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## Reassessment of the laparoscopy role in the investigation of infertility and treatment plan determination

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### ABSTRACT

**Objective:** To reassess the importance of laparoscopy in infertility investigation treatment plan determination. **Methods:** The study enrolled 237 patients with infertility duration > 1 year. A complete investigation was performed in all patients and male factor was evaluated by medical history and semen analysis. In the case of normal semen or mild-to-moderate oligozoospermia, the female evaluation included screening for infection diseases, transvaginal ultrasound, hormone parameter, hysterosalpingography, and laparoscopy. The final treatment plan was decided according to laparoscopy findings and any modification of the initial proposal was taken as treatment change. **Results:** At laparoscopy, normal pelvic cavity was found in 5.5%, endometriosis in 76.4%, pelvic adhesion in 17.2%, ovarian adhesion in 24.8%, peritubal adhesion 15.2%, unilateral tubal occlusion in 21.1%, bilateral tubal occlusion in 5.5%, and tubal sacculation, kinking, constriction, or fibrosis in 46.3%. Operative interventions during laparoscopy were endometriosis ablation/excision (74.6%), adhesiolysis (27.4%), and endometrioma cystectomy (4.6%). Laparoscopy determined to switch the initial treatment plan in 85 (35.8%) patients. **Conclusions:** Pelvic cavity abnormalities, primarily endometriosis, have high prevalence in infertile Brazilian women. Laparoscopy provides a precise diagnosis of tuboperitoneal factor and may switch the initial treatment plan in at least one third of patients.

## 1. Introduction

Abnormal tuboperitoneal factor at laparoscopy in all infertile women ranges from 35.0% to 83.0% and from 48.0% to 87.0% in the group assigned as unexplained infertility[1,2]. Endometriosis is found in 4.5%–82.0% of women with chronic pelvic pain, and in 2.1%–78.0% of infertile women[3,4]. Nevertheless, its prevalence depends on the patient profile and diagnostic tool utilized. Since the prevalence of endometriosis is 6–21 times higher in infertile as opposed to fertile women[5,6], several possible pathophysiological mechanisms are proposed to explain this association[7]. Because there is no agreement in published data concerning the need of laparoscopy to establish a

correct diagnosis before any treatment for infertility is planned, further studies are needed[8–11]. Unfortunately, instead of stimulating more investigation, several guidelines have recommended not to perform laparoscopy as a routine procedure to diagnosis of tuboperitoneal factor in infertile women[12–14]. However, in addition to provide a more precise diagnosis of the pelvic cavity condition, laparoscopy allows staging of the endometriosis when it is present[15,16], and even after normal hysterosalpingography, abnormal laparoscopic findings have been shown in 26.8%–87.2% of infertile women, mainly peritubal adhesions[10,11].

In the clinical setting, the selection of an appropriate infertility treatment plan, varying from ovulation induction plus timed intercourse to controlled ovarian hyperstimulation and *in vitro* fertilization will depend on woman's age, and nature and severity of the abnormal findings. Scarce evidence supports the use of ovarian suppression agents in the treatment of endometriosis-associated infertility[17], particularly in minimal and

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mild stages<sup>[12–14]</sup>. As some studies have demonstrated improvement in fertility rate in patient with endometriosis stages I and II treated by low complexity procedures, it is possible that some variables associated with pelvic endometriosis, such as tubal kinking, fibrosis, degree of pelvic vascularization or inflammatory reaction should be considered before initial treatment decision<sup>[19]</sup>. In addition, it was also demonstrated that small surgical procedures performed during laparoscopy may increase fertility rate more than laparoscopy alone even in the initial stages of endometriosis<sup>[10,13,14,20–22]</sup>. As it assures a forth fold increase in the pregnancy rate, medical treatment with GnRH analogue for 3–6 months is recommended before *in vitro* fertilization<sup>[14,18]</sup>. The reason for this different approach in not considering ovarian suppression before IUI, or other less complex treatments is not fully clear yet.

