 1985 and 1986 was 6.6% and 6.4%, respectively.[10] On the other hand, the birth rate by IVF increased rapidly during the 1990s. In the United States, the birth rate per IVF more than doubled from 12.3% in 1990 to 25.4% in 1999 and has been maintained at 28%–30% since 2002.[11-15]

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Through this review, we wish to suggest (1) the significance of TA in women with previous BTL, (2) TA as a treatment complementary, not competitive to IVF, and (3) TA may be more efficient than IVF in a selected group of women with previous BTL.

What to Consider when Choosing between Tubal Re-anastomosis and *In vitro* Fertilization?

The most important factor when choosing between TA and IVF will be the pregnancy rate since the main goal is to have a baby. Others include cost-effectiveness, convenience, complication and side effects, personal preference, other causes of infertility and whether an experienced surgeon is available.

Pregnancy outcomes

Direct comparison of the pregnancy outcome between TA and IVF is not easy because the reporting of pregnancies after IVF is mandatory or standardized, whereas that of TA is not. In addition, surgical success is reported as pregnancy rate per patient, whereas IVF pregnancy is determined per cycle.[16] Therefore, the pregnancy outcome between TA and IVF should be compared on a patient basis. Only two studies comparing the pregnancy outcome of TA and IVF on an individual patient basis in women who want to become pregnant after BTL has been reported. One is the study by Boeckxstaens *et al.,* which reported 59.5% and 52% liveborn delivery rate per patient in the TA and the IVF group, respectively, of which difference was not statistically significant.[17] In this study, the cumulative delivery rates in the TA and the IVF group by age were 52% and 72% for patients below 37 years, and 51.4% and 36.6% for patients over 37 years, respectively. The other study is a meta-analysis of van Seeters *et al*., which showed that the pregnancy and live birth rates tend to be higher in the TA group compared to the IVF group.[18]

However, most studies report the pregnancy rates of TA or IVF, separately, rather than comparing pregnancy rates of TA and IVF per patient in women who want to become pregnant after BTL. With respect to IVF pregnancy rates, the Society for Assisted Reproductive Technology (SART) 2016 data showed cumulative live birth rates per cycle (including fresh and subsequent frozen-thawed cycles) of 25.9% for ages 38–40 years, 13.4% for ages 41–42 years, and 4.1% for ages 43 years and older.[19] The 2020 CDC data from the United States show 7.2% live birth rate in women older than 40 years.[20]

In terms of TA pregnancy rates, Malacova *et al*.[21] reported a 5-year cumulative live-delivery rate according to age using the Kaplan–Meier curves for time to delivery from sterilization reversal. In this report, at 5 years, the survival curves show 30%, 25%, and 24% significantly higher live-delivery rates for women aged 30–34, 35–39, and 20–29 years, respectively, compared with women aged >40 years (26%), just as natural fertility decreases after the age 40 years (Malacova *et al*., 2015).[21] Similar results were confirmed in our experience of 961 patients who underwent TA from 1988 to 2007, which showed that the cumulative pregnancy rate for those 30 years or younger was as high as 97.5%, and the pregnancy rate seems to decrease with age but was 53.9% in women over 40 years old [Table 1].[22] Even in women over 40, various studies including ours showed the pregnancy rates ranging from 13% to 71% [Table 2].[23] These results showed a higher pregnancy rate of over 50% after TA compared to the low pregnancy rate of IVF in ages 40 years and older. Although some groups have insisted that IVF is the best approach for restoring fertility in women over 40 after BTL,[23] these results suggest that TA may be considered as the first choice even in women over 40.

