

# The role of hysteroscopy in the diagnostic work-up of infertile asymptomatic patients

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## Summary

**Purpose of investigation:** To demonstrate that office hysteroscopy has a key-role in the diagnostic work-up of infertile couples. **Materials and Methods:** The entire database of hysteroscopies performed in 572 menstruated women from 2008 to 2011, was retrospectively analyzed. A two-dimensional correspondence analysis among endometrial patterns, age ranges, and indication for hysteroscopies was made. A main-effect hierarchical log-linear model was built to assess the goodness of the correspondences found. **Results:** A clear cluster of aggregation appears in case of both primary and secondary infertility, with and without other indications for hysteroscopy, as well as in case of primary infertility with irregular menstrual bleeding. In such patients, chronic endometritis, normal pattern, and uterine malformations were frequently found. The most significant correspondence was found for normal pattern and chronic endometritis in case of secondary infertility and primary infertility, respectively. **Conclusions:** Office hysteroscopy should be reconsidered in the diagnostic work-up of infertile couples. It is able to assess or rule out endometrial factor for female infertility.

**Key words:** Hysteroscopy; Infertility; Asymptomatic women.

## Introduction

Infertility affects about 15% of couples worldwide [1,2]. The overall incidence of infertility has remained stable over the past decades [2]. Treatment options and success rates vary with the cause of infertility [3]. Infertile couples are usually advised to begin their investigations after 12 months of attempting to conceive or after six months if the female partner is more than 35-years-old or immediately if there is an obvious cause for their infertility or subfertility [4]. Since 1995, the preliminary advised investigations for the infertile couple have focused on semen analysis, detection of ovarian function by hormonal assay, and evaluation of tubal patency by hysterosalpingography or laparoscopy [5]. Currently there are no relevant differences that have been published concerning the guidelines for the basic evaluation of infertile couples. In fact, although hysteroscopy is the gold standard procedure for uterine cavity exploration, guidelines [6] recommend hysterosalpingography alone in the diagnostic work-up of infertile women. Hysteroscopy is only recommended when clinical or complementary exams (ultrasound, hysterosalpingography) suggest the presence of intrauterine abnormality or after in vitro fertilization (IVF) failure [7]. Moreover the effectiveness of removal intrauterine pathologies to improve the reproductive outcome is still under debate, even if some centres adopt the policy to perform hysteroscopy routinely in infertile patients [6, 8-10].

In 2010, a systematic review of Bosteels *et al.*, reported scarce evidence of the effectiveness of hysteroscopic removal

of uterine pathologies (endometrial polyps, sub-mucosal myomas, and intrauterine adhesions) or hysteroscopic metroplasty for improving fertility rate before IVF or intrauterine insemination (IUI) [11]. This review is limited to few randomized and controlled trials, and did not consider the effect of some other pathologies that may be involved in female fertility, such as endometritis, that was found to be associated to a wide number of female fertility problems [12, 13].

Thus the aim of this study was to assess, in a large number of cases, the most frequent findings in both asymptomatic and symptomatic patients that underwent hysteroscopic examination with a diagnosis of infertility in order to better define the role of hysteroscopy in the management of infertile women.

## Materials and Methods

Between 2008 and 2011, the hysteroscopic database of the Service of Gynecological Endocrinology and Physiopathology of Reproduction of the Institute of Obstetrics and Gynecology of Foggia, was analyzed. More in detail, the hysteroscopic reports and the relative indications for undergoing hysteroscopy of 572 menstruated patients were analyzed. As a policy of the Institute, patients with sonographic abnormal patterns of endometrial profile and patients with sub-fertility or infertility routinely underwent hysteroscopy, along with the ones with usual indications for hysteroscopy. Moreover the policy of “see and treat” of uterine pathologies in an office setting [14] and endometrial hysteroscopic biopsies were routinely performed. This extensive use of office hysteroscopy provides a better estimation of hysteroscopic findings in women with infertility, and was used to build a model of the likelihood for endometrial pathologies according with indications for hysteroscopy. Therefore, a number of patients analyzed

(106 out of 572) were symptomatic with or without sonographic abnormalities. Another part (77 out of 572) of patients were asymptomatic and had a normal sonographic examination.

