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# Endoscopy versus IVF: The Way to Go

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Additional information is available at the end of the chapter

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## 1. Introduction

### 1.1. Outlines

- Role of endoscopy in infertility. Microsurgical principles, reconstructive concept.
- Can endoscopy omit ART?
- Endoscopy Vs ART
- Advantages of ART over Endoscopy
- Fertility enhancing procedures:
  - Laparoscopic adnexal surgery.
  - Salpingoscopy
  - Hysteroscopy
- Endoscopy prior to ART (routine hysteroscopy, role of laparoscopy (tubes with or without hydrosalpinx and paratubal cysts, endometrioma).
- Endoscopically-assisted ART.
- Endoscopy for recurrent implantation failure.
- Future of endoscopy in the era of ART and keynote points.

## 2. Current approaches for infertility management

In modern practice, three schools are competitors for infertility management, namely expectant, endoscopic and assisted reproductive techniques (ART) approaches. There are no RCTs that compare the effectiveness of surgery against either IVF or expectant management. The following table demonstrates pros and cons of each approach (1).

### 2.1. Rationale of expectant therapy

Any treatment should be compared to expectant therapy.

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	Expectant treatment	Endoscopic management	ART
Advantages	Safe cheap	-Restores normal anatomy. -Enhances natural pregnancy. -Long-term results	-Time saving Excellent results
Disadvantages	Anxiety Unpredictable outcome	- expensive additional - specialist training -- experience -adverse effects (including ectopic pregnancies), and operative risks. -Unpredictable outcome	-Stress - Expensive - Risky -OHSS -Unpredictable outcome - Per trial result.

**Table 1.** Lines of infertility management

**2.2. Drawbacks of the expectant therapy**

- No strict criteria on which to base management decisions.
- Hence, the likelihood of spontaneous pregnancy for each individual couple must be weighed against the potential benefits or risks of interventional treatment.

**2.3. Is surgery better than IVF?**

**Logic studies:** Microsurgical reversal of sterilization is a highly cost-effective strategy when compared with IVF for women aged 40 years and above (2).

**Illogic studies:** some over enthusiastic studies demonstrated that endoscopy is much better than ART. In a bizarre study, Marana et al. (3) included 43 patients and subjected them to diagnostic or operative laparoscopy. Nine of them with submucous-intramural or multiple intramural fibroids underwent miomectomy by minilaparotomy following hysteroscopy and chromopertubation. The mean length of follow-up was 49 months (range: 11 to 118 months). They reported a very high pregnancy rate as 61 became pregnant (40%).

## 2.4. Advantages of laparoscopy over ART

- Excellent results.
- Long-lasting efficacy.
- Reconstructive concept.
- Physically and psychologically sound patient.

Tubal reconstructive surgery remains an important option for many couples and surgery should be the first line approach for a correct diagnosis and treatment of tubal infertility (4).

## 2.5. Advantages of endoscopic management over conventional management

- cosmetically most acceptable.
- shorter hospital stay.
- lower incidence of ileus.
- faster recovery.
- less post-operative pain and discomfort, and
- earlier resumption of normal activities and employment.
- reduced contamination of the surgical field with glove powder or lint.
- bleeding is reduced due to tamponade of small vessels by the pneumoperitoneum
- drying of tissues is minimal because surgery occurs in a closed environment
- easy intraoperative access to the pouch of Douglas and the posterior aspects of the genital organ.

## 2.6. Fertility-preserving reconstructive gynecologic surgery

- **Avoidance of serosal insults:** tissue trauma, ischemia, hemorrhage, infection, foreign-body reaction, and leaving raw surfaces.
- **minimizing tissue trauma:** by using atraumatic techniques, meticulous hemostasis, complete excision of abnormal tissues and precise alignment and approximation of tissue planes .

**Evidence of superiority of Laparoscopic reconstructive surgery:** one study proved that reconstructive surgery achieves a double pregnancy rate than non-reconstructive surgery (5).

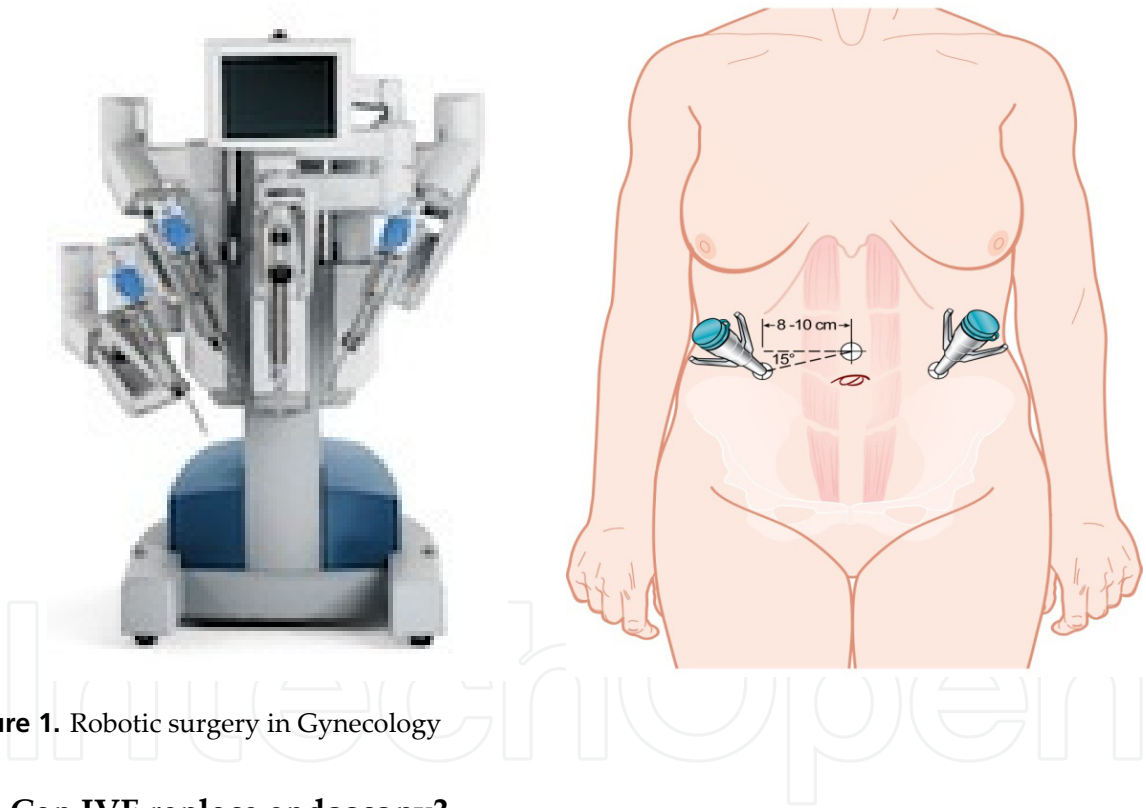
## 2.7. Is there a role for robotic surgery in improving pregnancy rate?