Then what would be the ideal strategy for conceiving in women aged 40 and older? Whatever the choice may be, we must make every endeavor to maximize the chance of our patients becoming pregnant during the 1 or 2 years they have. According to the 2020 CDC data from the United

Table 1: Pregnancy outcomes following tubal re-anastomosis

Age (years)	Pregnancy rate, *n* (%)
≤30	77/79 (97.5)
31–35	327/354 (92.4)
36–40	282/327 (86.2)
>40	68/126 (53.9)

*Extracted from the data of Moon *et al*.[22]

Table 2: Success of tubal anastomosis in women aged 40 years and older

First author (year)	*n*	Age (years)	PR, *n* (%)	LBR, *n* (%)
Trimbos-Kemper (1990)	78	>40	38/78 (49)	34/78 (44)
Glock (1996)	42	≥40	18/42 (43)	6/42 (14)
Yoon (1999)	17	40–45	12/17 (71)	-
Petrucco (2007)	47	≥40	26/47 (55)	19/47 (40)
Gordts (2009)	6	40–43	3/6 (50)	-
Hirth (2010)	11	>40	3/11 (38)	-
Caillet (2010)	16	40–42	8/16 (50)	7/16 (44)
Moon (2012)	126	≥41	68/126 (54)	-
Godin (2015)	19	40–42	13/19 (68)	10/19 (53)
Van der Water (2015)	14	≥40	4/14 (29)	1/14 (7)
Malacova (2015)	159	40–44	-	41/159 (26)
Berger (2016)	964	≥40	364/964 (38)	-
Gords (2009)	8	≥43	1/8 (13)	-

*Extracted from the data of Peregrine *et al*.[23] PR: Pregnancy rate, LBR: Live birth rate

States, live birth rate following IVF in women older than 40 years was 7.2%.[20] IVF may yield a higher pregnancy rate per cycle or trial than attempting natural pregnancy under similar conditions. Therefore, a woman with previous BTL trying to conceive through IVF makes sense. However, it can be inferred that the cumulative pregnancy, meaning the chance of an individual actually becoming pregnant might be lower with IVF since only a limited number of IVFs can be performed due to reasons including cost. On the other hand, the cumulative pregnancy for TA can increase as a woman who has undergone TA can try and anticipate conceiving every month. In our experience of 961 cases of TA, the cumulative pregnancy rate for women over 40 years old was 44.5%, 52.1%, and 53.9% at 12, 24, and 55 months' follow-up, respectively [Figure 1].[22] Thus, the pregnancy rate of an individual with BTL may be maximized by monthly attempts of natural pregnancy following TA in combination with IVF if needed. This strategy should be actively applied to women over 40 who do not have much time left regarding fertility or those with low anti-müllerian hormone.

However, patients undergoing TA are often fertile women who had previously undergone sterilization so direct comparison with subfertile women with tubal disease who have no choice except IVF might not be appropriate, and they will obviously differ in terms of reproductive outcomes. Therefore, this requires further assessment in controlled prospective comparative studies between TA and IVF.

Cost-effectiveness

Other than pregnancy, the second factor to consider would be cost-effectiveness. However, comparative analysis of cost is also difficult since funding for IVF is provided in many parts of the world (this applies to both state-funded IVF and IVF through many private insurance providers), but funding for TA is not so popular.

