

Rationale of first-line endoscopy-based fertility exploration using transvaginal hydrolaparoscopy and minihysteroscopy

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ABSTRACT: The transvaginal access for exploration of tubo-ovarian function in women with unexplained infertility has been revived since transvaginal hydrolaparoscopy (THL) was introduced in 1998. One prospective double-blind trial and several reviews have validated the diagnostic value of THL in comparison with laparoscopy for the exploration of women with unexplained infertility. A review of the recent literature confirms the efficacy and safety of the technique for first-line endoscopy-based exploration of fertility. The standard policy of 1-year delay for laparoscopic investigation in unexplained infertility is challenged. In older women and particularly in women experienced in fertility awareness methods, THL and minihysteroscopy can be performed after a waiting period of 6–12 months.

Key words: female infertility / laparoscopy / endometriosis / adhesions / surgery

Introduction

The investigation of the infertile couple by hysterosalpingography and laparoscopy and also the timing of the investigation are currently highly debated issues. The purpose is to review the rationale for a one-stop, endoscopy-based exploration including transvaginal hydrolaparoscopy (THL) in combination with minihysteroscopy and a chromopertubation test as the first-line investigation.

Culdoscopy

The first successful technique for endoscopic visualization of the pelvic organs was culdoscopy introduced in the early 1940s by Decker (1952). However, the knee–chest, or genupectoral position, was uncomfortable and the procedure was uncomfortable for both the patient and physician. Laparoscopy introduced in the 1960s became the standard method for gynecologic endoscopy, particularly when it became widely used for surgical procedures such as tubal sterilization (McCann and Cole, 1978). However, pioneers of pelvic endoscopy, such as Palmer (1974) in Europe and Diamond (1978) in the USA, continued to promote culdoscopy as the method of choice in at least one special application—namely, the diagnosis of infertility. The transvaginal access provides a closer, clearer and more detailed view of the ovaries, Fallopian tubes and surrounding pelvic structures. Diamond published in 1978 a personal series of 4000 outpatient procedures of diagnostic culdoscopy in infertility with a low rate of failures

and complications. Fimbrial phimosis and perifimbrial adhesions were more readily detected. Endometriosis and adhesions could be detected on all the surfaces of the ovary, the distal end of the tube, the lateral pelvic wall, the utero-ovarian and uterosacral ligaments and even in locations revealed with difficulty or not at all by laparoscopy. In particular, culdoscopy revealed the fine, filmy adhesions that are only rarely picked up by laparoscopy, but may be responsible for a significant amount of ovarian and tubal malfunction. Diamond (1978) advised that the technique should be returned to gynecologic training programs and he concluded: ‘True, culdoscopy requires laboriously won special skills, but its advantage to patient and physician are well worth the trouble. Once mastered, culdoscopy endows the gynaecologist with a rapid and minimally traumatic outpatient technique that supplies rich information not only in the initial diagnosis of infertility but also in circumstances where laparoscopy might be inappropriate’. However, the technology of laparoscopy continued to advance. Some improvements were suggested, such as dorsal decubitus (Mintz, 1987), hydroflotation (Odent, 1973) and miniculdoscopy (van Lith *et al.*, 1997), but failed to revive the interest in culdoscopy.

Transvaginal hydrolaparoscopy

In 1998, the Leuven group (Gordts *et al.*, 1998a) described THL for exploration of the pelvic exploration of infertile patients without obvious pelvic pathology. The technique uses the transvaginal route,

the patient lies in dorsal decubitus and access to the pouch of Douglas is achieved by a culdocentesis technique using a combined Veress needle-trocar system (Fig. 1). In this way, the new technique adds the benefits of hydroflotation to the closer, clearer and more detailed view of the Fallopian tubes and ovaries achieved by culdoscopy.

THL also differs in several ways from the standard laparoscopy. First, the use of the Veress needle as a trocar for insertion of the optic avoids the blind trocar insertion. Secondly, the use of a saline solution for distension avoids the side effects of a CO₂ pneumoperitoneum. Thirdly, the transvaginal access provides the optimal angle for full inspection of the tubo-ovarian structures. Finally, several steps required at laparoscopy, such as gas insufflation, Trendelenburg position, insertion of a second trocar and manipulation and rotation of the tubo-ovarian structures for full inspection, are avoided.