Current controversies on the use of laparoscopy as a routine procedure in infertility investigation had begun after publication of the only two randomized controlled trials on this matter, comparing fertility rates in women with minimal–to–mild endometriosis after laparoscopy alone or laparoscopy plus surgical ablation<sup>[8,9]</sup>. Both reported inconsistent results. Two other randomized clinical trials reporting on the use of ovarian stimulation with IUI in infertile women with minimal or mild endometriosis at laparoscopy showed better pregnancy rates with this treatment<sup>[10,20]</sup>. Despite the number of studies demonstrating the importance of laparoscopy for precise diagnosis and establishment of an optimal treatment plan for infertility women<sup>[10,16]</sup>, due to the costs, risks, and inconsistent improvement in fertility rates observed in some studies<sup>[20]</sup>, the use of laparoscopy in infertility management remains debatable. In fact, there is insufficient evidence to support or deny the positive effect of surgical treatment of endometriosis in early stages. Because lack of a definitive recommendation, the aim of this study was reassess the importance of laparoscopy in infertility investigation and its role in determining change in the initial treatment plan.

## 2. Material and methods

The study enrolled 237 infertile patients who attended the Tropical Institute of Reproductive Medicine and Menopause, Cuiabá, MT, Brazil, from August 2008 to August 2011. After approval by the local Committee for Ethics in Research, informed consent was obtained from each patient. The sample size was calculated assuming a prevalence of tuboperitoneal factor of 35%, precision of 80%, and a confidence of 99%. The inclusion criterium was infertility duration >1 year; exclusion criteria were severe oligozoospermia (<10×10<sup>6</sup> mobile spermatozoa) or azoospermia. All the patients underwent a full infertility investigation after the initial visit. Male factor was evaluated

by medical history and semen analysis. In the case of normal semen, or mild–to–moderate oligozoospermia, the female evaluation included screening for infections disease, transvaginal ultrasound, hormone parameter, hysterosalpingography, and laparoscopy. Laparoscopy was performed in all patients under general anesthesia by two of the authors (SFM, MMWY). The primary outcome measures of laparoscopy was verify its ability in changing the initial treatment plan. Other outcomes of interest were to assess the tube patency, tubal sacculation, tubal obstruction, fibrosis or tubal constriction, peritubal adhesions, pelvic adhesion, and peritoneal or ovarian endometriosis. Tubal patency was tested by methylene blue dye and the results were compared with those obtained with hysterosalpingography.

When necessary, adhesiolysis, excision or electroablation of endometriotic implants, and endometrioma cystectomy were performed. Surgical procedures performed during laparoscopy, or use of GnRHa to decrease inflammatory tubal or pelvic processes, were not considered as change in initial treatment plan by themselves. Nevertheless, the final treatment plan was decided according to laparoscopy findings and any modification of the first proposal was considered as treatment change, as follows: (1) if no abnormalities were found the infertility was assigned as unexplained and the patient was treated as planned before laparoscopy; (2) if endometriosis or other structural abnormalities were found, direct surgical treatment was performed, but the case was taken as change in treatment plan only whether the initial method of assisted conception was changed; (3) patients who had moderate or severe endometriosis associated with high pelvic inflammatory reaction, increased peritoneal fluid, tubal edema, or tubal sacculations were submitted to proper surgical procedure and complemented by GnRHa for at least three months. All these patients had changed the initial treatment plan and treated by ovulation induction plus intrauterine insemination instead of ovulation induction plus timed intercourse; (4) Patients with bilateral tubal occlusion, hydrosalpinx, filmy adhesion with enclosure of tubes and/or ovaries, or frozen pelvis, were treated by *in vitro* fertilization (IVF) or intracytoplasmic sperm injection; these case were considered as changed their initial treatment plan.

Data are presented in tables as percentages. When necessary they are described as median and 95% confidence interval.