The indications of hysteroscopy were summarized as following: primary infertility (without other indications for hysteroscopy), secondary infertility (without other indications for hysteroscopy), primary infertility with irregular menstrual bleeding, secondary infertility with irregular menstrual bleeding, primary infertility with other indications, secondary infertility with other indications, irregular menstrual bleeding (without infertility), and other indications (without infertility) (Table 1). Under "other indications" the following were grouped: abnormal sonographic endometrial patterns, presence of a cervical polyp, pap smear abnormalities needing to be addressed with an endocervical evaluation, and in case of vaginal polyp. Endometrial pattern retrieved were: normal pattern, endometrial polyp(s), cervical polyp(s), sub-mucosal myoma, chronic endometritis, cervicitis, uterine malformation(s), dysfunctional endometrium, malignancies, synechiae, vaginal polyp, and tubal micropolyps.

In order to check factors involving infertility that may condition endometrial patterns, the patients' age, and the polycystic ovary syndrome (PCOS) have been considered in the likelihood model. Unfortunately, no other causes of infertility were reported in the database, so no other causes of infertility were considered in the model.

Two-dimensional correspondence analysis was used to provide a perceptual map of the correspondence among indications for hysteroscopy and hysteroscopic findings, patients' age, and PCOS. The less far is the distance among the points in the map (hysteroscopy indications, PCOS, patients' age, and patterns points), the stronger was the correspondence found.

To control if the correspondence was significant, the main effect hierarchical log-linear model was built, assessing the behavior of standardized residuals. The behavior of standardized residuals indicated which were the more significant correspondences.

## Results

Table 1 describes the rate of indications for hysteroscopy and hysteroscopic findings among the 572 patients analyzed. Additionally, Table 1 describes the rate of PCOS cases and the rate of the patients' class age. Among 375 cases grouped as "other indications", 286 (76.3%) patients were addressed to hysteroscopy for abnormal sonographic scan examination of endometrial pattern, 86 (22.9%) for cervical polyps, one for a vaginal polyp (0.3%), and two for abnormal pap smear (0.5%). Dysfunctional endometrial patterns were described as "atrophic endometrium" (five cases – 6.1%), "focal cystic atrophic pattern" (two cases – 2.4%), "hypotrophic endometrium" (one case – 1.2%), "hyperplastic endometrium" (41 cases – 50%), "hypertrophic endometrium" (two cases – 2.4%), "secretive thickened endometrium" (nine cases – 11%), "endometrium not appropriate for the cycle phase" (25 cases – 30.5%), "decidualized endometrium" (one case – 1.2%).

Results from two-dimensional correspondence analysis are depicted in Figure 1. The squared block points in Figure 1 identified the indications for hysteroscopy, while the circular points are the patterns that grouped together patients' age and PCOS. Three clusters of aggregations could

Table 1. — *Descriptive statistic: rates.*

Indications for hysteroscopy	
Primary infertility	57 (10%)
Secondary infertility	20 (3.5%)
Primary infertility with irregular bleeding	13 (2.3%)
Secondary infertility with irregular bleeding	7 (1.2%)
Primary infertility with other indications	27 (11.4%)
Secondary infertility with other indications	11 (1.9%)
Irregular bleeding	106 (18.5%)
Other indications	375 (65.6%)
Hysteroscopic findings	
Normal pattern	141 (24.7%)
Chronic endometritis	68 (11.9%)
Cervicitis	19 (3.3%)
Endometrial polyps	205 (55.1%)
Cervical polyps	86 (15%)
Sub-mucosal myoma	58 (10.1%)
Malignancies	6 (1%)
Uterine malformations	35 (6.1%)
Synechiae	9 (1.6%)
Tubal micropolyps	1 (0.2%)
Vaginal polyp	1 (0.2%)
Dysfunctional endometrial patterns	82 (14.3%)
PCOS	7 (1.2%)
< 21 years old	8 (1.4%)
21 – 30 years old	81 (14.2%)
31 – 40 years old	279 (48.8%)
41 – 50 years old	170 (29.7%)
> 50 years old	34 (5.9%)