Among experienced endoscopists, it's well known that it's not the robot that does the surgery, it's the surgeon!

In a retrospective study, both robotically-assisted laparoscopic and standard laparoscopic treatments of endometriosis had excellent outcomes. The robotic technique required significantly longer surgical and anesthesia time, as well as larger trocars (6).

Myth	Facts
Three-D vision	no demonstration that it increases speed or safety
The surgeon sees up to 30% more endometriosis.	No RCT
Less recurrence and slowly	No RCT
Rapid recovery and smooth postop course	No RCT
The dexterity (ability to bend at the “wrist”) of the robotic instruments makes it possible to perform some surgeries laparoscopically that would otherwise require laparotomy.	this point is debated among experts.

**Table 2.** Pros and cons of Robotic surgery



**Figure 1.** Robotic surgery in Gynecology

**2.8. Can IVF replace endoscopy?**

Due to advances in the field of IVF/ICSI and stratification of management plans worldwide, the overall pregnancy rate following IVF/ICSI overcame that following endoscopic surgery in many centers. These encouraging results made some authors consider ART superior to surgery and should be offered as a first-line treatment (7).

**2.9. Which approach should we use: expectant, endoscopy or ART? (8)**

The treatment choice depends upon:

- Severity of the tubal disease.
- Duration of subfertility.
- Maternal age.
- Coexisting infertility factors.

Despite the widespread utilization of assisted reproductive techniques in recent years, hysteroscopic as well as laparoscopic surgery should be firstly offered for patients with adnexal and uterine lesions desiring fertility. Permanent correction of the patient's problem with frequent chances of pregnancy is a definite advantage of endoscopic surgery over assisted reproductive techniques. Reconstructive endoscopic procedures could be performed for fertile women as well e.g. hysteroscopic or laparoscopic myomectomy for abnormal bleeding. The concept of reconstruction following microsurgical principles coupled with refinement of instrumentation and techniques is would improve the results of hysteroscopic and laparoscopic approaches. It is expected to expand to cover many gynecologic aspects in the coming years particularly with the continuous advances in technology of fine endoscopic surgery and the development of more suitable robotic instrumentation.

## **2.10. Laparoscopy and IVF/ICSI are complementary since a long time (9)**

The first in vitro fertilization (IVF) child ensued following the partnership by a scientist with a focused ambition (Nobel laureate Robert Edwards) joining with the gynecologist who introduced laparoscopy to Britain in the late 60's (Patrick Steptoe). Egg retrieval was done laparoscopically. In modern practice, laparoscopic egg retrieval is still required whenever inaccessible ovaries are encountered. A trial of transabdominal sonographic aspiration was recently published with lower success rate of egg retrieval if compared to transvaginal sonographic aspiration (10).

**Laparoscopic GIFT:** a blastocyst intrafallopian transfer was associated with an intrauterine pregnancy; however, when the indication for blastocyst tubal transfer of an obstructed cervix is associated with a foreshortened cervix requiring cervical cerclage, there can be major health risks for infant and mother (11).

## **2.11. What's the best approach?**

Always try to use the appropriate approach for a suitable couple at the appropriate time. To achieve the best results, try to stratify the lines of management according to pathology putting in mind other circumstances. The following are examples of how to think in each case separately.

## **3. Pelvic endometriosis: A good example of how to individualize treatment**

The optimal management of endometriotic ovarian cysts in infertile patients is less well defined. Recent evidence of reduced responsiveness to gonadotrophins following

laparoscopic ovarian cystectomy has challenged the traditional surgical approach to treatment (12). Indeed, it has been suggested that surgery should be undertaken only for the treatment of large endometriomas or pain that is refractory to medical treatment, or to exclude malignancy (13).

Laparoscopic surgery may be of benefit in treating subfertility associated with mild to moderate endometriosis. However, additional studies in this field are needed before definitive conclusions can be drawn (14). Laparoscopic excision of ovarian endometriomas more than 3 cm in diameter may improve fertility. (level II evidence). The effect on fertility of surgical treatment of deeply infiltrating endometriosis is controversial (level II evidence).

### **3.1. Is there a need to treat endometriosis in patients undergoing IVF?**

In a meta-analysis (15) the chance of achieving pregnancy after IVF was significantly lower for patients with endometriosis (odds ratio, 0.56; 95% confidence interval, 0.44-0.70), as compared to those with tubal factor. They also reported decreased fertilization rates, implantation rates and in the number of oocytes retrieved.

### **3.2. Mild endometriosis Vs severe endometriosis prior to IVF/ICSI**

The same study (15) reported that the probability of pregnancy was reduced in women with severe endometriosis as compared to those with mild disease.

Contrarily, a recent retrospective poorly designed study (16) demonstrated that ovarian endometriosis does not reduce IVF outcome compared with tubal factor. Furthermore, laparoscopic removal of endometriomas does not improve IVF results, but may cause a decrease of ovarian responsiveness to gonadotropins. Nevertheless, they included a bizarre group of patients with one or more endometrioma, unilateral or bilateral with a size of 6 cm and more importantly symptomatic as well as asymptomatic cases. In addition to being a retrospective analysis, these heterogeneous criteria would weaken this study. We believe that stripping off cyst wall of a unilateral endometrioma wouldn't be expected to affect ovarian reserve or ovarian response to gonadotropins.

### **3.3. Advantages of laparoscopic surgery for endometriosis prior to IVF (ESHRE Recommendations, 2005) (17)**

- confirms the diagnosis histologically
- reduces the risk of infection
- improves access to follicles
- Improves ovarian response.

### **3.4. More advantages include**

- Spontaneous pregnancy in mild and moderate disease.
- Elimination of pelvic pain by destruction of the peritoneal endometriotic lesions which may be mistaken by OHSS if the patient is subjected to IUI.



### 3.5. Precautions of laparoscopic surgery prior to IVF/ICSI

- The woman should be counseled regarding the risks of reduced ovarian function after surgery and the loss of the ovary.
- The decision should be reconsidered if she has had previous ovarian surgery.
- RCTs showed that the excision technique is associated with a higher pregnancy rate and a lower rate of recurrence although it may determine severe injury to the ovarian reserve.
- Improvements to this latter aspect may be represented by a combined excision-vaporization technique or by replacing diathermy coagulation with surgical ovarian suture.

## 4. Role of hysteroscopy prior to assisted reproduction

Failure of IVF treatment can be broadly attributed to embryonic, uterine or transfer factors, but remains unexplained in most cases (18). A number of interventions have been proposed to improve IVF outcome, many of which are not strictly evidence-based and their efficacy in improving pregnancy rates remains controversial (19,20). One of the main causes of failure of implantation after proper embryo transfer is intrauterine pathology. Whether to perform hysteroscopic evaluation of the endometrial cavity prior to IVF/ICSI especially in patients with repeated failures is a controversial issue that is open for criticism and deserves further studies (21).