## 3. Results

A total of 260 laparoscopy procedures were performed from September 2008 to December 2010 and 237 patients were eligible. Two hundred and six patients (86.9%) were Caucasian, 15 (6.3%) African descendants, and 16 (6.7%) of other races. The mean age was (31.6±4.6) years. Out of these

237 infertile patients, 161 (67.9%) had dysmenorrhea, 63 (26.5%) reported dyspareunia, and 86 (36.2%) presented with diarrhea or increased peristalsis movements. A history of abdominopelvic surgery was reported by 57 patients (24.0%). The average length of infertility was 2 years (95%CI: 1.5–3.0) for primary infertility and 3 years (95%CI: 2.0–13.0) for secondary infertility ( $P=0.499$ ).

There were no high-risk complication associated with surgical laparoscopy but two cases of deep bladder wall cauterization; one was resolved with Foley catheter kept open for two weeks postoperatively and the other required surgical procedure. The main findings on laparoscopy are displayed in Table 1. In 89 out of 237 patients (37.5%) hysterosalpingography and laparoscopy showed discordant results. In 26/237 patients (11.0%) tubal patency was not examined with the blue dye test because the finding of frozen pelvis in 4 and technical difficulties in 22 patients. The primary tube abnormalities identified were tubal sacculation 24/237 (10.1%) tubal sacculation with other abnormalities 46/237 (19.4%); tubal constriction, fibrosis anywhere along the tubes, tubal kinking or thickening of the tubal wall in 86/237 (36.2%), and peritubal adhesions in 36/237 (15.2%). Using methylene blue dye, bilateral tube patency was documented in 148/237 patients (62.4%), unilateral patency in 50/237 (21%), and bilateral tube occlusion in 13/237 (5.5%).

**Table 1**  
Pelvic cavity findings at laparoscopy in Brazilian infertile patients.

Findings	n (%)
Normal	13 (5.5)
Abnormal	224 (94.5)
Endometriosis	181 (76.4)
Stage I	93 (51.4)
Stage II	28 (15.5)
Stage III	40 (22.1)
Stage IV	20 (11.0)
Endometrioma	11 (4.6)
Pelvic adhesion	41 (17.2)
Ovarian adhesion	59 (24.8)
Peritubal adhesion	36 (15.2)
Tubal disease	173 (72.9)
Unilateral tubal occlusion	50 (21.1)
Bilateral tubal occlusion	13 (5.5)
Sacculation	24 (10.1)
Kinking, constriction, fibrosis	86 (36.2)

**Table 3**  
Change in initial treatment plan of infertile women after laparoscopy intervention.

First treatment plan	Final treatment plan	Number of changes	% of change
Ovulation induction plus timed intercourse	Ovulation induction plus IUI	61/237	25.7
Ovulation induction plus IUI	<i>In vitro</i> fertilization	22/237	9.6
<i>In vitro</i> fertilization	Ovulation induction plus IUI	2/237	0.8
Total of changes		85/237	35.8

<sup>a</sup>Surgical procedures at laparoscopy were not considered as treatment change.

Essential operative interventions during laparoscopy, some in combination, are shown in Table 2. Endometriosis ablation/excision was needed in 74.6% of patients. After laparoscopy, GnRHa was given for 3–6 months in 108 (45.5%) patients with endometriosis associated with an extensive pelvic inflammatory reaction or tubal abnormalities. Though laparoscopy surgical procedures have not been considered as change in treatment plan by themselves, laparoscopy has shown the need to switch the initial treatment plan in 85/237 (35.8%) (Table 3).

**Table 2**

Operative intervention during laparoscopy in Brazilian infertile women.

Intervention	n/N	%
Endometriosis ablation/excision	177/237	74.6
Adhesiolysis	65/237	27.4
Endometrioma cystectomy	11/237	4.6
Myomectomy	15/237	6.3
Ovarian drilling	15/237	1.7
Excision of dermoid cyst	3/237	1.2

#### 4. Discussion

The best treatment plan must be offered to infertile couple. The present study demonstrated that endometriosis is highly prevalent in Brazilian infertile women and that laparoscopy had the ability to change the initial management plan in at least one-third of the patients. This is especially important if one considers the high degree of anxiety within these couples and their dissatisfaction with unsuccessful treatment result. To reevaluate the still debatable opinion concerning the use of laparoscopy in infertility workup, the current study included an adequate sample size, reached a power of 80%, and followed a complete workup in infertility investigation. In addition to report the findings at laparoscopy, the study provided a clear definition of the abnormal conditions that motivated changes in intended initial treatment plan.

