

Reproductive surgery in the 21st century

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Abstract

The result of infertility treatment can be assessed accurately by the monthly fecundity rate and the cumulative pregnancy rate (CPR). The monthly fecundity rate, decreasing over time, and the time needed to reach the ultimate CPR are key factors in decision making. Depending on the clinical assessment, infertility treatment will be either with in vitro fertilization (IVF)/assisted reproduction technologies (ART) or with a diagnostic laparoscopy associated with reproductive surgery, which thereafter may require IVF/ART. The comparison of IVF/ART treatment versus reproductive surgery is therefore the wrong debate as the CPR's of reproductive surgery and of IVF are additive. Decisions should be based on the ultimate CPR's and on effort and time, not on personal preferences. The large majority of women with infertility should have a diagnostic laparoscopy during which reproductive surgery can be performed if needed. IVF/ART treatment without a diagnosis decreases the ultimate CPR and is not without potentially serious adverse effects. Having excellent reproductive surgery readily available to patients, similar to the availability of IVF would increase CPR in women with infertility and decrease the overall cost.

Keywords: Infertility, IVF, ART, Reproductive surgery, Laparoscopic surgery, Endometriosis

Diagnosis and treatment of infertility have changed rapidly. Key events that improved and facilitated diagnosis were radio-immunoassays and our understanding of endocrinology, together with diagnostic laparoscopy and imaging techniques as ultrasound and magnetic resonance imaging. More recently we began to understand some genetic and molecular biological mechanisms. Milestones that changed therapy of infertility were hormonal treatments, ovulation induction, microsurgery^[1,2], in vitro fertilization (IVF), and assisted reproduction technologies (ART). Over the last 2 decades results of IVF treatment and ART improved spectacularly. In a parallel manner diagnosis became less important as IVF could be used for all causes of infertility ranging from mechanical, male and unexplained infertility to endometriosis. During the same period, results of reproductive surgery rather declined when microsurgery was replaced by plain

laparoscopic surgery without application of microsurgical principles. Indeed reproductive surgery became mainstream surgery, and the focus on adhesion formation prevention was lost as laparoscopy was considered “minimal invasive surgery.” In addition IVF or ART treatments were more suited than reproductive surgery for randomized controlled trials which had become the new evidence-based medicine standard. Not surprisingly reproductive surgery was declared dead and a relic from the past^[3].

Around the turn of the century it had become clear that post-operative adhesion formation had remained an important clinical problem and new strategies were developed that permitted virtually adhesion free surgery^[4]. Today, however, IVF treatment and reproductive surgery are often considered as 2 opposing treatment alternatives and IVF is increasingly started without a laparoscopy and/or a clear diagnosis. The driving mechanisms are the increasing success rate of IVF, the decrease in reproductive surgery training, the time pressure associated with the increasing number of women in late reproductive age seeking treatment. In addition organizational aspects of an IVF center stimulate to increase the number of IVF cycles, while including younger women with a shorter duration of infertility will increase the success rate.

In order to discuss diagnosis of infertility and surgical or IVF treatments the basics of infertility should be understood^[5]. The results of a treatment should be expressed by monthly fecundity rates (MFR) and cumulative pregnancy rates (CPR) (Fig. 1). The MFR for each type of treatment always decreases over time, because the most fertile couples will conceive faster, and the mean fecundity of the remaining group therefore decreases. The CPR is the percentage of women that started treatment who ultimately will have a baby. The choice of treatment should be based on the estimated MFR and CPR adapted for age and clinical findings, together with other variables as cost and preferences of the patient. Unfortunately MFR and CPR of surgical and IVF treatments vary for each individual infertility factor, including age,

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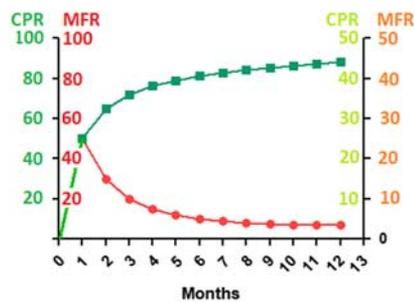


Figure 1. Monthly fecundity rate (MFR) and cumulative pregnancy rate (CPR). Fertility ranges from very fertile to very infertile. Therefore the MFR decreases over time as the remaining group becomes less fertile. CPR therefore will approach slowly the maximal CPR. Important is that the shape of these curves remain the same if the maximal CPR is much <100%. Indicated on the left is a simulation with an initial MFR of 50% and a maximal CPR of 100%. On the right side a simulation with an similar initial MFR of 50% but a maximal CPR of 50% is indicated.

duration of infertility, and with the skill of the individual surgeon or IVF center. To calculate exactly all these variables prohibitively large datasets would be necessary. In the absence of these comprehensive data, reproductive surgery will emphasize CPR because after surgery women can conceive each consecutive month. IVF on the contrary emphasizes the pregnancy rate of each IVF cycle which is the MFR. The CPR of IVF treatment is less clear as this comprises also the counselling to continue or to discontinue treatment. Therefore the comparison of the results of IVF and of reproductive surgery is often like a discussion using different languages.

