Role of hysteroscopy in evaluating chronic pelvic pain

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Objective: To provide a survey of various gynecological conditions causing chronic pelvic pain (CPP) that might be diagnosed by hysteroscopy.
Design: Review article.
Setting: Departments of obstetrics and gynecology and pathophysiology of human reproduction at a university in Italy.
Patient(s): Women affected by CPP.
Intervention(s): Hysteroscopy.
Main Outcome Measure(s): Effectiveness in diagnosing intrauterine pathologies that cause CPP.
Result(s): Hysteroscopy is highly effective in diagnosing various gynecological causes of CPP, including adenomyosis, chronic endometritis, Müllerian anomalies, retained fetal bones, endocervical ossification, and intrauterine abnormalities. Furthermore, hysteroscopy may play a primary role in the resolution of some of these conditions.
Conclusion(s): Because it can be executed safely in an office setting without anesthesia, hysteroscopy may be indicated, together with the other noninvasive procedures such as transvaginal ultrasonography, as a first-level investigation in women who are affected by CPP. (Fertil Steril® 2008;90:1191–6. ©2008 by American Society for Reproductive Medicine.)

Key Words: Chronic pelvic pain, hysteroscopy, laparoscopy, office

Chronic pelvic pain (CPP) represents the single most common indication for referral to gynecology clinics, accounting for 10%–40% of all gynecological visits and 50% of all diagnostic laparoscopies (1).

There is no universally accepted definition of CPP. However, according to the guidelines of the Society of Obstetricians and Gynaecologists of Canada, CPP can be defined as nonmalignant pain that is perceived in structures related to the pelvis; it must have been continuous or recurrent for $\geq$6 months (2).

Often, the etiology of CPP is not discernible. Many disorders of the reproductive tract, gastrointestinal system, urological organs, musculoskeletal system, and psychoneurological system may be associated with CPP in women. The most important gynecological causes of CPP include endometriosis, adenomyosis, chronic pelvic inflammatory disease, pelvic congestion syndrome, and intrauterine or cervical pathologies (contraceptive device, leiomyomata, endometrial or cervical polyps, cervical stenosis, or chronic endometritis) (3).

Gynecological causes of CPP usually are detected by the patient's history, physical examination, transvaginal sonography (TVS), and laparoscopy (4, 5).

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A thorough patient history may identify the cause of pain, as well as the factors that may exacerbate or alleviate it, its relationship to the menstrual cycle, and its different locations. The physician also should elicit a history of previous pelvic or abdominal surgery, previous pelvic infections, and other significant gynecologic disorders. The physical examination should include a comprehensive, multiorgan evaluation that concentrates on the lower abdominal and pelvic regions.

Noninvasive procedures such as TVS and magnetic resonance imaging (MRI) may provide important information, because they investigate both intrauterine and extrauterine environments, without significant patient risk or discomfort. In particular, TVS often is used as the first-line diagnostic tool in the evaluation of CPP, because it is relatively inexpensive and does not use ionizing radiation (6).

Okaro et al. (7) created the ultrasound term *soft marker* to indicate pelvic pathology in women with CPP, the soft marker being the presence of immobile ovaries and/or specific tenderness and/or loculated pelvic fluid at TVS. They found such soft markers to indicate significant pelvic pathology, with a positive likelihood ratio of 1.9.

Magnetic resonance imaging commonly is considered when TVS is nondiagnostic or equivocal. Although MRI may be the best overall test for clearly evaluating abdominal and pelvic anatomy, it has some limitations: it is relatively expensive, images may be degraded by metal implants in the body, and there are some contraindications to

having the test (e.g., ferromagnetic aneurysm clips or pacemakers) (6).

Some invasive procedures, such as laparoscopy, are major components in evaluating CPP, and many physicians believe that a workup is incomplete without this procedure. At present, gynecologists liberally use laparoscopy or microlaparoscopy under general anesthesia as the gold standard for the assessment of women with CPP. Laparoscopic observation of abdomen and pelvis will identify potential sources of CPP in most women. The most common findings at laparoscopy are pelvic endometriosis and adhesions (3). However, in $\leq$40% of women with CPP, laparoscopy fails to identify any obvious cause for the pain (7, 8).