Most of the surgeons currently provide THL in an ambulatory or 1-day care unit with conscious sedation. The same facilities as used in the IVF egg-retrieval procedure are required. The supplementary cost of the THL is the trocar puncture system and the operative sheet which cost around 2000–2500 € (excl. telescope) and are reusable. The total cost is related to the local variables, such as country, hospital admission and anesthesia.

Risks and complications of THL

The data of recent studies published since 2005 on access and complications of THL are summarized in Table I. They confirm the safety of the technique. Access is achieved in more than 90% of the patients. In a review of 4232 procedures from 10 studies, bowel injuries occurred in 0.61%. In a multicenter study, the incidence of bowel

perforation was 0.65% and decreased to 0.25% after an initial learning experience of 50 THL procedures: 92% of these bowel injuries were managed expectantly without consequences (Gordts *et al.*, 2001; Shibahara *et al.*, 2007). No major complication of vessel damage has been reported. The most common contraindications include obliteration of the cul-de-sac, fixed retroverted uterus and deep rectovaginal endometriosis (Mgaloblishvili *et al.*, 2007).

Transabdominal ultrasound has been proposed to guide the vaginal access to the peritoneal cavity (Sobek *et al.*, 2008). Ma *et al.* (2012) found that the technique was particularly useful in women with retroverted uterus.

Comparatives studies of THL versus laparoscopy

Table II summarizes the results of studies that have evaluated the value of THL in comparison with current methods of investigations in women with unexplained infertility. Comparative studies of THL and laparoscopy show grossly similar findings for adhesions, tubal lesions and endometriosis for the two techniques. Obviously, bladder endometriosis cannot be detected by the rigid endoscope, but on the other hand, THL facilitates the detection of endometriotic adhesions in the fossa ovarica and small endometriomas which were not detected by transvaginal ultrasound examination. A prospective double-blind comparative study showed that the interobserver agreement on endometriosis and tubal lesions is comparable for both techniques, but for adhesions is greater at THL than at laparoscopy (Brosens *et al.*, 2001).

Cicinelli *et al.* (2001) showed that THL with minihysteroscopy was better tolerated than a hysterosalpingogram (HSG) and revealed more information. THL was also found to be an inexpensive and safe outpatient procedure to exclude benign tubal spasm and confirm the presence of true occlusion at hysterocontrastsonography (Ahinko-Hakamaa *et al.*, 2009).

Khouri and Magos (2005) calculated and compared the costs for laparoscopy under general anesthesia and culdoscopy under local anesthesia and found that out-patient investigation in a one-stop fertility clinic produced a saving of over £380 per case, or 28%, to the hospital compared with in-patient investigation. Most patients appreciated the need for a single hospital visit and the availability of immediate results.

Benefits of hydroflotation for pelvic inspection in women with subfertility

The technique of THL offers major advantages for accurate exploration of the tubo-ovarian structures in patients with subfertility. First, the tubo-ovarian structures are directly accessible and can be inspected without manipulation in their natural position. The fimbriae remain distended and the infundibulum with the mucosal folds is in most cases accessible for inspection. The accurate observation of the tuba-ovarian function by hydroflotation has been illustrated by the first direct visualization in the human of the ovum retrieval process at the time of spontaneous ovulation. In one patient with unexplained infertility, THL was timed on the evening at 6 p.m. on the day of the LH peak. THL allowed the observation of the pulsating

