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Does Diagnostic Laparoscopy Have Value in Unexplained Infertile Couple? A Review of the Current Literature

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ABSTRACT

Context: Correct timing of diagnostic laparoscopy for unexplained infertility management remains as a debate for clinicians. A cost-effective strategy of diagnostic laparoscopy utilization for unexplained infertile patients is much needed.
Evidence Acquisition: Detailed evaluation of the articles extracted from a "Pubmed" and "Cochrane database" search using "unexplained infertility and diagnostic laparoscopy" word group between 1993 and 2012 was the preparation style of this review.
Results: Diagnostic laparoscopy should be considered when there are abnormal hysterosalpingography results, a past history of pelvic infection, pelvic surgery and/or unexplained secondary infertility during management of an unexplained infertile couple. Currently, omitting diagnostic laparoscopy following a normal hysterosalpingography in couples suspected to have unexplained infertility and proceeding with ovulation induction for several cycles before referring to assisted reproductive techniques are recommended. The additional value of diagnostic laparoscopy after a normal hysterosalpingography was found to be very low prior several attempts of intrauterine insemination. In the absence of pathological findings precluding fertility during an unexplained infertility evaluation, routine diagnostic laparoscopy for infertility evaluation is not necessary because 77% of these patients become pregnant following ovulation induction and/or assisted reproductive techniques treatment.
Conclusions: Omitting diagnostic laparoscopy after a normal hysterosalpingography in infertile patients with unexplained infertility and without risk factors for pelvic pathologies related to infertility is reasonable because the majority became pregnant after several cycles of ovulation induction, and/or assisted reproductive techniques treatment while diagnostic laparoscopy is indicated when pelvic endometriosis and/ or tubal pathology is strongly suspected.

▸ *Implication for health policy/practice/research/medical education:*
This article implicates correct timing of diagnostic laparoscopy for unexplained infertile couples. Readers who are interested in the management of unexplained infertility will benefit from this article.

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1. Context

Dealing with unexplained infertility (UI) is a challenge for clinicians involved in reproductive medicine. Despite evidence presented by current literature, it remains questionable as to whether a diagnostic laparoscopy should be performed prior making a treatment plan for those patients struggling with UI.

2. Evidence Acquisition

This review has been prepared following evaluating the articles extracted from a "PubMed" and "Cochrane database" search using "unexplained infertility and diagnostic laparoscopy" word group between 1993 and 2012. Good quality designed prospective, retrospective, meta-analysis and review articles have been selected based on their strict patient selection criteria for UI.

3. Results

By definition, UI is termed as infertility in which the cause of the fertility impairment cannot be detected by use of standard diagnostic measures like semen analysis, tests for ovulation and tubal patency (1-5) (Level II-2 for 2, Level III for 3-5). UI accounts for 20-40% of infertility after other obstacles like disturbances in endocrinology, immunology, genetics and reproductive physiology (6) (Level II-2) have been eliminated for those couples struggling to conceive. Exclusion of the other common causes of infertility including male factor, tubal insufficiency and anovulation establishes the diagnosis of UI, other factors such as fibroid tumours, endometriosis, unilateral tubal problems, mild male-factor infertility, immunologic causes, and genetic defects are all potential contributors to unexplained infertility (4) (Level III). However, when the tubal patency has been demonstrated by a hysterosalpingography (HSG), per tubal adhesions and/ or endometriosis can still exist and preclude conception. Patients with bilateral tubal disease should be offered either assisted reproductive techniques (ART) or microsurgery according to the patient's age and the extent of tubal disease but not diagnostic laparoscopy. The specific infertility cause must first be determined prior any decisions for intervention. The chance of a spontaneous live birth, success rates as well as costs and complications for different treatment modalities should be kept in mind when advising individualized treatment strategies offered to couples with UI. The value of diagnostic laparoscopy in current fertility practice is under debate.