In a systematic review (Level Ia evidence), 5 reliable studies were included (22). Two RCT showed a statistically significant improvement in the clinical pregnancy rate in the group who had office hysteroscopy (pooled RR = 1.57, 95% CI 1.29–1.92,  $P < 0.00001$ ). The miscarriage rate was not statistically different between the office hysteroscopy and control groups in either study (24% versus 29%, respectively, RR = 0.83, 95% CI 0.56–1.21,  $P = 0.33$ ). Three non-randomized controlled studies suggests that office hysteroscopy improves the pregnancy rate in the subsequent IVF cycle (pooled RR = 2.01, 95% CI 1.60–2.52,  $P < 0.00001$ ). In addition to the well known diagnostic as well as therapeutic advantages of performing hysteroscopy, even if the endometrial cavity was completely free, high pregnancy rate was achieved after diagnostic hysteroscopy since uterine instrumentation during hysteroscopy would inevitably cause a degree of endometrial injury and provokes a posttraumatic reaction that involves release of cytokines and growth factors (23,24), which in turn may influence the likelihood of implantation (25). Commencing IVF treatment soon after hysteroscopy may take advantage of this immunological response (26). Performing diagnostic hysteroscopy before assisted reproductive technologies (ART) may be advisable not only from the clinical but also from the economic point of view (27). Enhanced clinical pregnancy rates would be achieved on adding office hysteroscopy as a complementary step prior to IVF especially patients with recurrent IVF embryo transfer failures even after normal hysterosalpingography findings. Some abnormal intrauterine findings that would affect the prognosis of IVF/ICSI can be easily diagnosed by hysteroscopy like chronic endometritis, Müllerian anomalies, retained fetal bones, or endocervical ossification. Moreover, contact hysteroscopy may reveal additional valuable findings such as polyposis, strawberry pattern,



hypervascularisation, irregular endometrium with endometrial defects, or cystic haemorrhagic lesion which are commonly seen with adenomyosis (28). Future high-quality randomized trials are needed to confirm the favorable effect of standard hysteroscopy in different IVF populations and examine whether newer and less invasive techniques of uterine cavity evaluation such as mini-hysteroscopy (29) or hysterocontrast sonography (30) would have an equally beneficial effect when compared with no intervention before IVF.

With the advent of technical refinements and advancement in hysteroscopic surgery, it is expected that preoperative hysteroscopic evaluation of uteri prior to IVF/ICSI would be widely performed. Unfortunately, many of studies on this topic focus on the central role of hysteroscopic examination of the endometrial cavity in cases with recurrent failures (28,31,32). This concept should be reviewed since office hysteroscopy or minihysteroscopy is a simple outpatient conscious procedure (33-34) that provides excellent information on the implantation site in the endometrial cavity in a very short time. Relying on hysterosalpingography alone may be fallacious in some cases of fine intrauterine adhesions that may be masked by dye especially oily dye. Likewise, transvaginal ultrasonography as well as sonohysteroagrahy may miss some important fine intrauterine lesions that would simply contribute for failures (3). In one study, hysteroscopy succeeded to diagnose and treat intrauterine lesions in 26% of patients prior to starting trials of assisted reproduction (31). In a big sample sized study (36), intrauterine pathology was diagnosed in about 23% of 2500 cases prior to IVF trial. Another study diagnosed abnormalities in only 11 out of 678 cases. On reevaluation of DVD records of hysteroscopy by an experienced team, the same team reported perfect diagnosis in 77.6% of cases (37).

Following recurrent IVF failure there is some evidence of benefit from hysteroscopy in increasing the chance of pregnancy in the subsequent IVF cycle, both in those with abnormal and normal hysteroscopic findings. Various possible mechanisms have been proposed for this beneficial effect, but more randomized controlled trials are needed before its routine use in the general subfertile population can be recommended (38).

#### **4.1. What is the ideal approach prior to IVF?**

In recent years, conflicting opinions on the role of hysteroscopy before any case of IVF/ICSI or after failure once or more times. This conflict is due to different circumstances in different parts of the world regarding: availability of free health insurance for IVF, experienced hysteroscopists, availability of high-resolution 2D ultrasonography with or without SIS, use of office versus conventional hysteroscopes, use of vaginoscopic approach or not and socioeconomic level of the couple. Our opinion is summarized as follows:

- In centers where health insurance is covering the cycles, experienced sonographers performing high-resolution 2D ultrasonography with or without SIS, we believe that they can proceed for IVF without prior hysteroscopy.
- In centers where health insurance is not covering the cycles, experienced sonographers performing high-resolution 2D ultrasonography with or without SIS are not available, we believe that hysteroscopy specially office is very useful in such cases.

- In cases of failed IVF once, hysteroscopy is valuable and recommended.
- In cases with recurrent implantation failure, hysteroscopy is mandatory.

#### **4.2. Office hysteroscopy versus saline-infusion sonography (SIS)**

In 1999, we published our first series of SIS for screening in infertile patients utilizing 0.9% saline as an infusion solution and Nelaton catheters for injection (39). We reported satisfactory results. One year later, we published a study (40) on the efficacy of SIS for the detection of endometrial polyps in comparison to the conventional hysteroscopy. These studies compared SIS versus conventional hysteroscopy with excellent results in favor of SIS. Later on, we introduced office hysteroscopy (I use it since 2002 utilizing 2.6 mm telescope). With the advent of vaginoscopic approach, the procedure gained more acceptability among our patients. Now, after these years of experience we changed our mind and strongly say that office hysteroscopy can easily replace indirect diagnostic tools like SIS or 4D ultrasonography. Moreover, more detailed description of the endometrial cavity particularly the blood vessels would be obtained only with office hysteroscopy as we recently published (41).

### **5. Role of hysteroscopy after embryo transfer**

In a study evaluating the incidence of endometrial injury following embryo transfer, office hysteroscopy was performed immediately following embryo transfer and demonstrated marked endocervical and endometrial damage following rigid catheters more than soft catheters (42). Even for cases of early abortion following IVF/ICSI, hysteroscopy was proved to be very valuable. In one study (43), among 84 early abortion patients after IVF-ET, it succeeded to diagnose intrauterine abnormalities in 58 (69.05%) of the patients, including intrauterine adhesion in 32 (32/84, 38.10%), endometrial polyps in 12 (12/84, 14.29%), endometritis in 10 (10/84, 11.90%), submucous leiomyoma in 3 (3/84, 3.57%) and septa in 1 (1/84, 1.19%).

### **6. Hysteroscopic embryo transfer**

As a trial of improving implantation rate following IVF/ICSI, some scattered papers described hysteroscopically-guided embryo transfer. Principally, hysteroscopic approach was selected in difficult cases of embryo transfer (44).