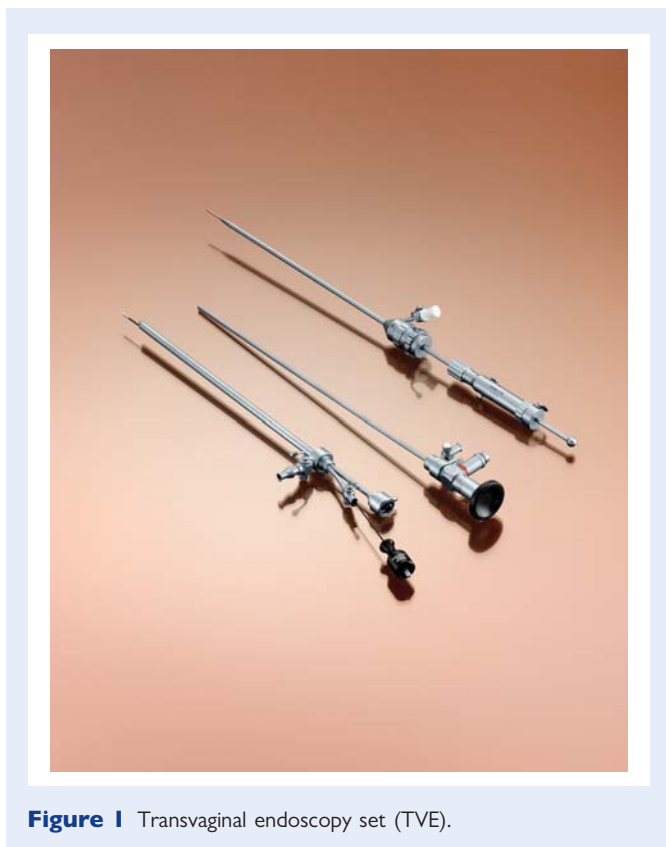


Figure 1 Transvaginal endoscopy set (TVE).

Table I THL in subfertile women without obvious pathology.

Author	Cases (n)	Access	Abnormality	Complications
Kissler <i>et al.</i> (2011)	239	99%	33.5%	0
Yang <i>et al.</i> (2011)	51	96%	47.9%	0
Pjevic (2010)	400	96%	47.5	0
Ahinko-Hakamaa <i>et al.</i> (2009)	56	91%		0
Sobek <i>et al.</i> (2008)	562	100%	30.5%	0
Van Tetering <i>et al.</i> (2007)	272	96%	56%	2 rectum 2 bleeding 1 suspected PID
Shibahara <i>et al.</i> (2007)	177			1.1
El-Shalakany <i>et al.</i> (2006)	22	95.5%	54%	0
Kowalczyk <i>et al.</i> (2006)	56	100%	57.2%	0
Tanos <i>et al.</i> (2005)	78	70–100%	49%	1 bowel 1 bleeding
Hu <i>et al.</i> (2005)	110	95.7%		0

PID, pelvic inflammatory disease.

Table II Controlled studies of THL in women with unexplained infertility.

Author	n	Access	Comparison with laparoscopy		
			A	T	E
Comparative studies of THL versus laparoscopy					
Nawroth <i>et al.</i> (2001)	43	93%	=	=	>
Dechaud <i>et al.</i> (2001)	23	95.7%	=	=	=
Takeuchi <i>et al.</i> (2001)	35	94.3	>	=	<
Darai <i>et al.</i> (2000)	60	90.2	=	=	=
Prospective studies of THL versus laparoscopy					
Campo <i>et al.</i> (1999): Comparable in accuracy to standard laparoscopy for the diagnosis of adhesions and endometriosis					
Brosens <i>et al.</i> (2001): More endometriotic ovarian adhesions and greater interobserver agreement at THL than laparoscopy					
THL versus hysterocontrastsonography					
Ahinko-Hakamaa <i>et al.</i> (2009): THL is an inexpensive and safe outpatient procedure to exclude benign tubal spasm and confirm the presence of true occlusion					
THL+mini-hysteroscopy versus HSG					
Cicinelli <i>et al.</i> (2001): THL combined with minihysteroscopy provides more information and is better tolerated than HSG in an outpatient infertility investigation					

A, adhesions; T, tubal lesions; E, endometriosis.

movements of congested fimbriae sweeping over the ovulatory opening as well as retrieval of the cumulus mass from the ovary (Gordts *et al.*, 1998b). Secondly, filmy pathological structures, such as free-floating adhesions or micropolypoidal formations on the surface of the ovary, which are collapsed during laparoscopy, can be

more accurately observed during THL than laparoscopy (Brosens *et al.*, 2001). The clinical significance of these ovarian micro lesions has to the best of our knowledge been investigated inadequately. Thirdly, the direct access to the infundibulum allows for accurate observation of the tubal mucosa and detection of mucosal adhesions, which are associated with pelvic inflammatory disease and increased risk of tubal pregnancy (Marana *et al.*, 2003). Finally, the microvascularization of the subtle peritoneal lesions, which is a typical result of the neoangiogenesis associated with endometriosis, collapses with pneumoperitoneum and is largely masked during laparoscopy but is clearly observed during THL. It is no surprise that in the current American Society for Reproductive Medicine classification system, the subtle peritoneal lesions are described by their color, but not by the presence and extent of angiogenesis. Further research may reveal whether or not the microvascularization of the peritoneal lesions is a useful parameter for defining endometriosis activity.

Significance of minimal and mild endometriosis in women with subfertility

Endometriosis has been a major argument to opt for an endoscopy-based rather than ultrasound-based fertility investigation. The main question is whether minimal or mild endometriosis is a potential cause of delay in conception and whether surgical treatment is effective. Several studies have investigated the significance of the presence of mild endometriosis in infertility.