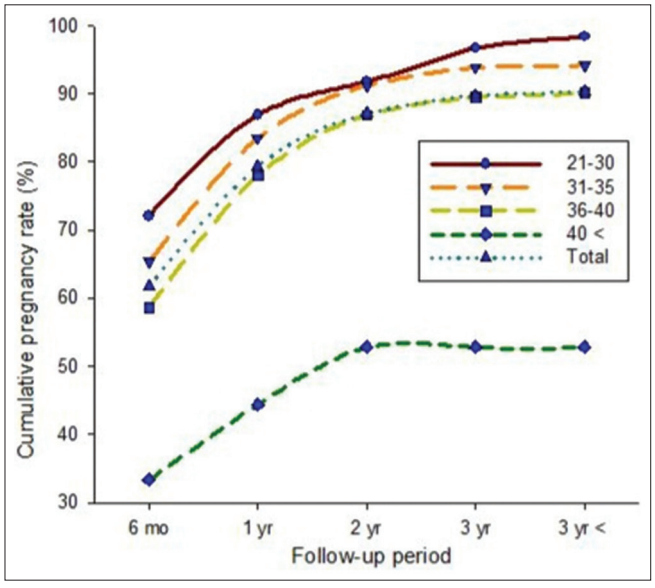

Figure 1: Cumulative pregnancy rate after tubal reanastomosis

In 2013, Hirshfeld-Cytron and Winter, for the first time, compared the outcomes of laparoscopic TA and IVF in terms of cost and suggested that laparoscopic TA was the most cost-effective procedure for women under 40 years of age, whereas IVF may be favored if the lower limit of IVF cost is $4500 in women older than 40 years.[24] Messinger *et al*. compared the total cost until reaching an ongoing pregnancy between 2256 TS cases and IVF cycles collected from the 2012 SART data. They concluded that TA was the most cost-effective method for those younger than 41 years and IVF for those older than 41 years. In women older than 40, TA became more cost-effective if IVF costs were $30,000 or more per cycle.[21] However, Messinger *et al*.[25] reported a live birth rate after TA of only 5% for women over 40 years old, which is very low compared to those (mostly 50%) of many other studies, as shown in Table 2. In addition, the cost of IVF in Hirshfeld-Cytron and Winter's[24] report was very low at $4500, whereas the cost per ongoing pregnancy following IVF according to Messinger *et al*.[25] was $32,814, $45,839, and $111,445 for <35, 35–40, and >40-year-old women, respectively. The cost of TA is similar to that of 1 cycle of IVF in Korea, and this also seems to be the case in the United States. As IVF is likely to require more than one cycle until becoming pregnant, it can be said that TA is more cost-effective since only a single procedure is needed. As the ASRM Committee Opinion has suggested, many studies have reported that TA is more cost-effective for all women including those older than 40 years of age.[26-32] Recently, Estes *et al*. also stated in an invited article contributed to the *Journal of Fertility and Sterility* in 2018 that TA is the most effective minimally invasive method for women desiring childbearing after BTL.[33]

Convenience

Convenience is also important as TA requires general anesthesia and 3–7 days hospitalization, thus calling for a longer recovery time compared to IVF, which delays the return to daily life.[17,34,35] On the other hand, IVF can be done without interruption daily life. However, IVF requires daily injections for ovarian hyperstimulation and frequent office visits for monitoring in different stages, whereas there is not much to do once the surgery is over for TA.

Side effects and complications

Another important factor to consider when choosing between TA and IVF is the side effects and complications which may occur during the process of the procedure or after pregnancy. Many studies have reported that IVF carries multiple risks that do not occur in naturally conceived women. The

most common complication is ovarian hyperstimulation syndrome (OHSS). Its frequency is as low as 1%–3% of cycle, and it can lead to serious conditions, including death and borderline ovarian cancer in extreme cases.[36-38] IVF can also cause obstetrical complications such as preeclampsia, placenta previa, and gestational diabetes. Neonatal risks, including low birth weight and preterm delivery can also occur in IVF-conceived pregnancies.[39] All of the risks directly and indirectly related to IVF eventually result in increase of the total cost.

TA can also cause various complications related to general anesthesia and surgery, and the complication rate is reported to range from 1.9% to 4.3%.[35,40] This is somewhat higher than the frequency of OHSS. However, in the hands of an experienced surgical team, TA is generally considered to have a very low risk of surgical complications. One of the critical potential risks after TA would be ectopic pregnancy. The ectopic pregnancy rate is slightly higher at 3%–8% in TA patients compared to 1.3% in IVF.[35,41,42] In our experience, the site of anastomosis was an important factor influencing the ectopic pregnancy rate. Our study showed a different ectopic pregnancy rate according to the site of anastomosis, with the interstitial–ampulla site being highest at 20%, which was significantly higher than 0%–3.2% at other sites. This can be attributed to the largest discrepancy in tubal diameters between the pin-point diameter of the interstitial portion and the wide diameter of the ampullary portion. Therefore, appropriate counseling on the possibility of ectopic pregnancy should be given before TA, especially if the interstitial–ampulla site is to be re-anastomosed.