#### **6.1. A new hysteroscopic tubal embryo transfer catheter was developed**

Catheterization was performed in 60 patients at hysteroscopic insemination into tube, using 3 French catheters, in which the distal 3, 4, and 5 cm tapered to 2 French. Hysteroscopic tubal embryo transfer and conventional IVE-ET were performed in 30 patients with normal tubes, who failed to achieve pregnancy after 2 IVF-ET trials. The success rate of complete insertion with the catheter tapering at the distal 3 cm was significantly higher than that at the distal 5 cm. Since we obtained the highest success rate of insertion with the catheter tapering at the distal 3 cm, we selected this catheter for the h-TEST. The rate of pregnancy in h-TEST was significantly higher than that in conventional ET (45).

## **6.2. Hysteroscopic Endometrial Embryo Delivery (HEED) (46)**

It refers to visually confirmed placement of the embryo(s) at a specific area on the surface of the uterus. It is done in an office setting, using a special fiberoptic scope and camera plus special tubing, and it takes approximately two minutes to perform. It uses nitrogen gas to avoid deleterious effect of CO<sub>2</sub> gas on the embryos. HEED can also be used for earlier (day 2 or 3) embryos as well as the more advanced embryos. This is especially advantageous in situations where the numbers of embryos are limited, or embryo quality is of concern. It is particularly useful in patients with advanced reproductive age, or when egg production is low, or in patients with poor sperm parameters. Patients will actually see the process on video monitor. The entry into the uterus is not always easy, as the non-stirrable tip of the catheter must usually go through different curvatures in the cervical canal and the uterine cavity while minimizing injury to the lining of the uterus, before it reaches the final destination. The flexible hysteroscope has a stirrable tip, helping guide the endoscope in a gas expanded uterine cavity. The slightly expanded uterine cavity also helps avoid contact between the hysteroscope and uterine surface. The final destination of the tip of the catheter is visually confirmed. This more precise placement and lower volume of transfer fluid may help reduce incidence of ectopic pregnancies even further. It may also reduce chances placenta previa, where the after birth is lying over the uterine opening. Presence of uterine contraction at the time of transfer that are otherwise not noticeable by using the "Blind" embryo transfer technique, can be visually confirmed and embryo transfer deferred. Precise and visually confirmed placement, may reduce percentage of multiple pregnancies, by reducing number of embryos transferred because of the less uncertainty of the placement of embryos with the "Blind" technique. Nevertheless, since the embryo(s) are laid on top of the uterine surface, due to inherent uterine contractions over the next few days after the embryo delivery and prior to their natural implantation in the uterine cavity, the embryo(s) may be expelled either into the fallopian tube (causing ectopic pregnancy) or out of the uterus, as they do with the current "blind" embryo transfer technique.

## **6.3. Subendometrial embryo delivery (SEED) (47)**

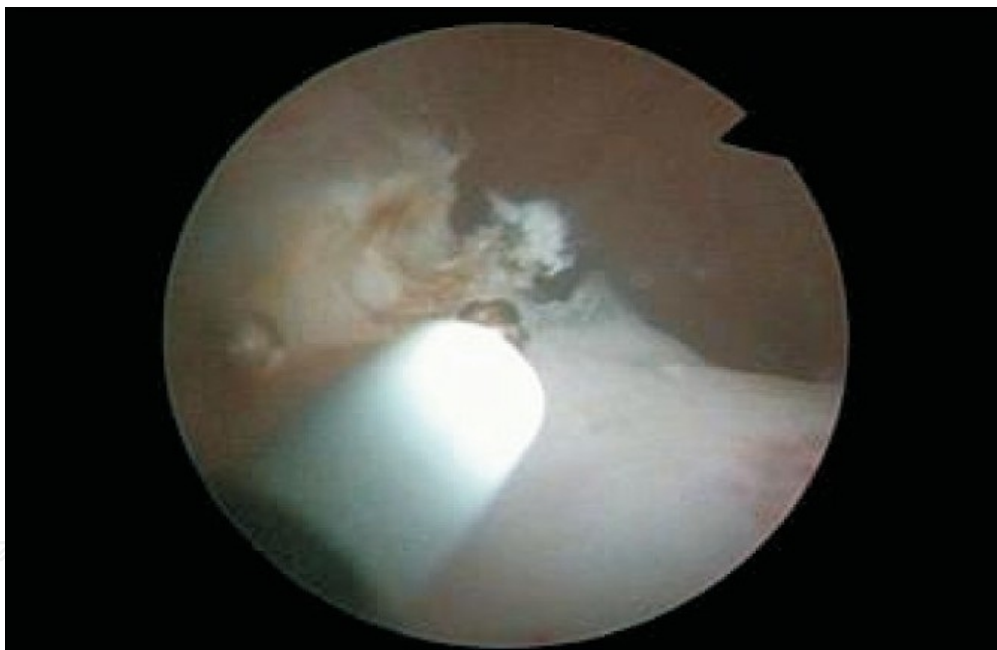
Patients will actually see the process on video monitor. It will reduce the chances that the embryo will fall out of the uterus, or that it will fall into the fallopian tube causing tubal pregnancy. Post embryo implantation, the woman does NOT need to stay in bed for 2 days.

The main disadvantage includes a possible scratching of the lining of the uterus so that pregnancy may not ensue. Candidates include any patient undergoing IVF, specially patients with previously failed standard embryo transfers, patients with ectopic pregnancies and tubal disease.

It is done in an office setting using a special fiberoptic scope and camera plus a special tubing with a needlepoint, and it takes approximately two minutes to perform. It utilizes flexible hysteroscope and an inert gas (nitrous gas) to avoid the deleterious effect of CO<sub>2</sub> gas on the embryos.

#### 6.4. Hysteroscopic cervical canal refashioning prior to difficult embryo transfer (48)

In some cases, access to the endometrial cavity is extremely difficult or even impossible. In some scarce studies. Sonographically-guided fine needle transmyometrial embryo transfer was tried but this technique is not universally accepted. An attractive recent hysteroscopic approach was described. The procedure is performed under general anesthesia. Patients are taken into the theater with a full bladder in case ultrasound guidance is required to access the uterine cavity. A Versapoint electrode (twizzle electrode) with a 1.9 mm Versascope (Gynecare division, Johnson and Johnson) is used for the procedure. The Versapoint electrode works on bipolar energy, so saline is used as the distension media. Versascope sheath has a small diameter (3.5 mm) and it can be inserted into the cervical canal without prior dilatation or with minimal dilatation. In two patients the canal is extremely tortuous and fibrotic and it is not possible to negotiate with the delicate Versascope. Cervical dilatation is achieved under ultrasound guidance in these women and the Versapoint twizzle electrode is introduced through the operating channel of an operating hysteroscope (Olympus).



**Figure 2.** Hysteroscopic cervical canal refashioning

For women with a false passage and acute angulation of the uterus, the tissue between the actual cervical canal and false passage is cut thus leaving a clean path which could be negotiated with an ET catheter. For the problem of a severely fibrotic OS, 1 or 2 linear releasing incisions are made with the Versapoint electrode, extending from the posterior aspect of the internal OS towards the external OS for approximately 1 cm. In patients who had a tortuous cervical canal, several projecting ridges are seen arising from the anterior, posterior and/or lateral walls of the cervical canal. The hysteroscope is introduced into the uterine cavity and then withdrawn towards the external OS. As the hysteroscope is moved

outwards the cervical canal projections distorting linearity of the canal are visualized. Linear releasing incisions of approximately a centimeter are made into these projections and a straightening of the canal is achieved. Subsequent to the procedure, dilatation is done to further stretch the incised fibrous tissue, and it is now possible to dilate the cervix up to size 10/12 Hegar in even the most resistant cervix.