There are a number of reasons that laparoscopy may fail to identify an organic cause of pain: the condition may not be visible at laparoscopy (i.e., adenomyosis, intrauterine pathologies, and so on), or an inexperienced surgeon may not recognize the disease, as with some forms of endometriosis (9). This results in an underdiagnosis of some gynecologic causes of CPP and, consequently, in an inappropriate referral of the woman and an inadequate treatment of the pain.

At this point, the following question spontaneously arises: can hysteroscopy provide significant information concerning the causes of CPP? In other words, can hysteroscopy diagnose some causes of CPP that otherwise may be hard to diagnose or that may not be detected when using TVS and/or laparoscopy?

Although some clinicians already use hysteroscopy in the evaluation of CPP, other investigators refute its usefulness.

In the international literature, data are lacking on the prevalence of hysteroscopic findings in unselected women with CPP, with the exception of those reported by Nezhat et al. (4).

Those investigators have conducted a study on 499 women who are affected by CPP and are undergoing diagnostic laparoscopy, plus hysteroscopy to identify the potential causes of pain. Their work has shown that hysteroscopy is effective not only when laparoscopy fails but also in patients in whom laparoscopy is performed successfully. Indeed, independently of the pathophysiology of CPP, the investigators showed that approximately one third of patients with abnormalities diagnosed at laparoscopy had concomitant intrauterine pathology. Leiomyomas and cervical stenosis were the most common hysteroscopic diagnoses and were considered to be potential sources of CPP.

The aim of our analysis is to provide a survey of various gynecological conditions causing CPP that may be diagnosed by hysteroscopy.

ADENOMYOSIS

Adenomyosis is a common, benign gynecological disorder that is characterized by the heterotopic presence of endometrial glands and stroma within the myometrium, surrounded by smooth muscle proliferation.

It traditionally has been diagnosed by the pathologist on hysterectomy specimens or by means of invasive techniques, such as laparoscopic uterine biopsies.

However, the recent development of high-quality, noninvasive techniques (TVS and MRI) has renewed interest in diagnosing adenomyosis before any treatment (10).

Adenomyosis particularly is amenable to MRI diagnosis, with accuracy rates of $\leq$99% (11–13). Compared with MRI, TVS is less sensitive for diagnosing such pathology, with sensitivity of 86%, specificity of 50%, and positive predictive value of 86% (11, 14).

Hysteroscopy has been demonstrated to be an important additional procedure for the evaluation of uterine pathology, even in the case of adenomyosis, because it offers the main advantage of direct visualization of the uterine cavity and the possibility of obtaining histological specimens under visual control (10, 15).

Recently, Molinas and Campo (16) proposed office hysteroscopy and TVS as first-line diagnostic tools in case of suspicion of adenomyosis.

Notwithstanding the fact that diagnostic hysteroscopy of the cavity cannot definitively diagnose or exclude adenomyosis, because its field of observation is limited to the endometrial surface, some investigators have described some hysteroscopic findings that are suggestive for such pathology: an irregular endometrium with endometrial defects (superficial openings), hypervascularization, a strawberry pattern, or cystic hemorrhagic lesions (10, 16, 17).

In particular, an irregular endometrial vascular distribution has been detected in more than half of patients (16). Ota and Tanaka (18) used morphological analysis of the endometrium to demonstrate that the mean surface area, total surface area, and total number of capillaries increased in the adenomyosis group, both in the proliferative and secretory phases. These findings strongly support the concept that endometrium is functionally abnormal in patients with adenomyosis. However, it should be emphasized that the superficial vascularization can be inspected correctly only by reducing the intracavitary pressure at the time of hysteroscopic examination.

In addition to the direct visualization of the uterine cavity, the hysteroscopic approach offers the possibility of obtaining histological specimens under visual control, allowing more accurate information to be obtained and correlations between images and histopathology to be made. During hysteroscopy, target biopsies of the endometrium and underlying myometrium can be obtained, either with the mechanical-punch technique or with electrical-loop resection. Furthermore, the visual appearance before, during, and after the loop resection also may demonstrate typical signs for adenomyosis.

McCausland (19) first described the technique of myometrial biopsy through the hysteroscope with loop resection and reported a prevalence of adenomyosis of 66% in patients with

abnormal uterine bleeding. That work also demonstrated a correlation between the depth of the lesion and the severity of the menorrhagia.

Furthermore, in a comparative study, Darwish et al. (20) demonstrated the superiority of loop resection over punch biopsy with rigid biopsy forceps.