Personal preference and other causes of infertility (male, ovarian reserve, and uterine)

Personal preference, for example, religious influence will also play a role when choosing between TA and IVF. If there are other causes of infertility such as the malefactor, low ovarian reserve, and uterine factor, IVF might stand a better chance of achieving pregnancy.

Experienced surgeon

From the factor listed above, we can see that TA is not an out-of-date procedure that is inferior to IVF, but rather it can be more effective in a selected group of women. The reason why the number of TA is decreasing to the point of extinction can be attributed to the fact that there is a serious shortage of experienced surgeons who are able to perform TA these days.

Why is Tubal Re-anastomosis Not the First Choice?

As previously described, TA has many advantages over IVF in terms of cost and pregnancy outcomes, as well as side effects and complications. Nevertheless, TA is not considered the first choice for posttubal ligation fertility, but rather IVF is preferred as the primary treatment. Peregrine *et al*. support IVF as the best approach for posttubal ligation fertility, especially in women aged 40 years and older.[23] They explained the reason for this in the following five aspects.

The first is the lack of experienced surgeons. While the outcome of TA is absolutely dependent on the expertise of the surgeon, the number of experienced surgeons is declining.[43] In a survey, it was reported that 43% of fellows had not performed a TA as the primary surgeon.[44]

Second is the trend of the times. Since the birth of the first IVF baby in 1978, the development of IVF technology led to a steady increase in the use of assisted reproductive technique (ART) and the number of fertility clinics providing ART services worldwide, including the USA and Europe [Figure 2].[45] As a result, IVF became more accessible. Korea also experienced a double in the number of infertility clinics from 86 in 2005 to 156 in 2022.[46] However, most infertility clinics are relatively small, and they do not have the system or capacity to perform TA, nor train the next generation of reproductive surgeons. It may seem obvious, but without an experienced surgeon who is comfortable with performing TA, TA will not even be an option.

Third is that IVF is more convenient than TA in several ways: (1) no general anesthesia is required, (2) quick recovery to daily life, and (3) no additional contraception is required. TA allows multiple pregnancies with a single procedure, while IVF allows only one successful pregnancy with a single procedure. If only one additional child is desired, TA would require subsequent contraception, whereas IVF would not.

The fourth reason for choosing IVF over TA is that various insurance policies started to cover the cost of IVF, although the extent and type of coverage (public or private) may vary among countries. More than half of the European countries registered with European IVF Monitoring publicly cover 100% of the cost, while the overall average coverage is 70%.[47] In the USA, as of August 2023, 21 states have passed fertility insurance coverage laws, 14 of those laws include IVF coverage, and 16 states have fertility preservation laws for iatrogenic (medically-induced) infertility.[48] However, TA costs are not covered by government funding or insurance system in most countries.

The fifth reason is that IVF has relatively less strict patient selection criteria compared to TA. IVF is preferred over TA in women with inadequate tubal length remaining. IVF is also indicated in women with partners with abnormal semen analysis.[43]

2021 ASRM Committee Opinion

The ASRM committee opinion published last year mentions that when counseling patients with tubal infertility regarding