There remains a great controversy about clinical utility of diagnostic laparoscopy among couples with UI as to whether this diagnostic tool affects the choice of the infertility treatment. Infertile couples ask for the most efficient treatment modality in the earliest time period and have little patience for potentially unnecessary surgeries or diagnostic measures that will take what they view as precious time during the infertility work-up. According to a meta-analysis conducted in 1995, tubal patency and peritubal adhesions can be estimated by HSG technique with a sensitivity of 65% and a specificity of 83% (7) (Level I). In 2001, Brosens I *et al.* compared transvaginal hydro laparoscopy (THL) with standard laparoscopy for detection of unexplained ovarian adhesions in patients with minimal and mild endometriosis and UI. They demonstrated that transvaginal hydro laparoscopy is superior to diagnostic laparoscopy especially for detection of subtle ovarian endometiotic adhesions that interfere with ovum capture and retrieval by the tubal fimbriae by creating an inflammatory environment (8) (Level II-2). In 2001 and 2002 respectively, Dechaud H *et al.* and Casa A *et al.* considered transvaginal hydro laparoscopy as an alternative procedure for evaluating female infertility in UI couples. When compared with diagnostic laparoscopy, diagnostic accuracy of THL was 40% and 92% within these two studies respectively (9, 10) (Level II-2). In 2002, Fatum M *et al.* suggested neglecting diagnostic laparoscopy after a normal HSG in couples suspected to have UI and they also recommended proceeding with ovulation induction for several cycles before referring to ART (11) (Level III). In 2003, Capelo FO *et al.* assessed the value of laparoscopic evaluation of the pelvis after failure to achieve pregnancy with clomiphene citrate usage for ovulation and they found that one third of these patients had significant pelvic pathologies that interfered with fertility potential (12) (Level II-2). They emphasized that pelvic pathologies found during diagnostic laparoscopy such as advanced stage endometriosis, pelvic adhesions complicating tub ovarian relationship and tubal disease affects a woman's chance to conceive spontaneously or by use of ovulation induction alone. Such findings influence the physician's treatment strategy and decrease the emotional stress and financial burden resulting from unnecessary and ineffective treatment plans decided upon before diagnostic laparoscopy results. The gold standard for evaluation of tubal patency is laparoscopic chromopertubation. Unlike the results of the study by Fatum M *et al.,* other studies demonstrated that laparoscopic evaluation of an unexplained infertile female pelvis is found to change the decision making process for the best and the quickest management plan like referring to ART when dense pelvic adhesions and/or tubal disease not amenable to treatment are encountered or performing surgical treatment of per tubal adhesions or endometriosis implants and/or endometrium's (11-13) (Level II-2). Following standard diagnostic evaluation procedures for infertility, approximately 20-30% of couples are found to have no identifiable cause for their infertility that is defined as UI (14, 15) (Level III). Diagnostic laparoscopy of these infertile women will probably lower this rate by determining the exact cause of infertility like per tubal adhesions, tubal disease and endometriosis (9, 10) (Level II-2). In 2009, a

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cost-effectiveness analysis of laparoscopy in women with UI was made by Moayeri SE *et al*. They found diagnostic laparoscopy a cost-effective component of infertility management in young couples with UI particularly when patients are likely to discontinue fertility treatments (16) (Level II-1). As intrauterine insemination (IUI) requires optimal conditions for ovum pick-up and transport mechanism for clinical efficiency to achieve a clinical pregnancy, diagnostic laparoscopy may be of value in confirming the functional tub ovarian integrity (15) (Level III). In 2003, Tanahatoe SJ *et al*. retrospectively evaluated the accuracy of diagnostic laparoscopy among patients with male subfertility, cervical hostility and UI before IUI with respect to pelvic pathologies found on laparoscopy leading to a change of treatment strategy (13) (Level II-2). The authors found abnormal findings on laparoscopy in 35% of patients and 25% of patients' treatment plan have changed after diagnostic laparoscopy. They assumed that omitting laparoscopy would probably lead to lower pregnancy rates, longer times to achieve pregnancy and more patients referred to ART treatments provided the change of treatment decision is effective following laparoscopy. In the same study, the additional value of diagnostic laparoscopy after a normal HSG was found to be very low for recommending laparoscopy before several attempts of IUI. In 2008, Tanahatoe SJ *et al*. investigated the additional value of diagnostic laparoscopy with respect to diagnosis and further treatment plan change to ART after an abnormal HSG retrospectively (17) (Level II-2). Only 29% of patients of whom laparoscopy results showed bilateral abnormalities precluding fertility potential were found to be referred to ART. In this study, the agreement between abnormalities found by HSG and laparoscopy was found to be poor. The authors recommended diagnostic laparoscopy after an abnormal HSG in the infertility treatment prior to making a decision for IUI or ART. These findings indicated that after an abnormal HSG, an infertile couple should not be made an ART candidate without visualisation of female pelvis for the pathologies impeding tub ovarian relationship by diagnostic laparoscopy (12, 13, 17) (Level II-2). When patients with unilateral tubal obstruction on HSG were considered, whether diagnostic laparoscopy should be made prior to IUI or delayed after several cycles of IUI still remains as a debate (17) (Level II-2). Contrarily, after a normal HSG, it is not cost-effective to proceed with diagnostic laparoscopy for an infertile woman without a history of pelvic surgery, pelvic inflammatory disease, a positive Chlamydia antibody test, endometriosis and unexplained secondary infertility (11, 16, 18) (Level III). These UI patients with normal HSG results should be treated with gonadotropins and IUI for 3-6 cycles before referring to ART as diagnostic laparoscopy has a relatively low contribution to the decision making process for UI patients with a normal HSG (16) (Level III). In 2007, Nakagawa K *et al*. strongly recommended diagnostic laparoscopy for UI patients because of the high rate of abnormal findings on laparoscopy (87%) (19) (Level II-2). In a cross- sectional study in 2009, Kahyaoglu S *et al*. evaluated the treatment strategy change after diagnostic laparoscopy for primary and secondary unexplained infertile patients. The rate of pelvic abnormalities related to infertility was found to be 60% and 69% among primary and secondary infertile patients that was reflected with a rate of 43% and 49% of treatment strategy change following laparoscopy respectively (20) (Level II-2). In 2010, in a prospective randomised controlled trial Badawy A *et al*. compared the clinical pregnancy rates of two groups of UI patients who have had and who have not had laparoscopy followed by ovarian stimulation and timed intercourse for six cycles. Based on the pregnancy rates among these two group of patients, the authors concluded that the diagnostic laparoscopy could be omitted for UI patients until ovarian stimulation and timed intercourse had been found to be successful for achieving pregnancy (21) (Level I). In a prospective study in 2012, Bonneau C *et al*. recommended diagnostic laparoscopic evaluation of female pelvis for UI patients during the infertility investigation by demonstrating a high rate of pelvic pathologies related to infertility (22) (Level II-2). In 2009, Goldman MB *et al*. investigated the role of diagnostic laparoscopy in couples treated for UI in the fast track and standard treatment (FASTT) trial. The pregnancy rates and time to establish a sustained pregnancy as the outcome measure were evaluated in this prospective randomised trial. They concluded that in the absence of pathological findings precluding fertility during an unexplained infertility evaluation routine diagnostic laparoscopy for infertility evaluation is not necessary because the majority of these patients become pregnant who proceed to ovulation induction and/or ART treatment. Sixty eight percent of the patients who have had a diagnostic laparoscopy conceived a sustained pregnancy when compared to 77% of patients who did not have diagnostic laparoscopy before fertility treatment ($P = 0.27$) (23) (Level II-1).