A comparison of the results of IVF treatment and of reproductive surgery is intellectually attractive. Clinically, however, it is important to take into account the approach and sequence of diagnosis and treatment of infertility.

IVF

IVF has become a very successful treatment and the MFR's for most indications are well known. However, the decreasing MFR during subsequent attempts and the ultimate CPR's are less documented. Discontinuation of IVF treatment can occur for many reasons varying from the cost and effort of an IVF cycle, to poor responders, couples with a poor fertilization and/or with a reduced prognosis for other reasons such as age. For these reasons the CPR or the percentage of women that become pregnant out of those that started IVF is rarely available in the literature. The ultimate CPR cannot be predicted from the MFR. The CPR will vary with the indication and increases when IVF is used more liberally in younger women. To the best of our knowledge the real CPR of IVF rarely exceeds 60%–80%.

The clinical sequence of diagnosis and treatment

One of the clinical questions in women with infertility in the absence of a male factor is whether and when a diagnostic laparoscopy should be performed during the infertility work-up. Indeed many causes of infertility as mild endometriosis and severity and extend of adhesions can only be diagnosed by laparoscopy. Therefore the necessity to resort to a laparoscopy is obvious in all women with pelvic pain and/or a history of pelvic surgery. However, in asymptomatic women with infertility a

diagnostic laparoscopy is a calculated risk and thus based on clinical judgment. In the absence of any pathology it may be considered overtreatment; however, in those with a pathologic finding treatment can be carried out during the same intervention and saves the patient valuable time. Some infertility groups will prefer an early laparoscopy in order not to lose time while others will try to postpone a laparoscopy as long as possible in order to avoid a laparoscopy in normal women. As a balance we suggest that a diagnostic laparoscopy and hysteroscopy should be performed in all women with an infertility of > 2 years in order not to miss easily treatable disease especially in older reproductive women, and in order to avoid unnecessary IVF.

This diagnostic laparoscopy and hysteroscopy performed in such women permits to make a diagnosis. Some women need surgery for gynecologic reasons other than infertility such as those with severe pain and cystic or deep endometriosis, or with a symptomatic myoma or a frozen pelvis. A second group are women in whom surgery seems indicated beyond a reasonable doubt, such as those with an endometrial polyp, a submucous myoma, a severe uterine septum, with superficial pelvic endometriosis or with filmy adhesions around the oviducts, ovaries or the ampulla. A third group are women in whom surgery can be considered controversial such as ovarian drilling in polycystic ovaries, deep endometriosis without pain, cystic ovarian endometriosis of <2 cm in diameter, and women with severe tubal disease. If the surgeon has the proper skills, surgery can be performed during this diagnostic laparoscopy, hence it is certainly preferable for such intervention to be carried out in a properly equipped center. As for IVF, comprehensive data describing MFR's and CPR's following each type of surgery for each degree of severity do not exist because of the inherent variability. The best data available are a CPR of 50%–60% after 1 year after surgery for ovarian endometriosis.

When surgery is necessary for gynecologic reasons other than infertility, the indication is beyond discussion. When in asymptomatic women the indication for surgery is only infertility as for reconstructive surgery for tubal occlusion, the results of surgery and of IVF should be balanced^[1,2]. This extreme situation of asymptomatic women in whom surgery has a poor prognosis, however, is rare. The clinical reality remains that in most women undergoing surgery either the preservation of fertility is important or they have gynecologic symptoms as pain or a pelvic mass together with their infertility.

After reproductive surgery over 90% of the subsequent spontaneous pregnancies occur within 6–12 months. This is compatible with the concept that after surgery fertility was restored close to normal while those who did not become pregnant, are likely to have had a reocclusion of the tubes. In such cases after a period of 6–12 months IVF should be advised. Surgery and IVF treatments for infertility therefore are complementary treatments in the large majority of women. However, surgery comes first especially when performed during the diagnostic laparoscopy.