At the moment, there is no consensus on the diagnosis of adenomyosis by hysteroscopic resectoscopic biopsy with respect to handling, orientation of the resected pieces, and depth of penetration (21); however, adenomyosis may be highly suspected when the following signs are found: [1] irregular subendometrial myometrium (whorled, fibrotic, and so on), [2] absence of typical myometrial architecture during the resection, and [3] intramural endometriomas (19, 20).

CHRONIC ENDOMETRITIS

Chronic endometritis is a subtle condition that is difficult to identify with noninvasive examinations. Indeed, it is not detectable by TVS and MRI and can be suspected only in patients who have complications such as adhesions, pyometra, or hydrometra. It may cause abnormal uterine bleeding, although in most cases it is asymptomatic or is accompanied by mild disturbances such as spotting and undefined CPP. A recent study has demonstrated that >70% of cases of chronic endometritis result from non-gonococcal, non-chlamydial infections, with common bacteria and mycoplasma representing the most frequent etiologic agents (22).

No general agreement exists in the literature about the diagnostic usefulness of hysteroscopy in the detection of chronic endometritis (23, 24).

Recently, Cicinelli et al. (25) described diagnostic criteria for chronic endometritis at fluid hysteroscopy with low pressure. Fluid hysteroscopy is more efficacious than is CO_2 hysteroscopy for detection of this entity; indeed, saline has no effect on endometrial microcirculation and provides smoother distension and continuous washing of the uterine cavity, allowing endometrial ingrowths to float.

The diagnostic criteria for chronic endometritis at fluid hysteroscopy are the following: stromal edema, focal or diffuse hyperemia, and endometrial micropolyps (<1 mm in size).

Stromal edema, mostly when combined with hyperemia, is a sign of inflammation that can be detected easily at fluid hysteroscopy, because the endometrial mucosa, although it is in the proliferative phase, appears pale, whitish, and nonhomogeneously thick; in some cases it may fold, thus simulating a polyp.

Micropolyps, in particular, represent a very reliable sign of inflammation. They are small, vascularized ingrowths that are covered by endometrium and characterized by an accumulation of inflammatory cells (lymphocytes, plasma cells, or eosinophilic granulocytes) and edema in stroma; they probably are an expression of an active and strong endometrial reaction and of massive release of interleukins and local growth factors (26, 27).

The combination of hyperemia, edema, and micropolyps has a diagnostic accuracy of 93.4%, confirming hysteroscopy to be a reliable and useful technique for investigating chronic endometritis (25).

MÜLLERIAN ANOMALIES

Even if Müllerian anomalies usually are associated with infertility and abnormal uterine bleeding, it should be emphasized that some of them may cause CPP (28). Hysteroscopy together with laparoscopy may contribute to the diagnosis of such anomalies. Steinkampt et al. (29) recently reported the case of a non-communicating accessory uterine cavity as a cause of pelvic pain. Hysteroscopy together with TVS was useful for detecting the cavity.

Recently, Nawroth et al. (30) described a significantly higher incidence of endometriosis in patients with a septate uterus, suggesting that in such cases, a combined hysteroscopy and laparoscopy should be performed. If this association is confirmed in further, larger studies, additional CPP may support the decision to operate. Indeed, clinical experience suggests that hysteroscopic resection of the uterine septum (even without laparoscopic treatment of endometriosis) often is followed by a significant improvement in, or complete resolution of, severe dysmenorrhea.

INTRAUTERINE BONE STRUCTURES

The presence of intrauterine bone structures is a rare condition (31–35) that mostly is caused by retained fetal bone fragments, as a complication of induced abortion, spontaneous intrauterine fetal death, and missed abortion (36, 37). In some cases, it may be caused by metaplasia of mature endometrial stromal cells, in response to chronic inflammation or trauma (38, 39). It is interesting to note that the presence of retained fetal bones may be more common in cases of uterine anomalies (34, 40).

This situation may cause CPP, infertility, abnormal uterine bleeding, vaginal discharge, and passage of bony fragments in menstrual blood (31, 41).

Transvaginal sonography usually represents the first-line diagnostic tool. Retained bone fragments are displaced on an ultrasound as bright echogenic areas with posterior shadowing. Hysteroscopy has been demonstrated to be effective for confirming the diagnosis and achieving the successful removal of fetal bones (35, 42–44), either with a resectoscope or with grasping forceps inserted through the operative channel of a hysteroscope (34, 40, 45).