The high prevalence of pelvic abnormalities in the present study is in agreement with the prevalence of abnormal peritoneal factor between 17.0% and 94.7% reported in recent studies[2,10,20,23]. Worldwide endometriosis has been found in up to 63% of infertile women[10]. The presence of endometriosis in 76.3%, confirmed by biopsy in 74.6% of

patients included in the current study may be linked to the regional characteristics of the population included in the current study. One possible cause, not examined yet, is the possible environmental contamination with polychlorinated dibenzo-p-dioxin, an organochlorine widely used in this Brazilian region.

The inclusion of not commonly mentioned small tubal abnormalities such as tubal edema, kinking and constriction as part of endometriosis consequences explains the higher prevalence of abnormal tuboperitoneal factor in the current study. Though small, these findings suggest that inflammatory reaction also seen in the early stages of endometriosis may affect the Fallopian tube function and impair tubal mucosal architecture. This new observation may explain the increased fecundity rate seen in patients with minimal and mild endometriosis treated by ovulation induction plus IUI[8,11,24]. Large-scale randomized controlled trials are needed to measure the impact of these specific alterations in fertilization and pregnancy rate. It is also necessary to harmonize the basic knowledge of the mechanisms by which endometriosis causes infertility with the results of the treatments currently recommended as guidelines by several medical associations for infertile patients with endometriosis [12–15,21,22].

The prevalence of peritubal/perifimbrial adhesions and pelvic adhesions found in the current study is consistent with the prevalence of 5.5%–41.0% reported by others[2,11,25,26]. Adhesiolysis was performed at the time of laparoscopy in all cases. Though the current available information comparing fecundity rate after laparoscopic adhesiolysis with no treatment is scarce, it seems that surgical lysis of adhesion increases pregnancy rates[26]. The current study did not address this matter. It has also been shown that endometriosis lesion cauterization/ablation improves fertility rate even in minimal–mild endometriosis[8,12]. In the current study, this procedure was performed in 74.6% of patients but it was not assumed as a change in initial treatment plan by itself and the reproductive results were not considered. Even those who do not agree with routine laparoscopy in the investigation of infertility, do not deny the possibility that laparoscopic lysis of adhesion or pelvic endometriosis implants excision leads to higher fecundity rate[8,12,26]. Currently, the number need to treat minimal or mild endometriosis with resection or ablation to yield one additional pregnancy ranges from 8 to 12[8]. It must be considered however that this number depends on the prevalence of endometriosis and may be lower.

Small defects in the appearance of tubes are rarely mentioned in published studies. The percentage of these tubal abnormalities found in the current paper (46.4%) is higher than the findings of other study reporting tubal sacculatation, constriction, fibrosis, and kinking with segmentation[9], likely due to different inclusion criteria. Those authors excluded patients with prior pelvic surgery, history of pelvic infection, and signs or symptoms of endometriosis, and we did not. A definitive conclusion

concerning the use of ovarian suppressive agents to improve the pregnancy rate in these tubal/pelvic conditions is not possible at this time and requires further well-designed studies[12,27,28]. So, the impact of GnRH suppression on these small tubal abnormalities is being investigated by our group.

In the practice of infertility management, the impatience of the couple, stress of ineffective treatment, low pregnancy rate assured by some current treatments, and health care costs greatly influence the type of diagnostic tools and treatments selected. In the search for a precise diagnosis and optimum initial treatment plan, laparoscopy allows one to avoid unnecessary trials of unsuitable treatment. In the current study, at least 35.8% of the initial treatment plans were changed during or after laparoscopy intervention, therefore two out of three patients were benefit. Worldwide, laparoscopy has changed the initial treatment plan in 15.8%–60.0% of infertile patients, even after normal hysterosalpingography[10,29–32]. While some authors have considered modification in initial therapeutic plan only in those patients needing IVF, therefore excluding all surgical procedures performed during laparoscopy[10], others, like us, have considered to be a change in treatment plan any modification of the assisted conception technique proposed before the laparoscopy. When laparoscopic interventions are considered, the percentage of patients who had the initial management plan changed increases to 45%–60%[10,16,19,30].