If during diagnostic laparoscopy, surgery could not be performed because the expertise was not available, the expected results—MFR's and CPR's—of IVF should be balanced with the results of reproductive surgery followed by IVF. The CPR's of surgery and IVF indeed are obviously additive. An example are women with a thin-walled hydrosalpinx. It is well known that in these women salpingectomy increases the fertility rate of IVF treatment. In contrast, a salpingostomy performed in women without severe intratubal damage and without extensive

peritubal adhesions will add a 20%–50% spontaneous pregnancy rate to the overall CPR after the additional IVF treatment.

In conclusion, the comparison of the results of reproductive surgery and of IVF/ART is the wrong debate. Clinical reality is the comparison of CPR over time following reproductive surgery + IVF versus IVF without reproductive surgery.

The reproductive surgeon

It is obvious that for the woman it is much preferable to have the surgical treatment performed during the initial diagnostic laparoscopy as it avoids a second intervention. This, however, requires a surgeon with sufficient clinical knowledge to recognize and assess the pathology and have the necessary surgical skills to perform the indicated surgery.

Reproductive knowledge comprises an estimation of the post-operative MFR and CPR for each type of surgery. Surgical expertise should be sufficient to recognize hidden pathology as deep endometriosis, to recognize and avoid extensive coagulation of pathologies as endosalpingiosis and to avoid eventual nerve damage. The reproductive surgeon should have the skills to perform surgery without or with minimal damage to tubes, ovaries and ovarian reserve, and with minimal postoperative adhesion formation. Deep endometriosis excision should be sufficiently complete also when surrounding the ureter and penetrating the bowel wall. The required expertise and skill raises the delicate question of quality of surgery including the prevention of postoperative adhesion formation. Today adhesions can fortunately be prevented with conditioning provided adequate surgical skills^[6,7].

The required combination of reproductive knowledge, expertise, and surgical skills is not obvious. Reproductive surgery is not mainstream surgery. It also raises the question of the surgical skills of fertility/IVF specialists and of reproductive knowledge of even excellent endoscopic surgeons.

Mistakes of reproductive surgery and of IVF

Inadequate reproductive surgery ranges from absence of diagnosis, wrong indications, ovarian damage, decreased follicular reserve to postoperative adhesions causing infertility. As this (mechanical) infertility is an indication for IVF, a potential vicious circle emerges.

IVF without a diagnosis/diagnostic laparoscopy risks causing problems. Besides the many missed diagnoses and the many opportunities of a spontaneous pregnancy, IVF with a rectovaginal nodule can make endometriosis worse with subsequently a frozen pelvis and very difficult surgery (P.R. Koninckx et al^[8], personal communications, 2016). Alternatively a not-treated deep endometriosis nodule may result in bowel perforations during pregnancy^[9].

The resulting costs for society and the emotional pressures for the patient are obvious and beyond this manuscript.

Conclusions

Training in reproductive surgery has been a concern for many years^[1,2]. Laparoscopic training in endoscopic surgery remains a worldwide difficulty if judged by the still limited percentage of total laparoscopic hysterectomy. Training in reproductive surgery constitutes an even bigger problem because of the technical difficulty of deep endometriosis surgery together with the limited number of

severe interventions in reproductive medicine. Also the alternative of training deep endometriosis surgeons in reproductive medicine and in quality surgery is not obvious. This difficulty resulting in a decline in the training and quality of reproductive surgery is moreover fuelled by subspecialty programs. Most fertility centers have become IVF centers without complete reproductive surgery which ranges from minor surgery to the very severe deep endometriosis surgery. Most fertility centers indeed do not have the number of interventions required to maintain training in advanced surgery. They, however, want to maintain minor surgery as most gynecologists like to do surgery. This indeed was their motivation to become an OBGYN. Unfortunately also minor surgery requires adequate training in order not to damage the reproductive organs and to avoid postoperative adhesions, which can become a cause for infertility.

Considering the difficulty of training in reproductive surgery resulting in a very variable quality, it might be useful to organize a quality control of reproductive surgery. We therefore suggest that video-registration^[10,11] should become mandatory, at least for recognized centers of excellence in endometriosis or reproductive surgery. As discussed, video-registration is the only way to assess indication and quality of surgery in the individual women. The possibility of subsequent evaluation is expected to increase quality as reproductive surgical skills and indication and difficulty of surgery will become better balanced albeit by auto-regulation. The impact of a having excellent reproductive surgery readily available to patients, similar to the availability of IVF would increase CPR in women with infertility and decrease the overall cost for society and/or the health care and/or for the patients themselves should not be underestimated.

Conflict of interest statement

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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