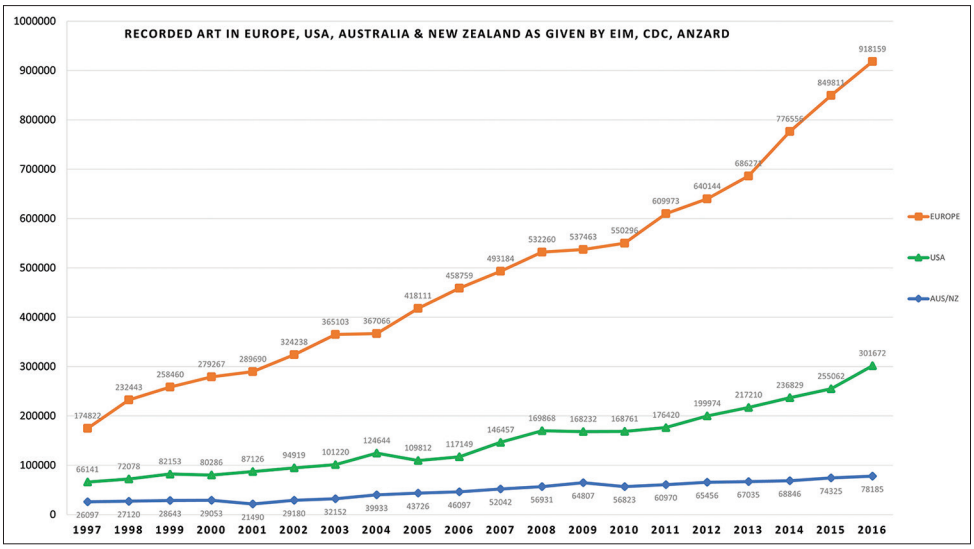

Figure 2: The number of the *in vitro* fertilization cycles from 1997 to 2016 in USA, Europe, and Australia/New Zealand. Note: This figure was partially extracted from the data of De Geyter *et al*.[44]

tubal surgery or IVF, one must consider the age, ovarian reserve, number and quality of sperm, number of children desired, site and extent of tubal occlusion, presence of other infertility factors, risk of ectopic pregnancy and other complications, experience of the surgeon, success rates of the IVF program, cost, and patient preference. It also says that IVF has a higher per-cycle Pregnancy rate (PR) and pregnancies happen within 1 year. In contrast, TA has a higher cumulative PR than IVF, but the time to delivery is substantially longer. The opinion was concluded by recommending microsurgical anastomosis for tubal ligation reversal.[8]

Measures to Further Increase the Pregnancy Rate and Efficiency of Tubal Re-anastomosis

To increase the pregnancy rate and efficiency of TA, the following three principles should be considered.

The first is selecting the most efficient surgical method because the best approach offers significantly improved outcomes. In the early 1970s, TA was performed by open laparotomy.[49,50] It can now be performed in three ways; (1) microsurgical approach, (2) laparoscopic approach, and (3) robotic approach. Laparoscopic access has several advantages including less postoperative discomfort and analgesic requirement, shorter hospital stay and time to recovery, and superior cosmesis.[51] However, laparoscopic microsurgery is time-consuming and has technical limitations.[52] Robotic surgery is not only very expensive but also significantly increases operative time and intraoperative complications.[53] In this regard, it has been acknowledged that microsurgical tubal ligation reversal is a better option.[24,41,54] Estes *et al*. commented that microsurgical TA is a cost-effective and successful technique.[33] The 2021 ASRM Committee Opinion recommended microsurgical anastomosis for tubal ligation reversal.[8] However, Madison *et al*. recently reported that conventional laparoscopy is also the overall most cost-effective approach because when compared with laparotomy, it has several advantages, such as excellent cosmesis and shorter hospital stay, reducing costs by about $500 per operation. In addition, it is significantly less expensive compared with robotic surgery.[53] Therefore, it is thought that there will be little difference in the pregnancy outcome according to the method whether it is microsurgical or laparoscopic surgery as long as it is performed by an experienced surgeon.