It was concluded that abnormalities within the pelvic cavity, primarily endometriosis, had a very high prevalence in this infertile Brazilian population. The present study confirmed that laparoscopy provides a precise diagnosis of tuboperitoneal factor and may switch the initial infertility treatment plan in at least one-third of patients. However, standardization of what should be considered a change in initial treatment plan in infertility treatment after laparoscopy is much-needed. Because the cost of infertility treatment and inflicted stress of negative results no couple should be treated, even for a few cycles, if there is no certainty that the chosen treatment is the optimum one.

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### Conflict of interest statement

We declare that we have no conflict of interest.

### References

- [1] Tanahatoo SJ, Hompes PGA, Lambalk CB. Investigation of the infertile couple: should diagnostic laparoscopy be performed in the infertility work up programme in patients undergoing intrauterine

- insemination? *Hum Reprod* 2003; **18**: 8–11.
- [2] Jayakrishnan K, Koshy AK, Raju R. Role of laparohysteroscopy in women with normal pelvic imaging and failed ovulation stimulation insemination. *J Hum Reprod Sci* 2010; **3**: 20–24.
- [3] Mahmood TA, Templeton A. Prevalence and genesis of endometriosis. *Hum Reprod* 1991; **6**: 544–549.
- [4] Meuleman C, Vandenabeele B, Fieuws S, Spiessens C, Timmerman D, D'Hooghe T. High prevalence of endometriosis in infertile women with normal ovulation and normospermic partners. *Fertil Steril* 2009; **92**: 68–74.
- [5] Rawson JM. Prevalence of endometriosis in asymptomatic women. *J Reprod Med* 1991; **36**: 513–515.
- [6] Louis GMB, Hediger ML, Peterson CM, Croughan M, Sundaram R, Stanford J, et al. Incidence of endometriosis by study population and diagnostic method: the ENDO study. *Fertil Steril* 2011; **96**: 360–365.
- [7] Gupta S, Goldberg JM, Azziz N, Goldberg E, Krajcir N, Agarwal A. Pathogenic mechanisms in endometriosis-associated infertility. *Fertil Steril* 2008; **90**: 247–257.
- [8] Marcoux S, Maheux R, Berubé S. Laparoscopy surgery in infertile women with minimal or mild endometriosis. *N Engl J Med* 1997; **337**: 217–222.
- [9] Parazzini F. Ablation of lesions or no treatment in minimal– mild endometriosis in infertile women: a randomized trial. Gruppo Italiano per lo Studio dell'Endometriosi. *Hum Reprod* 1999; **14**: 1332–1334.
- [10] Tsuji I, Ami K, Miyazaki A, Hujinami N, Hoshiai H. Benefit of diagnostic laparoscopy for patients with unexplained infertility and normal hysterosalpingography findings. *Tohoku J Exp Med* 2009; **219**: 39–42.
- [11] Nakagawa K, Ohgi S, Horikawa T, Kojima R, Ito M, Saito H. Laparoscopy should be strongly considered for women with unexplained infertility. *J Obstet Gynaecol* 2007; **33**: 665–670.
- [12] Kennedy S, Bergqvist A, Chapron C, D'Hooghe T, Dunselman G, Greb R, et al. ESHRE guideline for the diagnostic and treatment of endometriosis. *Hum Reprod* 2005; **20**: 2698–7204.
- [13] United State Department of Health and Human Services. National Guidelines Clearinghouse. Endometriosis: Diagnosis and management; 2010.
- [14] College National of Gynecologies et Obstetriciens Français. CNGOF Guidelines; 2006.
- [15] Bosteels J, Herendael BV, Weyers S, D' Hooghe T. The position of diagnostic laparoscopy in current fertility practice. *Human Reprod Update* 2007; **13**: 477–485.