ENDOCERVICAL OSSIFICATION

Endocervical ossification is an osseous metaplasia in the cervical canal, usually complicating chronic endocervicitis

(46–48). The mechanism through which endocervicitis leads to endocervical ossification is still unclear; however, it has been hypothesized that the release of the increased amount of intracytoplasmic calcium after the death of the cervical cells may trigger further deposition of calcium and formation of macroscopic bone structures (46). These patients may have CPP, infertility, hypermenorrhea, and dysmenorrhea. The diagnosis is based on TVS and hysteroscopy, which is useful for confirming the diagnosis as well as for treating the pathology. During hysteroscopy, the presence of white-colored endocervical fragments with a sponge-like aspect and hard consistency at contact with the tip of the hysteroscope supports the diagnosis of endocervical ossification and chronic endocervicitis (46).

INTRAUTERINE ABNORMALITIES

Some uterine abnormalities may cause CPP. These include cervical stenosis, intrauterine adhesions, polyps, and submucosal myomas (49). In case of cervical stenosis and adhesions, pelvic pain usually is caused by the occurrence of different sizes of hematometras, with consequent increase of the intrauterine pressure.

Large polyps and submucosal myomas may cause pain, especially when the uterus tries, by means of contractions, to expel them.

Some of these intrauterine lesions (i.e., polyps, submucosal myomas, hematometra) may be easily diagnosed with TVS, whereas other abnormalities may only be suspected or not diagnosed (i.e., intrauterine adhesions, cervical stenosis).

At present, office hysteroscopy commonly is regarded as the gold-standard technique in any situation in which a major or minor intrauterine or cervical anomaly is suspected or has to be ruled out (50). Furthermore, several investigators have demonstrated that most intrauterine and cervical lesions also may be successfully treated by hysteroscopy in the outpatient setting, during the diagnostic workup (*see and treat*) (51–53).

DISCUSSION

The term *office setting* refers to the performance of hysteroscopy, either diagnostic or operative, on an outpatient basis, while the patient is not in the operating room. Improvements in office hysteroscopy, both in technology and technique, such as the use of saline solution as distension medium (54), the availability of high-resolution mini-endoscopes (55), and the atraumatic insertion of the instruments (56), have led to the development of its current form. It is, therefore, now recommended as a first-line diagnostic tool for the evaluation of abnormal uterine bleeding (57) and infertility (58), because it is associated with minimal patient discomfort, excellent visualization, and very low complication and failure rates (58).

Moreover, as an operative tool, the new-generation office hysteroscope has the advantages of including an operative channel of ≥ 5 Fr, which enables the simultaneous diagnosis and treatment (see and treat) of various uterine and cervical pathologies in an outpatient setting (56–60).

Office hysteroscopy can be considered to be a valid diagnostic instrument for numerous pathological conditions causing CPP that can be hard to diagnose by, or that may not be diagnosed by, noninvasive techniques (TVS or MRI) or even by laparoscopy (i.e., chronic endometritis, intrauterine pathologies, Müllerian anomalies, superficial adenomyosis) (16, 51–53, 61, 62). Furthermore, it should be emphasized that a negative laparoscopy does not mean that there is no disease or that a woman has no physical basis for her pain (3).

Moreover, office hysteroscopy may play a primary role in the resolution of many causes of CPP, such as Müllerian anomalies (28, 62), intrauterine bone structures (34, 35, 40, 42–45), endocervical ossification (46), and intrauterine abnormalities (51, 52, 62).

For these reasons, although laparoscopy still represents the gold standard for the assessment of women with CPP, hysteroscopy may be considered a useful technique, mostly when the cause of CPP remains a diagnostic dilemma (4, 7).

Nowadays, the validity of hysteroscopy has been well demonstrated. However, unfortunately, most gynecologists still are unable to take advantage of the many potentialities of this technique or do not perform hysteroscopic procedures in the office setting.

Because it can be executed safely without anesthesia and has high patient compliance, office hysteroscopy may be indicated, together with the other noninvasive procedures such as TVS, as a first-level investigation in women affected by CPP. This could reduce the number of unnecessary laparoscopies that are performed in women with CPP.

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