### **6.5. Hysteroscopic site-specific endometrial injury (49)**

A site-specific hysteroscopic biopsy-induced injury of the endometrium during the controlled ovarian hyperstimulation cycle has been shown to improve subsequent embryo implantation in patients with repeated implantation failure. The procedure starts with performing panoramic hysteroscopy. A flexible claw forceps is introduced through a 2.2 mm working channel which is used to generate a local injury on the posterior endometrium at midline 10-15 mm from the fundus on D4 to D7 of the stimulation cycle. The depth and width of the injured site is  $2 \times 2$  mm (i.e. a bite of the claw forceps). No antibiotic or hemostatic drug is administered after the procedure.

Endometrial injury may have a beneficial role in implantation and improve the pregnancy rate. However, there are still many unanswered question including patients selection, timing, technique and number of endometrial biopsies needed (50).

## **7. Role of endoscopy in cases of hydrosalpinx**

- Tubal pathology, particularly hydrosalpinx, is associated with a low embryo implantation rate in IVF as well as an increased risk for early pregnancy loss.
- The role of surgery for tubal disease to improve IVF outcomes, in the absence of hydrosalpinx, requires further evaluation.

In recent years, considerable attention has been given to the possible impact of the presence of hydrosalpinx on implantation and ongoing pregnancy rates following IVF/ICSI (51,52). The mechanism of disruption remains uncertain. However, proposed mechanisms may be attributed to alteration in endometrial receptivity or direct embryo toxic effect (53). Furthermore, hydrosalpinx is liable be unintentionally punctured at the time of egg retrieval or it may disturb the access to the ovary if it is too big. A systematic review of three RCTs (54) showed that tubal surgery such as laparoscopic salpingectomy significantly increased live birth rate (OR 2.13; 95% CI 1.24 to 3.65) and pregnancy rate (OR 1.75; 95% CI 1.07 to 2.86) in women with hydrosalpinges before IVF when compared with no treatment. There are no significant differences in the odds of ectopic pregnancy (OR 0.42; 95% CI 0.08 to 2.14), miscarriage (OR 0.49; 95% CI 0.16 to 1.52), treatment complication (OR 5.80; 95% CI 0.35 to 96.79) or implantation (OR 1.34; 95% CI 0.87 to 2.05). Since hydrosalpinx reduces IVF pregnancy rates (14,55), it is therefore suggested that women with hydrosalpinges should be offered diagnostic/operative laparoscopy and a trial of salpingoneostomy. If failed or inaccessible, salpingectomy could be offered prior to IVF/ICSI to improve the chance of a live birth. Sometimes, laparoscopic access to the isthmic part of the tube is not feasible even in experienced hands particularly in patients with history of repeated laparotomies,



intestinal reanastomosis, or kidney transplantation. This situation may pave the way to hysteroscopic occlusion of the fallopian tubes based on the reported success in hysteroscopic tubal cannulation and sterilization techniques. The effectiveness of draining of hydrosalpinges or performing salpingostomy on improving live birth rate prior to IVF/ICSI needs further evaluation.

### 7.1. Methods of endoscopic proximal occlusion of functionless and harmful hydrosalpinx

1. **Laparoscopic:** this can be easily performed using a bipolar grasping forceps or monopolar grasping forceps. In either approach, take care to apply a little traction on the tube medially to avoid scattered secondary coagulation towards the lateral pelvic wall particularly when utilizing monopolar diathermy. By this way, the ureter would be perfectly secured. Some center using clips.
2. **Hysteroscopic:** this approach can be performed whenever laparoscopic approach is impossible or dangerous like cases with history of extensive abdominal surgery like resection anastomosis of the intestine or previous colonic surgery, or patients with a history of extensive or recurrent surgery for pelvic endometriosis. Practically, endoscopists may face some cases without feasibility to perform laparoscopy from the start. These cases deserve searching for an alternative approaches. Hysteroscopy comes as an attractive valuable alternative. Some studies used Essure devices to hysteroscopically occlude the proximal part of the fallopian tube. They reported some case reports of successful pregnancy. Nevertheless, we believe that leaving a foreign body in-utero would lead to decreasing implantation rate. Herein, I'll discuss in details our previous unique study on hysteroscopic tubal occlusion in cases with hydrosalpinx (56). The in-vitro safety phase of this study is done on fresh uterine specimens removed by abdominal or vaginal hysterectomy. In this phase the study, fresh hysterectomy specimens are placed on the return electrode of diathermy, then the corneal ends of both tubes are coagulated simulating the same manner as in the clinical phase. Temperature study is done using digital thermometer over the uterine serosa at site of the coagulation. Histopathologic sections are made to assess tissue effects and depth of penetration using Nitro Blue Tetrazolium (NBT) to evaluate the extent of coagulation on the tubal uterine junction. Computerized image analyzer (Leica Q 500 MB Computerized Image Analyzer) is used to measure the depth of diathermy damage to the surrounding myometrium. The clinical phase of this study is conducted at the out-patient Infertility clinic of Women Health hospital, Assiut University, from April 2004 to October 2006 and included 27 patients with definite uni- or bilateral laparoscopically-proved functionless hydrosalpinges scheduled for IVF/ICSI. All patients gave a written consent and the study is approved by the institutional ethics committee. They were randomly divided into 2 groups. Randomization is done using simple computer generated randomization tables method. Group A comprised 14 patients who were randomly allocated for laparoscopic occlusion. Laparoscopy is performed under general endotracheal anesthesia using a standard double puncture technique. Once the