have been identified. The first one encompasses patients under 21 and over 50 years of age, undergoing hysteroscopy for other indications than infertility. The hysteroscopic findings in those patients were: vaginal polyp, sub-mucosal myoma, endometrial malignancies, endometrial polyp, and cervical polyp (Figure 1). The second cluster of aggregation encompasses patterns of cervicitis or dysfunctional endometrium, observed in patients with irregular bleeding, aging usually between 31 and 40 years. The third cluster of aggregation appears in cases with both primary and secondary infertility, with and without other indications for hysteroscopy, and in primary infertility with irregular menstrual bleeding. In these patients, usually aging between 21 and 30 years, chronic endometritis, normal hysteroscopic pattern, and uterine malformations were more often found. Patients undergoing hysteroscopy for secondary infertility with irregular bleeding do not seem to have a likelihood of more common hysteroscopic findings. Moreover, PCOS and synechiae points are far from points of the indications for hysteroscopy, suggesting poor correspondence with specific indications for hysteroscopy. The pattern of tubal micropolyps is the most far from anything, suggesting no correspondence.

The main-effect hierarchical log-linear model proves that the overall correspondence found is significant (likelihood ratio:  $p < 0.001$ ; Pearson chi square:  $p < 0.001$ ). Figure 2

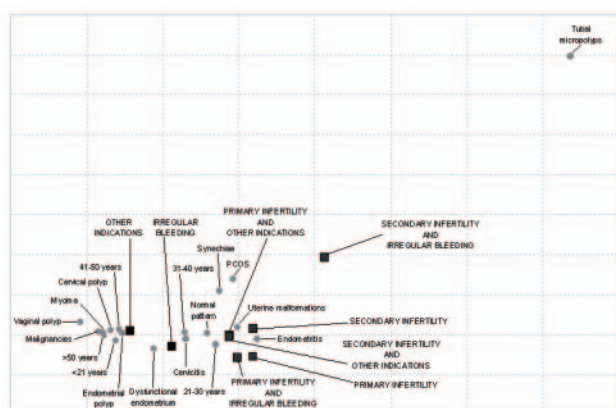


Figure 1. — Two-dimensional correspondence analysis.

depicts the behavior of the standardized residuals, highlighting where the correspondence was more significant. To facilitate the interpretation, the value of the 0,1° percentile on the left of x-axis and the value of 99,9° percentile on the right of x-axis are highlighted in Figure 2 (indicated by arrows). Bars crossing those limits provide a measure of the best correspondence. No correspondence was found for tubal micropolyps pattern (Figure 2). On the other hand, dysfunctional endometrium was more likely to be found in case of hysteroscopy for irregular menstrual bleeding. PCOS patients do not have specific indication for undergoing hysteroscopy. The PCOS patients are more likely to complain of primary infertility with irregular bleeding and secondary infertility with irregular bleeding (Figures 1 and 2) Normal pattern and chronic endometritis were likely to be found in patients with secondary infertility and primary infertility, respectively (Figure 1 and 2). Less strong correspondence may be found for less extreme percentiles.

## Discussion

According to the aim of the study, the correspondence analysis performed on 572 hysteroscopies, revealed an interesting association of some hysteroscopic findings and the indications to the exam. More in detail, all cases of infertility were found to be more often associated with chronic endometritis (Figures 1 and 2), with the exception of the cases with secondary infertility and irregular menstrual bleeding. However, the limited number of these cases (just seven cases) assessed in this study, biased the absence of association found. It has been reported in literature that chronic endometritis is easily detected by hysteroscopists [13] and that hysteroscopy is the best diagnostic tool for detecting chronic endometritis [15]. The present study highlights that chronic endometritis is often diagnosed at hysteroscopy in infertile asymptomatic patients, suggesting the opportunity to perform hysteroscopy since chronic endometritis is often