4. Conclusions

In conclusion, conducting an early diagnostic laparoscopy for specific unexplained infertile patients suspected of pelvic pathologies that preclude achieving pregnancy allows clinicians to examine an unexplained infertile female's abdominopelvic cavity and facilitates the decision making progress about infertility treatment strategy, with the added benefit of by maximizing time spent and reducing financial expenditure. However, based on the current literature, when the woman's HSG is normal, one cannot recommend laparoscopy as a first line diagnostic tool for infertility work-up due to lack of cost-effectiveness. Furthermore, diagnostic laparoscopy should be postponed until several ovarian stimulation and intrauterine insemination attempts had been found

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to be unsuccessful in achieving pregnancy. According to American Society of Reproductive Medicine (ASRM) diagnostic laparoscopy is indicated when there is evidence or strong suspicion of pelvic endometriosis, pelvic/adnexal adhesions, or significant tubal disease. Prior applying aggressive empirical treatments like ART, involving significant cost and/or potential risks to unexplained infertile patients, laparoscopy should be strongly considered (24) (Level III). However, the presence and absence of risk factors related to infertility does not always indicate a patient's need for diagnostic laparoscopy; it should be strongly considered by the clinicians when they encounter with an abnormal HSG result, a past history of pelvic infection, pelvic surgery and/or unexplained secondary infertility during management of an unexplained infertile couple. A laparoscopist should also be capable of performing operative procedures like adhesiolysis and endometriosis surgery during diagnostic laparoscopy especially for secondary unexplained infertile patients (20).

Omitting diagnostic laparoscopy after a normal HSG in infertile patients with UI and without risk factors for pelvic pathologies related to infertility is reasonable because the majority became pregnant after several cycles of ovulation induction, and/or ART treatment while diagnostic laparoscopy is indicated when pelvic endometriosis and/ or tubal pathology is strongly suspected. Based on the current literature, when HSG is normal, one cannot recommend laparoscopy as the first line diagnostic tool for infertility work-up due to lack of cost-effectiveness, so diagnostic laparoscopy could be postponed until several ovarian stimulation and intrauterine insemination attempts had been found to be unsuccessful in achieving pregnancy. Unfortunately, there are a few randomised controlled studies to investigate the value of diagnostic laparoscopy in unexplained infertile couples and the heterogeneity of published articles regarding pregnancy outcomes based on different follow- up durations of the patients. Diagnostic laparoscopy should be considered when there are abnormal HSG results, a past history of pelvic infection, pelvic surgery and/or unexplained secondary infertility during management of an unexplained infertile couple.

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Authors' Contribution

Data collection, selection, evaluation, design and concept of this article were accomplished by the author Dr. Serkan Kahyaoglu.

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