peritoneal cavity is entered, a panoramic evaluation of the pelvis is done. If the pelvis looks frozen or if the access to the fallopian tubes is impossible, the patient is considered failed laparoscopic approach. Those cases are subsequently treated by open laparotomic or hysteroscopic approach but the results of these procedures are not included in this study. If the procedure seems feasible, a third auxillary puncture is done. Utilizing a bipolar forceps, the isthmic part of the fallopian tube is coagulated and incised to ensure complete tubal occlusion as a case of tubal sterilization. The procedure is completed after securing hemostasis. The patient is discharged after 3-4 hours under antibiotic prophylaxis. Group B included 13 patients scheduled for hysteroscopic approach. The cervix is primed in all cases using 200 Mg misoprostol 8 hours prior to the procedure as previously described (57). The procedure is done immediately postmenstrual without specific preparation. Local paracervical anesthesia is selected in 5 cases while spinal anesthesia in 6 cases, and general anesthesia in 2 cases. Selection of the anesthetic technique is chosen according to patient preference after proper explanation by the anesthesiologist. The cervix is gently dilated till Hegar's 10 which is followed by insertion of a rotatory continuous flow monopolar resectoscope. Once the peritubal pulge (the proximal part of the intramural segment of the tube is clearly seen, a roller ball electrode of 3 mm size is bluged inside it and activated at 50 watts for about 8 seconds. A thorough comment on the fundus and the rest of the endometrial cavity is reported. The patients are discharged immediately if the procedure is done under local paracervical anesthesia, while the remaining cases are discharged few hours later. In both groups, the procedure is preceded and done under prophylactic broad spectrum antibiotic coverage to guard against any risk of flaring up of infection of the functionless hydrosalpnix. In both groups, patients are instructed to come back the next cycle postmenstually where hysterosalpingography (HSG) is done for most cases especially those with unilateral functionless hydrosalpnix. If the patient refused and has bilateral hydrosalpnix, sonohysterography (SHG) is done utilizing a simplified technique as previously described (39). Tubal occlusion of the affected side is confirmed if marked resistance is encountered on repeated injection of saline without evidence of intraperitoneal leakage from the occluded side which is the main outcome measure. Second-look office hysteroscopy is done for patients in group B whenever possible. The in-vitro safety phase resulted in bilateral complete coagulation of the proximal part of the tubes with secondary coagulation shown of up to 3 mm as shown in the histopathologic sections. When the power of coagulation is 50-60 W and operating time not prolonged more than 20 seconds, the thermal damage covered corneal end as complete coagulation in addition to 2mm -3 mm secondary coagulation of the adjacent cornualendo- myometrium. Serosal temperature is not exceeding 41.9 C° (range 39 C° - 41.9 C°) at any time during the procedure. No full thickness injuries are demonstrated either histologically or suggested by the temperature studies. Hysteroscopic access is achieved in 12 (85.7%) and occlusion is achieved in 9 (64.2%) cases. If the peritubal pulge is not clearly visible, the case is considered as failed access to the proper site of occlusion. In group B, diagnostic hysteroscopy showed fine marginal adhesions in 2 cases (15%) and a small polyp in one case (7.7%). Hysteroscopic tubal occlusion showed



shorter operative time ( $9 \pm 2.76$  min vs.  $23.6 \pm 4.75$  min,  $p = 0.0001$ ) and hospital stay as well ( $2 \pm 1.84$  hours vs.  $5 \pm 1.13$  hours,  $p = 0.0001$ ). No case of intraoperative complication in either group is reported. There is no case of exaggerated postoperative pelvic pain or fever in either group. HSG or SHG demonstrated complete tubal occlusion of the affected side in all cases in both groups). Second-look office hysteroscopy is done in 8 cases of group B which revealed no significant corneal lesions at the site of hysteroscopic occlusion. Pregnancy is achieved in 4 (28.5%) and 4 (30.7%) cases in both groups respectively following IVF/ICSI without any significant difference between both groups.

## 7.2. Comments on hysteroscopic tubal occlusion in hydrosalpinx

Hysteroscopic tubal occlusion of functionless hydrosalpinges is a unique one. It demonstrates a valuable role of hysteroscopic approach that can be performed in difficult cases with poor access to the isthmic part of the tubes via laparoscopy even with experienced hands. The idea is attractive but further large-sample sized studies are required to define the exact role of this approach.

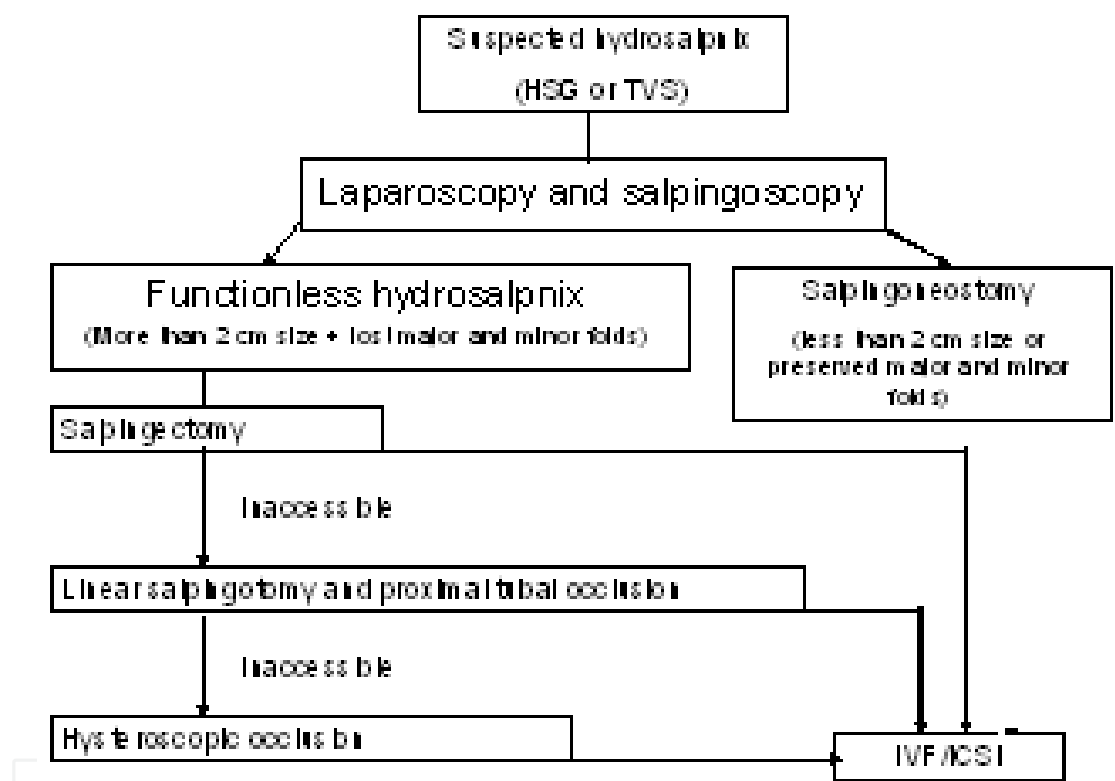
One of the interesting additive items of this paper to the literature is the term "functionless" hydrosalpinx. The proposed definition is very crucial to stratify cases suitable for microsurgical salpingoneotomy and those cases suitable for occlusive procedures. By this way, the place of reconstructive surgery is still preserved in modern practice even in the era of IVF/ICSI. Ethically, every effort should be exerted to restore normal anatomy whenever possible. This concept is of utmost importance particularly for the developing countries with limited resources where no national programs to support assisted reproductive techniques. Microsurgery to correct localized damage has the advantage of long-standing restoration of fertility. A simple prognostic classification is lacking. The severity of the tubal damage and the health of the mucosa is key in determining outcome. Proper selection of the tube for either line of management requires expert knowledge with the principles of salpingoscopy. Salpingoscopy during laparoscopy yields the best prognosis in patients with hydrosalpinx. Performing salpingoscopy with laparoscopy could significantly increase accuracy in predicting short-term fertility outcome. Whenever the mucosa is unhealthy, surgery is not justified; early referral for IVF is indicated.