- [16] Kahyaoglu S, Kahyaoglu I, Yilmaz B, Var T, Ertas IE, Mollamahmutoglu L, et al. Should diagnostic laparoscopy be performed initially or not, during infertility management of primary and secondary infertile women? A cross-sectional study. *J Obstet Gynecol Res* 2009; **35**: 139–144.
- [17] Hughes E, Fedorkow D, Collins J, Vandekechhove P. Ovulation suppression vs. placebo in the treatment of endometriosis (Cochrane Review). In: *The cochrane library*; 1999.
- [18] Sallan HN, Garcia-Velasco JA, Dias S, Arici A. Long-term pituitary down-regulation before *in vitro* fertilization (IVF) for women with endometriosis. *Cochrane Database Syst Rev* 2006.
- [19] Corson SL, Cheng A, Gutmann JN. Laparoscopy in the “normal” infertile patient: A question revisited. *J Am Assoc Gynecol Laparosc* 2000; **7**: 317–324.
- [20] Capelo FO, Kumar A, SteinKampf MP, Azziz R. Laparoscopic evaluation following failure to achieve pregnancy after ovulation induction with clomiphene citrate. *Fertil Steril* 2003; **80**: 1450–1453.
- [21] Jacobson TZ, Duffy JMN, Barlow D, Farquhar C, Koninckx PR, Olive D. Laparoscopy surgery for subfertility associated endometriosis. *Cochrane Database Syst Rev* 2010.
- [22] American College of Obstetricians and Gynecologist. Practice bulletin; 2010.
- [23] Khawaja UB, Khawaja AA, Gowani SA, Shoukat S, Ejaz S, Ali FN, et al. Frequency of endometriosis among infertile women and association of clinical signs, and symptoms with the laparoscopic staging of endometriosis. *J Pak Med Assoc* 2009; **59**: 30–34.
- [24] Tummou IS, Ascher LF, Martin JSB, Tulandi T. Randomized controlled trial of superovulation and induction for infertility associate with minimal or mild endometriosis. *Fertil Steril* 1997; **68**: 8–12.
- [25] Abuzeid MI, Mitwally MF, Ahmed AL, Formentini E, Ashraf M, Abuzeid OM, et al. The prevalence of fimbrial pathology in patients with early stages of endometriosis. *J Minin Invasive Gynecol* 2007; **14**: 49–53.
- [26] Tulandi T, Collins JA, Burrows E, Jarrell JF, McInnes RA, Wrixon W, et al. Treatment-dependent and treatment-independent pregnancy among women with periaadnexal adhesions. *Am J Obstet Gynecol* 1990; **162**: 354–357.
- [27] Marcus SF, Edwards RG. High rates of pregnancy after long-term down-regulation of women with severe endometriosis. *Am J Obstet Gynecol* 1994; **171**: 812–817.
- [28] Hughes E, Brown J, Collins JJ, Farquhar C, Fedorkow DM, Vanderkerchove P. Ovulation suppression for endometriosis for women with subfertility. *Cochrane Database Syst Rev* 2007; **3**.
- [29] Tanahatoe SJ, Lambalk CB, Hompes PGA. The role of laparoscopy in intrauterine insemination: a prospective randomized reallocation study. *Hum Reprod* 2005; **20**: 3225–3230.
- [30] Tanahatoe S, Hompes PG, Lambalk CB. Accuracy of diagnostic laparoscopy in the infertility work-up before intrauterine insemination. *Fertil Steril* 2003; **79**: 361–366.
- [31] Cundiff G, Carr BR, Marshburn PB. Infertile couples with a normal hysterosalpingography. Reproductive outcome and its relationship to clinical and laparoscopy findings. *J Reprod Med* 1995; **40**: 19–24.
- [32] Lavy Y, Lev-Sagie A, Holtzer H, Revel A, Hurwitz A. Should laparoscopy be a mandatory component of the infertility evaluation in infertile women with normal hysterosalpingography or suspected unilateral distal tubal pathology? *Eur J Obstet Gynecol Reprod Biol* 2004; **114**: 64–68.