Akande *et al.* (2004) found in a follow-up study of a group of 192 infertile couples that the likelihood of pregnancy was significantly reduced in infertile women with minimal or mild endometriosis compared with those infertile women with a normal pelvis.

Abuzeid *et al.* (2005) investigated 315 infertile patients with early-stage endometriosis in comparison with a control group of 152

infertile patients and found significantly more fimbrial pathology including agglutination, phimosis and blunting in the endometriosis group. The author suggested that the relationship between the fimbrial pathology and early-stage endometriosis deserved further endoscopic studies.

The results of the Canadian Collaborative Group on endometriosis (Marcoux *et al.*, 1997) support the view that the diagnosis and treatment of minor endometriosis in an early stage of subfertility is beneficial. The study involved 341 infertile patients with minimal and mild endometriosis who were randomized to laparoscopic ablation or expectant management. In the ablation group, the cumulative fecundity rate after a follow-up period of 36 weeks was 30.7 versus 17.7% in the no treatment group.

A similar randomized Italian study involving 101 patients found no difference in fecundity rates after a follow-up period of 1 year (Parazzini, 1999). A meta-analysis of the data of both randomized controlled trials showed that surgical treatment is more favorable than expectant management (odds ratio for pregnancy 1.7; 95% confidence interval 1.1–2.5) (Olive and Pritts, 2002).

After a meta-analysis of pregnancy outcome in IVF patients, Barnhart *et al.* (2002) concluded that patients with endometriosis of any stage should be referred for early aggressive infertility treatment, including IVF, to increase chances of conception. The data are in line with view of Dmowski *et al.* (1997) that the diagnosis of mild endometriosis is still unduly delayed in many patients with infertility.

Transvaginal endoscopy as the first-line investigation in subfertile women

Several studies have suggested that the optimal management of infertility requires an early and accurate evaluation of the reproductive tract, including uterine cavity, tubal patency and tubo-ovarian structures (Capelo *et al.*, 2003; Oliveira *et al.*, 2003; Tanahatoc *et al.*, 2003). It is no surprise that at present, HSG is challenged by more advanced ultrasound- or endoscopy-based approaches (Kelly *et al.*, 2001; Gordts *et al.*, 2002) such as transvaginal hydrosalpingography and THL. It remains, however, to be proven whether the use of any of the new techniques is cost-effective and whether the interventions are effective in improving pregnancy rates. Although equivalence or superiority of THL versus HSG as the first-line investigation in infertile women has not been demonstrated, the diagnosis of disorders like endometriosis is important as its presence infers increased risk of major obstetrical disorders (Brosens *et al.*, 2012).

Today, the exploration of female reproductive organs, which traditionally includes as the first step hysterosalpingography and at a later stage transabdominal laparoscopy, can be achieved as a one-step investigation by office transvaginal endoscopy combining minihysteroscopy, THL, a chromopertubation test and, in selected cases, such as sequelae of pelvic infection, salpingoscopy. This approach provides, in a single procedure, the most accurate and complete information of the reproductive organs and is performed as a one-stop office investigation under local anesthesia or conscious sedation (Gordts *et al.*, 1998a). Therefore, transvaginal endoscopy is intended to replace hysterosalpingography as a first-line investigation, and to avoid diagnostic laparoscopy in infertile patients without

obvious pelvic pathology. In addition, transvaginal endoscopy has the benefit to restore in the infertile patient the normal stratification of a surgical procedure, which proceeds from diagnosis to accurate information of the patient and to perform the surgical procedure after informed consent. In the case of pathology, the findings can be viewed and discussed with the patient before surgery is performed.

Timing the subfertility investigation

The duration of subfertility, or the time to conception, is at present a major parameter for timing routine exploration and starting treatment. It has been assumed that the longer the interval, the lower is the probability of conception, and therefore investigations should normally not start before 1 year of infertility (van der Steeg *et al.*, 2005). On the other hand, a prolonged duration of infertility is also an indication for the use of assisted reproduction technology (ART). The need for routine investigation of the female subfertility has been questioned. Therefore, current practice may paradoxically favor both under- and overuse of ART.