Hysteroscopic tubal occlusion of proximal part of the hydrosalpinx is feasible and promising as a safe, effective, fast, and easy approach. It can be done as an out-patient procedure under local paracervical block. It has the advantage of adding valuable evaluation of the endometrial cavity prior to IVF/ICSI. Further large sample-sized studies are required specially those utilizing bipolar resectoscope. The impact of hysteroscopic tubal occlusion on subsequent implantation and pregnancy rates needs to be addressed in another larger study. Since it is a preliminary study, the current role of hysteroscopic occlusion should be limited to cases of failed laparoscopic approach. Further studies are required before moving hysteroscopic occlusion to replace laparoscopic occlusion prior to IVF/ICSI.

### 7.3. A suggested flowchart for management of functionless hydrosalpinx prior to IVF/ICSI

**Laparoscopic tubal surgery:** tubal factors include proximal tubal occlusion, distal tubal phimosi or occlusion or peritubal adhesions. Endoscopy (whether laparoscopy or hysteroscopy) play a central role in the management of tubal disease.

- Tubal pathology, particularly hydrosalpinx, is associated with a low embryo implantation rate in IVF as well as an increased risk for early pregnancy loss.
- The role of surgery for tubal disease to improve IVF outcomes, in the absence of hydrosalpinx, requires further evaluation.

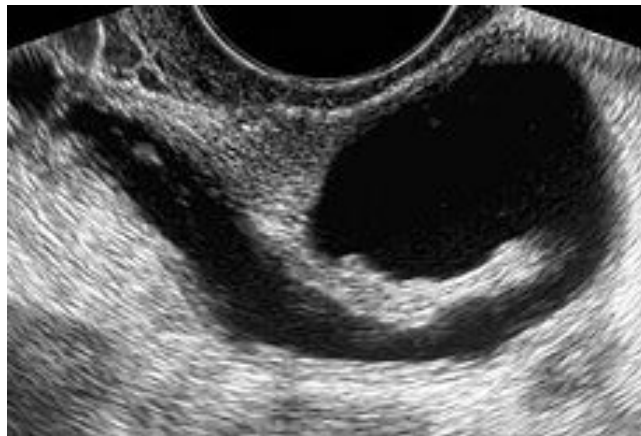


**Figure 3.** HSG: Hysterosalpingography. TVS: Transvaginal ultrasonography.

### 7.4. Laparoscopic management of distal tubal disease

Distal tubal occlusion may be due to hydrosalpinx, pyosalpinx or peritubal adhesions. Obstruction of the distal fallopian tube is one of the most common causes of female infertility (58). In cases of pyosalpinx, just tubal opening, drainage of pus and proper peritoneal toilet are sufficient. Don't forget to take a tubal wall biopsy. Don't proceed for tubal occlusion at the same setting for fear of disseminating infection and the possibility of tubal bilharziasis with reported cases of spontaneous pregnancy after proper treatment. Nowadays, it is conceived that the presence of hydrosalpinx is associated with a compromised outcome for IVF/ ICSI. Hydrosalpinx is associated with lower implantation and fecundability rates even if the contralateral tube is sound which may be attributed to alteration in endometrial receptivity

(59) or direct embryo toxic effect. Furthermore, it is liable to be unintentionally punctured at the time of egg retrieval or it may disturb access to the ovary if it is too big. In a meta-analysis, it has been demonstrated that there is a reduction by half in the probability of achieving a pregnancy in the presence of hydrosalpinx, and an almost doubled rate of spontaneous abortion (60). In an animal study, hydrosalpinx fluid is shown to contain toxins that are potentially teratogenic (61). Proposed mechanisms of impaired implantation rate due to hydrosalpinges are well addressed in the literature (62). Selected patients with unilateral hydrosalpinges and a patent contralateral Fallopian tube may exhibit increased cycle fecundity after salpingectomy or proximal tubal occlusion of the affected tube, and may conceive without the need for IVF. In a retrospective case-control study, bilateral salpingectomy due to hydrosalpinges restored a normal delivery as well as implantation rate after IVF treatment compared to controls (63). Randomized controlled trials recommended performing laparoscopic salpingectomy prior to IVF, especially inpatients with ultrasound-visible hydrosalpinges (64). In a Cochrane review (65), it is concluded that further randomized trials are required to assess other surgical treatments for hydrosalpinx, such as salpingostomy, tubal occlusion or needle drainage of a hydrosalpinx at oocyte retrieval. Functionless hydrosalpinx can be defined as a large blocked tube with lost major and minor folds, as seen at salpingoscopy after laparoscopic salpingoneostomy.



**Figure 4.** Sonographic appearance of a typical hydrosalpinx.

On sonography, the dilated fallopian tube presents as a thin- or thick-walled tubular fluid-filled structure that may be elongated or folded (figure). Longitudinal folds that are present in a normal fallopian tube may become thickened in the presence of a hydrosalpinx. The dilated fallopian tube may or may not show longitudinal folds. These longitudinal folds are pathognomonic of a hydrosalpinx. If the elongated nature of these folds is not noted, they may be mistaken for mural nodules of an ovarian cystic mass. Identification of a separate ovary helps distinguish a hydrosalpinx from a cystic ovarian mass, an important distinction because malignancy is rare with an extraovarian cystic adnexal mass. A significantly scarred hydrosalpinx may present as a multilocular cystic mass with multiple septa creating multiple compartments. These septa are generally incomplete, and the compartments can be connected. However, with more pronounced scarring, differentiation from an ovarian mass may not be possible (66). Potential pitfalls in the diagnosis of hydrosalpinx include

paratubal, paraovarian, or perineural cysts. In some cases, CT or MRI may be helpful to differentiate these conditions from a hydrosalpinx (67).