The second is the surgical technique because great variations (50%~81%) in live birth rates have been reported depending on techniques used [Table 1].[10,23] Especially, perfect re-canalization of the two tubal segments is an essential factor for a successful pregnancy after TA. Various methods, including single-layer, two-layer, 1-stitch, 2-stitch, 3-stitch, or seromuscular fixation with microstaplers and biological glue, have been introduced.[55-57] To achieve perfect canalization, three major factors must be considered above all else; (1) overcoming the discrepancy in the diameter between the two segments, (2) keeping parallel alignment of the tubes, and (3) adequate suture method to maintain the patency of the tube. We developed a temporary loose parallel 4-quadrant suture method that satisfies these three conditions. http://www.apagemit.com/page/video/show.aspx?num=316&kind=2&page=1. The suture is performed sequentially in a 6, 12, 3, and 9 o'clock position. Each suture is tied loosely at about 1.5 cm from closing tie position so that the sutures are not released. After placing four sutures, we check if the sutures run parallel, and if so, the sutures are tied tightly starting at 9, 3, 6, and 12 o'clock. With this technique, we were

Table 3: Pregnancy outcomes of tubal reanastomosis

	n (%)
Overall pregnancy rate	754/886 (85.1)
Intrauterine pregnancy rate	732/886 (82.6)
Spontaneous abortion rate	76/732 (10.4)
Known deliveries	680/732 (92.3)
Ectopic pregnancy rate	22/886 (2.5)
Time length from anastomosis to pregnancy	6.2±6.7 (1~55) months

*Extracted from the data of Moon *et al*.[22]

able to obtain a high pregnancy rate (85.1%) comparable to that of natural fertility [Table 3].[22]

The third is securing the most experienced surgical team. Many studies have emphasized that the success of the TA procedure requires the most experienced surgeons with a highly selective patient population.[10,21,33] The Asia-Pacific Association for Gynecologic Endoscopy and Minimally Invasive Therapy have recognized the fact that the differences in training make a vast difference of outcomes in clinical trials. As a result, they have been committed to the accreditation and training of minimally invasive surgery and have suggested the need for qualified training centers from worldwide to participate in this certification.[58] We also fully agree with this group's opinion and hope that an accreditation and training system to train the most experienced surgeons in the field of TA can be established.

Suggestion and Conclusion

TA and IVF are the two main approaches that can be applied to women desiring posttubal ligation fertility. These two options are not competitive but rather complementary. However, if some issues are solved, TA can be considered as the first option even in this era where IVF seems to be the only option. Thus, we suggest the three following measures.

First, as previously mentioned, an experienced of surgeon is absolutely crucial to the success of TA. However, the number of expert surgeons is on the decline. More surgeons are reluctant in choosing TA over IVF, which seems so easily approachable. Therefore, it is necessary to establish a system that can train and nurture many experts in TA. Currently, we are introducing our technique in TA, microsurgical TA by temporary loose parallel 4-quadrant sutures technique through YouTube so those in need can easily access it.[59]

Second, we propose a support system for insurance coverage of TA expenses. In 1948 in Paris, the United Nations General Assembly first declared the universal protection of fundamental human rights, "rights inherent to all human beings." Then, in 1994, the International Conference on Population and Development in Cairo began to consider reproductive rights as grounded in the existing human rights obligation.[60] With this historical background, fertility care has been covered by insurance, and most developed countries support IVF costs through public or private funding. At present, the insurance system for IVF costs covers medication, doctor/medical fees, and laboratory bills. Like IVF, TA is another medical approach that supports and cares for the most fundamental human right of having babies. Therefore, it is only reasonable that TA costs are also supported by insurance coverage in the same way as IVF. Insurance coverage of TA costs will allow TA to be selected before IVF, considering the pregnancy success rate and less complication.

Third, long-term family planning following TA should be discussed thoroughly because TA might permit several pregnancies from the initial expanse. At present, a variety of contraceptive methods has been widely used. According to the review by Trussell *et al*.,[61] 15% of women would choose repeat sterilization, 18% short-acting contraceptive methods, and 9% long-acting methods, whereas 57% would use natural family planning, male sterility, and/or condoms. Therefore, the TA surgeons will have to provide the patient with the most efficient and cost-effective method according to the patient's condition.

Data availability statement

The datasets generated during and/or analyzed during the current study are available in the Youtube, https://www.youtube.com/watch?v=0G0AAOhaNNQ.

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Conflicts of interest

There are no conflicts of interest.

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