Recent prospective studies on fecundity have shown that human beings may be more fertile than has previously been estimated (Parazzini, 1999; Barnhart *et al.*, 2002; Olive and Pritts, 2002). Brosens *et al.* (2004) proposed that in view of the availability of less invasive and more accurate diagnostic tools and effective treatments, our current approach in timing the exploration of female infertility needs to be revisited. The issue is no longer when an invasive and expensive procedure, such as laparoscopy, should be performed but at which stage a comprehensive minimally invasive fertility investigation should be performed in order to respond with an accurate diagnosis to the question of the couple who worries about the delay in pregnancy. More than ever, the timing needs to be individualized depending on factors such as age, medical, menstrual and sexual history, previous experience with contraceptive methods, use of fertility awareness method for conception and other individual factors. With the progress in minimally invasive exploration, the decision of timing the fertility investigation depends, as for other medical disorders, in the first instance not on an abstract duration in time, but on the rational demand of the woman who worries about the delay of conception.

In older couples, the question arises whether laparoscopy can be omitted from the infertility work-up when the hysterosalpingography is normal and there is no abnormal contributing history. It is assumed that hereby the cost of fertility treatment is reduced without compromising success rates (Fatum *et al.*, 2002). However, some diseases such as pelvic adhesions and endometriosis are more frequently found in older women and apparently, there is no unique pattern of infertility diagnosis in older women (Balasch *et al.*, 1992; Balasch, 2000). This supports the view that the method of investigation of infertility should not differ based on the age of the patient. Women should be informed that the chance of a live birth following IVF is significantly decreased after the age of 35 years, and is <10% after the age of 40 years. On the other hand, after surgical treatment, as shown in well-selected cases of tubal infertility, such as reversal of tubal sterilization, the results may be surprisingly good in women after the age of 40 years.

Table III Ovarian capsule drilling during THL in anovulatory women with polycystic ovaries.

	<i>n</i>	Lost	Ovulatory	Pregnancy ^a	Complications
Fernandez <i>et al.</i> (2001)	13		46%	71% at 6 months	0
Casa <i>et al.</i> (2003)	28		66.7%	76% at 6 months	1 laparoscopic conversion
Fernandez <i>et al.</i> (2003)	80		91%	60%	0
Gordts <i>et al.</i> (2009)	39	6		81%	0
Poujade <i>et al.</i> (2011)	77	3		33.7%	5 laparoscopic conversion

^aExcluding IVF.

The current definition of subfertility as 1 year of unprotected intercourse without conception can be challenged as being valid for all populations. In selected groups of patients, it seems justifiable to investigate female as well as male fertility at an early stage of subfertility such as women using the vulvar mucus symptom or the LH peak day for timing intercourse (Keulers *et al.*, 2007; Brosens *et al.*, 2009). Postponing the investigation 1 year in women using fertility awareness methods can be regarded as undertreatment.

Ovarian surgery at THL

A recent advance in infertility surgery in THL has been the ovarian capsule drilling in women with clomiphene citrate-resistant polycystic ovary syndrome. The preliminary results suggest that capsule drilling by bipolar coagulation can be safely performed during THL (Table III). The majority of patients became spontaneously ovulatory and achieved pregnancy spontaneously or after ovarian stimulation. Experimental work in a porcine model suggests that monopolar drilling causes more tissue damage than the bipolar needle in saline (Ma *et al.*, 2010).

The feasibility of transvaginal reconstruction of the ovarian endometrioma has also been demonstrated (Gordts *et al.*, 2000). The transvaginal technique facilitates the access to the site of inversion and adhesion in the ovarian fossa and, in contrast with the fenestration and drainage technique, ablative surgery is carried out under hydrofloatation inside the distended cystic cavity allowing clear visualization of the tissues and performance of atraumatic reconstructive surgery (Brosens *et al.*, 2001).

Conclusion

Infertility is a distressing condition where the prolonged waiting period without diagnosis and appropriate counseling is frequently a source of depression and a risk of inappropriate or excessive treatments. A review of the current literature shows that the minimally invasive techniques of THL and mini-hysteroscopy are efficient and safe for pelvic exploration and can replace the traditional techniques of hysterosalpingography and laparoscopy. They allow for full investigation of the reproductive tractus in an out-patient setting. Therefore, the current policy of 1-year delay before the pelvic structures are fully investigated can be challenged. Infertility of 6 months duration in the older woman with unexplained infertility or in the woman using fertility

awareness methods is an indication for exploration by THL and minihysteroscopy.

Authors' roles

I.B. contributed to (i) the conception and design and analysis and interpretation of data, (ii) drafting the article and (iii) approval of the version to be published; R.L.W. initiated the concept, contributed on the writing and illustration and approved the final text.

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