### 7.5. Technical tricks of laparoscopic management of hydrosalpinx

- a. **Salpingoneostomy:** One of the keys of success is to evaluate the tube externally and internally. If peritubal adhesions exist, microsurgical adhesiolysis should be performed at first. Be sure that the tube is freely mobile. Imagine the site of the new ostium before dealing with the hydrosalpinx. It should be directed towards the pouch of Douglas to help ovum pick-up. Start by salpingoneostomy using a fine monopolar or bipolar needle. The finest the needle, the better ostium. Incise the distended distal part of the tube “+ shaped” (cruciate incision). Then, evaluate the tubal mucosa using a salpingoscopy. Practically, use the diagnostic hysteroscopy which consists of a 4 mm telescope and a 5 mm outer sheath. Connect it to a normal IV infusion set and use saline as an irrigating fluid. Grasp the new ostium with an atraumatic grasping forceps and insert the hysteroscope with comment on the major and minor folds till reaching the narrowest part of the tube. If major and minor folds are lost this means that the prognosis is poor even after proper refashioning. The next step is to grasp the tubal lumen with atraumatic forceps and to evert it outside. Lastly, fix the edges of the new ostium either with monopolar spray coagulation just distal to the incised parts to evert them or with the aid of fine sutures.
- b. **Salpingectomy:** This procedure is indicated if a pathologic unilateral huge hydrosalpinx is present to enhance spontaneous pregnancy or bilateral big hydrosalpinx before IVF/ICSI. It is performed in the same manner as mentioned in the section of EP.
- c. **Tubal occlusion:** Once the peritoneal cavity is entered, a panoramic evaluation of the pelvis is performed. If the pelvis looked frozen or if access to the fallopian tubes is impossible, the patient is considered a failed laparoscopic approach. Those cases are subsequently treated by open laparotomic or hysteroscopic approach. If the procedure seems feasible, a third auxiliary puncture is carried out. Utilizing a bipolar forceps, the isthmus part of the fallopian tube is coagulated and incised to ensure complete tubal occlusion, as a case of tubal sterilization. The procedure is completed after securing hemostasis. The patient is discharged after 3-4 h under antibiotic prophylaxis. Laparoscopic salpingectomy or bipolar proximal tubal occlusion yielded statistically similar responses to controlled ovarian hyperstimulation and IVF-ET cycle outcome. Proximal occlusion might be preferable in patients who present with dense pelvic adhesions and easy access only to the proximal fallopian tube (68). Occlusion is considered a minimally invasive procedure, requires less experience, feasible in most cases, and has fewer burdens on the psychological status of those infertile women. Hysteroscopic approach is recently described by our team at Assiut University Institution (69). The cervix is primed in all cases using misoprostol (200 µg) 8 h prior to the procedure. The procedure is carried out immediately postmenstrual without specific preparation. Local paracervical, spinal or general anesthesia could be used. Selection of the anaesthetic technique is chosen according to patient preference after

proper explanation by the anaesthesiologist. The cervix is gently dilated with Hegar 10 and a rotatory continuous flow monopolar resectoscope is inserted. Once the peritubal bulge (the proximal part of the intramural segment of the tube is clearly seen, a roller ball electrode (size: 3 mm) is introduced inside it and activated at 50 Watts for about 8 seconds. A thorough comment on the fundus and the rest of the endometrial cavity should be reported. The patients are usually discharged immediately if the procedure is carried out under local paracervical anesthesia, while the remaining cases are discharged a few hours later.

## 8. Proximal tubal occlusion

Usually diagnosed by HSG and confirmed by laparoscopic chromopertubation test. The most important job of the endoscopist is to find out contraindications for hysteroscopic tubal cannulation procedure which include:

- florid infection
- genital tuberculosis
- obliterative fibrosis and long tubal obliterations that are difficult to bypass with the catheter.
- severe tubal damage.
- previously performed tubal surgery.
- salpingitis isthmica nodosa.
- isthmic occlusion with club-shaped terminal, ampullar or fimbrial occlusion, and tubal fibrosis
- coaxial TO: combined distal and proximal tubal occlusion.

Don't try to cannulate the tube in such cases as failure would be expected and you would be disappointed. In cases with isolated tubal occlusion, cannulation would be successful.

## 9. The following is our protocol for tubal disease management

- Pathologic PTO: IVF
- Isolated PTO: TC
- Midsegment O: IVF
- Small hydrosalpinx+ normal salpingoscope: OL
- Functionless hydrosalpinx: PTO then IVF
- Combined PTO and DTO: IVF
- Peritubal adhesions: OL Vs IVF

## 10. Endoscopic uterine surgery

### 10.1. Endoscopic myomectomy prior to IVF/ICSI

The impact of uterine myoma on the outcome of IVF/ICSI is a very controversial topic. Many centers are overdoing myomectomy for nearly all myomata regardless size and site considerations. Contrary, other investigators have shown that fibroids don't exert a

deleterious effect. Nevertheless, many studies have provided evidence that uterine myomas have a significant effect on IVF outcomes and there is a large body of evidence that treatment of uterine myomas increases fertility and pregnancy rates, and decreases the rate of pregnancy loss (70). There is no doubt that any cavity-distorting myoma should be removed whether completely submucous or interstitial myoma with submucous encroachment. This highlights the central role of prior hysteroscopy as well as saline infusion sonohysterography (SIS) as previously described (39). Not only does sub mucous myoma cause mechanical interference with implantation, but it also alters endometrial receptivity (71)

Controversy exists for interstitial and subserous myomata. The evidence supports treatment of all very large myomas (>7 cm) (70). Subserosal myomas that are smaller than 7 cm in size and intramural myomas of less than 4–5 cm in diameter appear to have little effect on IVF outcomes. Larger intramural and subserosal myomas present a clinical dilemma and more studies are needed to clarify a definitive plan for management (70). In a prospective controlled study, the distance between the intramural myomas and the endometrial lining did not appear to affect the IVF outcome. An insignificant tendency towards improvement of IVF outcome is found in myomas at more than 5 mm from endometrial lining (72).

In a recent review of literature (73) on myoma and assisted reproduction technology and spontaneous conception, hysteroscopic sub-mucous myoma resection is found to increase pregnancy rates. Intramural fibroids appear to decrease fertility, but the myomectomy does not improve assisted reproduction technology and spontaneous fertility. More high-quality studies are needed to conclude toward the value of myomectomy for intramural fibroids. Subserosal fibroids do not affect fertility outcomes, and removal does not confer benefit.

## 11. Keynote points

### 11.1. Tubal infertility

Endoscopy and ART are not competitors but complementary.

First trial is the best trial for tubal surgery.

Performing laparoscopic surgery for endometriosis prior to IVF is very valuable in many cases.

There is NO adequate trial comparing pregnancy rates with tubal surgery versus IVF.

Per cycle pregnancy rate of IVF: higher

Tubal anastomosis for reversal of sterilization has significantly higher cumulative pregnancy rate than IVF and is more cost effective even above 40 years.

Factors affecting counseling for tubal surgery or IVF:

- Age of the woman.
- Ovarian reserve.
- Number and quality of sperms/ejaculate.



- Number of children desired.
- Site and extent of tubal disease.
- The presence of other infertility factors.
- The risk of ectopic pregnancy.
- The experience of the surgeon.
- The success rate of IVF program.
- The patient preference.

## 11.2. Uterine myoma and infertility

Uterine myoma may affect fertility according to its size, site and associated pathology. Endoscopic approach has a definite role in its management. HM is the gold standard line of management of submucous myoma of suitable size. LM doesn't seem to be superior to conventional open myomectomy regarding fertility and is characterized by both short and long term drawbacks. Uterine myomata would affect IVF/ICSI outcome whenever disturbing the endometrial cavity or large sized. The impact of other types of myomata on IVF/ICSI deserves further studies. Hysteroscopic myomectomy is indicated for intracavitary myomas and submucous myomas having at least 50% of their volume within the uterine cavity. The management of the subfertile women with small intramural fibroids (<5 cm) is still a subject of debate (75,76).

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