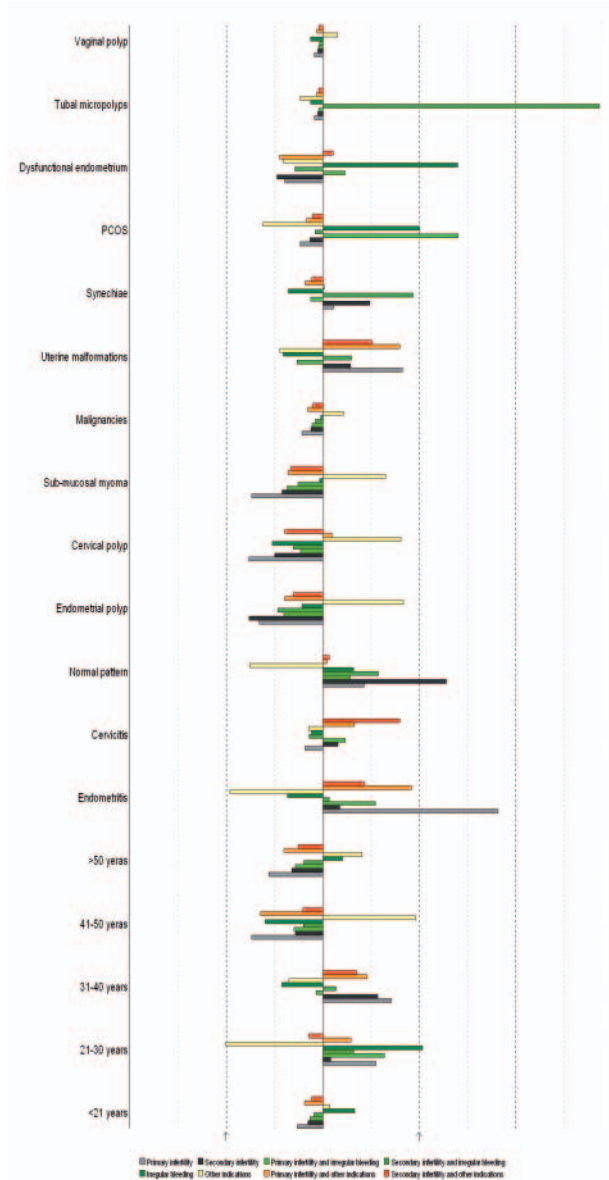


Figure 2. — Behaviour of standardized residuals.

asymptomatic in such patients. The present findings contradict a recent paper of Kasius *et al.* showing that the clinical implication of CE seems minimal since it can be rarely diagnosed in a population of asymptomatic infertile patients with a normal transvaginal ultrasound examination [16]. On this basis, the present authors can suggest that among infertile female population, hysteroscopy should be indicated also in cases with asymptomatic infertile women without other specific indications to perform hysteroscopy.

A normal endometrial pattern was found most of all in case of secondary infertility which could be in any case, a useful information, in order to exclude an endometrial factor as a possible cause of infertility. It would be interesting to know the associations, if any, between hysteroscopic in-

dications and all the specific causes of infertility or sub-fertility (i.e. premature ovarian failure, endometriosis, and pelvic inflammatory disease), after localizing their points in the Figure 1. This information allows to address the more common cause of female infertility to specific hysteroscopic indications and the relative hysteroscopic pattern. Another interesting finding of the present study is that patients with PCOS did not show any specific indication for hysteroscopy, since the distance of the PCOS point from the squared points of infertility did not differ from the distance from the squared point of the irregular bleeding indications (Figure 1). This leads to speculate that infertile patients with PCOS may show an endometrial dysfunctional pattern which may concur to explain their infertility disorder [17, 18], as well as women undergoing hysteroscopy for irregular menstrual bleeding.

## Conclusion

This study demonstrates that chronic endometritis is the most frequent hysteroscopic finding associated to infertility, even in asymptomatic women.

Moreover results showed that hysteroscopy is a key-examination in infertile patients, which is able to detect chronic endometritis in both asymptomatic and symptomatic women. On the other hand, hysteroscopy allows to rule out an endometrial factor for female infertility in the other cases. Thus, in the authors' opinion, the role of office hysteroscopy in the diagnostic work-up of infertility should be reconsidered.

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